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Contemporary Developments and Perspectives in International Health Security

Volume 2

Edited by Stanislaw P. Stawicki, Thomas J. Papadimos, Sagar C. Galwankar, Andrew C. Miller and Michael S. Firstenberg

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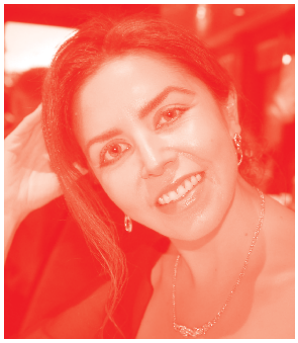

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Contents

Preface

International Health Security In The Era of COVID-19

The COVID-19 pandemic has changed the world forever. Some of its consequences are already apparent, but many are yet to be truly appreciated. The changes we can readily "see" include widespread use of personal protective equipment (PPE), social distancing measures, and, sadly, decreased overall life expectancy. At the same time, major technological advances have been made across multiple areas of life, from messenger RNA vaccines to telemedicine, novel therapeutics, Internet- and blockchain-based applications, and a plethora of innovative public health tools.

But perhaps most important in the context of this book is the emergence of International Health Security (IHS) as an essential component of modern public health. Not only has the pandemic affected all of us directly via the harm inflicted by a merciless and impersonal pathogen, but it has also exposed numerous weaknesses and blind spots across various domains of our society's operating fabric, from critical supply chains to mass transportation, civil unrest, and healthcare system inefficiencies. Many of these "systemic symptoms" continue to persist well beyond the well-defined "waves" of the pandemic.

We must acknowledge that largely unprepared, humanity was collectively deeply humbled by the ongoing pandemic. As has been true in the past, we must all-too-frequently learn and re-learn the same lessons of overconfidence, passivity, and missed opportunities. Yet we must also emphasize the victory of human resolve and our ability to "rise to the occasion" when facing overwhelming odds. In addition, the COVID-19 pandemic reinforced the fact that we are all part of a true "global community." After all, what used to be an isolated problem for one region of the world can no longer be contained in the era of inexpensive, easy-to-access, universal mass transportation, even when the strictest of precautions are taken.

Within this general context, a thorough evaluation of the relationship between COVID-19 and IHS is warranted, including a detailed examination of all pertinent domains that directly or indirectly influence the wellbeing of human health and wellness. Using the expanded definition of "health security" as it evolved during this current pandemic is especially important and central to highlighting the impact of future emerging infectious diseases (EIDs) on multiple other spheres of human life, with medical and direct healthcare aspects constituting only a small proportion of factors that actively modulate wellness and health across the planet.

Moving forward, it appears that more comprehensive, inclusive, and multidimensional approaches to any future pandemic event may represent a much better way to reduce both human and economic costs of any such "once-in-a-century" global event. In the end, our ability to successfully navigate this complex crisis is a true reflection of human resolve and a testament to our collective accomplishments. After all, when we all work together as close partners, in a well-orchestrated manner, outcomes tend to be significantly better than when corresponding alternatives are concerned.

Pandemics are known to force our existing systems, established patterns, and the way we operate in general to rapidly evolve and change. While it is generally acknowledged that there is often an inherent "reluctance to change," especially if there is contentment with the status quo, major transformational events are defined as such because they mandate change, often in ways that are difficult to initially anticipate or accept. Although short-term change can be reactive, the longer-term response to the pandemic tends to be both more deliberate and constructive. The latter may include scientific research, development, and distribution of therapies, vaccines, and medical devices, as well as an in-depth reflection on various limitations and "lessons learned" that became evident in the process.

The early pandemic created a perfect environment for the accelerated maturation and implementation of various existing technologies. Two particular examples include telehealth and artificial intelligence. At the same time, the adoption process of novel technologies and approaches must also ensure that we carefully consider appropriate safety and ethical considerations, any potential limitations, well-defined staff responsibilities, evolution of team roles, as well as adherence to protocols. While such new technologies very quickly become a part of the modern medical lexicon, widespread acceptance was often challenged, not just by individual human reluctance or aversion but also by various other limitations that may not have been known until the corresponding implementation was complete.

Although the post–COVID-19 future is still difficult to conceptualize, we will eventually—and hopefully sooner rather than later—enter this new and eagerly awaited "state of the planet." It will hopefully be an environment where politics, interpersonal violence, acute and chronic disease, economic, racial and healthcare disparities, the viability of healthcare systems, delivery of care, mental health, homelessness, and aging are all thoroughly re-evaluated and properly addressed. Of importance, both skills and knowledge regarding pandemic preparedness fundamentals should become an established competency for those holding or running for key public office positions. After all, ignorance and complacency toward problems for which there are clear political, social, economic, and scientific solutions are simply not acceptable (and more so if there is clearly associated harm).

Within the expanded IHS framework, the response to the current pandemic has been a kind of "one-size-fits-all" public health policy without sufficient strategic assessment of the local and regional situation. The relatively diminished capacity of peripheric surveillance and control systems has forced local governments to "copy and paste" control strategies from abroad, often with suboptimal results. Consequently, we must always remember that "one size may not fit all." Finally, there is a tendency to extrapolate from previous scientific approaches to pandemic management. However, this way of managing the current crisis may not adequately consider variables such as the evolution of human social, political, medical, economic, and financial changes over time. Lessons of pandemic management in the 19th and 20th centuries, for example, need to factor in the reality that the 21st-century IHS framework is vastly different and inherently more complex. Moreover, in the last few decades, there has been a dramatic disinvestment in the area of public health, a phenomenon that clearly needs to be reversed.

The expanded and redefined scope of IHS provides a unique opportunity for the public health community to embrace a more holistic approach to an area that was traditionally much more narrow in scope. Our current crisis reminds us, on a daily basis, how unprepared we continue to be for the current Public Health Emergency

of International Concern (PHEIC). As we tackle one of the greatest challenges to IHS in recent decades, that of the COVID-19 pandemic, it becomes increasingly important to shift our focus to a more global yet significantly more granular and scientific perspective on IHS threats and emergencies. Such a perspective will help facilitate quicker, more effective, and more equitable responses for future PHEICs. We hope that this book will provide a solid springboard for an insightful and captivating discussion in this rapidly developing and important area of academic international medicine and public health.

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Chapter 1

Introductory Chapter: International Health Security in the Era of COVID-19

Stanislaw P. Stawicki, Thomas J. Papadimos, Sagar C. Galwankar, Ricardo Izurieta, Andrew C. Miller and Michael S. Firstenberg

1. Introduction

Since December 2019, the world experienced one of the most traumatic global events in modern history – the emergence of a devastating coronavirus disease 2019 (COVID-19) pandemic that continues its ravages more than 18 months later [1, 2]. Such once-in-a-generation or even once-in-a-century events have profound impact on our perception of the global *status quo*, and are a testament to the overwhelming and humbling power of nature over man [3]. Inherent to any pandemic-related considerations is the impact of the recent events on international health security (IHS) – a complex and highly heterogenous area under the broader umbrella of health sciences [4]. Not only does the pandemic affect us directly via the harm inflicted by a merciless and impersonal pathogen, it also exposes numerous weaknesses and blind spots across various domains of our society's operating fabric – from critical supply chains, to mass transportation, to civil unrest, to healthcare system inefficiencies [5, 6]. Key concepts discussed in this chapter (and the book) are outlined in a word cloud format (**Figure 1**).

Figure 1.
Composite word cloud depicting key terms and dominant concepts in the current book.

2. The story of human resolve

As much as we must acknowledge that humanity was deeply humbled by the ongoing pandemic, and that all-too-frequently we had to re-learn the collective lessons of declaring premature victory, we also need to emphasize the story of human resolve and our ability to "rise to the occasion" when facing overwhelming odds [5, 7–9]. The COVID-19 pandemic taught us much about being a true "global community" [10]. Within this general context, a thorough evaluation is warranted of the relationship between COVID-19 and IHS, including a detailed examination of all pertinent domains that directly or indirectly influence our ability to maintain human health and wellness. Using the expanded definition of 'health security' in the context of a global pandemic is especially important and central to highlighting the real-time impact of an emerging infectious disease (EID) on multiple other spheres of human life, with medical and direct healthcare aspects constituting only a small proportion of factors able to actively modulate wellness and health across the planet [11–18]. In fact, one might argue that a more comprehensive, inclusive, and multi-dimensional approach to the current pandemic contributed to a significant reduction in both human and economic costs of this once-in-a-century global event. And even more importantly, the above is a true reflection of human resolve and a testament to our collective accomplishments when we all work together as a community.

3. The COVID-19 pandemic as a transformational event

Global challenges, including a devastating pandemic, often force our existing systems, established patterns, and the way we operate in general, to rapidly evolve and change in response. While it is generally acknowledged that there is often an inherent "reluctance to change," especially in the presence of contentment with the *status quo*, major transformational events are defined as such because they mandate change – and often in ways that are difficult to initiatially anticipate. Thus, the initial change can be – quite understandably – reactive. However, the longer-term response to the pandemic tends to be more deliberate as well as more constructive. This is especially true in the context of research, development, and distribution of therapies, vaccines, therapeutic devices; an acknowedgmet of treatment limitations that are assessed within an ethical framework; as well as serious consideration of cultural, religious, and family centered approaches [19, 20].

4. Technology-driven transformation of healthcare

The early pandemic created a perfect milieu for various existing technologies to enter mainstream implementation and use [21]. Two particular technological advances worth mentioning in this context, both already well in the state of "transition into mainstream" irrespective of the ongoing pandemic, are tele-health and artificial intelligence [22, 23]. At the same time, the adoption process of novel technologies and approaches must also ensure that we carefully factor in appropriate patient safety considerations, any potential limitations, well-defined staff responsibilities, evolution of team roles, as well as adherence to protocols [24]. While such technologies very quickly become a part of the modern medical lexicon, widespread acceptance was often challenged, not just by individual human reluctance or aversion, but also by the simple reality that such digitial tools, despite the need for rapid and widespread implementation, have not quite matured for the intended role(s) they were originally conceived to fulfill.

5. Post-pandemic recovery: toward sustainable future

Although current events make it challenging to clearly picture the post-COVID-19 future, it is likely just a matter of time before we enter this new and eagerly awaited "state of the planet." It will hopefully be a state where politics, economic health, violence, acute and chronic disease, racial disparities, health care access, the viability of health care systems, delivery of care, mental health, homelessness, and aging are seriously re-evaluated and addressed. It will be critically important that this future is constructed in a manner that The United Nations proposed in their landmark document discussing 17 sustainable goals for the future [18]. These suggestions are a roadmap to assist in overcoming challenges such as poverty, environmental concerns, various socio-economic injustices, the climate change, among other agenda points. Within this context, we must ask, "Is the social, economic, and political infrastructure of the planet ready for such demands?" There is no doubt that community participation on local, regional, national and international levels will be necessary for a successful and sustainable outcome for the planet and for the humanity [25]. Of additional importance, it is also vital that the knowledge of pandemic preparedness fundamentals becomes an established competency for those holding or running for political office, where ignorance and complacency toward implementing viable solutions for problems with established political, social, economic, and scientific evidence is simply not acceptable [5].

6. Humans and humanity

As the pandemic continues beyond 2020 the world will likely see an imbalance between the vaccinated and the unvaccinated, the 'pro-maskers' and the 'anti-maskers,' the believers of science and the non-believers of science, the true warriors (health workers on the ground) and the media warriors (the speakers in media), the false news mongerers and the seekers of truth [11, 26, 27]. As we battled to save lives, the pandemic tested our resilience at an individual level and also tested our values as a global society. Sharing, caring, supporting, collaborating, empathy, compassion, resilience and resolve were actively tested, every minute of every day, at every location, and for every human being. Food, water, hospital beds, medications, and oxygen were simultaneously in high demand and in short supply [22].

Across intensive care units on every continent, critically ill patients fought for every breath, fought to live, fought for another opportunity to be with their loved ones. The entire humanity was fighting to survive as COVID-19 mercilessly affected individuals, families, nations, political and economic spheres. The pandemic changed geopolitical relationships, industry partnerships and economic projections. It changed and will continue to change the way things humans do well into the future, and potentially forever across some domains (e.g., pandemic preparedness and management) [5, 22].

When looking at the COVID-19 pandemic events from a truly global and comprehensive perspective, it is a giant test of how humans approach and embrace international health security. In the context of 'health security,' the actual degree of security is closely related to the overall degree of 'health insecurity' that exists around us. Maintenance of health security requires ongoing efforts and a constant focus on all mission-critical elements [18]. As this herculean task is being undertaken, the attainment of 'health security' thus becomes a careful balancing act that involves politics, competing interests, social, and economic considerations. Humanity plays a major role when we evision a 'secured world.' Here, IHS should be considered to be universal, and it should be the main sustainable goal that humans

should strive to attain and work toward consistently. As such, 'health security' is a long journey with only a few periodic punctuations that provide just enough time for self-reflection and re-orientation.

7. Synthesis

Within the expanded IHS framework, the repose to the current pandemic has been a kind of one-size-fits-all public health policy without a strategic assessment of the local and regional situation. The relatively diminished capacity of peripheric surveillance and control systems has forced local governments to 'copy and paste' control strategies from abroad [22, 28]. However, when pursuing such course, we must remember that "one size does not fit all." Moreover, quick, effective, and vigorous actions have been lacking.

Of importance, there is a tendency to extrapolate from previous scientific approaches to pandemic management that did not factor in the variables of the evolution of human social, political, medical, economic, and financial changes over time. Lessons of pandemic management in the 19th and 20th centuries, for example, need to factor in the reality that the 21st century IHS framework is vastly different and, inherently, more complex – both for better and for worse. Also, in the last few decades, there has been a dramatic disinvestment in the area of public health and the concept that investment in the workforce's physical well being and mental health positively influences productivity has been either abandoned or significantly de-emphasized. Nevertheless, the immense costs for the global economy of the COVID-19 pandemic have changed this paradigm and forced all stakeholders to re-emphasize the need for robust and consistent public health funding. As a matter of fact, no other pandemic has affected the U.S. and the global economy with such historical precedent [29, 30], at least in absolute terms.

8. Conclusion

The expanded and redefined scope of International Health Security provides a unique opportunity for the public health community to embrace a more holistic approach toward an area that was traditionally much more narrow in scope [18]. Our current crisis reminds us, on a daily basis, how unprepared we continue to be for the events of a Public Health Emergency of International Concern (PHEIC) [23, 31–33]. As we tackle one of the greatest challenges to IHS in recent decades (if not of the past several centuries) – the novel coronavirus 2019 (COVID-19) pandemic – it becomes increasingly important to shift our focus to a more global, yet significantly more granular and scientific, perspective on IHS threats and emergencies. Such a perspective permits quicker, more effective, and more equitable responses for future PHEICs. We hope that the foundation created by this Editorial team will provide a solid springboard for an insightful and captivating discussion in this rapidly developing and important area of academic international medicine and public health.

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Chapter 2

Which Plagues are Coming Next?

Ricardo Izurieta, Adriana Campos, Jeegan Parikh and Tatiana Gardellini

Abstract

Plagues and pandemics are no longer distant thoughts of the past. Previously referred as moments in history, infectious diseases have re-emerged as potential existential threats to mankind. International Health Security researchers have repeatedly warned society about impending pandemics and in 2020, the world experienced its first major pandemic in over a century. The SARS-CoV-2/COVID-19 pandemic came fast and hit hard, impacting the entire world within months of discovery. Although SARS-CoV-2 was a completely novel virus, there are an assortment of novel and timeworn pathogens fostering the potential to become the next pandemic. This chapter focuses on pathogens ranging from yeast to virus, capable of transmission through food, water, air, or animal, that could emerge as the next International Health Security threat.

Keywords: pandemic, vector-borne diseases, airborne diseases, waterborne diseases, foodborne diseases, public health, infectious diseases, International Health Security

1. Introduction

The current COVID-19 pandemic has given the world a new lesson that the war against human pathogens is not over. The next plagues are coming, that is for sure, we just do not know when and where they will emerge. The transcontinental global movement of human populations, animals, products, and food in unprecedented numbers and at immeasurable speeds has determined the emergence of new plagues. The International Health Security panorama is changing with the incorporation of vast geographical areas to the agroindustry; the displacement of large population groups either due to problems of floods, drought, wars, or people that search for better living conditions. In addition, the disposal of biological waste and the weaponization of pathogenic microorganisms are phenomena with serious consequences. International multinational cooperation is needed to improve the development and availability of drugs and vaccines at a global level, as well as, improving preventive health services, keeping safe all repositories of infectious agents, and the establishment of an International Health Security System focused on Infectious Disease Surveillance and Control.

2. Methods

An organized, systematic, four-step methodology for collecting key information was carried out to write this chapter. In a first step a search in websites such

as the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH) was conducted to identify emerging infectious diseases pathogens. In a second step, the main emerging infectious diseases pathogens were classified in viruses, bacteria, parasites and fungi as well as by their mechanism of transmission. In a third step, all updated manuscripts related with each one the selected pathogens were extracted from scientific databases including Pubmed, MEDLINE, Google Scholar, and SCOPUS. Finally, all pathogens were classified using the WHO Pandemic Phase Descriptions and Main Actions by Phase [1].

3. Pathogens to study

3.1 Vector-borne

Vector-borne diseases are transmitted, either biologically or mechanically, via insect vectors or animal vectors. Vector-borne diseases were the cause of great plagues in the previous centuries and continue to take human lives every year. Although the invention of pesticides, better hygiene and sanitation, and improved physical barriers have contributed to the decreased incidence of these type of infections, globalization, deforestation, and global warming are causing Vector-borne diseases to experience a comeback [2]. With enough conditions in their favor, Vector-borne diseases are capable to expand from being endemic in some areas to becoming a pandemic. Vectors range from insects to mammals and are present in all parts of the world. The pathogens described in this section are transmitted by mosquitoes, ticks, rodents, lice, and fleas.

An important factor regarding Vector-borne diseases and their respective vectors compared to other mechanisms of infectious disease transmission (e.g., airborne, foodborne) is the emerging data indicating vectors are capable of hosting more than one pathogen at a time [3–7]. Co-transmission and co-infection are not well understood yet are raising questions regarding clinical manifestation, virulence, and possible future implications. Although the mechanisms of co-infections are not well comprehended, there are documented case reports with individuals presenting more than one Vector-borne disease at the same time [8–10]. Specifically, there is rising concern about mosquitoes and their capability to co-infect humans, with recent studies showing *Aedes aegypti* [4, 7] and *Ae. albopictus* [3] capable of transmitting Zika, Chikungunya, and Dengue viruses within one bite.

3.1.1 Viruses

3.1.1.1 Yellow fever virus

Yellow fever (YF), one of the deadliest infectious diseases less than a century ago [11], was historically a neglected infectious disease unit the 1902 creation of the Pan American Health Organization (PAHO) and International Sanitary Bureau of the American Republics [12]. Yellow fever is caused by the etiological agent yellow fever virus (YFV), belongs to the flavivirus genus and, is a part of the arboviruses group (i.e., a commonly used, yet unofficial, name for viruses transmitted by arthropods). [11]. YFV circulates between humans, non-human primates, and several species of mosquito vectors (*Aedes, Haemagogus, Saberges)*. Currently, YFV has not adapted as well to humans as Dengue virus, leaving YFV as a zoonotic disease but with a future capability to extend to an anthroponotic. In the past decade there is an increase in

concern of non-primate transmission which could go unnoticed and spillover to large human populations [13]. Due to the nature of the virus requiring epizootic transmission, unfortunately, YFV cannot be eradicated from the planet. *Aedes aegypti* and *Aedes albopictus* which are present in over 150 countries suggest nearly half of the global population is at risk of YFV transmission [14]. Traditionally, YF affects the Americas and the African continent with its warm temperatures and suitable habitat for the mosquito vectors of the virus. There are seven major genotypes of YFV, differentiating the American and African cases – with 5 circulating within Africa and 2 in the Americas. Depending on the location of cases and the type of mosquito species native to the area there are three main types of YF transmission – urban, sylvatic, and intermediate (only Africa). Urban transmission is caused mainly by *Aedes aegypti* or a similar urban mosquito as the transmitter in humans [11, 15]. Sylvatic transmission appears between non-human primates and sylvatic mosquitoes, typically apart of the *Haemagogus* or *Sabethes* genera. In Africa alone, YF is estimated to kill over 70 thousand individuals a year [16]. The case fatality rate (CFR) depends on the location of infection, with South America having a higher CFR (40–60%) compared to Africa (closer to 20%) [17]. However, most cases are mild and resolve with supportive care. Moreover, in areas with co-transmission of both Dengue and YF viruses, it is possible that previous Dengue infections may protect against severe YF infections [18]. Similarly, to how YFV is thought to have traveled from the African continent to the West Indies centuries ago on shipping routes, it is capable to continue expanding in the current age with increased globalization and construction within the vector habitat. As mentioned above, YF is endemic in mostly South American and Africa, with outbreaks consistently seen each year. Although not often heard about in North America and Asian countries, Yellow Fever was endemic hundreds of years ago in cities like New York, Philadelphia, Memphis, and New Orleans [19] and has the possibility to emerge in Asian countries [20, 21]. Although *Aedes* mosquitoes are also native in parts of Asia, the absence of YF cases has long been a scientific enigma [21, 22]. Common theories to the lack of YF cases in Asia are: the east African mountain range provides a natural barrier for Asia [21], competition with Dengue virus limits YF transmission [23], and vector competency [20] among others. However, in the recent years an increased number of imported YF cases into Asian countries have raised alarms to the potential introduction of YFV to the local environment [20]. The most important factor describing whether or not YFV will be transmitted in a specific area is the vector. Fortunately, YFV can only be transmitted via the bite of an infected mosquito, making mosquito control programs essential in YFV transmission reduction. However, the world currently is experiencing a re-emergence of YF due to increased globalization, deforestation, and climate change, with recent outbreaks occurring in Brazil [24, 25]. With globalization, both humans and mosquitos may hitch rides to different parts of the world where YF transmission is uncommon and becoming an International Health Security issue. Furthermore, the present deforestation occurring throughout the world, especially in the South American and African forests, is closing the distance between humans, infected non-human primates, and mosquitos. Lastly, the increasing temperatures seen due to climate change may have implications on YFV vectors and their global distribution [16] – increasing the risk for contracting YF. In a recent study, an increase in temperature is estimated to increase the chance of the annual amount of YF death by over 90% [16]. Currently, countries with endemic YFV transmission have mosquito control programs capable of decreasing/controlling mosquito populations. Furthermore, the use of Geographic Information Systems (GIS) in conjunction with mathematical models [11] assist in predicting future YF outbreaks and viral transmission [16].

Lastly, one of the most important tools available to fight infectious diseases exists against the Yellow Fever virus – a vaccine. The earliest version of a YF live-attenuated vaccine was created in 1936 and the same vaccine strain (17D) is still presently effective and used in areas with endemic transmission [11].

3.1.1.2 Dengue virus

Dengue virus (DENV) occurs in over 100 countries causing nearly 100 million acute infections and half a million deaths each year [26, 27]. The disease itself is characterized by an acute fever which is transmitted from mosquitos (*Ae. aegypti* and *Ae. albopictus*) to humans, however, most cases are asymptomatic. Anywhere from 5–20% of cases progress to severe dengue which includes bleeding, shock, organ failure, and death. Severe forms of Dengue are known as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Dengue is described as early as 1600 and continues to be endemic to many parts of the world [27]. Similarly, to the Yellow Fever efforts initiated by PAHO, a major *Aedes aegypti* eradication program between 1947 and 1970 aimed to eliminate this mosquito species and therefore, eliminate Dengue. However, *Ae. aegypti* reinfestation occurred shortly after and has even increased in dispersion in the recent decades [27]. Like other infectious diseases, Dengue is thought as an exotic disease – perhaps many individuals have not even heard of Dengue before. It may surprise many individuals in developed countries that Dengue's main vector *Ae. aegypti* is capable of living in almost all continents except Antarctica [28]. Dengue was common in port cities in the Caribbean and all throughout the Americas and continues to cause outbreaks in developed areas such as the Florida (2020) and Hawaii (2015) [29]. A significant barrier in the diagnosis and reporting of Dengue is the commonality the disease shares with other Flaviviruses such as Yellow Fever virus and Zika and its cross-reactivity in serological testing. The aforementioned diseases share similar flu-like symptoms and serological misdiagnoses are believed to fuel the underreporting of DENV and other Flavivirus infections. As Dengue cases continue to increase it is essential to understand the current epidemiology and public health programs in place to reduce the outbreak risk and reinforce International Health Security. Dengue virus shares many similar characteristics with YFV - it is a part of the Flaviviridae family, and its main vectors are *Aedes aegypti* and *Ae. albopictus* mosquitoes. Typically, DENV is found in tropical and subtropical regions and unlike other viruses, individuals may be re-infected by different serotypes. This is especially important in public health prevention programs and epidemic mitigations. Unfortunately, individuals infected with one serotype only produce antibodies capable of neutralizing that specific serotype, leaving the individual unprotected against the other 3 serotypes. Moreover, through antibody-dependent enhancement, re-infection by a different serotype increases the risk of severe dengue disease [26]. In 2019 a vaccine against DENV was approved for individuals aged 9–45 years and who had experienced a prior DENV infection. However, providing this vaccine to individuals without prior DENV infection also increases the risk for the antibody-dependent enhancement and therefore greatly limiting who may be immunized [30]. In a pandemic scenario this limitation would be disastrous.

3.1.1.3 Zika virus

One of the most famous infectious diseases of recent decades, Zika came into the international spotlight during its 2015 epidemic. Although Zika virus (ZIKV) was discovered in a Ugandan forest over 50 years ago, in 2015 it emerged as a global epidemic affecting multiple countries and causing widespread panic [31]. In 2016,

the World Health Organization (WHO) declared the outbreak as a Public Health Emergency of International Concern, with ZIKV affecting throughout the Americas and Caribbean. One of the main reasons for the declaration and widespread worry is the increase in microcephaly cases and other neurological disorders that ZIKV brought with it. Interestingly, prior to the outbreaks in the recent decade, ZIKV infections were considered benign [32]. It was the increase in neurological disorders such as Guillain-Barré syndrome in older children and adults and microcephaly and other birth defects in newborns in the 2015 Brazil outbreak that forewarned the local and international community of the potential adverse effects from a ZIKV infection [32]. Although the incidence of Zika cases has decreased since the 2015–2016 epidemic, a substantial amount of Zika research continues to provide new data and information on this infectious disease. Current research suggest Zika will be around until the foreseeable future with research indicating ZIKV actually circulates in areas previously unknown. Moreover, in 2019 Europe's first autochthonous case [31] was identified and further confirmed the importance of vector control and public health programs. Like the flaviviruses mentioned above, ZIKV's main vectors are *Ae. aegypti* and *Ae. albopictus* placing a large proportion of the global population at risk of infection; therefore, threatening International Health Security [31, 33]. Although *Aedes* mosquitos are the confirmed vector for ZIKV, *Culex* genera mosquitoes, mostly *Culex quinquefasciatus*, are theorized to be capable to transmit Zika, further expanding its geographic reach [34]. However, recent studies did not support the ability for Culex mosquitoes to transmit ZIKV [35, 36]. In conjunction with its vectors wide global reach, a high proportion of Zika cases are asymptomatic and those who are symptomatic mirror symptoms to dengue and the flu (e.g., fever, rash, muscle and joint pain) compounding the barriers to diagnosis, treatment, and epidemic mitigation efforts.

3.1.1.4 West Nile Virus

An emerging zoonotic arbovirus, West Nile Virus (WNV), was first described in a sick woman located in the West Nile Uganda district in 1937 [37]. Sixteen years later WNV was detected in birds living in the Nile delta region, suggesting its transmission cycle involves mosquito vectors and birds – yet may infect humans [38]. It is now known WNV is capable of infecting both humans and other vertebrate species, with its sylvatic cycle infecting horses and humans as dead-end hosts and birds as the amplifying host. Unlike the previously mentioned viruses, WNV uses the *Culex* genus mosquitoes as its primary vector. Recently, additional mosquito genera, *Aedes* and *Ochlerotatus*, were identified as possible WNV vectors. Although this virus historically caused outbreaks in Africa, Asia, and the Middle East, cases of WNV are now common in Europe and the Americas. The first US case occurred in 1999 and within a decade cases were identified in Canada, Mexico, and South America – with cases as south as Argentina [37]. WNV has spread to all continents except Antarctica, increasing the risk of future and larger epidemics worldwide. WNV is now considered endemic in the US with as many as 47 US states reporting WNV cases each year [38]. Although the incidence of WNV has increased throughout the decades, most human WNV infection are asymptomatic [39]. About 1% of infected individuals experience severe neuroinvasive disease such as meningitis, encephalitis, and flaccid paralysis [39, 40]. The movement of migratory birds in addition to the local movement of sedentary birds are hypothesized to contribute to the global distribution of WNV [38]. Current public health programs aiming to reduce the spread of WNV rely on GIS and mosquito population control techniques. Furthermore, since WNV is able to infect horses and birds, many endemic areas have equine and sentinel programs focused on surveillance

and monitoring of WNV transmission. Moreover, recent mathematical and GIS models identified risk factors pushing WNV transmission such as populations living in poverty, environmental factors, and mosquito populations [41]. There are no current approved vaccines against WNV, leaving public health prevention programs and vector surveillance the main barrier between WNV causing larger human outbreaks.

3.1.1.5 Crimean-Congo hemorrhagic fever virus

A Nairovirus, Crimean-Congo hemorrhagic fever (CCHF), is an emerging infectious disease using *Hyalomma* genus ticks as its vector with distribution in Africa, Asia, and Europe [42]. CCHF was first described in the Crimean Peninsula less than a century ago, in 1944, during World War II when cases were brought on Soviet soldiers. Since then, the importance of CCHF has grown so much so that in the last 3 years the WHO considers it one of eight priority emergent pathogens [42]. Currently this zoonotic virus is endemic in approximately 50 countries throughout the world. Domesticated animals such as sheep, cattle, and goats as well as birds serve as the amplifying host, maintaining the transmission cycle alive in diverse regions. The Crimean-Congo hemorrhagic fever virus is transmitted to humans mainly through the bite of hard-bodied ticks yet can be transmitted with direct contract with blood and other infected bodily fluids. An infection typically comes directly from an infected tick or ticks on livestock that then bite humans. For those reasons many CCHF cases originate in individuals in agricultural jobs (direct) and nosocomial environments (direct bodily fluid contact). Most cases are asymptomatic or present mild symptoms such as fever, headaches, dizziness, and abdominal pain and myalgia [43]. In severe cases the course of infection includes an incubation period, pre-hemorrhagic, hemorrhagic, and convalescent phases [43, 44]. It is estimated approximately 10% of the cases will present severe disease with mortality rates ranging from 20- to over 30% in these severe cases [44]. Due to high mortality rates and global risk, the Centers for Disease Control and Prevention (CDC) considers CCHF virus a level 4 biosecurity risk pathogen [42]. There is currently no approved CCHF vaccine and treatment is usually supportive and symptomatic [42]. Fortunately, the current geographic distribution of the *Hyalomma* tick is limited to 50 degrees north latitude [45], preventing the disease to expand beyond this geographical limitation for now. Nonetheless, the climate change and increased environmental temperatures may provide the vector an opportunity to expand its traditional reach which may become an International Health Security threat. Consequently, CCHF prevention focuses on public health education, environmental programs, and physical barriers (e.g., thick clothing, long sleeve shirts, long sleeve bottoms) [43].

3.1.1.6 Mayaro virus

This emerging zoonotic pathogen is an enveloped +ssRNA virus belonging to the alphavirus genus of Togaviridae family [46]. Mayaro virus (MAYV) is part of the viruses of Semliki forest antigenic complex and causes Mayaro fever [46, 47]. Transmission of MAYV into humans occurs primarily through the bites of infected mosquitoes of the genus *Haemagogus* spp., especially *Haemagogus janthinomys*, with experimental studies showing the ability of MAYV to infect mosquitoes of another genus such as *Aedes aegypti*, *Culex*, *Mansonia*, *Psorophora*, and *Sabethes* [46, 48]. The sharing of common antigenic sites among viruses of Semliki complex causes serological misdiagnosis and underreporting of MAYV infection in endemic areas [46, 49]. MAYV infection produces self-limiting symptoms of fever, headache,

myalgia, arthralgias, maculopapular rash with more than 50% of them developing long-term incapacitating arthralgias. Sometimes Mayaro fever can result in complications resulting in hemorrhagic manifestations, neurological manifestations, myocarditis, intermittent fever, and death [46, 49]. Pharmaceutical countermeasures such as specific antiviral agent or licensed vaccine are not available against MAYV. Thus, prevention and control of MAYV infection is dependent on vector control techniques and barriers to prevent human-vector contact. This neglected tropical virus was first isolated from the sera of forest workers of Mayaro county, Trinidad and Tobago in August–September 1954 [50]. Even earlier evidence of transmission of MAYV in Panama and Colombia between 1904 and 1914 was provided by a retrospective study [51]. This was followed by reporting of MAYV infection in Brazil, Bolivia, Colombia, Surinam, Peru, Ecuador, French Guinea, Venezuela, and Haiti [46, 52]. Currently, the pathogen is endemic in regions of Central Brazil and the western coast of South America [52]. The import of MAYV cases in North America, Netherlands, France, and Germany in last decade shows the potential of travelling in introduction of agent in new areas [46, 52]. Infection with MAYV is detected in many vertebrate hosts such as nonhuman primates, rodents, sloths, small mammals, and birds with nonhuman primates (monkeys) being suspected of maintaining the enzootic cycle [46, 47]. The zoophagous nature of the *Heamagogus* spp. species results in the restriction of MAYV to rural areas with occasional outbreaks in humans [49]. However, the ability of MAYV to infect urban vectors like Aedes (*Ae. aegypti* and *Ae. albopictus*) suggest a potential future expansion and invasion of MAYV into urban areas of the world becoming an International Health Security threat [46, 52]. Anthropogenic changes, genomic mutations, insecticide resistance in vectors, globalization, climate change, and infection of urban mosquito vectors could result in epidemiological evolution of MAYV and MAYV fever becoming an International Health Security threat.

3.1.1.7 Chikungunya virus

First reported in 1952 in Tanzania, Chikungunya virus (CHIKV) is an alpha virus apart of the Togoviridae family and transmitted by Aedes mosquitoes [53]. The word Chikungunya translates as "the disease that bends up the joints", which is one of the severe symptoms of the disease (i.e., arthritis) [54]. The main transmission among humans occurs through epizootic cycles, where vertebrates are the viral reservoirs and the mosquito acts as the vector [55]. Since its discovery, there were CHIKV outbreaks throughout Europe, India, and Asia. CHIKV was a mostly a forgotten infectious disease until its 2006 resurgence and widened global reach. In 2007, Europe reported its first autochthonous CHIKV infection and by 2013 it had found the Americas, first landing in Saint Martin and then spreading throughout South America [53]. In spite of underreporting and misdiagnoses cases have occurred in more than 45 countries [55]. Active outbreaks allow humans to become the reservoirs and continue to fuel the outbreak. Like Zika, the first autochthonous cases in the Americas were fairly recent, with CHIKV's first outbreak in the Northern and Northeastern regions of Brazil [53]. The most serious outbreak was probably the Reunion Island outbreak between 2005 and 2006, where nearly a third of the island's population (255,000) was infected and over 250 individuals died [56]. A CHIKV infection typically causes symptoms such as fever, arthralgia, myalgias, and skin rashes [55]. In a subset of cases, joint inflammation and arthritis lasting up to 4 months may occur [55]. The increased incidence of CHIKV over the recent decades in areas previously unaffected, in addition to the wide geographical range of its vector (i.e., the Aedes genus) lead to heightened concern of future outbreaks and adverse health outcomes. Moreover, recently CHIKV infection is

associated with abortion during the first and last trimesters of pregnancy, further emphasizing the need for CHIKV research and therapeutics [55].

3.1.2 Bacteria

3.1.2.1 Rickettsia prowazekii

As one of oldest infectious diseases known to mankind, Typhus, caused by the bacteria *Rickettsia prowazekii* and *R. typhi*, continues to be an International Health Security threat. Due to the nature of the outbreaks caused by *R. prowaszekii*, having higher mortality rates [57] and a recently discovered animal reservoir (i.e., flying squirrel) [58, 59], only *R. prowazekii* will be covered in this section. *R. prowazekii*'s, the cause of epidemic typhus, history is unclear. Some scholars believe epidemic typhus to be have caused the 430 BC plague of Athens [57, 60, 61] where it killed 25% of the population [61]. While the origins of this pathogens may be unclear, it is certain it continues to be part of an International Health Security program today. Typhus is also referred to as a pestilential disease, or an infectious disease killing a large number of individuals, that is commonly used in old world diseases. Epidemic typhus is usually associated with cold months and poor sanitary conditions are conducive to lice proliferation [60]. Until the late 1900s, *Pediculus humanus corporis* (i.e., human body lice) was thought to be the only vector for *R. prowazekii* until the late 1970s when a US outbreak seemed to inculpate *Glaucomys Volans* (i.e., southern flying squirrel) [58, 59]. Infection occurs when an infected human body louse defecates on an individual and its feces, containing R. prowazekii, enters the bite site or wound [57, 60]. Transmission via flying squirrel is not yet completely understood [60], however it is thought to spread through aerosolized ectoparasite feces [57, 60]. Currently, epidemic typhus is endemic in South America, Africa, and Asia [57, 60]. Outbreaks propagate especially following famines, climate changes, wars, and social unrest all of which are currently present in the world [57, 60]. One of the most recent largest outbreaks was reported during the Burundi civil war in 1997, where approximately 100,000 individuals were infected and the case fatality rate was 15% [60]. Clinical manifestation of Typhus includes skin rashes (crucial for clinical diagnosis), fever, headaches, and cough [57, 60]. Without treatment, the case fatality rate could be as high as 60%, however, currently with treatment is closed to 4% [60]. Unlike the previously mentioned pathogens, once infected with *R. prowazekii* individuals may stay infected for life. This is even more alarming given a recrudescence may cause Brill-Zinsser disease [57, 60, 62]. Currently, epidemic typhus is treated using antibiotics (doxycycline) and there is no approved vaccine. Given infection by inhalation it is possible R. prowazekii may be used as a biological weapon and is warrants additional research and funding [60, 63, 64]. With the current International Health events including refugee camps, wars, and populations living in unsanitary condition, epidemic typhus may continue to produce outbreaks similar to the Burundi outbreak and therefore vaccine development should be encouraged.

3.1.2.2 Yersinia pestis

Perhaps the most infamous infectious disease, the Black Plague or Black Death, is caused by *Yersinia pestis*. *Y. pestis*, a bacterium, has caused multiple plagues throughout the history of mankind [60, 64]. The earliest epidemic caused by *Y. pestis* killed approximately 30 to 50 million people in the 541–542 AD Plague of Justinian [64]. Since then, there were four additional pandemics caused by this pathogen, the Black death (1347–1351), Italian plague (1629–1631), Great plague of

London (1664–1666), and the Third plague (1885) [64]. In total, the five pandemics caused by *Y. pestis* are estimated to have killed over 250 million people. Cases of the plague still exist, yet the discovery of antibiotics has greatly reduced the global burden of this disease [60]. There are five forms of plague, all affecting the human body differently and having different mortality rates, bubonic, septicemic, pneumonic, meningeal, and pharyngeal [64]. However, there are typically three types of plagues described in the literature and main causes of outbreaks: bubonic, septicemic, and pneumonic [64, 65]. Today most human cases of plague are of the bubonic or pneumonic form, caused by spillover of an infected flea (bubonic) or by the inhalation of infectious droplets (pneumonic) [66]. The transmission of *Y. pestis* relies on rats (*Rattus rattus*) and its ectoparasite the rat flea (*Xenopsylla pheopis*). Conversely, in 1941 body lice and human fleas were found to be infected with the plague, indicating other vectors may exist. Currently there are no documented cases of plague being transmitted by body lice or human fleas to humans [66], yet some scholars suggest previous epidemics were caused by plague infected lice based on genomic evidence and paleomicrobiology [60]. Buboes or swollen lymph nodes are classical characteristics for Bubonic plague and typically are transmitted from rodents [66]. Septicemic plague is a severe form of bubonic plague where the bacteria enter the blood stream. Pneumonic plague affects the lungs and is transmitted by aerosolized bacteria [66]. Due to the respiratory nature of pneumonic plague, pneumonic plague can be spread person to person yet usually the high case fatality rates end the outbreaks quickly [66]. The case fatality rate, in the absence of treatment, for pneumonic plague can near 100%, while bubonic plague being around 40–70%, and septicemic around 50% [65, 66]. As mentioned, the plague took millions of live throughout the history of mankind and continues to do so to this day. The largest (n = 2348 cases) latest outbreak occurred in Madagascar late in 2017, with 70% of the cases diagnosed as pneumonic plague and 202 deaths occurring [67]. While the probability of a pandemic caused by the plague has decreased, a recently discovered multidrug resistant strains of *Y. pestis* has raised alarms for potential future outbreaks becoming of International Health Security concern [65, 67]. The Madagascar strain (MDR *Y. pestis* plasmid pIP1202) was found to be resistant to eight common antibiotics (i.e., streptomycin, chloramphenicol, tetracycline, sulfonamides, ampicillin, kanamycin, spectinomycin, and minocycline) [68, 69]. Currently, there are still antibiotics (e.g., doxycycline) successful in treating MDR plague. Moreover, the high mortality rate in conjunction with the ability to be transmitted person-to-person leads *Y. pestis* to be classified as a Category A biothreat agent (i.e., high priority agent) [70, 71]. Without an approved vaccine available and the presence of a multidrug resistant plague, the Black Death may re-emerge from the history books.

3.1.2.3 Francisella tularensis

The causative agent of tularemia, *Francisella tularensis*, is transmitted to humans by different types of arthropods (e.g., ticks, flies, mosquitoes) or ingesting contaminated meat or water [65, 66]. First described in the 16th century, Tularemia affects mostly in the northern hemisphere [67]. It is now hypothesized Tularemia arrived from the Middle East to Central Anatolia since 14th century BC [67]. Due to its survival in water and its transmission, it may also be considered a waterborne pathogen [66]. The two main transmission cycles, terrestrial and aquatic, utilize different reservoirs and vectors and are differentiated by subspecies tularensis (also called Type A) and holarctica (also called Type B) [65]. Type A, being terrestrial and using mainly ticks, mosquitoes, and flies in its transmission cycle will be covered in this section. The most understood and established vector for *F. tularensis* is

the tick (e.g., *Dermacentor andersoni*, *D. variabilis*, and *A. americanum*). Mosquitoes and flies are thought to be mechanical vectors and their role in transmission is not fully understood [65]. The infectious dose for contradicting tularemia is extremely low, with only 10 *F. tularensis* bacteria needed to establish an infection subcutaneously and 25 when in aerosol form [65]. Disease typically is one of two forms either the ulceroglandular form (i.e., the most common) or the typhoidal form (i.e., the most severe form) [65]. There is currently no vaccine available against Tularemia and antibiotic treatments (doxycycline and ciprofloxacin) exist [68]. Due to its multiple forms of transmission in addition to mortality rate (30–60%) [65, 68], the pathogen is considered a Category A biothreat agent and requires a level 3 biocontainment [65, 68, 69]. This would not be the first time *F. tularensis* is considered a biological warfare agent, according to some scholars *F. tularensis* was used in the 1320–1318 BC Neshite-Arzawan conflict as a biological agent [67], warranting a need for further research and vaccine development as it constitutes an International Health Security threat.

3.1.2.4 Elizabethkingia anophelis

A newly uncovered bacterium, *Elizabethkingia anophelis* was discovered in 2011 in the midgut of an *Anopheles gambiae* mosquito [70–73]. Less than a decade since its discovery this pathogen has caused human disease in Asia [73–75], North America [76, 77], Europe [72, 78], and Africa [79]. The route of transmission remains unclear, although it is theorized mosquitoes transmit the bacteria to humans [80]. In Hong Kong there is evidence of perinatal vertical transmission [80] and both an outbreak in Singapore and Greece link *E. anophelis* cases to the water sources [78, 81]. The pathogen recently gained international attention by a large outbreak occurring in Wisconsin, USA, where over 60 cases were identified and 18 deaths occurred [71]. Clinical symptoms may include mostly sepsis, meningitis, fever, bacteremia, and pneumonia [71, 72, 76, 78], among others. Currently the case fatality rate is estimated between 23–70% [71–74, 80]. Disease was usually present in neonates, the elderly, chronic illness or immunocompromised individuals [80]. With increasing prevalence of people with co-morbidities this agent may see increased cases in the years to come. Since discovery, *E. anophelis* is found to be resistant to beta-lactam antibiotics and aminoglycosides [82], yet susceptible to minocycline, levofloxacin, among others, complicating treatment. With less than a decade since its discovery there are many knowledge gaps in all aspects of this pathogen from transmission cycle to disease manifestations. More research is warranted in addition to sustaining current mosquito control programs and surveillance.

3.2 Airborne

In the last century, some of the deadliest pandemics were spread through respiratory droplets or aerosols. Globalization and shortening of travel time have further increased the speed of spread of airborne diseases. Scientific advances in vaccine development and antimicrobials has helped to counter these outbreaks however risk of massive outbreaks due to emerging and re-emerging pathogens remain and is an International Health Security issue. The 2019 coronavirus disease (COVID-19) pandemic has shown the susceptibility of human population to novel emerging or re-emerging pathogens and its significant effect on economic, social, and human health. It has also shown the ability of a pathogen to rapidly disseminate through airborne or respiratory route and the difficulties associated with prevention and control measures. The majority of pathogens require isolation, quarantine and

respiratory precautions (surgical masks, personal protective equipment in hospitals, cleaning of surfaces, disinfection of surfaces, and hand hygiene) as prevention and control measures. Dangerous pathogens such as viruses, bacteria, or fungi transmitted from environment, animals or humans through respiratory route and having potential to cause epidemics and/or global pandemics are listed below along with the available medical countermeasures.

3.2.1 Viruses

3.2.1.1 Variola virus

Variola virus, a member of the *Orthopoxvirus* genus is the causative agent of smallpox. Before the 15th century, the disease was limited only to the continents of Europe and Asia. The smallpox was introduced into the Americas, Africa, and Australia between 15th and 18th century due to European colonialism and resulted in massive outbreaks with high case-fatality rates due to immunological naïve populations [83]. The variola virus was transmitted in humans predominantly through respiratory droplet nuclei. It can also transmit the infection through contact with body fluids, skin lesions, and scab fluids of infected person. The smallpox virus is limited to the human population with no animal reservoir [83, 84]. The global health campaign for smallpox eradication resulted in the eradication of smallpox in 1980 with the last natural case of smallpox in Somalia in 1977 [83]. In 1978, the accidental laboratory release of variola virus in Birmingham, United Kingdom and the resulting infection and death of a photographer due to smallpox is the last known death due to smallpox in the world with her mother being the last known case of smallpox. The eradication of smallpox was followed by cessation of smallpox vaccination programs and that has resulted in the mankind losing immunity to smallpox and other orthopoxviruses [84].

The variola virus is recognized as a huge threat to human health if used as bioweapon. This was based on the ability of Soviet Union to weaponize smallpox in the 1980s [83]. In 1994, the WHO Committee on orthopoxviruses decided, the stocks of variola virus DNA should be kept at only two international laboratories in world, namely Centers for Disease Control and Prevention (United States) and State Research Center of Virology and Biotechnology -VECTOR institute (Russia) [84]. However, fear remains that secret variola virus stocks could be kept illegally somewhere and be used in bioterrorist attacks; therefore, it is a threat for the International Health Security [83]. Genomic studies on orthopoxviruses has suggested the deletion of genes as an important concept for the reductive evolution of orthopoxviruses in adapting to new host species or emergence of new virus species [83, 85]. The existence of zoonotic orthopoxviruses with the ability to cause sporadic human cases raises the possibility of reemergence of variola virus as part of these natural evolution of orthopoxviruses [84]. Like the introduction of the smallpox in the Americas, either the release of variola virus intentionally or its reemergence as part of natural evolution can result in public health emergency of global concern with high fatality. This concern is mainly due to a huge proportion of the world being immunologically naïve, increased percentage of immunologically suppressed population, and globalization resulting in rapid spread of virus [83]. The effective vaccine and two antiviral drugs (brincidofovir and tecovirimat) are available pharmaceutical measures to fight any future outbreak due to either natural evolution or bioterrorist attack [83]. However, the lack of practical knowledge among healthcare professionals related to smallpox clinical characteristics may further delay early diagnosis, treatment and control of the outbreak.

3.2.1.2 Monkeypox virus

Monkeypox virus, has emerged as the most common pathogenic Orthopoxvirus and causes a zoonotic disease Monkeypox [86]. Similar to the variola virus, transmission is through respiratory droplets/secretions or contact with the lesion material [86]. Monkeypox is endemic in Central and West Africa with similar clinical manifestations as smallpox and a case-fatality rate of 10% [83, 84]. The clinical manifestations include fever, myalgia, exhaustion followed by appearance of rash and lymphadenopathy in 1–3 days [86, 87]. Monkeypox virus can infect a wide range of mammalian species with various species of African rodents acting as natural reservoir [88]. Monkeypox virus usually results in sporadic cases due to low efficiency of person-to-person transmission and occurs mainly from primary human cases but never from secondary cases [83, 84, 86]. However, during the recent outbreaks in Nigeria and Democratic republic of Congo (DRC), increased person-to-person transmission was observed along with associated imported cases in UK, US, Israel and Singapore [83, 89]. Additionally, in the US Midwest outbreak, the virus showed the ability to infect intermediate hosts (prairie dogs) from natural reservoirs and subsequently infect humans [90]. Infection with a Orthopoxvirus or smallpox vaccination provided protection against monkeypox virus and thus smallpox eradication and cessation of vaccination has resulted in decreasing number of vaccinated individuals [90]. Currently the monkeypox virus is in stage-3 of pathogen evolution to cause disease and phase-3 of WHO pandemic security alert level. The risk factors of absence of population-scale immunity, increasing efficiency of person-to-person transmission, and the presence of animal reservoir along with potential intermediate host suggests that monkeypox is no longer a rare disease and has potential to cause widespread epidemics becoming a threat for International Health Security. There is currently no approved antiviral or detailed case management for monkeypox however, selective agents developed for smallpox virus could be tested for treatment efficacy in case of outbreaks [89].

3.2.1.3 Nipah virus

Nipah virus is an emerging zoonotic -ssRNA virus belonging to the Henipavirus genus and Paramyxoviridae family. The natural reservoirs of Nipah virus are the Pteropid bats (fruit bats) with pigs acting as intermediate hosts [91, 92]. The fruits bats are limited to farms and orchards in the tropical and subtropical regions of Asia, East Africa, and Australian continents [91, 92]. The consumption of fruits by pigs which are contaminated or partially eaten by the Nipah virus infected Pteropod bats results in the spillover of the virus to intermediate hosts [93]. The transmission of the virus from intermediate hosts to humans is through direct contact with the excretions and secretions of infected pigs such as urine, saliva and respiratory secretions [92, 93]. The animal to human route is the primary mode of transmission with limited person-to-person transmission through direct contact with respiratory droplets or fomites. The major clinical manifestation of Nipah virus infection is acute encephalitis with headache, fever, vomiting, and dyspnea [92].

The Nipah virus outbreaks are limited to Asian continent with Malaysia (43%), Bangladesh (42%), and India (15%) reporting the incident cases worldwide [92]. The first outbreak of Nipah virus was identified in Malaysia in 1998 which spread to Singapore in 1999. This was mainly due to the importation of infected pigs from Malaysia to Singapore and the spillover of infection among pig farmers and abattoir workers [94]. This was followed by outbreak in Bangladesh in 2001 and neighboring India. In Bangladesh cases are identified nearly every year while India has reported outbreaks in 2001, 2007, and 2018 [92, 93]. All the Nipah virus outbreaks reported

till now had limited person-to-person transmission with R0 < 1 [93]. However, due to the high rate of mutations in the RNA virus, it has the potential of generating a strain with R0 > 1 [93]. Currently the disease is in the stage-3 of pathogenic evolution with phase-3 on pandemic alert scale. There is currently no medical countermeasure (antiviral or vaccine) approved or available against Nipah virus [92]. The genomic heterogeneity combined with the known susceptibility in humans and ability to cause person-to-person transmission suggests a future pandemic risk of Nipah virus and thus the listing of Nipah virus diseases as one of the WHO priority diseases with greatest danger for International Health Security [93, 95].

3.2.1.4 Hendra virus

Similar to the Nipah virus, Hendra virus is an emerging zoonotic pathogen belonging to the genus Henipavirus and family Paramyxoviridae. The Pteropid bats (Australian flying foxes) are the natural host with horses acting as amplifying hosts [91, 96]. Human disease follows transmission through contact with respiratory secretions of infected hosts while no person-to-person has been documented until now [96]. The clinical feature of Hendra virus disease in humans is acute encephalitis with or without influenza-like illness [96]. The first outbreak was identified in 1994 in Australia and the disease has been limited to Australia. There have been 7 human cases until now with a high case-fatality rate of 57% [96]. Currently, the disease is limited to stage-2 of evolution with phase-2 of pandemic alert level. There is currently no medical countermeasure (antiviral or human vaccine) approved against Hendra virus; however. an equine subunit vaccine is approved in Australia [92, 96]. The identification of virus in horses and presence in Pteropid bats underpins the potential of virus to cause large outbreaks in future becoming a threat for International Health Security.

3.2.1.5 Influenza viruses

These are a group of four types of enveloped -ssRNA Influenza viruses (A, B, C and D) belonging to the Orthomyxoviridae family of virus and are the common etiologic agent of respiratory infections in humans [97]. The virus is transmitted from person-to-person through respiratory droplets or contact with fomites [68]. Of the four types of influenza viruses, Influenza A and B cause disease in humans with influenza A having the ability to infect hosts of multiple species (pigs, horses, aquatic birds and poultry) in addition to humans [68, 98]. Influenza A undergoes antigenic drift and antigenic shift and thus causes seasonal epidemics and global pandemics while Influenza B undergoes only antigenic drift and is responsible for only seasonal epidemics [68, 99]. Antigenic drift is due to point mutation and results in minor genomic changes while antigenic shift is due to genetic reassortment and results in major genomic changes [68]. The antigenically different 18 hemagglutinin and 11 neuraminidase proteins further divides influenza A viruses into various subtypes i.e. H1N1, H3N2, H5N1, H7N9, H5N8.

Influenza A viruses have caused the highest number of known global pandemics in human history with Spanish flu (H1N1) in 1918, Asian influenza (H2N2) in 1957, Hong Kong influenza (H3N2) in 1968, and Swine flu (H1N1) in 2009 [100]. The seasonal influenza is responsible for annual epidemics in the human population with approximately 5–15% of the total world population being affected annually [68]. The clinical features of influenza infection include myalgia, headache, fever, sore throat, and non-productive cough with nearly 50% of infections asymptomatic [98]. The worldwide dissemination of avian influenza A viruses in domestic poultry flocks and birds and the demonstrated ability to infect humans has raised

the potential of future pandemic due to avian influenza A viruses which is of main International Health Security concern [101]. In 1997, an outbreak of H5N1 in Hong Kong resulted in 18 human cases and resulted in six deaths [102]. This was followed by continuous circulation of H5N1 strain in China with the widespread geographical distribution of this epizootic strain. Between 2003 and 2009, H5N1 resulted in 403 human cases with a high case fatality rate of 63%. Despite the high fatality, biological barriers prevent efficient binging of influenza virus to human receptors and thus the virus continues to have inefficient person-to-person transmission [102]. Similar human infections resulting in small outbreaks have been seen in H5N8 and H7N9 strains of avian influenza A viruses [101, 102]. However, the high propensity of influenza virus to undergo mutational changes may result in a complete species switch and lead to a pandemic which becomes an International Health Security threat.

M2 proton channel inhibitors (amantadine and rimantadine) and neuraminidase inhibitors (oseltamivir, zanamivir, peramivir) are the traditional antiviral drugs approved for influenza prevention and treatment [103]. All the influenza A viruses are resistant to M2 proton channel inhibitors making the neuraminidase inhibitors the drugs of choice against influenza viruses. Balovir Marboxil, a viral replication inhibitor was approved by FDA in 2018 but rapid emergence of resistance has prevented its routine use [103]. The seasonal influenza inactivated vaccine requires yearly evaluation due to genomic heterogeneity and is effective mainly against the vaccine strains [68]. Thus, the antigenic shift that results in emergence of pandemic strain would make seasonal vaccines ineffective. Currently, the influenza A virus are in different stages of pathogenic evolution ranging from stage-2, stage-3 or stage-5 and have a phase-3 or phase-5 pandemic alert level depending on serotype [68, 101]. The ability of influenza virus to infect multiple species, cross species barrier, and high genomic variability resulting in novel viruses with low immunity among the population are the reasons behind the constant threat of pandemic by influenza A viruses.

3.2.1.6 SARS-CoV-2

In 2019, a novel zoonotic beta-coronavirus (+ssRNA) emerged as the cause of viral pneumonia in Wuhan, China and was later named as *Severe Acute Respiratory Syndrome-related coronavirus-2* (SARS-CoV-2). SARS-CoV-2, the etiologic agent of COVID-19 is transmitted from person-to-person predominantly through respiratory droplets and secretions [68, 104]. The SARS-CoV-2 causes an influenza like illness with severe cases presenting with dyspnea, septic shock, and acute respiratory distress. The mammalian reservoir for the virus is believed to be bats and contact with contaminated live animals is believed to be the cause of spillage of virus into humans [68, 104]. The virus rapidly spread globally affecting 218 countries in 6 continents with the outbreak being declared a global pandemic by WHO on March 11th, 2020 [104, 105]. According to WHO, a total of 83,910,386 cases of COVID-19 has been reported till January 4, 2021 with 1,839,660 of them having fatal outcome. A new variant of SARS-CoV-2 known as B.1.1.7 emerged in the United Kingdom in late September, 2020 due to N501Y mutation and has nearly 71% (95% CI: 67%–75%) higher rate of transmission than previous variant [106]. As of January 4th, 2021, three types of vaccines have been approved in United States and United Kingdom for emergency use for prevention of COVID-19 [107, 108]. This includes the mRNA vaccine by Pfizer/BioNTech, Moderna and non-replicating vector vaccine by AstraZeneca/University of Oxford [107, 108]. Additionally, the Russian Sputnik (vector) and Chinese Sinopharm (inactivated) vaccines have been approved in other parts of world to fight the COVID-19 pandemic [109, 110].

Antiviral remdesivir is the only therapeutic agent approved by FDA against SARS-CoV-2 with baricitinib currently under emergency use authorization for therapy in combination with remdesivir [111]. Currently, the SARS-CoV-2 pathogen is in the stage-5 of pathogenic evolution with ongoing global pandemic and becoming a menace for International Health Security. Despite the authorization of vaccine, the challenges associated with logistics of vaccination and emergence of new variants of SARS-CoV-2 suggests that SARS-CoV-2 will continue to be an agent of public health concern for years to come.

3.2.1.7 SARS-CoV-1

The first of the beta-coronavirus (+ssRNA) to emerge in Guangdong Province, China by zoonotic transmission was called Severe Acute Respiratory Syndrome-related Coronavirus (SARS-CoV) and was responsible for the 2002/2003 Severe Acute Respiratory Syndrome (SARS) outbreak [68, 104]. The SARS-CoV-1 causes symptoms similar to SARS-CoV-2. The main mammalian reservoir host of this virus were bats with Asian civet cat believed be to the source of initial human infection [104]. The person-to-person transmission occurred due to contact with respiratory droplets or fomites. The epidemic started in November 2002 and spread rapidly to 29 countries in 5 continents resulting in 8437 cases and 813 deaths [68]. The outbreak was contained in July 2003 and since 2004 no cases of SARS has been reported [104]. Currently, there is no known transmission of SARS-CoV-1 to humans (stage-1) and it has a phase-1 pandemic alert level.

3.2.1.8 MERS-CoV

In 2012, a novel beta-coronavirus was identified to be the causative agent for acute respiratory disease in humans in Saudi Arabia and was named Middle East Respiratory Syndrome-related coronavirus (MERS-CoV) [104, 112]. Bats are the main mammalian reservoir for MERS-CoV with dromedary camels as the source of human infection [104, 112]. This enveloped +ssRNA virus is transmitted from animals to human through close contact with infected dromedary camels and/or person-to-person through respiratory droplets [104, 112]. The majority of cases of MERS-CoV are limited to Middle East with the lack of rapid global spread due to poor efficiency of person-to-person transmission [104]. MERS-CoV infection results in symptoms similar to other beta-coronaviruses and range from mild influenza like illness to severe disease with respiratory distress, septic shock, and multi-organ failure [112]. The initial case in 2012 was followed by an outbreak in Middle East in 2014 impacting 27 countries in Europe, Asia, Middle East, and North America with cases related to Middle East travel history [104]. The associated Korean outbreak in 2015 was precipitated due to a super spreader event with the individual having travel history to Middle Eastern countries [104, 112]. Till December 2019, a total of 2499 confirmed cases and 858 deaths have been reported due to MERS-CoV [68]. Research studies have shown the natural susceptibility among Alpacas and Llamas camelids to MERS-CoV [113, 114]. This raises the potential of widening of the geographic distribution of MERS-CoV to the South American region with high new world camelids population (Peru, Argentina, Chile, Bolivia) if the virus is introduced to these regions, becoming a threat for International Health Security in the Americas. Currently, the virus in stage-3 of pathogenic evolution and phase-3 of pandemic alert level. The lack of vaccine or treatment along with the potential for viral mutation that could increase zoonotic and/or person-to-person transmission may increase the epidemic potential of MERS-CoV and cause an International Health Security threat.

3.2.1.9 Hantavirus

Different than any previously mentioned pathogens, Hantaviruses are an entire genus capable of causing human diseases. In 1981, this group of -ssRNA viruses were introduced into the Bunyaviridae family [115]. Before 1993, Hantaviruses were thought to be solely responsible to cause hemorrhagic fever with renal syndrome (HRFS) in old world [115]. The main reservoirs for this type of viruses are rodents such as Cricetidae and Muridae. In 1993, the first new world Hantavirus was found in the Southwestern region of the US. This virus would later be named Sin Nombre virus (SNV) and be known to cause hantavirus cardiopulmonary syndrome (HPS) [115]. Since the discovery of SNV, the hantavirus genus includes more than 20 species and 30 genotypes [115]. Scientists have identified the deer mouse as the major host of SNV with cases confirmed in at least 30 US states [116]. The transmission of virus in humans is predominantly through inhalation of aerosolized rodent urine or salivary droppings. The pulmonary syndrome presents flu-like symptom lasting 3 to 5 days and after 7 days the cardiopulmonary phase may begin [115, 116]. Unfortunately, diagnosis of HPS has proved difficult and leads to misdiagnosis and underreporting [116]. Currently, the SNV has a high case fatality rate of 35% with no licensed antivirals or vaccine. Since close contact with or among rodents account for majority of exposures, rodent prevention and population surveillance is essential for transmission control. In 1996, a study found evidence of person-to-person transmission of another hantavirus in Argentine, raising concern of larger outbreaks in future [117]. Luckily person-to-person transmission is rare, if non-existent suggesting pathogen is in stage-2 of pathogenic evolution and thus, phase-2 of pandemic alert level. Yet, recent outbreaks of other Hantaviruses (e.g., Andes virus) are an alarm for International Health Security surveillance systems who worry about future local outbreaks or global pandemics due to potential for person-to-person transmission.

3.2.2 Bacteria

3.2.2.1 Burkholderia pseudomallei

This gram-negative bacillus is commonly found in environment and is the etiologic agent of a serious disease "Melioidosis" in humans and animals [118]. The agent was first identified in 1911 in Burma but was named *Burkholderia pseudomallei* in 1992 [119]. Melioidosis, also known as "Whitmore disease" mimics various other diseases such as community-acquired pneumonia, tuberculosis and sepsis and has a case fatality rate of 10–40% in humans [120–122]. Infection with *B. psuedomallei* is seen in numerous wild and domestic animal species with most cases seen in pigs, sheep, and goats [123]. The disease was first identified in Australia in 1950 and is currently endemic in Northern Australia and South East Asia [119, 120, 122]. In addition to the endemic areas, sporadic cases of *B. pseudomallei* occur in non-endemic areas of Central America, South America, and Africa and result in an estimated 165,000 cases per year worldwide with 89,000 of these cases having fatal outcomes [119, 122]. The predominant method of transmission is percutaneous inoculation, inhalation of aerosols, or ingestion of contaminated water with rare incidence of placental transmission [118–120]. *B. pseudomallei* infects both humans and animals but very rarely there is person-to-person, animal-to-animal or zoonotic transmission [120, 123]. The infectious form of *B. pseudomallei* can persist for prolonged periods in the environmental with soil or water acting as reservoir [123]. Improvement in diagnostic facilities and risk factors such as increased diabetes prevalence, anthropogenic changes, and globalization of humans and animals

may result in increase in infections by *B. pseudomallei* [123]. The lack of animal to humans or person-to-person transmission suggest the gram-negative bacteria is in stage-1 of pathogenic evolution. In the US, melioidosis is not a nationally notifiable disease but *B. pseudomallei* is a tier-1 select agent with a potential for use as a bioweapon due to its ability to infect humans and animals [123]. *B. pseudomallei* is resistant to penicillin, ampicillin, 1st and 2nd generation cephalosporins, and aminoglycosides like gentamycin, tobramycin and streptomycin. The therapeutic management consists of an 10–15 days intensive therapy with ceftazidime or carbapenems (meropenem/imipenem) followed by eradication therapy with trimethoprim-sulfamethoxazole [124]. The increase in areas with endemicity and susceptibility to infections in large number of species suggests a future risk in increase in reported cases and thus warrants increased awareness and attention from International Health Security experts. The lack of vaccine and long-term pharmaceutical therapy would further complicate the response in case of an outbreak.

3.2.2.2 Coxiella burnetti

Coxiella burnetti, the causative agent of Q fever in humans is an intracellular gram-negative coccobacilli that occurs in all geographic regions of the world except New Zealand [125–127]. The main reservoir of *C. burnetti* are cattle, sheep, and goats with marine mammals, birds, and arthropods reported to harbor the bacterium [127, 128]. Ticks are the main source of transmission of the bacterium in domestic animals but are not the source of transmission in humans [125]. Human Q fever is a worldwide zoonosis transmitted due to the inhalation of aerosolized bacteria from the environment. The bacterium is mostly spread in the environment due to shedding of bacteria in mammalian birth products, milk, feces, and urine with the bacterium surviving in the environment for long period [125, 128]. There have been only anecdotal reports of person-to-person transmission [127, 128] suggesting the pathogen is currently in stage 2 of evolution. The epidemiological profile of *C. burnetti* differs by countries and ranges from sporadic cases such as in US marines in Iraq, an epidemic in Cayenne, French Guiana, a major outbreak in Netherlands from 2007–2010, and a hyperendemic situation in Africa [127–129]. The widespread geographical distribution of *C. burnetti*, the recent outbreaks and description of disease in South-East Asia, India, and Brazil suggest the disease is very common cause of fever in the inter-tropical areas [127, 128]. The strains of *C. burnetti* resistant to doxycycline and erythromycin has been reported in many endemic areas of the world however most isolates still remain susceptible to doxycycline, fluoroquinolones, and trimethoprim-sulfamethoxazole [128]. The CDC has recently classified *C. burnetti* as select agent with potential to be used as in bioweapon [128]. Currently, *C. burnetti* causes zoonotic diseases but has not resulted in human-to-human transmission and thus is at the phase-3 of WHO pandemic alert level. The ability of *C. burnetti* to infect wide range of vertebrate and invertebrate hosts, persist in environment for long time, and cause massive outbreaks such as in Netherlands suggest that *C. burnetti* could become a major International Health Security threat in future with potential to cause pandemics.

3.2.2.3 Bacillus anthracis

This gram-positive spore forming bacilli is the causative agent of anthrax, a zoonotic disease which is rare in humans and common in animals. Human anthrax is a highly contagious disease and can be transmitted from animals to human through contact with infected animal or animal products or ingestion of animal meat. However, this highly virulent disease has no documented person-to-person

transmission [68, 130]. Herbivores animals are the primary reservoir of anthrax with all warm blood animals susceptible to *B. anthracis* infection [130]. Depending on the method of entry of the pathogenic endospores (inhalation, ingestion, skin), the disease can have respiratory (5%), cutaneous (94%), and gastrointestinal (1%) forms [130].

Worldwide approximately 20,000–100,000 cases of anthrax are reported annually, with the disease a major threat in arid regions of Central Asia, Africa, Middle East, Haiti, and South America [68, 131]. In the US, a total of 18 cases of inhalational anthrax and no case of gastrointestinal anthrax has been reported in the 20th century [132]. The largest outbreak of human anthrax was reported in Soviet Union in 1979, due to ingestion or contact with contaminated meat. The spores of the bacilli are resistant to environmental conditions such as drying, heating, ultraviolet (UV) rays, and gamma radiation and can survive for decades [68, 130]. This makes *B. anthracis* a major biological risk with a potential to be used in bioterrorist attack. In October–November 2001, intentional release of anthrax resulted in 22 cases of inhalational or cutaneous anthrax in US [133]. The drug of choice for treatment is oral or intravenous doxycycline or ciprofloxacin with the vaccine having no efficacy in post-exposure prophylaxis [130]. The causative agent is sensitive to most antibiotics with the exception of 3rd generation cephalosporins and trimethoprim-sulfamethoxazole but requires long duration of treatment due to endospores [130]. Currently, the disease in in stage-2 of evolution of pathogenic microbe resulting in limited animal to human outbreaks and phase-2 pandemic security level. This combination of factors such as high virulence, persistence in environment, and the fact that it has already been weaponized makes *B. anthracis* a major concern for International Health Security.

3.2.2.4 Mycobacterium tuberculosis

Tuberculosis (TB) is a chronic inflammatory disease caused by an acid-fast bacilli *Mycobacterium tuberculosis*. In addition to *M. tuberculosis*, *M. bovis* a member of the *Mycobacteriaceae* genus also can cause TB infection [134]. With the advent of antibiotics, public health experts believed they had achieved control over TB however, the emergence of HIV pandemic in 1980s resulted in the re-emergence of TB [135]. In 2019, TB was the infectious disease responsible for the largest number of deaths due to communicable diseases worldwide [136]. The *M. tuberculosis* bacilli is transmitted from person-to-person through small droplet nuclei while *M. bovis* is a zoonotic disease transmitted from cow to humans through ingestion of unpasteurized milk [134, 137]. *M. tuberculosis* has also shown to have bidirectional transmission between elephants and humans i.e. reverse zoonosis and zoonosis [138, 139]. The zoonosis- reverse zoonosis transmission is mainly possible due to close contact between humans and elephants during training of elephants, living in close proximity, and cleaning of barn [138, 139]. The inappropriate usage of antimycobacterial agents and antibiotics associated selective pressure led to the emergence of drug resistance strains of *M. tuberculosis*. Multi-drug resistant TB (MDR-TB) is defined as resistance to isoniazid and rifampicin, two of the first line antimycobacterial agents. Additionally, selective strains of bacteria have emerged with resistance to even second line antimycobacterial agents causing extensively drug-resistant tuberculosis (XDR-TB) and some with total lack of susceptibility to antimycobacterial agents causing total drug-resistant tuberculosis (TB) [140]. MDR-TB chemotherapy consists of drugs with severe toxicity to be given for 18–24 months and thus MDR-TB is associated with significant morbidity and mortality.

TB affects all regions of the world with nearly a quarter of the world's population infected with *M. tuberculosis* [136]. In 2017, worldwide TB incidence was 10 million

with 1.57 million fatal outcomes [136]. Approximately 5.6% of the total TB cases and 3.6% of the incident cases were MDR-TB [136]. Nearly 70% of the global burden of TB was found in South-East Asia and Africa with India, China, and Russia having more than 50% of the global burden of MDR-TB [140]. Only 57% of all MDR-TB cases receives and completes treatment [140]. Tuberculosis is primarily a disease transmitted airborne from person-to-person and thus is in stage-5 of pathogenic evolution. MDR-TB continues to be a threat to public health and international security due to the concerns related to long duration of chemotherapy, lack of safe and effective antimycobacterial agents, morbidity, mortality, socioeconomic impact, airborne transmission and recent zoonotic-reverse zoonosis transmission. Many International Health Security experts believe MDR-TB could be the plague of century 21st.

3.2.3 Fungi

3.2.3.1 Candida auris

Candida auris is an emerging pathogenic yeast belonging to the genus Candida and is responsible for multidrug-resistant invasive infections in nosocomial settings [141–143]. The species has been mainly isolated from nosocomial environment, where it survives for a long time and can form biofilms resulting in inter and intra-nosocomial transmissions [141, 142, 144]. *Candida auris* was first identified in 2009 in Japan and has rapidly spread to five continents (North America, South America, Europe, Asia and Africa) becoming an International Health Security threat [143, 145]. *C. auris* infections has been identified in Australia, Bangladesh, Kuwait, India, Japan, Pakistan, Oman, Singapore, Iran, Panama, Venezuela, Colombia, Brazil, Chile, United States, United Kingdom, Spain, Germany, Israel, France, and the Netherlands [141–143]. The emergence of *C. auris* has been attributed to widespread usage of antimicrobial (antibiotics and antifungal) agents and rising ambient temperatures [141]. *C. auris* results in skin or mucosal colonization in patients with the organisms being recovered from physical surfaces such as furniture, medical equipment or sinks [141, 142]. No animal or environmental reservoir for *C. auris* has yet been identified. Previous [141] studies done in the United Kingdom, India and United States suggest community transmission and community reservoir are unlikely [141]. However, *C. auris* has a very efficient person-to-person transmission that allows it to spread rapidly among patients [141, 142, 144]. The person-to-person transmission and presence of yeast on surfaces suggest a potential respiratory droplet mode of transmission but no specific mode of transmission has been established yet [141, 142].

One unique feature that differentiates *C. auris* from other *Candida* spp. is its ability to cause invasive infections in individuals with normal neutrophil counts [144]. This is due to the reduced activity of human neutrophils against *C. auris* leading to poor outcomes [144]. Individuals requiring multiple medical procedures that results in prolonged hospital stay such as surgical procedures, cardiac catherization, endoscopic gastrotomy tube insertion and mechanical ventilation are at higher risk of *C. auris* infections [146, 147]. Infection or colonization with *C. auris* is also found frequently in patients with co-morbidities such as chronic/acute renal failure, immunosuppressive conditions/diseases, cardiovascular diseases, liver disease, diabetes mellitus and benign/malignant solid tumors [148]. The *C. auris* yeast exhibits a high range of antifungal resistance with resistance to fluconazole as high as 93% [141, 142]. Amphotericin B has a wider range of MIC and thus are less likely to be used as empirical therapy. Echinocandins has a more favorable susceptibility making it the drug of choice for *C. auris* infections [141, 142].

The lack of knowledge related to any animal reservoir makes the *C. auris* pathogen currently in stage-5 (exclusive human agent) of pathogen evolvement. The combination of drug resistance, persistence on environmental surfaces, reduced neutrophil effectiveness, and rapid person-to-person transmission has resulted in increased nosocomial outbreaks around the world with significant mortality and morbidity [141, 142, 144]. Currently, these outbreaks are limited to nosocomial settings and thus are in Phase-3 of WHO Pandemic alerts. These factors of rapid transmission, outbreaks in widespread geographical regions and reduced human neutrophil activity makes *C. auris* a huge potential International Health Security threat in case of sustained community outbreaks.

4. Conclusions

Since ancient times, large number of pathogens (viruses, bacteria, parasites, fungi) found in the environment are responsible for causing severe morbidity and mortality. These pathogenic organisms mainly infect humans through respiratory droplets, aerosols, dust, vector bite, contaminated food or water, or direct contact with animal hosts. The emergence of SARS-CoV-2 in 2019 and its global spread resulted in the announcement of the sixth public health emergency of international concern in last 10 years after Influenza A (H1N1) in 2009, Ebola virus in 2014, Polio in 2014, Zika virus in 2016, and Ebola in 2019 [68]. Moreover, in the last 20 years the emergence of novel pathogens such as SARS-CoV-1, MERS-CoV, Candida auris, and drug resistant bacteria in addition to the ongoing epidemics/local outbreaks of vector-borne diseases such as Crimean-Congo Hemorrhagic fever and Zika has raised International Health Security alarms. This chapter mainly concentrates on the epidemiology, pharmaceutical tools, prevention, and control of pathogens having respiratory or vector mediated transmission. Infectious diseases continue to be major causes of fatality worldwide despite the significant advances in civilization, scientific technology, and medicine. On the contrary, these same advances may contribute to the emergence, re-emergence, and rapid spread of diseases due to climate change, deforestation, globalization, and over usage of pharmaceutical tools. In the last few decades, the rapid emergence/re-emergence of novel and resistant pathogens make it essential to establish surveillance and research programs into potential pandemic causing pathogens. It is important to take cognizance of the hazards posted by these vector-borne and airborne pathogens, already circulating among the animal or human population to prevent the risk of epidemics and global pandemics. Majority of the viruses with potential to cause pandemics lack antivirals and vaccines while fungi and bacteria have developed resistance to antimicrobials. Thus, special attention needs to be paid in the research and identification of effective drugs against these pathogens to have the medical countermeasures available to fight future pandemics and protect our International Health Security.

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Chapter 3

Reflections on Climate Change and Public Health in Africa in an Era of Global Pandemic

Edlyne Eze Anugwom

Abstract

The study examined the impact of climate change on public health provisioning in Sub-Saharan Africa. In addition to recognising the multifarious influence of climate change on health, it argues that the quest for global health security can only be achieved against the backdrop of concerted mainstreaming of climate change response into public heath provisioning, especially in the developing world. Adapting to climate change and mitigating its impact would logically require integrating it into public health planning, programming and interventions. Therefore, if health security entails provisioning and catering to the full range of health needs of people, climate change given its undoubted implications for health should be in the forefront of health security globally. Despite the global discourse of climate change and health security, tangible actions and programmes at different levels are needed to achieve the goals of good health and effective health security. This is no less the case now that the pandemic has challenged and stretched health institutions and provisions. However, the complex and intertwining effects of climate change and its manifold nexus with public health and health security can easily be apprehended through the systems perspective. There is the need for both radicalization of the public health system in Sub-Saharan Africa and concerted efforts across disciplines and actors to achieve effective climate change mitigation and adaptation and thus further strengthen health security.

Keywords: Climate Change, Sub-Saharan Africa, Public Health, Health Security, Climate Change Mitigation and Adaptation, Pandemic

1. Introduction

The chapter examines the impact and influence of climate change on public health in Sub-Saharan Africa which is a developing region of the world. It contends that in addition to its noted impact on agriculture, the environment, economy and migration, climate change also exerts far-reaching consequences on people's health and occupies a prominent position in any serious discourse on health security. As a result, adapting to climate change and mitigating its impact would logically require its mainstreaming into public health planning, programming and interventions especially in developing parts of the world where public institutions and structures are in most cases incapacitated. In other words, there is no doubting the nexus between climate change and health as well as the various deleterious impacts of climate change on public health [1–3] and health security.

There is no gainsaying the fact that health security entails provisioning and catering to the full health needs of the people in a fair and equitable manner especially against acute health issues that may have global origin and ramifications. In other words, such global events as climate change and pandemics are the main thrust of health security provisioning. Health security thus involves buffering citizens against the present and future threats and impacts of such global events. As argued here, one critical strategy for achieving this goal may be through mainstreaming climate change into public health provision.

Therefore, responding to the new challenges of climate change is certainly a critical way of ensuring health security now and in the foreseeable future. The reassurance that climate change mitigation and adaptation strategies embody provisions for health goes a long way in ensuring health security. Without doubt, building health security niches on the well-known or orthodox health challenges including the explosive issue of COVID-19 pandemic without taking adequate cognisance of climate change is surely deepening health insecurity inadvertently. Therefore, the focus on climate change and public health should be seen as part and parcel of the broad agenda of ensuring health security especially in developing nations where weak institutions and other structural constraints may undermine even the best health intentions.

Be the above as it may, the extant literature is replete with narratives on how climate change affects natural disaster including health related risks for different categories of the human population globally [4–7]. In other words, climate change impacts on natural disaster which in turn leads to fatalities, injuries and other short-term and long-term health issues for affected members of the population.

While some of what passes as climate change may be attributable to changes and transformations in the natural system overtime, a significant contributor to climate change results directly or indirectly from human actions and obtuse inaction. In other words, human influence or activities have been the dominant force of climate change especially the easily observable phenomenon of global warming [8].

There is no doubt that climate change and other human induced stressors negatively influence human health and well-being in various ways. While some of these threats are apparently obvious others are directly observable. However, the impact of climate change and adverse weather events on health is gradually becoming an accepted phenomenon which challenges health policy and planning especially in the areas of public and community health. Thus, while climate change as a distinct phenomenon poses its various challenges there is need for public planners to incorporate climate change issues into the mainframe of health planning. In other words, while climate change calls for adaptation and mitigation efforts, such efforts should be extended and mainstreamed into public health planning especially in the developing parts of the world where public health infrastructure may be commonly weak and bedevilled by structural constraints of different types; which also have a sum negative impact on efforts towards health security whether conceived from a global or national perspective.

Health security even though mainly apprehended from a global perspective equally entails well-planned and systematic action at national and regional levels to deal with global health threatening events. Without doubt, environmental degradation and the increasing consequences of climate change are global concerns that threaten health and which demand concerted action at different levels.

However, assessing the impact of climate change on health, health security and other spheres of national life would benefit from the realization that climate change is not really a single driver of repercussions but is in reality mediated by exiting contextual factors or forces in producing adverse impacts on human life [9]. It is in this regard that climate change response should be context-specific

and targeted at the observed and expected adverse impacts of climate change in any given world region.

2. Methodology

The chapter relied on information from documentary data and the content analysis of extant literature on climate change and health. The literature search was anchored on such inclusive terms as climate change; climate change and health; climate change and public health; health security; adverse weather events; climate change and new and emerging infectious diseases; climate change vulnerability and adaptation; climate resilience; climate change and poverty; climate change and human impacts; health effects of climate change; systems thinking in public health. However, literature with parochial local and solely national focus as well as extreme dated literature were excluded. Sources of literature include: University of Nigeria electronics library collection; IPCC; PLOS; Lancet; Elsevier health; BMC Public Health; Research Gate; and Academia.

2.1 Conceptualising climate change as distinct from weather

There is often a tendency to confuse weather changes or the state of the weather with climate change. As a matter of fact, some of the pessimism around climate change and its implications cohere with a failure to distinguish climate change from weather changes. Therefore, a good starting point in this article or chapter may be to summarily make a distinction between the two phenomena. Even though weather events or changes are related to climate change the two things are clearly different. In a very simple sense, severe weather events like droughts, tornadoes, blizzards, hurricanes and heavy downpours are indicative of adverse weather, climate change occurs in a situation where such adverse weather events persist over long periods of time i.e. over decades or longer. In other words, climate change refers to average weather conditions (in fact, whether adverse or not though emphasis is usually ascribed to the adverse ones for obvious reasons) that have been observed to have persisted or continued over long periods of time.

Thus, while weather state can change over hours and days, climate change occurs only when such events are observed as consistent or increasing in dimension or magnitude over a long period of time usually over decades. Interestingly, climate change in the above sense would encompass both increases and decreases in temperature as well as changing risks and probability of some adverse weather events, shifts and changes in amount and direction of precipitation and significant changes in other features of the general climate system whether globally or in some parts of the globe. But in terms of relationship, adverse weather events graduate to climate change when they are persistent and significant over decades and even centuries.

While vulnerability or susceptibility is a commonly invoked concept in climate change science, it is also a good expression with regards to tackling the climate change effects on human health. In this case, vulnerability becomes the tendency or susceptibility to being adversely affected by climate change induced health effects. However, in the case of public health and climate change, vulnerability is affected by three critical elements viz. exposure (contact by any means between the person and one or more psychosocial, chemical, biological or physical stressors especially those affected or induced by climate change); sensitivity (degree to which the person or group is affected by climate variability or change overtime); and susceptibility to harm or adverse effect which also includes the individual's capacity or ability to adapt or cope [10].

From the point of view of Africa and the developing world in general, adaptive capacity is very critical since the impact of climate change is directly proportional to adaptive capacity of the given group or individual though adaptive capacity is affected in turn by the strength and availability of institutions and common public good beyond the individual. There is no doubt that adaptive capacity also affects resilience or the ability to recover from, absorb and adapt to climate change or adverse weather events. Both adaptation and resilience as already indicated are affected not only by the individual personal attributes and possessions but more crucially by public institutions and policies targeted at engendering climate change adaptation. In this sense, public health as a common good and property of the group becomes crucially in building adaptation and resilience to climate change. While it is right and conventional to limit the public health role in climate change to mainly health benefits, it is equally important to realise that health is pivotal to other manifestations and activities of man in the society. Therefore, building public health systems that are resilient to climate change and which enable adaptation is imperative to improving social functioning in such other spheres as politics, economy, social and culture.

2.2 Theoretical framing of public health response to climate change

There is enough persuasion to believe in the value of the systems approach or systems thinking as a theoretical and philosophical base upon which to anchor public health response to climate change in Africa. However, unlike typical social science notions of the systems approach, the systems approach here privileges the interaction between the natural system and the activities and actions of humans and their agencies. Thus, such natural phenomena as ice sheets, forests, vegetation usually interact with human activities and practices like financial markets, transportation needs, farming systems, public policies and practices, indigenous knowledge, cultural patterns etc. All these cohere with the basic reality that the systems approach allows a holistic and integrative framing of climate change challenges and responses that are anchored on the inevitable reciprocity, mutual impact, heterogeneity and common influence that characterise both the natural and social systems.

The systems approach from one influential perspective is "a paradigm or perspective that considers connections among different components, plans for the implications of their interaction, and requires transdisciplinary thinking as well as active engagement of those who have a stake in the outcome to govern the course of change" ([11] p. 403).

Incidentally, public health is attuned to the realization that health is not solely a question of the bio-medical conditions of the individual or society. It embodies a fundamental recognition that public health is founded on the conception of health as beyond simply the biology and even behaviour of the individual. The above perspective makes it possible for public health to embody perspectives and viewpoints beyond the bio-medical and this is what makes public health suited to tackle the multi-pronged challenges of climate change which requires concerted efforts from different professionals and experts.

Also, the systems approach becomes recommended because it goes over and beyond conventional or orthodox conceptualization and framing of problems and actions. It thus embodies features and orientations that help capture the undoubted complexity of public health and the innovative responses demanded in coming to terms with climate change.

Components of the systems approach that recommends it to public health and climate change concerns include: its emphasis on relationships among phenomena; enables generalised studies even while preaching multidisciplinary orientation;

transcending academic or disciplinary boundaries in the bid to foster effective interaction; apprehending and building robust responses to social issues including climate change, health and even peace building; heterogeneity of philosophical roots and methodological orientation that generally produces a bewildering range of philosophies and array of methodologies that are extensive enough to embody different aspects of public health and generate innovative responses and framing new challenges like climate change. However, underlying and coupling the unique features of the systems thinking in public health is the emphasis on information sharing, collaborations across disciplines, active borrowing from others; eclectic orientation to both philosophical roots and methodologies; co-production of knowledge and more critically openness to new ideas and methods in spite of disciplinary orientation.

Beyond the above, the systems approach allows the conceptualization of both climate change and public health beyond a one-dimensional or uni-disciplinary perspective. It makes us realise that the public health challenges of climate change necessitate both concerted actions and the breaking of disciplinary barriers.

But the systems approach while lending itself to robustness, innovation and transcending of disciplinary boundaries or its eclecticism still enforces academic rigour and methodological sensitivity as we pursue understanding and solutions to health challenges including climate change. In this sense, "systems thinking compels us to study complex health-related phenomena rigorously, but with appropriate techniques" ([11] p. 404).

2.3 Climate change and health: an established and evolving nexus

It is really matter of fact to argue that, "public health planners and professionals at the state and local level, policymakers, and members of the public all need to consider health a central dimension of climate change and to plan and act accordingly" ([12] p. 435). In this sense, climate change does not just require framing into health planning but equally calls attention to the need for concerted action across all sectors in order to evolve adequate and timely responses to climate change especially in the area of health where the multifarious impacts of adverse weather events on health are still emerging.

In other words, while there is incontestable evidence of the impact of climate change on a good number of health issues, there are still emerging evidence of further nexus between adverse weather or climatic conditions and human health. The above reality underlines the need for a public health response that is both innovative and encompassing.

There are so many ways that climate change impacts on health. Thus, such things as the survival and distribution of mosquitoes, ticks, disease carrying rodents and the general environment (droughts, floods, and environmental hygiene) are all affected significantly by weather events and climate change. Also, climate change and weather affect the survival and distribution of helminths and their implications for such health issues as nematodes or roundworm infections (lymphatic filariasis, onchocerciasis); soil transmitted helminthiases; trematode infections (schistosomiasis and others); cestodes or tapeworms that cause a broad range of infections and diseases in human hosts.

Apart from the above, such other vector borne diseases like malaria and Dengue fever are proliferating from increasing climate and weather adversity in Africa while meningitis or Meningococcal meningitis which is caused by the bacteria *Neisseria meningitides* is also a climate sensitive disease which even though existing globally takes it heaviest toll in Africa and other developing parts of the world. Thus, there is no doubt that quite an impressive array of evidence exists in the extant literature

on the real and potential health effects of climate change globally [10, 13–16]. As already established a climate change induced event like drought can be linked to such illnesses as diarrhoea, scabies, conjunctivitis and trachoma [17].

Some easily verifiable negative health implications of climate change include (**Table 1**).

2.4 Specific nexus between climate change and pub health in Africa

There is no gainsaying the obvious fact that climate change can impact on public health in Africa in a variety of ways. Thus, "climate change effects on human health, along with the additional impact on the environment and on the economies of African countries, are likely to impede development. African countries will suffer health consequences related to the effects of climate change as their people are among the most vulnerable to climatic change in the world. This vulnerability is due in part to existing problems of poverty, weak institutions and armed conflict" ([18] p. 1). Therefore, peculiar African challenges ranging from widespread poverty, weak and failing institutions, internecine conflicts to poor public health systems, weak governance, and leadership incapacity make the continent literally in the eyes of the storm with regards to climate change. Confronting climate change and adverse environmental factors would entail improving and enhancing social and governance systems and processes.

As, as has been contended, "climate change can therefore affect human health in two main ways: first, by changing the severity or frequency of health problems that are already affected by climate or weather factors; and second, by creating unprecedented or unanticipated health problems or health threats in places where they have not previously occurred" ([10] p. 31). Specific nexus between health and adverse climatic conditions is illustrated in **Table 1** below.

In summary, climate change in Africa would adversely affect water resources (floods and droughts); severe decline in precipitation especially in South Africa and the Southern Africa region; increasing extreme and longer heat periods especially in tropical West Africa [19]; agricultural production especially cereals [20]; savannah ecosystems [21]; increased aridity in the Southern Africa region especially Somalia

S/N	Health Issue	Adverse Climatic/Weather Event
1.	Hypothermia	Cold
2.	Hyperthermia	Heat (including heat waves and heat stress)
3.	Famine	Droughts; Floods
4.	Internal Displacement	Floods; Drought
5.	Personal injuries	Floods; Hurricanes; Wildfires; Tornadoes
6.	Death (including drowning)	Floods; Droughts; Wildfires; Landslides
7.	Vector Borne Diseases (malaria; dengue fever; rift valley fever)	General adverse climatic conditions especially precipitation; floods;
8.	Food contamination and shortages (impact on nutrition and disease resistance)	General adverse climatic conditions especially precipitation; floods;
9.	Emerging Infectious Diseases (West Nile virus; Ebola; hantavirus)	General adverse weather and climate
10.	Cardiovascular and respiratory diseases	General adverse weather and climate

Source: Author's compilation.

Table 1.
Specific health issue by adverse climatic/weather event.

and Ethiopia; ocean ecosystems especially in the form of declining fish catches; coastal populations; general infrastructure and myriad health issues ranging from infectious diseases (resurgence of New Tropical Diseases (NTDs), variants of known viruses) to fatalities and injuries resulting from adverse climate events like flooding, landslides and heavy rainfall [22].

The notable impacts of climate change in major regions in Sub-Saharan Africa include: West Africa – droughts, flooding in coastal plains, desertification, severe food production decline and food shortages with implications for health across varied groups [23]; Southern Africa – droughts resulting from decrease in precipitation, new and emerging vector borne diseases; East Africa – flooding, health risks and infrastructure damage. All these consequences would be seriously further worsened by poverty and incapacity of institutions. For instance, it has posited that the populations of such African nations like Mozambique and Nigeria would be most affected by sea-level rise in the future in terms of absolute number of those to be affected [24].

Climate change would also expectedly occasion a shift in the distribution of a good number of vector-borne diseases. In fact, it would appear that malaria is already encroaching in areas hitherto alien to it including the highlands of Ethiopia, Kenya, Burundi, Rwanda [25–27]. These areas are usually where malaria was not in existence a few years ago. Worrisomely, such projected shifts would also affect areas of the Sahel, East Africa as well as Eastern, Central and Southern Africa.

Perhaps, the specific role of public health in climate change adaptation and resilience can be further illustrated through a brief focus on three adverse weather events that are now almost rife in the continent viz. drought, flood, and wildlife:

Drought – the function of public health in this regard should commence with a thorough risk assessment which should normally focus on such critical health issues as sanitation, water, food security, shelter as well as such other structural considerations as the likely or probable political, economic and psychosocial impacts of the drought on a given population or community. All the above are contingent upon recognising that drought can produce the following adverse effects: contamination of water; compromising sanitation and hygiene facilities and activities, infections, and population displacement. Thus, activities should focus on how to stem, ameliorate or avoid the impact of the flood on the above and generating disease surveillance, infection control, temporary shelters and alternative water sources tailored to the drought in question. The activities also require both public education and information regarding water usage, specific social and health risks as well as behavioural and attitudinal orientation consistent with adapting to and overcoming the adverse event. There is no doubt that information even before, within and immediate cessation of the drought can go a long way in the quest for resilience.

Floods – floods entail the overflow of water or the submergence of normal land areas with water. Floods could result from excessive precipitation over a long period of time; the overflowing of rivers beyond their banks; streams that occasionally break their confines or limits and submerge neighbouring areas. In the above sense, flooding may be caused by either natural processes (excessive rainfall; massive melting of snows) or coastal processes (storm surge as a result of hurricanes; tsunamis; inundation of the coastal regions; excessive water currents).

However, apart from the tsunami, the other causes of flooding are directly related to climate change and can be made worse by human activities related to land use, farming, irrigation activities etc. The public health impacts of climate change induced flooding include: destruction of homes; population displacement; water contamination; personal injuries; stress and mental health issues; disruption of both sewage and waste disposal as well as death (either from drowning or other activities related to the onset of the flood or during the flooding).

Public health response to flood would include precautionary and early warning systems. Equally important are strategies and detailed action plans that anticipate the impacts and emerging needs to be produced by the flood as well as peculiar stop-gap approaches to tackle shortage of services and amenities within the flood period. These could be related matters like loss of shelter, personal hygiene, general sanitation, water, worsening of pre-existing chronic diseases, over-burdening of existing health-care facilities, likely increase in disease burden, onset of new and emerging infectious diseases especially at the cessation of the flooding or during it, loss of income among others. In sub-Saharan Africa in general, floods always increase the likelihood and burden of diseases like malaria and Dengue fever. Thus, there may be proliferation of mosquitoes and other vector borne diseases resulting from the flood. Incidentally, the impact of these health issues goes far beyond the cessation of the flood.

Wildfire – Even though not as much a problem in Africa as it has been in the United States since the last two decades, wild fires still pose considerable climate change challenge. Generally, wildfire is a humongous inferno; a large sweeping and destructive fire or conflagration which occurs especially in the rural areas and desert or wilderness. Wildfires usually poses a lot of adverse consequences for the affected population or community ranging from the probability of burn injuries, death, population displacement and loss of property. Just like in the case of the flood, the normal first step for public health agencies should be community wildfire risk assessment and evaluation of fire hazards within the community. There should be extensive and full plans relating to probability of wildfire and the fire hazards. Plans would involve the specific steps or strategies for evacuation and regular fire drills as well as mass evacuation and temporary resettlement plans.

2.5 Generalised poverty, climate change and health in Africa

One big problem with addressing climate change impacts especially adaptive capacity of household and individuals in sub-Saharan Africa is that of poverty. In spite of however poverty is defined and whatever indicators are used in measuring it, there is no contesting the fact that poverty is widespread or generalised in most countries in Sub-Saharan Africa. According to a recent World Bank Report [28] people living in poverty in Sub-Saharan Africa grew from 278 million in 1990 to 413 million in 2015. Furthermore, the average poverty rate for the region is about 41% and 27 out of the world's 28 poorest countries are in Sub-Saharan Africa [28, 29].

Poverty limits individual's economic and social functioning and exerts adverse impacts on nutritional intakes, access to health services and even sensitivity to climate change and adverse weather events. The poor are usually in the epicentre of impacts of climate change because those who are poor suffer generalised socio-economic debilitations and inadequacies even before the onset of climate change. Therefore, in the event of climate change adversity the poor are usually the first affected and the most impacted. As has been argued, "poverty can leave people more exposed to climate and weather threats, increase sensitivity because of associations with higher rates of illness and nutritional deficits, and limit people's adaptive capacity" ([10] p. 31). For instance, it is reported that malnutrition cause about 1.7 million deaths per year in the continent and is perceived as the largest contributor to mortality related to climate change around the world [18].

2.6 Refocusing and strengthening public health response to climate change in Africa

The response of public health to climate change should go beyond the usual focus on epidemiology and diseases prevention and control to anchor on social

framing of health issues and engendering appropriate behavioural and attitudinal responses in the public. In this sense, health workers and professionals should embody strategies towards motivating appropriate behaviours in people as well as the political capital and tool for eliciting innovative policies especially from political leaders and policy makers.

Public health should in terms of climate change focus on the promotion of safety and health (parts of its core mandates). It should ideally work towards reducing the pre-existing burden of disease and evolve activities that build social capital, community engagement and collaborative initiatives that enhance community resilience. From the point of view of responding to climate change challenges, the preparedness and response of public health institutions should enable activities that build community resilience as well as reduce vulnerability in the population [30].

In other words, while climate change reverberates with health security, its challenges can be approached from a robust public health system that facilitates both mitigation and adaptation processes. Thus, the relationship between health of the people and climate change within a public health framework can be depicted in a Venn diagram as shown below (**Figure 1**).

There is no doubt that intervention in climate change adaptation is clearly in the core mandate of public health. Therefore, focusing on the public health impact of climate change is really consistent with key medical ethics of beneficence (protection of people from harm now and in the future and more generally in terms of boding good for people), non-maleficence (avoids harm or injury), and justice (equitable and fair to all concerned). The problem or issue of justice resonates with health provision even prior to climate change given noted inequalities in health. These inequalities are especially heightened in the case of Africa and other developing parts of the globe where economic and social limitations negatively impact

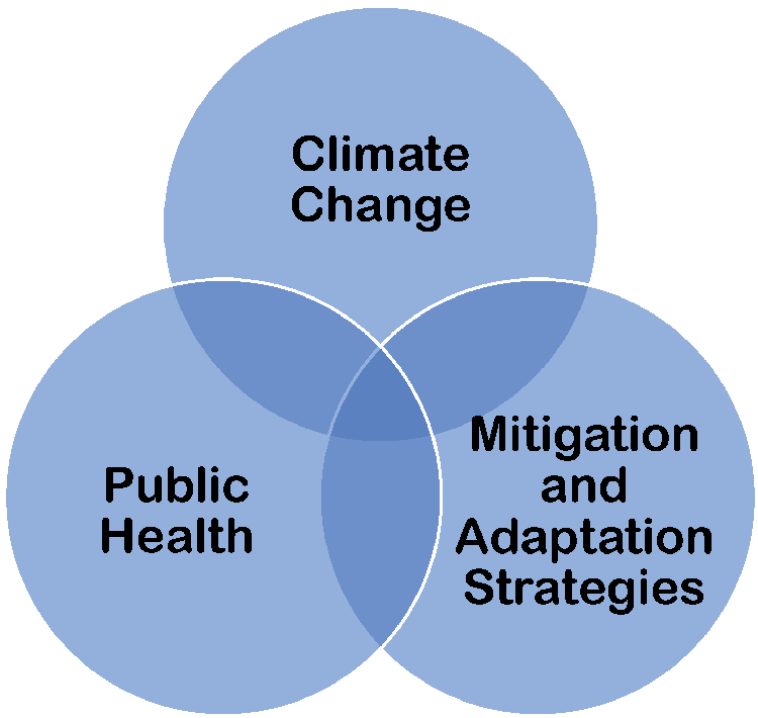

Figure 1.
Nexus between Climate Change and Public Health. Source: Author's compilation.

peoples access to health and health facilities. As has been insightfully posited, people in poor countries will willy-nilly face more health risks in the context of limited resources and thus less resilience than the situation in the developed or wealthy nations of the world [31–34]. It is a given that climate change has the tendency and potency to exacerbate existing health disparities and even introduce new ones. Incidentally, health disparities and inequalities are imbued in public health; and public health practices and policies aim to eliminate these disparities. These overriding goals of public health are more than desired now that climate change poses a formidable challenge to the health of people in these developing regions of the world. In these areas more than any other place, "public health action on climate change must include vulnerability assessments, identification of the most vulnerable populations, and a focus on eliminating health disparities" ([12] p. 438).

It is conventional wisdom that one approach to climate change is to improve the adaptation and resilience of people to adverse weather events. Adaptation to climate change incidentally occurs mainly at the individual, family and community levels. As a result, public health agencies and institutions given their location at the local communities are especially in a position to build the resilience of people to climate change especially climate change induced or generated disasters and afflictions. Public health institutions should be core part of the preparedness, response and recovery activities associated with climate change. In other words, public health agencies with their felt presence in the local communities can play critical roles at the three levels of building resilience to climate change.

Preparedness focuses on anticipating and making provision for the impacts and influence of climate change on people (activities and programmes that build and improve absorptive capacities); response has to do with a robust and timely response to the emergencies and problems that arise in times of adverse weather events like floods, wildfires and hurricanes (creating and deploying buffers that stunt or stop the influence of adverse events); and recovery is all about enabling the prospects and processes of overcoming the effects of adverse weather events at both the individual and community levels (activities and strategies towards engendering and facilitating recovery from such events in the community).

A very pragmatic approach to the evolvement of good practices and behaviours among the populace may be also emphasising co-benefits of health which have undoubted utility to climate change efforts. There is no gainsaying the fact that actions which embody health co-benefits (i.e., other benefits and gains beyond climate change) would more likely induce behaviour modification and attitude change than those that simply target only climate change issues which incidentally exist mainly on collective and aggregated forms. These issues are often construed as beyond the immediate influence of the individual; a view which often debilitates action on the individual level against climate change.

Responding to climate change would entail of necessity both innovation and radicalization of some conventions of policy and practice. For instance, climate change requires a longer time frame in public health planning than is usually the case [35]. Research is actively needed in order to continue to refine approaches to tackling the peculiar and general health challenges of climate change; also, to discover new and emerging nexus between adverse weather events and health. In other words, there should be endless quest for new evidence and innovative solutions. New evidence of association, whether in the short or long run between climate change and health as well as exerting efforts and resources on discovering innovative solutions to climate change induced or enhanced health challenges.

Interestingly, while preparedness is critical to public health interventions in climate change, it often occurs within the context of scientific uncertainty and inadequacy of facts. Thus, such events as pandemics, hurricanes and even tornadoes

cannot be predicted with precision, public health is expected to be innovative and prepared enough to respond within a limited time frame. It is in recognition of the above that preparedness is all about anticipation. This preparedness or anticipatory strategy finds support in both conventional wisdom and scientific orthodoxy. Thus, according to the Wingspread Conference, "when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically" [36].

Preparedness would therefore compel public health agencies to act or think strategically even when there are not enough or satisfactory precise scientific evidence. This would involve an element of risk management. Risk management as the name suggests is the systematic and evolving efforts towards identifying, tackling and reducing perceived risks to the health of a given population. Both the risk management principle and strategic thinking embodied in the notion of preparedness derives from the cognition that climate change could exert enormous costs on health but this could be significantly reduced if adaptation and mitigation efforts specific to health are undertaken at the onset. Therefore, "timely action to address the health impacts of climate change and makes good economic sense" ([12] p. 437).

3. Conclusion

Apparently, the discourse on climate change and public health does not seemingly embody health security. However, the above view is only tenable when health security is given a narrow or circumscribed definition and approached from a climate sceptical stance. But health security is concerned with all actions and systems that portend good health and wellbeing of citizens now and in the future. Thus, responding to the nascent health challenges of climate change within the framework of public health should be rightly conceived as crucial to realising the broad goals of health security. After all, health security as generally acknowledged is about actions and activities that are needed whether proactively or otherwise in order to curtail or minimise the impact or deleterious effects of acute or serious health events. In its conventional sense, health security is approached from a global perspective that privileges concerted action at different levels. In the same vein, climate change issues have been approached largely from a global perspective and have been perceived as portending acute public health challenges globally. However, while global efforts remain paramount, actions at regional and sub-regional levels can be coordinated in the case of climate change to build into the global health security agenda.

As part of the effort at adaptation and strengthening health security, public health should actively and robustly link people to needed and appropriate health service and support in the event of adverse weather events. Therefore, there is need for a strong and integrated infrastructure for delivering health service and interventions as part and parcel of the response to climate change at the community level. As has been argued, "climate change, an environmental health hazard of unprecedented scale and complexity, necessitates health professionals developing new ways of thinking, communicating, and acting" ([35] p. 403).

Besides the recent global challenge of COVID-19, climate change has been in the forefront of realistic efforts towards health security in the past three decades. Thus, climate change and its responses should be seen as lying squarely within the rubric of health security. Apparently, there can be no real or sustainable health security especially in developing regions of the world without accounting for climate change. Putting climate change within a responsive and robust public health system

logically responds to the glaring need for health security in almost the same way as a global compact on COVID-19 and its vaccines.

A good theoretical landing in responding to the health challenges of climate change is through adopting the systems theory. Systems thinking in this regard embodies multi-disciplinary and linkage propensity in the sense that it is oriented to drawing a nexus between disciplines. Therefore, in public health and climate change the systems approach become relevant in ensuring linkages and manifold nexus between disciplines that breeds concerted action. Without doubt, climate change is the area where multi-disciplinary approaches are needed in order to fully embody and respond to its various impacts and manifestations. Systems thinking also privileges diverse impacts and manifestations. It thus enables the understanding and acceptance of the impacts of both climate change and health on other spheres of the social system.

In spite of accelerating research on climate change in the last few decades, there is still no contesting the need for more research efforts especially in pinpointing specific and directional interaction between climate change and health or diseases especially in the case of new and re-emerging infectious diseases in Africa. In other words, nothing would be better than an evidence-based response to climate change i.e., the use of research and experience of epidemiology and disease patterns over the years in designing and informing climate change response in the area of public health in the continent. Despite the above, there is no gainsaying the need for radicalization of the public health systems in Africa and repositioning them towards innovative and concerted response to real, emerging and even anticipated impacts of climate change on health. These would entail not only fundamental mainstreaming of climate change into public health but equally building individual and community resilience through programmed interventions; tackling extensive health inequities or disparities especially those generated by or associated with poverty as well as reforming health institutions and infrastructure to embody robust innovations and concerted response to climate change especially in this era of global pandemic and beyond.

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Chapter 4

Improving International Health Security in Resource-Scarce Regions: Leveraging upon the Initial Success of Combating COVID-19 to Fight Emerging Health Threats

Daniel Lawer Egbenya

Abstract

In this Chapter, an overview of health security in different regions of the world will be considered with emphasis on the situation in low resource settings such as the global south and Asia since they share a lot in common. Additionally, how countries in these areas, especially sub-Saharan Africa, used existing health infrastructure, local resources and policy to somehow successfully (at least, presently) combat the ongoing COVID-19 pandemic will be elucidated. Ways in which the current approach being adopted by these countries could be used to fight other emerging health conditions such as rising cases of cardiovascular and chronic conditions in these countries will be considered in this Chapter. These measures may boost and ensure sustainability of overall healthcare capacities of these countries.

Keywords: international health security, COVID-19, emerging health threats, low-resource settings, healthcare

1. Introduction

Among the many lessons being learnt from the ongoing coronavirus disease 2019 (COVID-19) pandemic is that the state of health of each country may be intricately linked to all other countries on the globe. This comes to buttress what the world witnessed during epidemics in the recent past, particularly the Ebola virus disease of 2014–2016. Impliedly, whatever happens in the health system of any country in the 21st century is likely to have some effect on many other countries due to the high interconnectedness and interdependence of our world. Frequent and rapid travel possibilities have facilitated movement of disease causing agents such as seen in the emergence of COVID-19. Millions of lives and properties are lost in the wake of infectious diseases. Infectious diseases may have killed more humans than wars have ever done in human existence. These call for strengthening international health security especially in resource-constraint regions of the world so as to fight future epidemics and other diseases. This may be done by instituting appropriate healthcare policies based on local contexts and establishment of requisite healthcare infrastructure. Also, the World Health Organisation (WHO) should be

strengthened and resourced as well as a demonstration of a high sense of commitment on the part of countries to adhere to international health treaties [1, 2].

Emerging health threats are constituted by a number of new, unknown and evolving health conditions that a group of people encounter every now and then. These complications may result from environmental destruction, infectious diseases, population and lifestyle events, chemical exposure and natural disasters. The possibility of deliberate or accidental release of pathogens as bioweapons should also not be lost on us. These health threats may be faced from time to time and their effects may be experienced on a daily basis. Additionally, the emerging burden of disease in Africa, a resource-constraint region, shows a trend in which the predominantly infectious disease-burdened region is now grappling with non-communicable diseases [3].

In the midst of the deadly COVID-19 pandemic, resource-scarce countries may potentially marshal some inherent resources to combat emerging health threats. While the availability of a full functioning and inclusive healthcare system is desirable in all countries including low- and middle- income countries (LMICs), to effectively tackle emerging and re-emerging health threats, LMICs may start off by strengthening their low-level resources while scaling up with the construction of the needed huge infrastructural healthcare facilities.

As being witnessed in some places, particularly in developing countries, readiness of the populace to follow through with the COVID-19 protocols without extreme recourse to challenging the need for instituting those protocols vis-à-vis infringement on human rights, disease mitigating measures have the potential to achieve worthwhile results in the direst of circumstances. This is contrary to what transpired in the West, especially in the early days of the emergence of COVID-19, where there were elaborate roadblocks set in the path of these same protocols. For instance, while the generality of the Ghanaian population, and indeed some parts of Africa, largely accepted and embraced the wearing of face masks and used same as a fashion trend, that was to be missing in the West.

In protecting a country's health security, the said country is indirectly contributing to protecting and promoting international health. Unfortunately, about 70% of the world's countries assert that they cannot independently fight off an outbreak [4]. This calls for urgent steps in scaling up the healthcare resources of these countries. Technical and financial assistance for epidemic preparedness should be advocated and closely monitored. For example, intensive personnel training, spearheaded by the Centres for Disease Control and Prevention (CDC), highly contributed to Nigeria's success at fighting the 2014 EBOLA epidemic [5]. Prevention, early detection and treatment are the surest and most efficient ways to fight off epidemics. Despite advanced countries have the moral obligation to assist their less-developed counterparts, owing to our interdependence, the latter needs to harness local resources aimed at achieving same target.

2. Brief overview of international health security

Good health is essential for the full functionality of humans. Determinants of quality and adequate health security of a population include a number of factors. These include the availability of a well-laid out quality healthcare policy and programmes, health facilities including hospitals and fully-functional diagnostic laboratories as well as a qualified and highly-motivated healthcare workforce. The availability of these varies from place to place, globally.

Health security in the developed world is one of topmost priority to governments in those countries. In such places, there is massive investment in both basic

and applied health research, for example. The availability of comprehensive healthcare policy complemented with advanced, state-of-the-art healthcare infrastructure enabled these countries to adequately provide for the health needs of their people. Such countries have effective and elaborate surveillance system in place to quickly identify any emerging health threat and provide the necessary remedy in a timely and effective manner, in most stances. When they even delay in doing so, it sounds to reason that the turn-around time would have even be higher should same condition be found in the developing world.

In resource-scarce regions of the world such as parts of Africa and Asia, however, there is a wide gap in providing the essentials needed for quality healthcare. These affect the overall quality of healthcare services rendered to people in these areas. More importantly, should there be an epidemic such as the EBOLA virus disease of 2014–2016 in parts of West Africa, there might be dare consequences for the lives of people not only in the epicentres of the infections but potentially, everywhere else.

Inadequate healthcare infrastructure to combat infectious disease outbreaks is a major occurrence in many LMICs. Despite the need for foreign aids to scale-up the number of key healthcare infrastructures in LMICs, these should not in any way be strictly tied to complicated strings that have the potential to affect the sovereignty and overall human security of these countries.

Early detection of outbreaks, which is essential for containment, takes place in a well-functioning healthcare system [6]. In places where the healthcare system is not properly functioning and where some groups of people do not have access to the country's healthcare system, outbreaks of infections may go undetected and unreported for months hence causing more havoc in the population. This may occur mostly in developing and resource-scarce countries, as shown by the EBOLA virus disease of 2014 in Guinea, West Africa. Moreover, the implementation of sanctions such as travel bans instead of provision of financial and technical support to countries that report the presence of unusual pathogens and infections in their jurisdictions may deter some of these countries from reporting such outbreaks early enough to world regulatory bodies such as WHO despite being obligated under the international health regulations to report such issues.

3. Method

To obtain papers for the current work, literature search was conducted in electronic databases and search engines, namely; Google scholar, PubMed and Google search engine. Phrases such as international health security, WHO phases of pandemic, fighting COVID-19 in Africa, second wave of COVID-19 and emerging health threats in Africa were searched. After going through the suggested papers by the searches, the papers used were selected. Papers included were written in English language. Additionally, based on the content of the current chapter, WHO and CDC, two prominent healthcare agencies, were heavily relied on to obtain the requisite papers for the present work.

4. Phases of the COVID-19 pandemic

Pandemics are marked by phases which identify key observations including their emergence and possible interventions. Similarly, COVID-19 has noticeable phases. These phases are important as they reflect possible preventive and mitigation measures to adopt at any point in the course of the pathogen invasion.

For instance, instituting social and physical distancing protocols and the decision to close a country's borders to traffic (air, land and sea) may be largely influenced by the rate of spread of an epidemic or a pandemic. The COVID-19 phases presented here are based on the WHO pandemic phase descriptions used for influenza [7]. In phase one, no novel coronavirus found in animals was deemed to cause infections in humans hence no need for mitigating measures. In Phase two, however, a novel coronavirus in animals was deemed to be the causative agent of a human infection. Specifically, a pneumonia outbreak with unknown aetiology was noticed in Wuhan city, Hubei province of China in late December, 2019 [8]. Subsequently, this outbreak was found to have commenced at a seafood market in the Wuhan city. Thereafter (12 January 2020), China shared data on a newly discovered coronavirus, initially named 2019 novel coronavirus (2019-nCoV), which was found to cause the pneumonia reported in the previous month.

About a month later, 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) officially named the virus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and WHO named the condition caused by this virus, coronavirus disease 2019 (COVID-19) [9]. The name of the virus reflects the family of viruses from which SARS-CoV-2 emanates from. Collectively, SARS-CoV-2 together with the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) constitute a subfamily of coronaviruses called β-coronavirus, a viral group [10]. Coronaviruses infect both man and animals leading to both acute and chronic conditions [11]. A phase three of the viral spread would be the situation where the virus does not lead to community level transmission because there is no human-to-human contact transmission. Impliedly, the virus in the animal contact may have led to few cases of infection and appropriate containment measures taken to prevent its spread. However, this was not to be the case of COVID-19 as it led to community level or horizontal transmissions. Therefore, phase three of COVID-19 had the virus spreading within the Wuhan city and the Hubei province. Consequently, the first imported case of COVID-19 from Wuhan City, globally, was reported by Thailand on 13 January 2020 [8]. This commenced the cross-country transmission of the disease and phase four of the spread of the pandemic. On 11 March 2020, owing to the over 118,000 confirmed cases in 114 countries in which 4,291 lives were lost, WHO declared COVID-19 a pandemic [12]. This is the Phase five of the spread of the virus.

A post-peak period of the pandemic occurs where there is a reduction in pandemic levels (number of cases) in most countries to levels below the observed peak levels. While this might have occurred in specific WHO regions such as Africa (in July), South-East Asia (in September) and Eastern Mediterranean (in November), the global post-peak period is, presently, unknown due to increasing cases in the Americas and across Europe [13]. However, currently, there is a second wave of spread of the virus in which other variants, different from the initially reported strain of the virus, are being found in some countries. With the raging second wave in countries such as the United Kingdom and South Africa, all countries need to strengthen their surveillance as well as mitigating measures so as to avoid the spread of the virus. Finally, a post-pandemic phase will set in when the disease will be reduced to normal levels. During such periods, surveillance and infection preparedness should still be put in place so as to prevent any future outbreak. The WHO phases, largely, correlate with the CDC influenza phases being applied to the surveillance and management of COVID-19 in the United States. These phases are, namely; investigation, recognition, initiation, acceleration, deceleration and preparation with the first four phases termed prepandemic intervals and the remaining, dubbed; pandemic intervals [14].

5. How have countries in the different regions of the world fared during the COVID-19 pandemic?

As at 14 December 2020, globally, there are over 70 million confirmed cases of COVID-19 resulting in about 1.6 million deaths with about 47 million recoveries [15, 16]. The current epicentre of the disease which doubles as the region with the highest number of cases, the Americas, has recorded over 30 million cases, representing about 42% of global infection rate with the United States of America alone accounting for about 16 million of this. Asia, where COVID-19's patient zero is located, currently falls below Europe based on the number of confirmed cases of COVID-19. The lowest case infection rate, till date, has been recorded in the WHO African region where a total of 1.6 million cases have been reported, that is, about 2.3% of the global infection rate. Similarly, while the Americas have reported 780, 904 deaths so far, the Africa region has reported 35, 879 COVID-19 associated deaths (that is about 2.6% and 2.2% death rate, respectively, in the two regions; both of which are around the global death rate of about 2.3%). There are a number of possibility that may have accounted for the significant variations in the number of cases and deaths reported in the different regions of the world. These may include genetic and temperature variations. Presently, there is a second wave of COVID-19 infections in a number of countries across the globe particularly in Europe.

The outbreak of COVID-19 in China, Asia, and subsequent report of its spread to Europe led many researchers, scientists and policy makers to probe how well the different regions of the world may combat the deadly infectious disease. While there was high hope for the more advanced countries to fiercely fight off COVID-19, owing to the superior healthcare infrastructure in those countries, many wonder how resource-scarce regions will fare in dealing with the pandemic. As expected, many countries put in measures to combat the virus. These included closure of entry points like airports, lockdowns and purchase of personal protective equipment.

Per the current death rate data as well as adherence to COVID-19 protocols, Africa may be doing fairly well in the management of the pandemic. The region has one of the lowest COVID-19 death rate (as stated above) and a recovery rate of as high as 85% [17], exceeding the global average rate of 67%. With this appreciable recovery rate, some lessons might be learnt from the management of the pandemic so as to improve healthcare in the region.

6. Boosting the healthcare needs of resource-scarce countries to fight emerging health threats

The world's population is projected to witness a huge rise in its ageing index, particularly in developing areas such as Africa [18]. Ageing is associated with increasing probability of proneness to infections due to reduced immune strength. Should these occur without corresponding improvement in healthcare infrastructure and services, there may be dare consequences on the population in these areas in the years ahead. In cases where there are hospitals to admit the aged, in-hospital infection risk needs to be critically checked.

Also, the increasing population of LMICs portends a fertile avenue for the emergence and spread of infections. Infectious diseases account for about half of the total death in Africa [19]. With increasing population implies that inadequate and overcrowded healthcare facilities may serve as vital spreading grounds for infections. Closely related to the increasing population is unplanned and uncoordinated urbanisation in these countries. Due to a number of factors including,

predominantly, the burning desire to seek for jobs in the urban and peri-urban areas in these countries, there is bound to be excessive urbanisation. The effect of this was felt in major cities across Africa during the COVID-19 lockdowns initiated in some of these cities. In Accra, Ghana, for example, it was a nightmare providing for most of these people who moved to the cities in search of non-existent jobs hence have no savings to depend on during the brief period of lockdown. If left uncheck, increasing population and its associated urbanisation may pose major obstacles in the fight against emerging and re-emerging infectious diseases in LMICs.

The effect of human-induced global environmental health challenges as evidenced by the problems associated with climate change may be harshly felt by LMICs in the coming years. While these countries may argue that they contribute less to climate change, in comparison to advanced economies, they (LMICs) may severely experience the blunt of climate change-associated problems such as emergence of environmental health conditions owing to their insufficient healthcare resources to combat same. Conversely, the advanced countries have high quality and adequate healthcare infrastructure to, somewhat, more effectively fight off health complications resulting from the changing environmental trends. Low resource settings need to adopt some local, contextualised measures to combat emerging and re-emerging infections in the years ahead.

6.1 Community resource utilisation in healthcare management

Community and traditional leadership can be marshalled to combat some healthcare challenges particularly in remote areas where mainstream healthcare facilities are either lacking completely or highly insufficient. Community mitigation measures have to be initiated and/or intensified through education and awareness campaigns. A large part of the population of many LMICs including Ghana live in remote areas who, due to information gap, do not have a good understanding of developments in relation to many health conditions; just as the emergence of COVID-19 had shown.

To make good use of community involvement in disease prevention and control, effective and efficient community engagement approach needs to be designed and implemented. In particular, key community leaders such as chiefs, assembly and unit committee members/opinion leaders should be involved in the local awareness creation and educational campaigns against diseases. These individuals are well respected in their communities and so would contribute to the dissemination of multilingual, contextually relevant public education and awareness campaign [20]. Where there are Community-based Health Planning and Services (CHPS) centres (mini health centres), the work of the community leaders will complement the activities of the CHPS staff. Also, most villages now have public address platforms where relevant, local information are passed on to residents. This is being used in some places during the COVID-19 pandemic to educate inhabitants. Such awareness creation may be intensified and repeated a number of times on these community platforms. In Kenya, East Africa, for instance, daily broadcast of COVID-19 adverts in local languages in communities were carried out. Central governments should also encourage community-based non-governmental organisations (NGOs) and decentralised governmental institutions located across the various districts to assist in public education on key health issues. This is because these organisations have established good working relationship with their respective communities and so have good understanding and knowledge of the local dynamics hence are able to deliver impactful awareness and education on major health conditions in their catchment areas.

6.2 Harnessing ingenuity and innovation in resource-scarce regions

When it matters most, when the lives of entire communities, cities and countries in some of the world's poorest places is threatened, ordinary citizens rose to the call. These citizens drew on their inherent ingenuity and devised preventive or protective apparatus against COVID-19. From very simple devices such as a handwashing plastic container with a tap fixed at one side of its lower part, popularly called Veronica bucket in Ghana, mechanised washing devices to solar and electricity powered handwashing apparatus as well as locally-produced digitised thermometer, a number of devices were manufactured within a short space of time during the COVID-19 pandemic. Interestingly, each new device manufactured showed to be an improvement over an existing similar device.

Similarly, many African countries saw the need to increase local productions of personal protective equipment (PPE). Ghana, for example, had unprecedented governmental support for the local textile industry to produce PPE including medical gowns and face masks in large quantities. Hitherto, these PPE are imported from countries such as China. Also, the increased level of technological innovation during the pandemic will be essential if the continent can fight emerging health threats in the future. Since the virus was found to be localised on surfaces including currencies, the predominant cash economies in Africa were at a disadvantage. Technological improvement led to an increasing pace of cashless payments including mobile money payments for public transportation and cost of purchased items. These and other innovative strategies were seen in places such as Ghana, Nigeria and Kenya.

Giving the innovative ideas shared and devices produced during the COVID-19 outbreak in many LMICs, it is not far-fetched to suggest that when people feel that their very basic existence as a community or nation is threatened, they are likely to come up with strategies and programmes to ameliorate the supposed daunting challenges. These innovations can be utilised in fighting emerging infectious diseases in many places.

6.3 Building of capacity of healthcare personnel as well as the establishment of the requisite infrastructure

Capacity building of the requisite human resource capital is critical if resource-scarce regions of the world will be able to win the war against emerging health threats. The often too inadequate healthcare professionals in these countries can no longer stand the test of time. Healthcare professionals ranging from health promotion officers, public health experts, community health assistants, laboratory technicians, pharmacists, nurses and medical doctors ought to be trained and frequently undergo continuous professional development so as to boost their capacity to effectively tackle health challenges in contemporary times. As has been clearly shown by COVID-19, advanced countries which serve as health tourism destinations for some citizens of LMICs cannot be available for use at certain times since they are also overburdened by cases in their respective countries. It, therefore, implies that elaborate and concerted efforts should be taken, going forward, to boost the capacity of healthcare professionals in LMICs if these countries are to survive the next deadly epidemic or pandemic.

Establishment of a state-of-the-art advanced laboratory alone is not enough. While this is a critical necessity, its maintenance is even more important taking into perspective the lack of maintenance culture in many developing countries. The importance of advanced laboratories in infectious disease prevention and management cannot be overemphasised. Accurate diagnoses and case management

are dependent on accurate laboratory investigations. In the same vein, accurate laboratory investigations are obtained from well-equipped, advanced laboratories, with sophisticated equipment. Unfortunately, most countries in LMICs lack the availability of such laboratories. Apart from the need for the establishment of such laboratories, maintenance culture, ironically, in resource-scarce countries is abysmally poor. Ordinarily, one would expect that such countries would rather maintain the few equipment and facilities in their possession. A culture of maintenance needs to be urgently developed in these countries. Standard operating procedures, where they exist, should be strengthen and vigorously followed. In instances where these do not exist presently, strenuous steps should be taken to, as a matter of urgency, put in such protocols. Without this, even should the establishment of advanced laboratories come to fruition, they will not adequately serve the purpose for their establishment. People who default in adhering to the maintenance routine should be penalised severely. This is because refusal to strictly adhere to such practices will result in mass murder in the foreseeable future as those facilities cannot be utilised when they are needed should the next epidemic or pandemic occur.

6.4 Private sector and donor participation in healthcare system development

Active involvement of the private sector was seen in the fight against COVID-19. In Ghana, for instance, the private sector and individuals mobilised and built an infectious disease centre, in record time, for the government and people of Ghana. More importantly, this is the first centre wholly built to serve as an infectious disease centre in the country. This is a great initiative that must be modelled, going forward, so as to help strengthen healthcare infrastructure in the country. Likewise, it is an initiative worthy of emulation by other LMICs.

As could be seen from the ongoing pandemic, no one country can successfully fight against a deadly infectious disease. Foreign assistance and careful utilisation of grants/aids and loans obtained from donor agencies and countries must be considered in the development of the healthcare system of LMICs. Unfortunately, misuse and abuse of healthcare support and aids have retarded the development of healthcare system in many of these countries. If countries will make any headway in confronting the challenges posed by emerging health threats in the 21st century, appropriate strategies have to be put in place to curb corruption in the health sector. The abuse of such financial assistance only enriches the few individuals involved but leaves the lives of countless number of people in danger as the intended infrastructure to be built will not see the light of day. Both the receiving country and the donor agency should enhance monitoring measures to ensure effective utilisation of such donations and apply severe sanctions on culprits who will engage in nefarious acts. It is through such means that resources can be put to their intended uses and provide the needed healthcare infrastructure in LMICs enabling the world to prepare and contain emerging infections.

6.5 Intensification of health promotion

Many countries in the global south have instituted health promotion programmes as an integral part of their national health policies. This is a cost-effective approach that can be utilised by resource-constraint countries. Health promotion ensures the adoption and inculcation of appropriate behavioural changes in the population so as to produce desirable results. Health promotion promises to achieve appreciable success in fighting diseases such as malaria and tuberculosis (TB) in Africa.

Emerging health threats in Africa such as cardiovascular diseases and obesity whose causes are linked to sedentary lifestyle and associated behavioural tendencies can be fought through extensive and coordinated health promotion approach. With the increasing burden of non-communicable diseases on the continent, health promotion may be instrumental in managing these conditions [3]. The middle class in these countries spend hours unend in their air-conditioned houses, cars and offices with little room for physical exercise. Fast food, rich in calories, in recent years, is a major delicacy for many in some developing countries. Frequent and consistent exercise and change in dietary content, for instance, need to be taken up seriously by the middle class in these countries who due to the nature of their work tend to live sedentary lifestyles. For instance, immune enhancing diet was highlighted by the government and health experts during the peak of COVID-19 in Ghana. This strategy could be used to fight off many infections.

6.6 Public education in fighting zoonotic infections

Over the years, deadly epidemics and pandemics have originated from human-pathogen contacts [21]. Notably, deadly infectious diseases such as EBOLA virus disease, influenza H1N1 and COVID-19 have been linked to animals such as bat and swine. There is the need for determined efforts by countries to reduce, where appropriate, these possible contacts. Similarly, the increasing change in human-animal ecosystem needs to be checked since this may be an avenue for spread of zoonotic infections.

There might be increasing contacts with hitherto un-encountered animal species. Human-pathogen contacts leading to infections of zoonosis types, for instance, can be reduced if appropriate steps are put in place. It is expedient that governments should institute awareness creation campaigns to educate the populace on the need to avoid excessive contacts of suspected animals. Bushmeat (meat delicacy obtained from wild animals) should be reduced as many of these animals may carry pathogens which may be harmful to human health. Being a major hub of bushmeat, LMICs need to increase surveillance of the consumption of the delicacy so as to reduce zoonotic infectious diseases [18, 19]. Hunters and other persons who may patronise these delicacies should be on the lookout for unusual signs and symptoms so as to quickly report to the hospital should any unknown sign and symptom be seen or felt. These would help prevent or reduce the possibility of getting infected with zoonotic infections in the future.

7. Conclusion

The fight against emerging and re-emerging infections and diseases needs to be won by all; irrespective of geographical differences. Through the collective efforts of both resource-scarce and advanced countries, appropriate measures could be put in place to strengthen the healthcare system of all countries. This is very necessary to build a resilient international health security owing to the interconnectedness of our world in contemporary times in which an outbreak in the remotest places can in no time reach the busiest of cities with its damning trails. Despite the need for advanced countries and donor agencies to assist resource-constraint regions of the world in building both the human and infrastructural capacity in the less developed countries with the ultimate aim of safeguarding the health of both regions, it is expedient that the less-developed nations draw on the strength of their basic and local potentials, as being exhibited in the COVID-19 fight. The battle against the

next possible epidemic or pandemic will be won if and only if individual countries institute appropriate measures (or are assisted to) so as to prevent, detect and contain any future outbreak.

Conflict of interest

None.

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Chapter 5

Inclusion Policies and Territorial Welfare Networks between Society, Work and the Economy at the Times of Covid 19

Romano Benini

Abstract

The Covid 19 health crisis rose the level of unease in the global market, bringing about a need for national systems which favour the development model, capable of giving centrality to the system with notions of inclusion and human development. Italy, having been categorised as one of the countries with the highest mortality rates as a direct result of Covid 19, provides us with the context in which we can identity how the capacity for resilience and economic development increasingly depend on the adoption of effective policies and tools which pursue these notions of inclusion and quality, and how the response to crisis often falls hand in hand with the strengthening of health prevention and territorial social networks. Through the analysis of data across the Italian regions, we find that a connection exists between environmental risk and health risk; with the greater spread of Covid 19 being found in the most industrialized areas, which only highlights the importance of adopting a development model that promotes the environmental turnaround of the economy while, at the same time, strengthening the functionality of social ties. This article addresses the issues of how, through aggravated discomfort, the crisis has made some of the ongoing phenomena even more apparent, with the introduction of social pathologies and increasing risk of inequality. Italy, despite its difficulties, offers interesting social and welfare network systems characterised by eco-sustainable productions, which can be strengthened through measures supported by European programs for the purpose of recovery and resilience.

Keywords: inclusion, welfare, pandemic, development, public health

1. Introduction

Well-being depends more and more on human development, given the ability of nations to promote investments capable of providing care, training and employment to citizens. The ability to guarantee free and efficient healthcare, education, training and work services to a large proportion of the population free of charge, or at least with limited costs, constitutes not only the concrete principles and base level of civilisation, but is, in fact, a prerequisite for the system to be competitive, functional and capable of generating wealth. The paradigm of the new millennium, as supported by the Fourth Capitalism dimension, requires that social development and economic grown be held together. The magnitude of the recent Covid 19 health

crisis has illustrated the importance of the relationship, showing how the level of human development is capable of determining the level of resilience within a given system, and how the ability to deal with crises, while crucial, is not sufficient. One the one hand, we have seen how countries in which economic growth and social development are not well integrated, matched with a higher level of inequality, such as the United states and Brazil, have struggled to deal with the consequences brought about by Covid 19. On the other hand, we have also seen how the impact of the large-scale health crisis is greater in regions and territories which a have a higher level of economic and human development, matched with a greater urban concentration and higher levels of pollution, mobility and traffic. The social dynamics determined by the Covid 19 pandemic have made the importance of a system capable of taking care not only of the disease, in terms of functioning hospitals and health centres, but of the social and welfare repercussions even more apparent. Addressing the various forms of malaise and discomfort through a network of social inclusion and assistance when it comes to welfare, accompanying and following people throughout the course of treatments. The Covid 19 health crisis helps to shed light on the contradictions present in contemporary society, showing how the road to a prosperous economy passes through social equality, sustainable development and a quality of life that supports the intertwined relationship between these two underlying principles in an attempt to combat against the main factors of discomfort in today's society, loneliness and lost ties [1–3].

2. Evolution characteristics of the Covid pandemic in Italy and Europe

2.1 Diffusion and resilience factors

The analysis of diffusion factors and those of resilience and health risk reduction which have presented themselves in the Covid 19 pandemic, highlight a system contradiction: separating an economy that was united for many years, the resilience of the system and the ability to manage the risk of contagion and its consequences in territories where social equality appears to be greater is magnified, guaranteeing the presence of an effective health, assistance and inclusion system becomes all the more apparent. The Covid 19 pandemic has added gravity, and put emphasis on the contradiction of the system, when a system deemed wealthier, with higher levels of employment, especially in areas where the risk of infection is greater, faces greater risks. This phenomenon is evident in all European regions, but especially amidst the Italian ones, where the spread of infection is entirely linked to the present of air pollution factors and is event in areas with a higher rate of urbanisation and mobility. The risk of contagion, on the other hand, appears somewhat more attenuated in regions such as Emilia Romagna or Tuscany, where economic growth and the presences of a robust entrepreneurial fabric correspond to the presence of a high rate of social and human development and a lower presence of polluting factors.

The Health crisis appears as yet another episode in a sequence of phenomena that contribute to the connection between factors of social unease and the consequences of an economic, financial and productive model that ought to be structurally re-thought, considering aspects that impact the environment, health and society in terms of inequality. This data appears to be present and well confirmed also by the evaluation of the diffusion and resilience factors found in the Italian system, which appears particularly exemplary of the different conditions present in European nations. In fact, Italy includes in its territorial diversity almost all the socio-economic conditions present in Europe and the analysis of the impact of the pandemic shows factors of diffusion and resilience that confirm what can be seen of the broader European framework.

In particular, the data concludes that:

- The areas with the greatest spread of the contagion both in the first and section wave can be placed in urban contexts and with greater anthropization, but above all, in those contexts characterised by the presence of particularly structured production and economic systems alongside an increased environmental risk.

- The realities affected by the major contagion, have the capacity to reduce the risk of mortality, dependent on the presence of valid social and health aids as well as intensive care.

- Preventative actions and above all the contexts capability to mitigate the repercussions on families and individuals with respect to the discomfort and social malaise aggravated by the health crisis and the impact of the pandemic, depend on the presence, alongside health facilities, of advanced social networks and services that support the formation of social capital.

- The treatment of health pathology through hospitalisation is ultimately one aspect, despite its obvious importance, the overall solution concerns itself with more widespread and extensive prevention and contrast tools, which consider places as well as the ways of living, working and production.

The data helps to express how the internal areas of the country have been less affected by risk factors and how the more cohesive local communities with more personal services are able to mitigate the phenomena of post Covid discomfort, as a result, territories characterised by more eco-sustainable productions generally appear less affected by the risk. In light of this, the Covid 19 pandemic has set forth a basic rule of thought: that health security is dependent on how one lives and how one produces. The presence of a system of social services and the people who help to reduce the use of hospitalisation and promotion of production activities capable of limiting the emission of pollutants into the atmosphere.

The thousands of villages and small municipalities, which offer high touristic value albeit at the risk of depopulation, are territorial contexts in which the risk factors appear less serious, as do the conditions of social hardship, due to the presence of social networks and stronger community ties. The Italian situation confirms what has been known for some time, and has been reaffirmed in the recent months through the analysis of the impact of Covid 19 derived from individuals, society and the economy, namely that human beings are incredibly sensitive to social circumstances – as put forth in the R. Laing's work '*The Politics of Experience*' (1967) [4]. Verified by social sciences and the growing role of welfare systems, which in recent years see social pathologies being derived from economic-culture factors, the situation that the world is currently experiencing confirms this fundamental assumption of psychiatry, bringing about a risk of dissociative identity disorder, anorexia, schizophrenia and above all depression in the post Covid context. The spread of depression as the "social disease" of this decade stems from the profound sense of inadequacy for what one could do and are unable to do, resulting from the ethics of efficiency at any cost, which coincidently has been an common thought in shaping these past decades and that of late liberalism, such ideals have led to devastating consequences for the human condition and society – from the growth of inequality to the other various forms of unease [3, 5–8].

The risk factors and spread of the Covid pandemic have certainly brought these social issues to light, however, the elements of resilience show how the health crisis

is an expression of a wider environmental crisis and a development model that generates situations of crisis, hardship and difficulty. To recall the words of Pope Francis, and applying his rational to the current context in which the epidemic has spread; *"it's not possible to remain healthy in a sick world"*.

The response to crisis factors and the consequences on people within a territory ought not to be traced back to the sole dimension of health therapy and pharmacology as they have been in the last phase. Instead, the therapies must primarily concern themselves with risk reduction, and therefore be of a preventative nature. It's not possible to solve structural problems with the logic of merely containing consequences, instead it's necessary to shift the focus and act on the causes. Genetic and biological research is called upon to pay attention to social transformations and the consequences found in the everyday lives of people who live in an economic and productive model that exasperates the individual and the environment [9–12].

The Covid 19 pandemic ought to be considered as the latest example of a continuous acceleration of crises deriving from the current exasperation of economic growth which, like many of the preceding crises i.e. the financial and the employment crises as well as the continuous environmental crisis, puts too much emphasis on the speculative logic of 'short-term advantages' [13].

2.2 Inequality and social hardship

One characteristic of social impact which presents itself in the current economic model, on a global scale, lies in the increase of inequality, traditionally measured through the "Gini index" which considers the differentials that present themselves amidst the different income classes. The notion is increasingly important given its connotations with two of the world's largest economies, the USA and China, ranking top in both the West and the East within terms of inequality. It's interesting to note that China, while formally a communist country, has a much higher level of social inequality compared to that of Japan, despite Japan being generally accepted as the main capitalist nation in the Eastern world. Exasperated capitalism seems to spread better in this era in the less democratic countries. In any case, the dimension of inequality constitutes as one of the basic characteristics in the current and prevalent development model, which calls into question the function of welfare policies and social inclusion networks. A deeper analysis into the Covid pandemic seems to only exacerbate the critical elements of the current development model, given the connection between the spread of the pandemic and the growth of inequality factors. The apparent need to counteract the increased condition of inequality and related social dynamics is becoming more and more important in light of the recent pandemic and its aggravations:

1. Avoid the impoverishment of people and the worsening inequalities resulting from a fall income, or loss in employment, and the obstacles arising from social distancing

2. Avoid the collapse of the productive system, especially of those which contribute significantly to the competitive capacity of the country and its social infrastructure

3. Promote private, public and social activities that are, necessary in the short term to counteract the effects of the virus and, vital in the mid-long term to bring about a wider change with the participation of citizens and work development on the basis of environmental (ecological and agro-food transition) and social justice.

If we consider the trend of wealth in the West over the course of the pandemic, we can observe that OCSE countries have seen an unprecedented growth in bank deposits. Such data indicates that the crisis may be leading to an extra-economic situation, especially when compared to historical data, with the previous financial and unemployment crisis of 2009/2011 we saw a decrease in bank deposits and savings. The extra-economic situation is also plausible given the natural consequence of the containment measures adopted during the pandemic, in the months following the decrease in the infection, there will likely be, as usually the case after a crisis, an increase in consumption. Having said this, the decrease in propensity concerned itself primarily with expenses such as international tourism, generally speaking, it was those individuals with a higher level of income that had a greater effect of savings. This excess of savings affects not only families, but companies, particularly those in an advantageous situation, i.e. operating in technological innovation, or those who have had access to forms of financial support. According to analysts, this phenomenon also leads to an increased level of inequality, given that its likely these saved resources remain in the bank deposits of the owners. This is one of the ongoing phenomena that illustrates how the crisis, induced by Covid 19, is destined to aggravate inequality, a common factor among the recent economic crises faced in the past decades since the turn of the millennium.

While this phenomenon is more evident in countries already known for characteristics including a greater level of inequality, less welfare coverage and a less gradual tax systems, such as the United States, the risk in the West is still apparent. The sequence of crises that have spanned the last twenty years have contributed to a divide in people, a distance in social classes, decreases in opportunities and an impoverished middle class. It's a trend that can only be stopped through robust investments in human development, health, education, welfare in the workplace. It's the process of rebuilding social bonds weakened by the continuous attack of crises and the advance of inequality in a system that requires performance, feeds expectations and generates depression, a phenomenon that is widespread, especially among the richer counties.

One of the most important cultural changes that will prevail at the end of the pandemic is therefore a renewed focus on the responsible innovation of life models. Forms of social interaction and production of goods and services based on investments in innovation capable of promoting responsible growth, directly or indirectly linked to the use of digital technologies for more sustainable development, must be promoted. If the spread of the health crisis feeds factors of inequality, it is equally evident how inclusion policies aimed at reducing social inequality can contribute to not only contain, but also reduce health risk factors. There is, therefore, an interesting connection between social risk containment policies and interventions to reduce health risks.

3. Reasons for the high mortality rate among Italians and the implications of post Covid 19 trauma

In the long months drawn out by the Covid pandemic, Italy's found itself in a situation characterised by some basic contradictions. On one hand, being the first Western country hit in February 2020, the delays in the initial closures significantly worsened the impact of the first wave. Generally speaking, the Italian health system ranked second in the wold by the WHO for efficiency, according to the 2019 index, held up, though this is arguably due to the impact of the pandemic being somewhat concentrated from the outset in regions with the most solid health structures. In spite of this, Italy remains among the countries in the world with the highest mortality rate and a high rate of contagion, this is a likely result of the country having a high percentage of the elderly population matched with a decrease in the number

of intensive care units in health centres, especially when compared to countries like Germany. In any case, even in the Italian situation, the risk factors have been increased by the lower investment across health systems in recent years, in particular, the lowered investments in emergency therapy departments.

If we consider the comparison with the indicators of the state of concern among European citizens, we can evaluate how Italians today have a far greater concern for work and the fate of the economy than for their own or family's health conditions and the possibility of getting sick. The second wave of the virus has, in fact, increased the fears of Italians for the economy, while decreasing those for the disease. The emotional dimension remains in this decisive situation, having said this, there are also reports which indicate the inherent stress enforced upon Italian families as a result of the health crisis. This leads to an assessment of the fragility in families, which in turn highlights the importance and need to strengths social networks and communities as a means of alleviating burdens or stressing in isolation, such a notion is generally supported in the results of surveys carried out in countries such as Spain and Poland. In Italy, as in other countries, the family has represented a decisive factor of resilience, as is typical with countries with a prevailing Catholic culture.

Another form of discomfort during the months of the pandemic concerns itself with the younger side of the spectrum, poor socialisation, deprivation of play and sharing with peers. Social isolation has resulted in widespread forms of unease and fragility among the younger generation, to the point of real 'broken sociality' crises. Professor Massimo Ammaniti, developmental psychoanalyst and honorary professor of Developmental Psychopathology at the Faculty of Medicine and Psychology of the University of Rome, and member of the international Psychoanalytical Association, has published an important research on this very aspect. Professor Ammaniti argues that: "The identity of children is closely linked to the rhythms, habits, rituals of daily life and its environments, so, in the absence of these elements, the risks are disorientation and insecurity. In fact, everyday life reassures children and confirms them in their identity and in the fact that they live in a predictable environment on average. These shortcomings, together with the absence of other important stimuli (confrontation with other children, group games, school activities), have created a real syndrome of social deprivation" [14].

Research has highlighted the difficulties faced by the younger generation during the period of the pandemic, with around 30% of Italian children having faced difficulties and disturbances of emotional regulation, i.e. sleep disturbances, irritation, mood swings, and increased tendency to favour the opposition and increased anger.

All these phenomena lead to a situation that requires the adoption of tools and behaviours capable of dealing with the evident increase in situational discomfort. The turning point is the investment in human development and the ability to intervene on the pre-existing development models, increasing social ties and promoting the resulting economic activities. Through analysing the ongoing phenomena and evaluating its data, we can observe how socioeconomic and health resilience capacities find common ground in the relationship with the human development index: this is an interesting albeit diminutive studied convergence, measurable not only in European counties but also among Italian regions and the various factors of human development, the ability to react to the social and economic crises of the territory and the response to the health crisis in terms of care and assistance systems.

4. Welfare systems and work-related stress in the context of Covid 19

If we consider the evolutionary indicators of economic frameworks, such as the Excelsior forecast reports by UnionCamere as well as the various company

analyses carried out by the Foundation of Labour Consultants, we can see how the Italian economy might emerge in the coming months, generating or at the very least accentuating a tendency towards specialisation, which runs the risk of creating higher levels unemployment, or people who cannot easily be re-employed in the labour market. It would seem that the crisis has had a greater effect on sectors with low added value, for example catering or tourism, which during recent years have provided opportunities of employment even for people with low professionalism and/or low incomes. Considering this, the effect of the pandemic, in Italy just as in other counties, will weigh more on families with low-professionalism and income workers, contributing to both social and economic unease. This unease is only magnified in counties with less investment in social promotion and active policies. The criticalities linked to the exceptional nature of the economic and health phase, deriving from a client of uncertainty, include difficulty of planning, management of remote work, stress of workers, organisational problems and naturally, a worsened climate and quality of work. The long months of the pandemic as well as those following have imposed greater levels of work-related stress, which seem to be only partially mitigated by the presence of remote work, even more so given that such work is not always turned into effective 'smart-working'. The phenomenon of work-related stress undoubtably impacts a given company's productivity and is a route cause faced by many Italian companied today. Company priorities in the pursuit of resilience and recovery are therefore closely linked to the recovering and raising of productivity levels as well as the reconstruction of a peaceful working climate within the structures. The internal reorganisation of work processes, prompted by the many innovations introduced over the course of the pandemic, are instrumental in the growth of productivity and play an important role in helping to orientate corporate strategies on human resources, together with the acquisition of new skills and the introduction and strengthening of a work logic geared towards objectives and results. In Italy, Covid 19 has emphasised the differences between territories and social classes, as well as the differences between various economic sectors, penalising, as mentioned previously, economies with less added value or a weakened capacity for innovation. According to the analyses on the Italian employment situation, the majority of losses are recorded within the fields of accommodation and catering, suffering from a 20% reduction in staff, followed by trade, recreational, cultural and sports services. The expectations for manufacturing activities are generally less critical, especially for companies with a greater capability for innovation and sustainability as well as the production of Made in Italy excellence, and show signs of growth, albeit moderate. Fortunately, there are industry sectors that are significantly less affected by the crisis, and are in fact showing signs of improvement, such as credit and insurance, information and communication and social services and assistance. Generally speaking, the social and economic data reporting on the effects of the Covid 19 pandemic show how the crisis has weakened industries that were already considered as weak, emphasises fragility leads to further disintegration, inequality and social unrest which has been coming to light in the recent decades, the consequences weigh not just on the health system but also on the economic one.

5. Elements of resilience and control, and overcoming the Covid 19 crisis

To understand what the elements of resilience are with respect to health risk factors, it's useful to first verify how the Covid 19 pandemic affected Italian regions in different ways throughout 2020, and how the level of lethality does not strictly depend on the level of the elderly population within a given region. Covid 19 does

not result in the same mortality rate across the board but instead manifests itself with extreme variability, with positivity levels ranging from a maximum of 5.4% in Lombardy to a minimum of 1.3% in Campania, averaging out at 3.5% nationwide. The morality rates for Covid 19 vary significantly across the different regions, with the same prevalence of new infections irrespective of the age range in a given territory. This is what we are led to believe from the emerging analysis of data collected by the national health observatory in Italian Regions of the Catholic University (Rome campus). The recent analyses further confirmed the data which emerged in the outset of the pandemic, namely that Covid 19 had a different intensity and lethality both in Italy and in Europe. The evidence ought to be analyses and fully understood by medical science and experts within the field of organisational health systems, especially since the differences found do not solely concern the fragility of the elderly population, those whom seem to be most affected by the virus. The researchers underline that the reasons for the regional and European differences must be sought among a very wide range of factors; organisational deficiencies, initial delays in understanding the severity of the emergency, deficits in the infection tracing systems, variant levels of virus aggression or aggressiveness, individual behaviour and the choices of central and local governments.

Another possible interpretative path suggested by the study is that among the most affected territories, with many having high levels of anthropisation, urbanisation and mobility, where most of their social and economic relationships take place. These areas, in all probability, have been subjected to a greater risk of contagion. Take Lombardy for example, the Italian region has both the highest intensity of movements and also, the greatest number of recorded infections. Paying attention to the relationship between deaths and infected people (the lethality), European analyses even depicts a high level or variability in this case, even the comparison amidst the elderly population (over 65) shows a correlation that is not always significant. In other words, the rate of mortality does not depend on the elderly structure of the population (**Figure 1**). Across Europe, the analysis of lethality recorded in its individual counties in relation to the percentage of elderly people has brought to light significant differences. For example, in groups with the highest

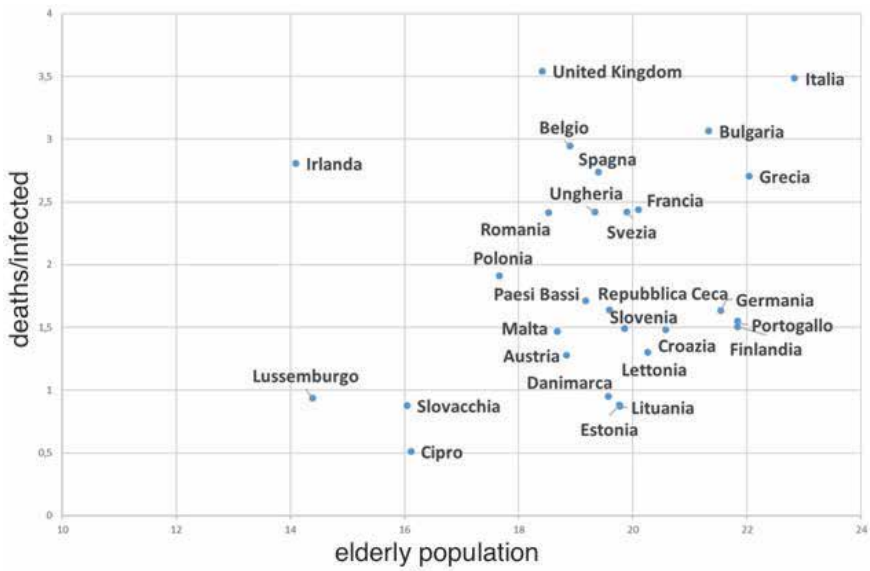

Figure 1.
A graph to represent the lethality of Covid 19 per country in relation to the proportion of elderly people.

percentage of an elderly citizens, lethality varies from 1.3 in Latvia to 3.1 per 100 inhabitants in Bulgaria; comparatively, in countries with the lowest percentage of elderly people, lethality varies from 0.5 recorded in Cyprus to 3.5 per 100 inhabitants in Great Britain.

Italy has a high level of lethality, with a contagion rate that places it within the central range of European rankings. Data has helped to verify that many of these deaths occurred within the elderly Italian population, Italy, in comparison to other European countries, ranks first for its share of elderly people, however this is only one factor that contributes towards mortality. In fact, the more worrying situation can be found in Great Britain, the cost with the highest level of lethality, despite having a relatively young population compared to many other European states. Similarly, Ireland also shows a high level of lethality in relation to the share of elders in the population. In general, there are very different situations with respect to lethality which do not necessarily rely solely on the share of the elderly population.

The analysis helps to clarify a plausible connection between the health crisis and the characteristic of the development model, and the connection between the lethality rate and the level of economic growth between Italian regions appears to be somewhat verifiable in this sense. The first phase of the epidemic was principally consolidated in northern Italy, while the second affected the whole national territory, albeit with varying intensity. What's interesting to note is that northern cities continued to record the highest mortality rate even in the second phase of the infection: in November 2020, for example, the mortality rate was 73 percent in north cities compared to 46 percent in the south. Despite the spread of the epidemic throughout the country in the second phase, the lethality rate remained higher within the urban context and in areas with a higher presence of productive settlements and mobility. Building on this, the highest mortality rate was found amidst Italian regions with a presence of territorial industrial systems, including Lombardy, Veneto, Friuli and Piedmont.

There is also a connection between the environmental risk factors and those relating to the health risk, which can also be found with regards to the spread of Covid 19. In particular, Italian provinces which, over past decade prior to the start of the pandemic, had the highest levels of atmospheric pollution (as reported in January 2020 by the Air Quality Index) appear to align themselves to the greater levels of spread-ability in the first phase of the pandemic, such was the case for Bergamo, Brescia, Lodi, Piacenza, Milan, Monza, Turin. Pavia, Parma and Modena. Unsurprisingly, the effect was greatest in northern Italy, one of the places in Western Europe with the highest levels of atmospheric pollution, and at the same time, home to the greatest presence of production sites. Over the course of the second wave, we can see a greater challenge in containing the rate of contagion especially in areas with a higher presence of pollutants. If the environmental element is an important factor in preventing health risk, arguably, the ability of social and welfare systems to contain and manage risk factors can be found in the greater capacity to contain and manage the consequences of said contagion that appear to be present in regions such as Emilia Romagna, Lazio and Tuscany. All of whom happen to have a better human development index compared to other regions that have been proportionally more affected by the health risk, namely, Lombardy, Umbria and Piedmont. The human development index is an official indicator that measures, among other things, the quality of social ties, the health and the welfare systems present in a given territory. In comparing Italian regions, which appear similar from a socio-economic point of view and neighbouring from a territorial perspective (which ultimately allows for a comparable level of exposure to the health risk), we can see how territories with a better human development index have been able to develop a greater resilience capacity and health risk

containment; i.e. Emilia Romagna reacts better than Lombardy, Trentino better than South Tyrol, and Lazio is considerably more resilient compared to Abruzzo or Umbria. This correspondence is further supported by pre-covid data, under the comparison between the management and containment of the health risk and the levels of social and health services measured through the official LEA indicator. If we combine this data with research indicators that attempt to measure 'social capital' (the presence of social participation, civic sense, non-profit enterprises and associative and voluntary networks within a territory) we can see a significant correspondence with the human development index and a partial alignment with measurements in health care quality levels. In fact, the relations they maintain with other subjects of the social protection system, both public and private, within a territory contribute to the value generated by non-profit institutions. The network of social and economic relationships that non-profits build ought to also be considered as an important indicator of social capital. Territories ranking top in this regard, i.e. Emilia Romagna, Trentino, Tuscany and Friuli, show a greater capacity for socio-economic resilience and at the same time a greater ability for containment with regards to the effects of the health crisis.

Such data can certainly stand to be depended and strengthened by further comparisons and feedback, but nonetheless seem to indicate that the various risk and crisis factors of this economic phase (from the productive crisis to a social one and from an environmental crisis one of health) have a common denominator that requires a reflection on the development model and shift in direction towards environmental and social sustainability. This empirical evidence establishes the needs for further fields of research and studies to highlight and support the following considerations;

- The Covid 19 health crisis appears to be determined by a series of contributing causes, a mix of elements that favour the spread of the virus
- The ability to either reduce or spread risk appears to be linked to the environment, the level of anthropisation and the presence of air pollution factors
- Urban contexts, both for environmental factors and for the presence of a continuous ad high contact between people, are considered to be places with the greatest diffusion of health risk
- The ability to contain and manage the effects on people's health is linked to the presence of adequate social health and welfare facilities within a territory
- The ability to intervene and reduce social hardship depends on the presence of networks supporting social inclusion and personal services within a given territory
- Both the resilience and resilience capacity of socio-economic dynamics as well as the promotion of development factors are dependent on the ability to invest in an eco-sustainable economic system, the promotion of an evolved welfare system, the centrality of investments in social protection, the prevention of health risk, as well as human development and civil liability.

The comparative analysis of the connected phenomena and the effects produced by the coronavirus pandemic from a social, health and economic perspective highlight the need to intervene and amend the current development model, promoting ecological reconversion of the economy that goes hand in hand with the promotion

of central social ties. Questioning the current neoliberal and global economic model, which can in part find references and tools in the innovation model of the Fourth Capitalism, providing interesting examples and good practises in Italy's own social and economic system.

6. The necessary integration between health, social and economic networks

6.1 The Italian example

Faced with crises, civil and cohesive communities react as plants do; strengthening the roots, developing shared bonds, protecting and including the weakest subjects and innovating and generating beauty. These are the realities of Italian production excellence, local networks, districts and supply chains of small to medium-sized enterprises that support both quality and sustainable production. The network system of Italian manufacturing excellence, studied throughout the world, is one of the few models where the increase in productivity and the innovation capacity of the economy is linked to the improvement of cohesion and social ties, as well as environmental investment: it's an example of the possible and desired relationship between social quality and the quality of the economy. There is a vast amount of data that confirms how the resilience of the Italian economic and social system, in its best expressions, relies on the distinctive characteristics of a 'vegetable economy', whereby the economy is considered as an expression of the territory and its environment. If Italy remains the fifth country in the world in terms of its trade surplus, and the seventh with regards to its manufacturing, it is likely a result of it having the highest percentage of waste reduction and recycling compared to other European countries (79 percent, double the European average). As the research of the Symbola Foundation (www.symbola.net) shows, Italy also ranks first in the world view for organically grown agriculture, with no European rivals to match their number of organic producers: approximately 70 thousand, almost double the average of other nations. Italian agriculture emits around 50% less greenhouse gases compared to the EU-28 average, significantly better than other large counties. Italian productions boast as many as three thousand geographical indications recognised at a community level for food products, considering this, it's no surprise that the added value of Italian agriculture is among the highest of large European countries.

If we consider the eco-efficiency factor (a synthesis of four factors: 1. Materials used 2. Energy used 3. Waste production and 4. Atmospheric emissions) the Italian system is among the most environmentally sustainable in Europe and among the major European economies. In recent years, Italy has grown the most in terms of its production eco-efficacy, thanks to the promotion of both recycling and circular economy. During the pandemic, 'green' companies, which have invested in eco-sustainability, appeared to be both more resilient (with a lessened decrease in turnover) and reactive, allowing for a a more confident outlook in the future. Generally speaking, these 'green' companies are more dynamic, innovative, digital and young. Investments in eco-sustainability and in the reduction of consumption also helps to establish a foundation for employment opportunities, the shift towards eco-sustainability has seen a rise in demand, both now and in the coming years, for professionals with green, environmental and digital skills.

Italy is also the first European country for companies operating within the cultural sector, deriving value from both its historical and artistic heritage. Generally speaking, Italy has a 'cohesive' business dimension well rooted in Italian history,

culture and economy linked to a given territory which creates value directly from social ties. Among these enterprises, the role of the cooperative enterprise is of special importance. While Italy has suffered from production and financial system crises in recent years, cooperative and mutual systems have been able to respond to said crises by strengthening networks, promoting participation and creating jobs. Since the beginning of the last century, non-profit companies have continued to promote an alternative model to financial capitalism, demonstrating how it is possible to consider economics primarily in terms of social well-being as opposed to not profit.

No reflection on overcoming a system based on the relationship between production and income through social and territorial networks can ignore the consideration of experience and value that comes with cooperative enterprises, very few countries in the world show the capabilities of this model as the national economy of Italy does. If the previous tendencies to lean towards a capitalist model were based on the hegemony of utilitarianism and competition, both between firms and within the internal organisation of work, the inclusion of Fourth Capitalism ideals allows the axis to shift in favour of a shared ability and cooperation within a system, present in the form of sharing knowledge and experiences. In this sense, the cooperative dimension that presents itself in the Italian model no longer appears solely in the non-profit economic dimension as a response to social needs, but as a possible means of organising the economy and society around the value of a person and for the purpose of well-being. Considering this it's fair to day that Italy not only has a strong tradition of cooperation and social enterprise, but also has a historically consolidated model promoting both human and social relationships; organising the territory and creating networks and relationships between people, businesses and the territory that they establish through an economy of collaboration and sharing. From these practises, examples and experiences, it's possible to build the conditions for a sustainable and stage development model on a health, environmental and social level.

6.2 From the recovery fund to a new development model

From the outset of the Covid 19 pandemic, originating areas surrounding Northern Italy, Southern France and Catalonia, some of the most developed areas across the continent, Europe saw a reactional divide. Two key directions emerged; Northern European countries as well as some eastern European counties gave priority to economic protection, whereas other countries, such as France and Italy, limited economic activity and prioritised above all, the health of their citizens. This division emphasises the first significant consequence of how the Covid 19 epidemic brought to light an important transition in the geopolitical relations perspective and the development model itself. The indications of the PNRR, the plan supported by the Recovery Fund for the recovery and resilience of countries within the European Union, offer a clear directive necessary to prevent current and future health risk situations: namely, the promotion of investments, infrastructures and incentives for an ecological conversion of the economy and greater social inclusion. For many nations across the world, especially the recently developed counties, this is likely to trigger an expensive change to production models that emit mass pollutants into the environment and have little regard for conditions of growth with respect to inequality. Many corporations and international companies, for example those operating in a highly polluting sector such as that of clothing, continue to produce in countries where there are no, or at least little, regulations and limited imposed on productions which negatively affect both humans and the environment. As such,

a global strategy for the purpose of pandemic risk prevention ought to be imposed upon nations with rigorous agreements aimed at supporting ecologically sustainable production, which at the same time, ought to reduce the emissions of gas and pollutants, even if this means the banning of products which appear difficult to recycle and dispose of. Nations know what they must do, but the path of a circular and environmentally sustainable economy, which involves both heavy costs and investments, cannot be explored only by Europe and the more advanced economies. In this sense, a directive heads towards the direction of re-converging two of the planet's largest economies, that of America and that of China, is necessary. Albeit difficult to imagine given their tendency to prefer security over enrichment at a cost.

The belief of scientists regarding the close correlation between environmental crisis and the health crisis much reach policy makers as soon as possible, necessary countermeasures for the purpose of resilience and recovery must be taken. The hope is that the European Union's recovery plan could stimulate change and initiate a change in direction, even if the world is not entirely binding. The new development model that needs to be determined in order to recover from the crisis and the sequence of crises that have characterised the last ten years, i.e. financial, environmental, economic and health, must be sustainable for man, society and the planet. Health sustainability ties itself to environmental sustainability, which in turn paves the way for human sustainability acts. Considering this, while quantitative productions, generated by the anxiety of the consumption of perishable goods as spawned by the rampant depression in a hyper-consumer society, must be expanded, services ought to be expanded to fully ensure citizens live better and together. The demand for solitary and selfish consumption must be replaced with the demand for sharing and social bonds. There is an economy of beauty and the well-made which opposes the consumerism of 'ugly' and perishable goods, the production of which generates pollution. There is a civil economy based on community-like-services promoting togetherness, increasingly requested not only by the elderly and generally weaker population, but also be those who want to escape from the social malaise that is fuelled by the current development model [15, 16].

The pursuit for another quality of life not measured by the conditions of production (a parameter used mainly by the US news and WEF model indicators), but instead, measured by psychological factors of well-being (i.e. parameters used by the BES). Both economic and social references call for a different model for the purpose of attaining sustainable development and are well presented within the Italian experience, even more so from an ethical and cultural point of view. The task of Italy, is therefore, in this phase of crisis resilience, to focus on the basic aspects of its model; quality, environmentally and socially sustainable productions with investments in networks and personal services.

7. Conclusion

The health crisis, which arrived in 2020 following a sequences of other crises, both an environmental and financial one – which continue to remain prevalent even today, have brought to light a need to reform social and economic models for the purpose of ensuring greater sustainability and balance between economic growth, social development and respect for the environment. In defining the conditions which some economists, including professor Stefano Zamagni, refer to as 'integral development', offers an appropriate means of determining decision makers in public policies. In light of this, actions must:

- Support social ties through forms of collective participation, associations, voluntary work and other forms associated with the aggregation of promoting a common good

- Promote methodologies, especially those which preserve initiatives and the creation of territorial networks of solidarity, learning and sharing

- Promote conditions for the participation in civic life and decisions regarding territorial development models

- Promote social mobility and the dissemination of personal, civic knowledge and growth, all the while ensuring development of social capital in areas which are determined by the conditions of economic growth

- Investing in the quality of human relationships, interventions for the inclusion of people in difficult conditions and considering work as a fundamental measure in the promotion of social development, through the support of effecting and present training and work-related services within a territory

- Promote activation and welfare interventions in the workplace and support a wage policy that limits inequality

All the challenges, which ties themselves to the underlying foundations of a system, gives reference to ethics. If the antidote to crises lies in the reconstruction of social ties, we must understand how to intervene in an attempt to counter the widespread ethics of individualism – which has seemingly been fuelled by decades of economic and political neoliberalism and only proves to feed the endless cycle of empty consumerism [17–19]. Humanity must free itself from the fragility and illusionary will to power, which is often expressed in the logic of accumulating useless goods and precarious experiences. The new development model must avoid the promotion of freedom to 'do as one want's and instead promote the freedom to change oneself. It is only in this way that we can truly take care of others and develop beyond a sick world.

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Chapter 6

Supply Chain Management and Restart of Economy in Post COVID-19

Venkataramanaiah Saddikuti, Sagar Galwankar and Akilesh Sai Saddikuti Venkat

Abstract

The increase in World Trade has led to significant growth in world GDP over last 100 years particularly. Supply chains have become the major enablers of world trade and the world is connected through supply chains. Any disruptions in any part of the world has led to disruptions in supply chains and economic recessions. Crisis like Tsunamis, earthquakes, 911 terror attacks, epidemics/pandemics like COVID-19 etc. have affected the businesses worldwide. COVID-19 pandemic has precipitated economic crisis due to disruption of supply chains and suppressed demand for many products and services worldwide. International Monetary Fund (IMF) has projected global economic growth to be negative 4.9%. This economic crisis has resulted in substantial erosion of market capitalization across the globe. The impact of COVID-19 is very significant on both health of the people and economy worldwide. Almost all businesses and governments are trying its best to save people from health and economic crisis. This requires rebuilding of supply chains through appropriate configuration with reliable sources of supply, collaboration, manufacturing and distribution of goods and services. Sectors like essential items, pharmaceutical, e-commerce have started early recovery of economy. However, other sectors require suitable interventions from government, business organizations in their policies and practices and use of digital technologies for economic recovery.

Keywords: COVID-19, E-commerce, economic development, economic recovery, GDP, healthcare, pandemic, supply chain management, world trade

1. Introduction

Trade is an integral part of economic activity and development. In global economic system, countries exchange various products as well as intermediate goods/inputs. International trade creates network of economic activity which are generally called trade networks or supply chains. Supply chains are the major enablers of world trade and the world is connected through supply chains. The world economy is strongly connected and influenced by supply chains and its developments. According various industry reports/studies, the best companies are the ones which are having best Supply Chains [1]. Global competition is forcing

organizations to build suitable competencies to reduce cost and improve customer service on continuous basis. Corporations have realized that substantial cost savings and market benefits can be achieved by more effective management of their supply chains globally. Advances in information/communication systems and quantitative modeling are also being widely implemented, which provide the potential for access and analysis of comprehensive data/information from each element of the supply chain. One of the main objectives of supply chain is to link the markets, distribution system, manufacturing and allied processes and the procurement to serve its customers across different parts of the world at lower cost and higher service levels. Various developments in technologies, trade policies lead to strong economic growth of the world. Supply chains facilitated globalization of trade for a long time. Various disruptions challenged the globalization. COVID-19 crisis has led to the greatest disruption of supply chains worldwide. COVID-19 crisis not only disrupted the global supply chains and it has thrown lot of challenges to politicians, business and overall economy. COVID-19 pandemic has precipitated economic crisis due to disruption of supply chain, manufacturing activities, and suppressed demand. International Monetary Fund (IMF) has projected global economic growth to be negative 4.9%. This economic crisis has resulted in substantial erosion of market capitalization across the globe.

This chapter focus on how supply chains helped in building the economic development before COVID-19 crisis and how these will help to restart the economic development post COVID-19. We present a brief overview of supply chain management with some examples, impact of COVID-19 on supply chains and economy followed by economy recover framework, sectors and strategies.

1.1 Definition of supply chain and supply chain management

A supply chain is a system consists of people, material, transformation activities, organizations, information and resources used in fulfilling the demand for a product or service by a customer. Supply chain management deals with transformation of raw materials and components into a finished product/service that is delivered to the end customer [2]. **Figure 1** shows a typical supply chain which consists

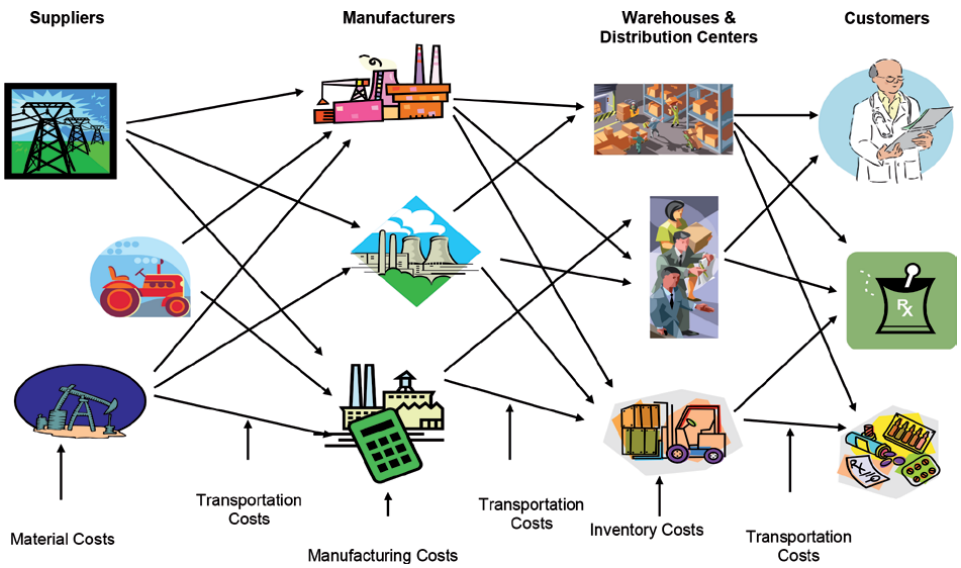

Figure 1.
A typical supply chain network [2].

of suppliers, manufacturers, distributors and final customer. These entities are connected through suitable transportation, warehousing and information sharing across the supply network.

A supply chain is a network between a company and its suppliers to produce and distribute a specific product to the final buyer. Generally, supply chains deal with different activities, people, material, information, financial resource, knowledge & skills. **Figure 2** shows various flows that need to be managed in a supply chain. Three important aspects of supply chains include adaptability, alignment and agility. The best supply chains identify structural shifts, sometimes before they occur, by capturing the latest data, filtering out noise, and tracking key patterns [3]. The supply chain also represents the steps it takes to get the product or service from its original state to the customer [2, 3]. Supply chain management is a crucial process because an optimized supply chain results in lower costs and a faster production cycle which helps companies to remain competitive in the business landscape. Some of the important areas that requires attention in supply chains include flow optimization, coordination, risk management, sustainability, safety and security. The best supply chains aren't just fast and cost effective. They are also agile and adaptable, and they ensure that all their companies' interests are aligned [3, 4].

Supply chain management uses different approaches for efficient integration of its stakeholders like suppliers, manufacturers, warehouses, retailers such that the merchandise is manufactured and supplied to the right customer on time at correct location at correct time at minimal cost and optimal service level [2, 3]. According to Institute for supply management, the supply chain management is defined as "the design and management of seamless, value-added process across organizational boundaries to meet the real needs of the end customer. The development and integration of people and technological resources are critical to successful supply chain integration". Similarly, Supply Chain Council defines it as "Managing supply and demand, sourcing raw materials and parts, manufacturing and assembly, warehousing and inventory tracking, order entry and order management, distribution across all channels, and delivery to the customer". Council of Supply Chain Management Professionals defined it as "the planning and management of sourcing and procurement, conversion, and all logistics management activities".

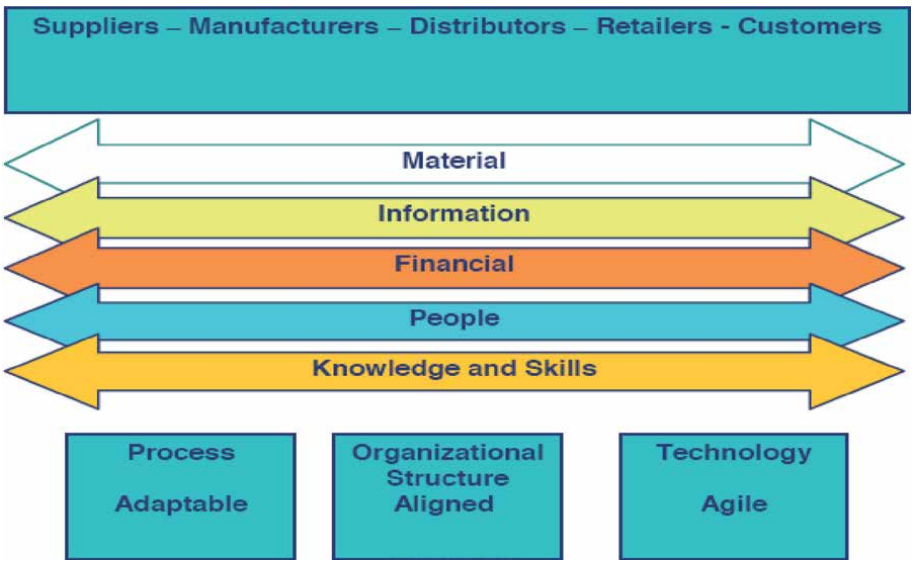

Figure 2.
Various flows in supply chain [3].

Also includes coordination with channel partners, which can be suppliers, intermediaries, third party service providers, and customers.

1.2 Supply chain building blocks

SCM is the management of a network of interconnected businesses involved in the provision of product and service packages required by the end customers. The network of interconnected businesses and comprises of three major building blocks Viz., structural, logical and informational [2, 3, 5, 6].

Structural Building Blocks include Suppliers, Manufacturing/Assembly Plants, Warehouses, Distribution Centers, Retailers/Customers, Logistics Network (inbound and outbound), Customers Orders etc. This can be visualized clearly from, **Figure 3**, a computer manufacturing company like IBM, HP, Dell etc. The relationship and their strength and number of entities drive the supply chain performance.

Logical building blocks of a supply chain include both horizontal and vertical functions of a supply chain and the same is shown in **Figure 4**. Logical building blocks include strategic, tactical and operational decisions cutting across various processes like procurement, production, sales and services. Integration of these building blocks across the supply chain network requires suitable organization structure and accountability. Both structural and logical building blocks are connected/integrated through informational building blocks.

Information building blocks focus on material requirement planning (MRP), enterprise resource planning (ERP), electronic data interchange (EDI), internet technologies, sensor networks, E-Commerce, E-Markets, E-CRM, Decision Support Software, standards etc.

1.3 Supply chain decision spectrum

Organizations involved in supply chains need to take several decisions are different levels and different processes. A typical decision spectrum is shown in **Figure 5** along with various decisions at different levels. Forecasting is one of the

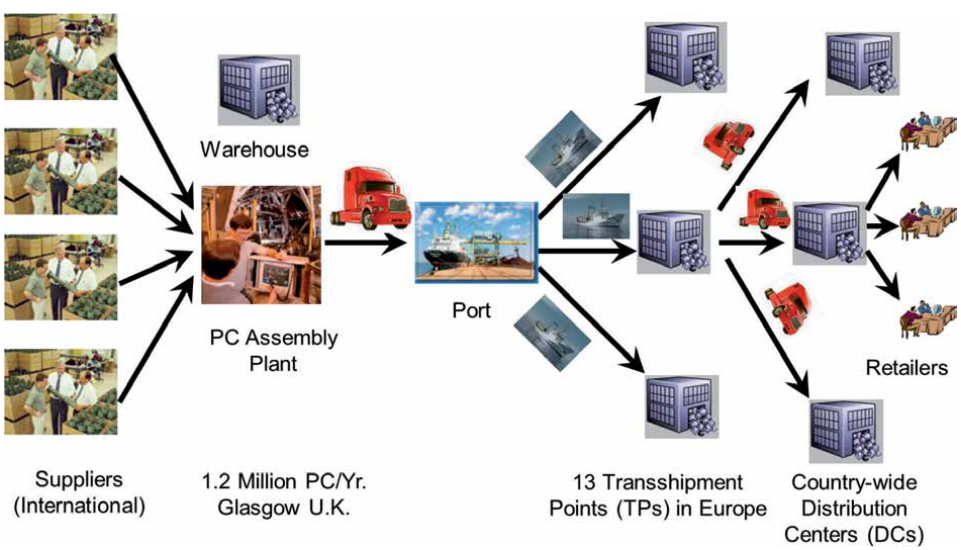

Figure 3.
Structural building blocks of a supply chain [2, 5].

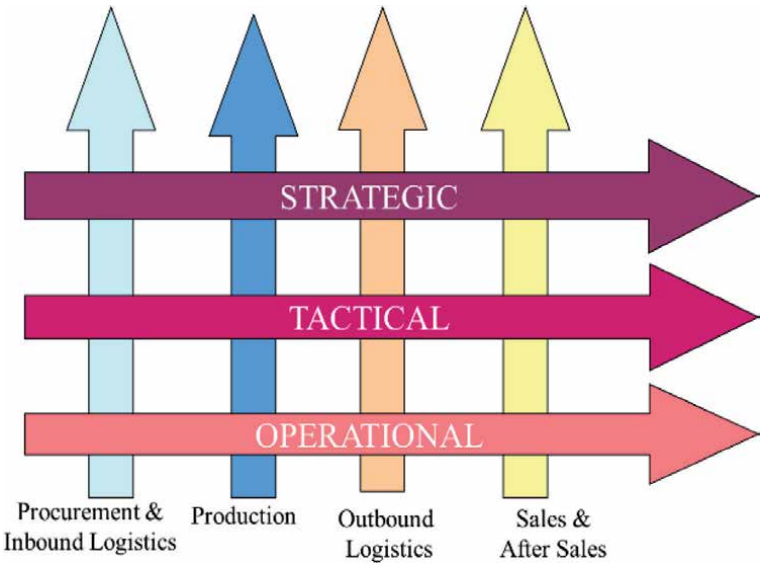

Figure 4.
Logical building blocks of a supply chain [5].

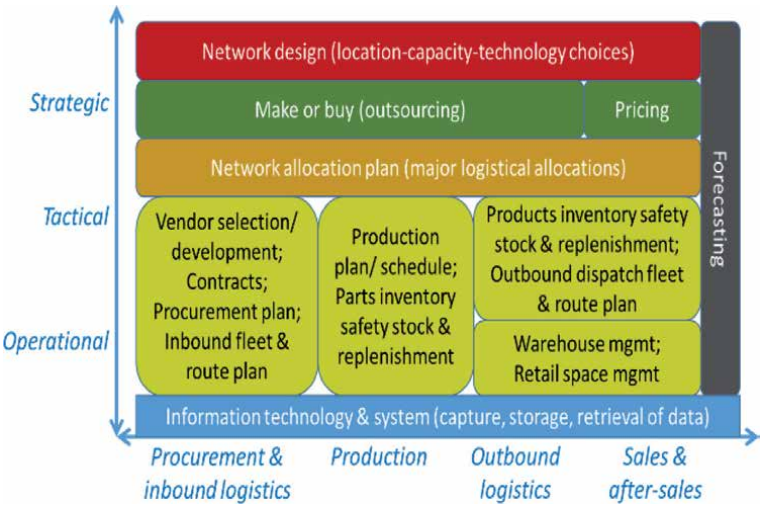

Figure 5.
Supply chain decision spectrum [5, 6].

critical inputs that affects the efficiency and responsiveness of the entire supply chain both in short term and long term.

Procurement & Inbound Logistics include two major components via., (i) managing procurements and (ii) manufacturing procurements. Managing procurement tasks comprise of control of inventory, development of quality standards, price negotiation, purchase of goods and services, financial purchases, aligning purchase to the company ethics and policies and disposal of waste. It also assists the organization to formulate strategies regarding criteria to choose suppliers for the company. The company can benefit from waste reduction and preservation of environmental assets, biodiversity and other finite assets. Manufacturing procurement efficiently manages the suppliers for the raw material with focus to obtain cheaper and quality raw materials.

Production Plan include safety stock and replenishment decisions and based on trends and market dynamics. If the production activities aren't planned properly there is high chance to face the issues such as shortage of stock and heavy inventory. During COVID-19 sudden lockdown was imposed across the globe which has hit the production lines badly because of unexpected gap between demand and supply for essential products.

Outbound Logistics include demand management and order fulfillment. It takes care of fulfillment of demand of goods and services of customers at right time and quantity with better responsiveness. Demand management helps in understanding important aspects of customer demand by better forecasting of requirements and enhanced visibility across the supply chain. It also assists in enhance customers' service, managing and improving inventory levels, enhance inventory planning and optimize promotion and trade planning, develop sales or demand forecasts. The main objectives of order fulfillment are to effectively help in faster order processing, faster order delivery to the customers' and frequent fulfillment of products. Network designing and process designing are two components of order fulfillment which assists an organization in meeting its order fulfillment goals while minimizing the delivery costs.

Order fulfillment also takes into consideration of networking strategies such as allocating inventories in the physical buildings, transportation strategies such as trying new processes and carriers and making changes in the distribution centers. Therefore, the order fulfillment considers cross-functionality of the organization which builds coordination among main suppliers and customers.

Sales & Post Sales service takes care of needs of the supply chain stakeholders like dealers wholesalers and retail outlets. Decent long-term relationships with the retailer and wholesalers, frequent inventory inspection/management and capturing customer feedback are key components to understanding the demand of the product in the market.

There are two major aspects to be considered in post-sales. They are Customer relationship management (CRM), customer service management (CSM). CRM helps in understanding how to provide tailor-made products and services to meet the needs and demands of a customer. CRM through supply chain network and through the delivery of products builds competitive edge of a company against their competitors. The main responsibility of a customer service management lies in refining the relationship with the customers. Customer service management in the SCM building blocks effectively focus on managing customer service on the basis of customer's preferences, tastes, and perceptions to deliver best of products and services.

1.4 Principles of supply chain management

Making rational decisions in the context of supply chain management is a complex one. To help managers decide how to proceed, [7] have suggested the following seven principles which were based on the stories of successful organizations in business. These principles include the following [7]:

1. Customer segmentation based on their needs
2. Logistics network customization
3. Observe market demand and plan accordingly
4. Postponement or delayed differentiation of product closer to the customer demand

5. Strategic sourcing

6. Use of SC wide technology strategy

7. Use of channel wide performance measures

Principle 1: Adapt supply chain serve customers based on their needs.
Principle 2: Use customized logistics network to serve requirements at lower cost based on segment.
Principle 3: Observe the market trends and plan to meet the demand across the supply chain consistently with suitable forecasts and optimal allocation of resources.
Principle 4: Use postponement or delayed differentiation in meeting the uncertain demand of the customer with better speed/response.
Principle 5: Use strategic alliances for sourcing of various raw materials/inputs at lower cost and better quality.
Principle 6: Use supply chain-wide technology strategy that supports multiple levels of decision making and gives a clear view of the flow of products, services, and information.
Principle 7: Use channel-spanning performance measures to measure success in fulfilling the end-user demand efficiently and effectively.
Many organizations around the work have benefited by using these principles and able to meet the customer demand effectively and profitably by strengthening their supply chains. Further, organizations have pursued various initiatives like integration of supply chain activities and these have resulted in improved asset utilization, reduced cost, and created competitive advantage on one hand and improved revenues on the other hand.

1.5 Performance measures of supply chains

Measuring supply chain performance is one of the most difficult tasks in business due to involvement of many stakeholders and different types of activities that they perform in different geographic locations and contexts. However, both industry practioners and researchers have evolved different performance measures which are based on cost, quality, delivery, efficiency, sustainability etc. Some of the mainly used performance measures include delivery performance to request, upside production flexibility/material availability, total supply chain costs, Cash-to-Cash Cycle Time, return on investment, inventory turns, fill rate, customer service level, revenue growth etc.

2. Methodology

In this study, we have adopted a generic method for literature search and industry practices in the area of supply chain management in different sectors, reports on economic development, global value chains, world trade and reports on COVID-19. Literature search has been carried out using key words like COVID-19, Supply Chain Management, economy recovery, world trade, global value chain, world GDP, healthcare from the databases like PubMed, Google Scholar, EBSCO, ENKI, ABI Info, etc. The search does not include other databases. Apart from these we have also used information regarding various stimulus packages and sectoral specific schemes for economic recovery in different countries. We have used the information from firms like McKinsey, The Economist, Gartner Inc., World economic forum, World

trade organization etc. The author's own research and consulting experience in the area of supply chain management and healthcare management. Apart from these we have also gathered the information from experts from different fields like policy makers, industry practitioners, consultants, medical physicians from healthcare sector at global level. We have excluded country specific details in the study.

3. Supply chain ecosystem and frameworks

Supply chains are in practice for a very long time in different forms facilitating the trade [5]. After world war II (WW-II), the importance of supply chains has increased significantly and from 1960s its influence has increased duo to developments in computers and information technology. Further, post 1990s due to advent of internet technologies and globalization of trade, the importance of supply chains has increased many fold and the GDP of the world has increased significantly [5, 6, 8] and the same is given in Section 3. Supply chain ecosystem and framework is brief described in the following sub sections.

3.1 Supply chain ecosystem

Figure 6 shows various stakeholders and their relationship in the context of supply chain ecosystem [9]. Supply chain ecosystem is a complex network connecting various stakeholders through suitable technology platforms and incentive systems. This include logistics service providers like third party, forth party logistics providers, reverse and returns, inbound and outbound. Transportation modes would include roadways, railways, airways and seaways. Other services like warehousing, courier and freight services and material handling. SC ecosystem would include platforms, software across different industry verticals like automobile, fast consumer goods, industrial goods, energy, health and other services.

SC platforms are very critical and include connectivity management, application management and data management. Connectivity management include WAN, Wi-Fi, Hotspot, Bluetooth, RFID etc. Due to increase in complexity of SC network, the importance of software has increased significantly and most of the activities

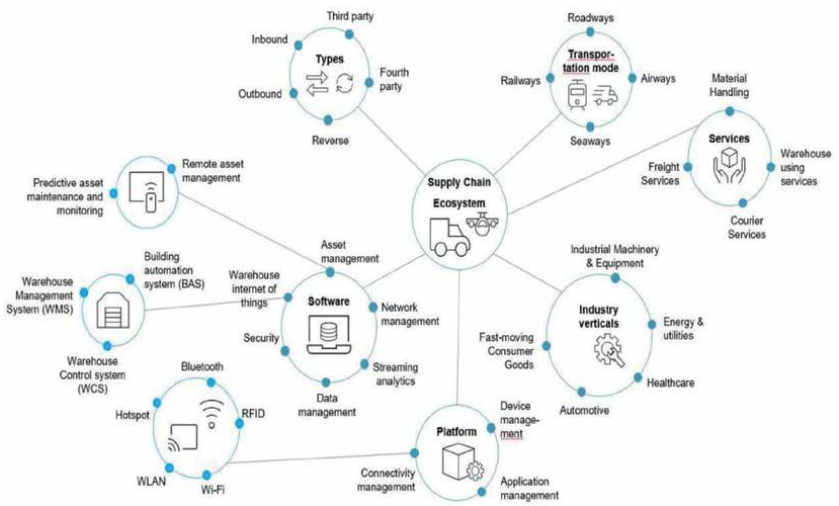

Figure 6.
Supply chain ecosystem [9].

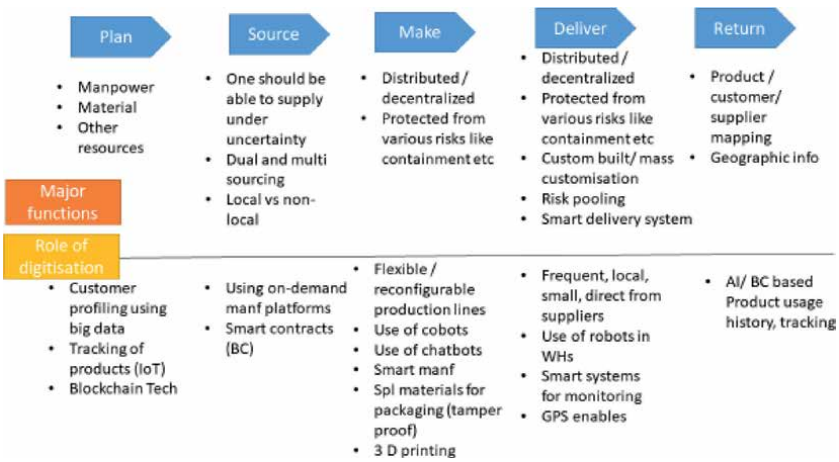

Figure 7.
SCOR model with traditional and digital focus [10].

are managed through software tools. Software management in the context of SC include network management, streaming, data management, security, internet of things, asset management, asset maintenance, warehouse management, building management, fleet management etc. Advances in information and communication technologies like GPS has further improved the performance and control of supply chain activities. Due to rich data and advances like Artificial Intelligence (AI), Machine learning (ML) are facilitating in more rational and timely decisions across the supply chain.

3.2 SCOR model

Supply Chain Operations Reference (SCOR) model is very widely used industry standard model developed by supply chain council in 1996 [10]. SCOR model follows a hierarchical structure and has three levels. Level 1 include five process types viz., plan, source, make, delivery and return. The elements of SCOR model is shown in **Figure 7** along with major functions and role of digitization at each stage of the supply chain. Level II include process categories which defines the configuration and level III include process activities in terms of inputs and outputs and performance measures. SCOR model employs five performance measures: reliability, responsiveness, flexibility, costs and asset management. In summary, the traditional SCOR Model has five processes, five performance measures and three levels describing SC comprehensively. Due to technological advancements in data capturing and analysis tools, the digitization across SC has attracted many stakeholders in improving the supply chain performance significantly. Digitization of supply chain functions at each stage is also shown in **Figure 7**. The most interesting and important element is handling of returns across various industry verticals. Returns in the supply chain have assumed significance due to electronic commerce industry. Of late, AI and Blockchain technologies are playing a critical role in managing the returns across various industry verticals by tracking the product usage history and other relevant information.

SCOR model covers the following activities:

- Covers all interactions of **customers** from order entry to final invoice/ payment.

- All transactions related to **product** (good or service) from supplier end to final customer, including product, spares, other equipment, software etc.

- All interactions of the **market** from demand aggregation to demand fulfillment for each customer/order.

SCOR model allows environmental measures like carbon emissions, air pollution, liquid and solid waste, percent recycled waste etc. SCOR model connects emissions to the processes at source and provide a structure for measuring environmental performance and improvement areas. The hierarchical nature SCOR model allows strategic environmental footprints to be translated to specific activities and targets.

3.3 Healthcare value chain capabilities model

Though the supply chains are widely used in manufacturing industry to start with, subsequently the supply chain concepts and practices have been applied in other sectors including healthcare industry, pharmaceutical, food and agriculture, ecommerce, humanitarian, disaster relief etc. Healthcare is changing at an unprecedented pace, due to the impacts of technology, cost pressures from both payers and patients who are seeking quality care. Healthcare organizations including providers, retailers, distributors and wholesalers, manufacturers. Some of the organization who have adopted supply chain practices include Johnson and Johnson, Cleveland Clinic, Mercy, CVS Health, McKesson, Novo Nordisk, Medtronic, Stryker, Roche, Pfizer, Owens and Minor etc. For example, Mayo Clinic has improved the care delivery and reduction in cost by collaborating with its suppliers and adopting digital technologies in its operations. **Figure 8** shows the framework suggested by Gartner in respect of healthcare organizations with a main objective of improving the human life at sustainable costs as well as quality. This model has five major processes viz., patient focus, collaboration, network visibility, cost to serve and change management supported by fundamental capabilities covering all the processes [11].

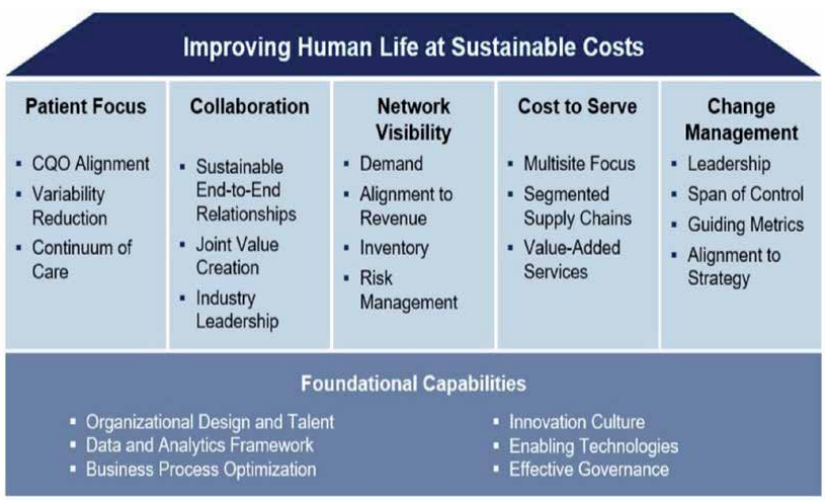

Figure 8.
Healthcare value chain capabilities model [11].

3.4 Sectoral specific supply chains

Due to inherent advantages and capabilities of supply chains, many organizations across different industry/business verticals have adopted supply chains and benefited immensely. Some of the major sectors include automobile, food and agriculture, e-commerce, healthcare including hospitals, pharmaceuticals, diagnostic services, medical devices etc., defense and government, energy and power, oil and gas etc. Supply chains of e-commerce, food and healthcare is briefly explained in this section.

3.5 Electronic commerce supply chains

Electronic commerce (e-commerce) supply chains have gained significant importance due to ability of supply chains in meeting the customer service and low cost. Many companies like Amazon, flipkart, Alibaba etc. have demonstrated the power of supply chain in their business operations. **Figure 9** shows typical supply chain network of e-commerce supply chains. **Figure 10** shows a macro view of supply chain management at Amazon [Amazon.com]. e-commerce supply chains are more robust compared to others mainly due to its ability to manage the disruptions during crisis like COVID-19. Particularly during COVID-19 crisis, Amazon, flipkart and other e-commerce companies were able to maintain the continuity of supply in spite restrictions like lockdowns, social/physical distance and limited time operations, shortage of manpower etc. These companies are able to recover fast due to its resilience and responsiveness capability. This can be seen from the latest trend in the share price of e-commerce and food supply chain companies.

3.5.1 Food supply chains

A typical food supply chain with food safety information system and quality assurance system is shown in **Figure 11** [14]. The food supply chain includes farm/

Figure 9.
E-commerce supply chain [12].

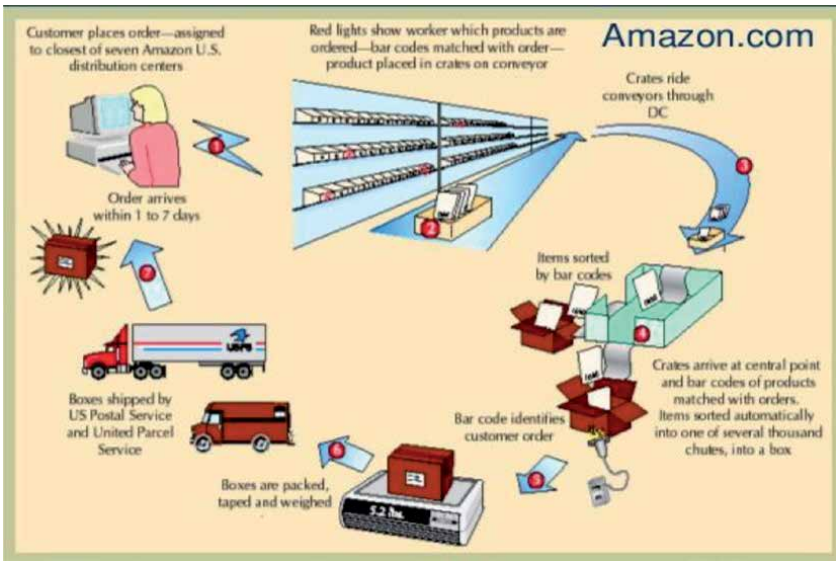

Figure 10.
Amazon supply chain [13].

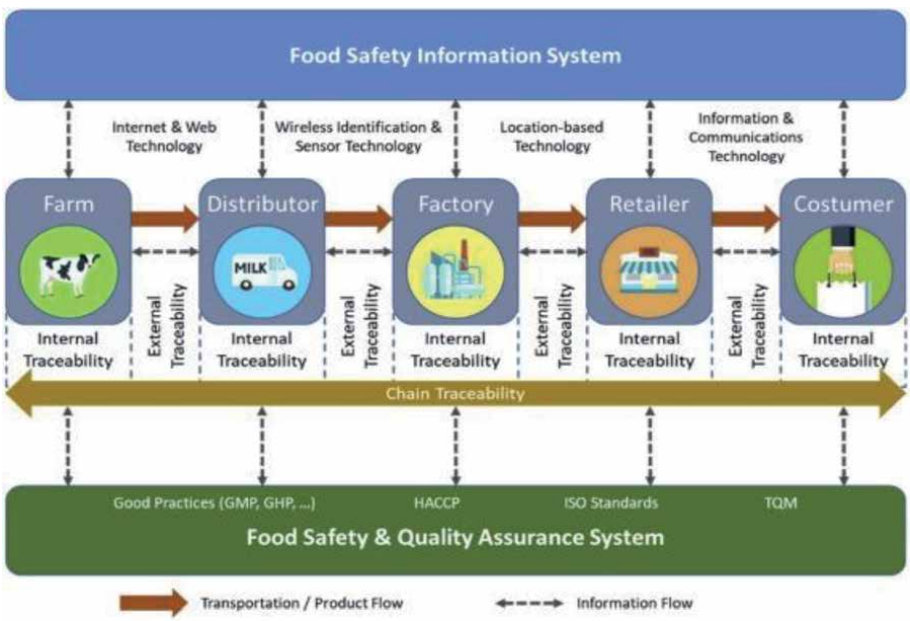

Figure 11.
Food supply chain [14].

farmer, distributor, factory, distributor/retailer and final customer. In case of food supply chains the most critical issue is food safety across the supply chain. These supply chains focus very heavily into food safety and traceability at each stage of the supply chain mainly at interfaces. Food supply chains uses information and communication technology widely. Quality and Compliance of standards across food supply chain is very critical and makes use of advanced technologies like RFID, temperature controls, GPS enabled systems for tracking and traceability. It follows standards like good manufacturing practices, ISO standards and TQM etc. [14].

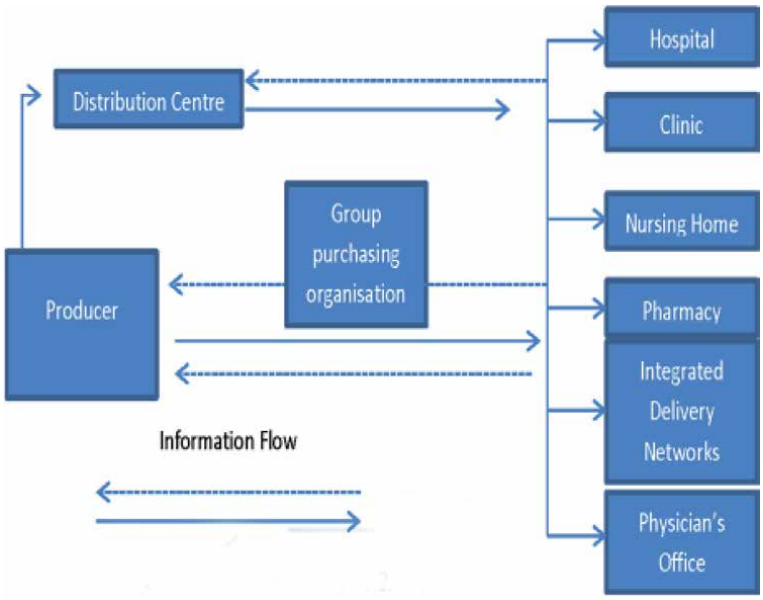

Figure 12.
Elements of healthcare supply chain [15].

3.5.2 Healthcare supply chains

Healthcare supply chains are more complex than other supply chains due to presence of many stakeholders and responsiveness requirements. A typical healthcare supply chain is shown in **Figure 12**. Healthcare supply chains poses several challenges due to stringent regulatory requirements, safety and security and quality requirements. In spite all these challenges, many healthcare organizations benefited by adopting supply chain management approaches. According to Gartner study [11] on top 25 healthcare supply chains, top 5 organizations include Johnson and Johnson, Cleveland Clinic, Mercy, CVS health and Duke University Health system. Many of these organizations are using best practices like collaboration, digitalization, robust processes that are aligned with the overall objective as well as the elements listed in healthcare value chain capabilities model. The major strengths of healthcare supply chains include agility, alignment, adaptability, resilience and responsiveness. These organizations follow people, process and technology solutions in the care delivery. Of late, many healthcare organizations particularly using AI and Blockchain technologies for personalized care in large scale. Telemedicine and home care is growing very fast due to COVID-19 crisis where supply chain is very critical. Some of the organizations are using drones for delivery of medicines, pathology samples, food and equipment. Many start-ups also emerging in healthcare by bridging the gap predominantly through digital technologies and supply chains.

3.6 Supply chain configurations (hub and spoke model, centralized vs decentralized SC)

Supply chain network structures and its configuration is very important in achieving the performance of supply chains. Predominantly used supply chain structures in the practice include centralized and decentralized [2] or Hub and spoke model. **Figure 13** shows typical structure of centralized and decentralized supply chains. Centralized systems are more efficient and are generally used for

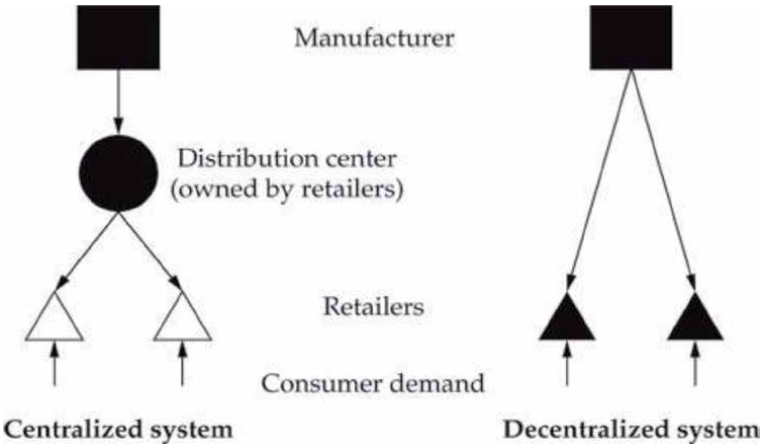

Figure 13.
Centralized and decentralized supply chain system [2].

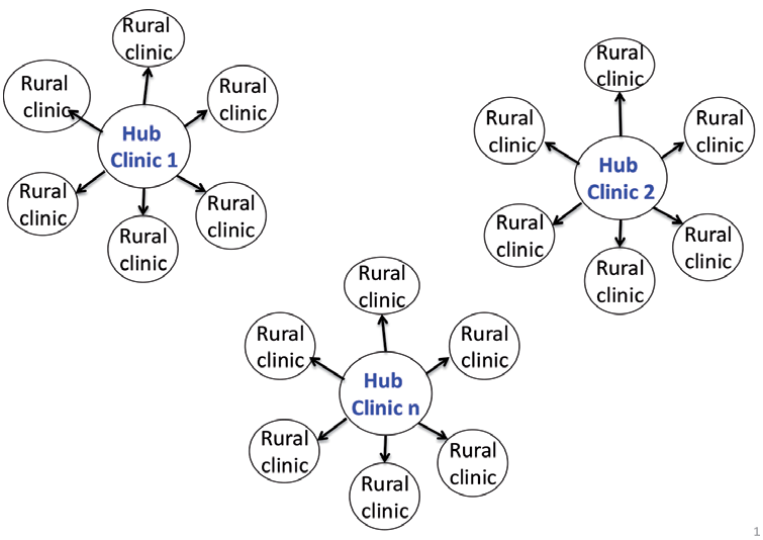

Figure 14.
Hub and spoke model of a healthcare start-up [16].

high volume low value commodities like steel, cement, automobiles, computers etc. where cost is important. Whereas decentralized systems are predominantly used in e-commerce, healthcare and other services where responsiveness is most important. Hub and spoke models are predominantly used is both product and service organizations. A typical hub and spoke model of a Start-up delivering health services in Rural areas in India is shown in **Figure 14**. Generally, the Hubs are equipped with more resources that can help serving the customers located spoke level. Typically, these share many resources and innovate through collaborative mechanism and employ multi skilled people and technology to improve the efficiency and reach.

4. Relation between economic development and global value chains

Supply chains have contributed significantly for the world trade for many years. Further, supply chains have facilitated the globalization of trade. **Figure 15**, shows

the world trade over last four decades [8]. There is a sensitive relationship between economic development and supply chain because efficient management of the supply chain can reduce costs, maximize customer value, and maximize competitive advantage. It entails effective coordination and control of linked sectors, departments, systems, and organizations. According to a study by world economic forum, reducing supply chain barriers could increase world GDP better over import tariffs. Further, the study shows that 50% reduction in supply chain barriers can increase world trade by 14.5% and world GDP by 4.7% and these gains are more evenly distributed across various countries and also it can generate more employment [17].

Global trade has increased owing to adoption of liberalization and globalization as national economic policies by several countries in post-Soviet era (post 1992). Global GDP has also expanded in tandem with global trade. An analysis of global merchandise trade and global GDP at market exchange rates with 2008 as base years shows coupled growth in global GDP and global trade as depicted in **Figure 16** [18]. Due to emergence of global value chains, the global trade is shifting fast. This can

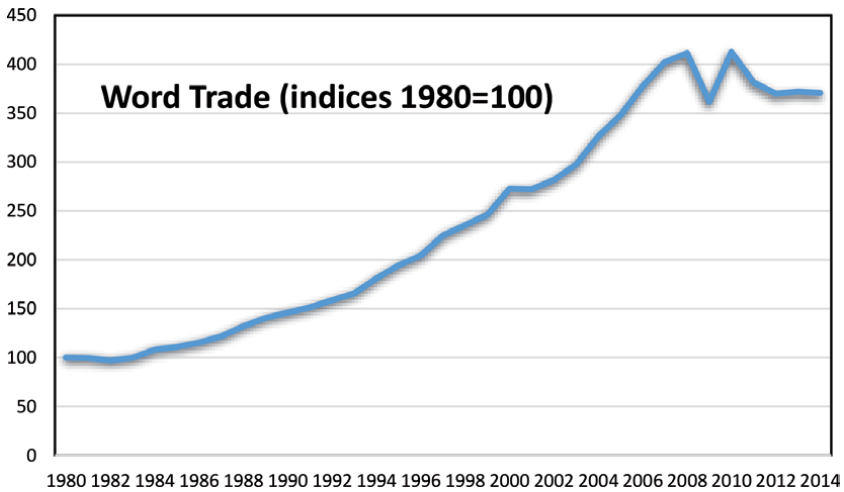

Figure 15.
World trade-exports [17].

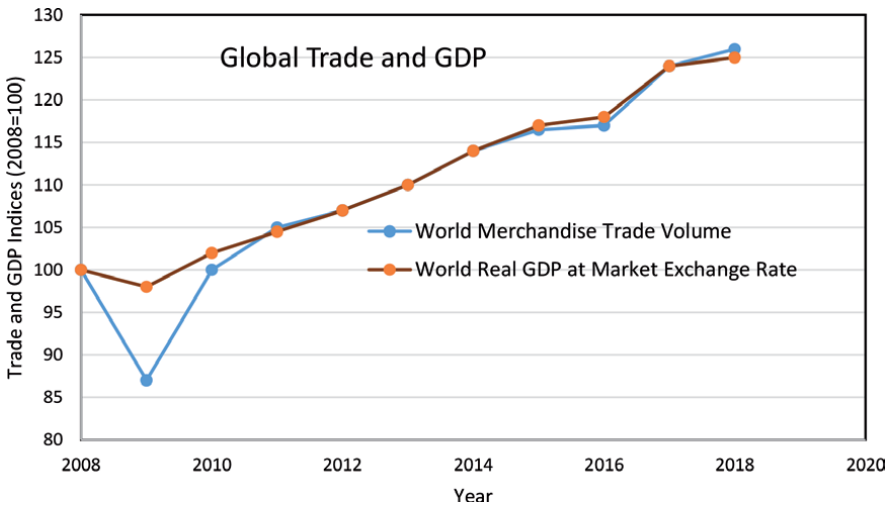

Figure 16.
Relation between global trade and GDP [8, 18].

be seen from **Figure 16**. Expansion of global GDP and its correlation with global trade increases the importance of worldwide network of production of goods. A study done by [8] suggests that contribution of intermediary goods in global trade of manufactured goods was more than that of finished goods during 2001–2008 and 2009–2014. This conclusion supports the existence of complex Global Value Chains (GVC) [19]. Furthermore, as per the available data, 57% of the global trade in 2015 was constituted by trade of intermediate goods [18]. OECD TiVA database shows that the Asian economies have the highest growth rates of contributions in GVCs [20].

Due to increasing network of global supplies, patterns in global trade have shifted from 'trade in goods' to 'trade in value added' and 'trade in tasks' [19]. The Global Value Chain (GVC) Framework has emerged due to shifting pattern of global trade. It focusses on expanding and strengthening supply chain and value generation therein. Both developing and developed economies get benefited by participation into GVC [8]. Participation into GVC provides an exposure to the global best practices, technological know-how, and competence development. These result in higher economic growth and development [21].

4.1 Supply chain and global value chain (GVC)

GVC framework provides a strategic overview of global supply chain and integration of different characteristics of complex supply networks into GVC would provide a holistic perspective of various methodologies- operational and strategic [17]. Development of robust supply chain management practices have strengthened GVCs thereby easing cross-border movement of goods. It promotes domestic manufacturing and consumption. These in-turn result in growth of national GDPs. Therefore, to boost global economic growth promotion of global trade is essential. Sustenance of rapid growth in global trade is a function of participation of various countries into GVC which requires a robust supply chain management. From this analysis, it can be concluded that, development in supply-chain practices have contributed substantially to global economic growth.

World class organizations like Walmart, Apple, P & G, Amazon, IBM, Toyota, General Motors, Best Buy, Marks & Spencer's, Zara, Sports goods companies, mobile companies, food chains have gained significantly by adopting supply chain practices in their business. Similarly, healthcare organizations like CVS Pharma, Cleveland clinic, Narayana Health of India, pharmaceutical companies, medical device and equipment companies and many others have gained significantly.

5. Impact of COVID-19 on supply chains

In 2019 the United States imported a staggering four $52 Billions of goods from China. COVID-19 crisis has created historical disruption to global supply chains. COVID-19 crisis has affected health of people, business and overall economy at global level. COVID-19 crisis is a wake-up call for supply chains and one way it created de-globalization of business and supply chains. Over dependence on one country like China had proved to be very disrupted at times of pandemic. Bloomberg reported in March 2020 that electronic makers are past the point of no return in the gradual migration from China. Further, the Chinese trade (both domestic and international) transactions dropped by around 56% in the mid- February 2020. Similarly, US, UK and Europe also gone through a drop of 26% in April 2020 and touched 17% in late April 2020. Sourcing from India it is recommended an

incremental approach in bringing all Indian suppliers i.e., carefully select some low-risk and high reward programs to try out in India while maintaining Chinese base.

Due to COVID-19 crisis companies have fallen into one of two categories those that do not do anything hoping such a deception will not ever happen again those firms that heed the lessons of this crisis and make investments in mapping their supply networks so that they do not operate blind when the next crisis strikes, these are the ultimate winners. Some of the major challenges faced by supply chains due to COVID-19 include the following [22, 23]:

- Lack of visibility due to higher levels of SC network complexity
- High uncertainty on both supply and demand end
- Limited production flexibility
- Limited financial flexibility

In several countries consumer surveys show a likelihood of greater spending on groceries and less spending on discretionary categories. According to McKinsey study on marketing and sales survey conducted in Italy, Spain, UK and US during March, 2020 reveals that except groceries (grown around 18%) other sectors like quick service restaurants, restaurants, footwear, apparel, jewelry, accessories, furnishing and appliances have recorded negative growth ranging from 50–85%. Among all sectors, restaurants are the worst affected.

Another important incident of 2011 Tsunami in Japan can also help the business organizations around the world to learn important lessons. After the 2011 earthquake and tsunami had devastated north-east in Japan it led to the application of a new methodology that was developed that enables a sophisticated way to understand the exposure to risk associated with unlikely events such as COVID-19 pandemic. The ability of the supply chain to recover from the disaster should be considered by the supplier as a performance factor of the supply chains.

6. Economy recovery sectors and strategies

6.1 Recovery framework

McKinsey [22] has suggested the following three step framework for rapid recovery:

1. **Identify and prioritize actions** based on clear understanding and demand patterns of activities that can capture revenues quickly (B2B and B2C- multiple SCs) and opportunities need to be continuously updated

2. **Act with urgency** judicious allocation of resources to the activities prioritized to capture the growth. Engage new partners and new channels (online and offline), reallocation of resources to safe places quickly and reconfiguring the SC, shifting the promotional sales etc.

3. **Develop a rapid-fire agile operating model** - speed of decision making and agile teams (market insights, cash liberation, growth, digital market and post Covid-19 growth)

6.2 Recovery sectors

According to some of the major studies by McKinsey, Economist and others [22–24], the early starters of economy include health care including pharmaceuticals, medtech, diagnostics, hospital and home care services, telehealth/telemedicine, essential items, food and agriculture, FMCG, 3D printing, internet of things (IoT), AI/ML, robotics, smart systems, e-commerce industry. COVID-19 has put the medtech industry at center stage with unparalleled demand for diagnostic test PPE, ventilators, and critical medical supplies. McKinsey [22, 23] has built a detailed model of COVID-19 impact on medical procedures mainly for the United States on the Europe which is used to create a model for predicting the potential impact on medical device sales in consumables and implants. The models consider two broad scenarios for COVID-19 case growth V shape recovery and W shape recovery. In V shape recovery, it is estimated that the material procedures decline by around 70% in the second quarter and up to 45% in third quarter when compared to 2019. It is expected to see a rapid ramp up for the next three forth to catch up on delayed elective procedures. Whereas in W shaped recovery, procedures would decline by 69% and 45% in the second and third quarters respectively.

Telehealth potential has been realized after the COVID-19 crisis and telehealth consumer adoption has increased from 11% in 2019 to 76% in 2020 in US along. Approximately $250 billion or about 20% of all Medicare Medicaid and commercial OP office and home health spend could potentially be virtualized with the help of telehealth. Similar trend has been observed in many countries worldwide.

6.3 Recovery strategies and actions

It will not be that easy for many organizations to have a detailed analytical understanding of demand variability at local and national level. However, *stress testing* of supply chains with different scenarios with viable product demand and procedures will be very critical for managing the current scenario. Some of the methods suggested to overcome the impact on supply chains [22, 23, 25] includes the following:

Develop a high-risk supply chain disruption-monitoring and response program for countries impacted by the virus and the potential supply chain exposure from Tier 1 and below.

Assign high-risk weighting to suppliers and sub-tiers from emerging and developing countries with less developed healthcare systems that are less prepared.

Conduct a contract review to understand any financial implications of not being able to deliver supplies to manufacturing locations and customers.

Special attention for balancing of supply and demand, building suitable safety stocks are essential for business continuity, particularly with the unpredictable volatility of supply chain functions.

Identify various opportunities at supply side and diversify suppliers to ensure manufacturing capacity and raw material availability.

Establish a robust risk management models to monitor and prepare for shortages in material, manufacturing capacity and work closely with supply chain stakeholders particularly with critical suppliers.

Implement and utilize enhanced risk management, including scenario planning to create preemptive action plans.

Review the New Product Introduction process and utilize design measures to discover or develop alternative sources and routes in order to diversify your value chains. At the same time, analyze cascading implications of changes in volumes, quality and markets.

The most common approach is to use the bill of materials and focus on key components.

Some of the major actions suggested by McKinsey for economy recovery [23] is given below.

- **Strategy:** Reposition the bran, Mergers and Acquisitions, Networked Ecosystems, create a new demand planning system.

- **Productivity:** Take initiatives such as Marketing, improving sales productivity, Inside sales, data analytics for performance management.

- **Digital channels:** Use scaled digital sales & services, E-commerce, Digital marketing etc.

- **Customer experience & insights:** This can include, customer experience, Personalization, improved CRM, creating value proposition through suitable products, Analytics-driven sales and distribution, revenue pricing and promotion optimization.

Some of the actions suggested for recovery of medtech industry [22] include the following.

Accelerate capacity of equipment like PPE, Ventilators, other surgical items etc. that is essential to save the lives of critical COVID-19 patients.

Maintain capacity of equipment used in COVID-19 treatment or that requires replacement such as CT machine dialysis equipment or ECMO machines etc.

D*eprioritisation* of equipment not useful in COVID-19 treatment such as MRI surgical and mammography equipment and etc.

Supply chain management and reliability: More than 90% of global annual medical device exports come from countries that are now in some form of quarantine. There for Medtech company should consider activating supply contingency plans repositioning inventory to areas of greatest need and making all reasonable attempts to protect the health and safety of workers on the manufacturing floor.

Preserving cash: according to the McKinsey benchmarking analysis the potential for a rapid 3–5% increase in cash flow could be shown additional changes to production like just-in-time inventory pooling and rationalization, and standardization can free up more cash. These initiatives should be rigorously tracked in conjunction with appropriate cash controls and customer considerations.

Resource relocation and portfolio strategy: Now is the time to establish processes that can anticipate market demand and shift staffing as needed to quickly accommodate changes this would require increased investment in cross training the employees as well as new processes to rapidly scale up support services.

The company is required to fundamentally rethink the supply chain network and key suppliers as they were already facing pressure to localize in certain markets, after the crisis it will continue to be important for the companies to consider how to balance these pressures that can impact local supplies with potential desires for greater flexibility in capacity. These adaptations could include building more agile organizations, speeding time to market and aspiring to "absolute benchmarks" for product design and development and manufacturing efficiency.

Some of the lessons learned from fast food service organizations like KFC, McDonald etc. include the following which are based on digitalization:

- **Co-creation:** use of user generated content with apps like radio KFC, RJ hunt and design your own bucket challenge.

- **Unique Experience:** the simple equation is (cutting edge technology + ingenious ideas = unique experiences) Example, interactive campaigns.

- **Feedback fanatics**- the secret to a great relationship is listening KFC ensure that every feedback was listen to and addressed.

Strengthening healthcare's supply Chain.

These are the five specific capabilities that can have a dramatic impact on performance of the healthcare supply chain [26]:

1. Better segmentation of products, markets and customers.

2. Greater agility to reduce cost and increase flexibility.

3. Measurement and benchmarking.

4. Alignment with global standards.

5. Collaboration across the healthcare value chain.

How to address the shortage and improve the safety?

Supply chain issues create opportunities for counterfeiters and gray market vendors threatening patient safety and cutting into revenues of legitimate companies. Supply chain security breaches are increasing by an average of 33% every year not only in the emerging markets such as China, India & Brazil but also in the developed world. Better supply chain processes are central to increasing patient safety. Therefore, it is recommended that adopting a common global data standard and upgraded grading supply chain processes could/counterfeiting in half returning up to $15 Billion to $30 Billion in revenue to legitimate companies to reinvest in further improvements to patient care.

Building a new healthcare supply Chain

Organizations can learn from the experience of laptop manufacturer in Indian who can accept an order and deliver a customized computers to a European customer in almost a week. Other organizations like pharmaceutical and medical equipment companies can adopt two broad approaches based on internal factors and external factors. Internal factors include – segmentation, agility, measurement while the external factors include- alignment & collaboration [27].

Segmentation: Companies such as pharmaceutical and medical device generally follow one size fits all type of supply chains which are proved to be disastrous particularly during pandemic times. Best companies address these problems by segmenting the supply chains according to the nature of product and customers demand and preferences by developing suitable forecasting, production and distribution strategies for each category.

Agility: This refers to building and operating supply chains that can better respond to demand shifts due to occurrence of unexpected disruptions in the business. The approaches include cross functional process, understanding of demand and supply scenarios and circumstances, effective communication and transparency across the supply chain.

Measurement: Generally, FMCG companies use data driven metrics such as manufacturing index for producing appropriate quantity of stock keeping units (SKUs) across countries and plants. Organizations also uses commercially available benchmarking tools and approaches for guidance and identification of opportunities along with supply chains.

Alignment: Refers to building of a cost effective supply chain that could align around global standards that support data interchange processes and capabilities to reduce the errors etc.

Collaboration: Many successful organizations collaborate in areas where they have a strength and share the benefits. Collaboration focus on (i) S*election of partners for the potential value of the collaboration; (ii) capabilities and willingness to act as a team; (iii) dedicate resources to collaboration and involve senior leadership in it; (iv) jointly manage performance and measure impact; (v) start out with a long-term perspective.*

According to [25], the supply chains needs a stress test in terms of time to recover (TTR) and time to survive (TTS). TTR is the time it takes for a particular player/stakeholder (supplier, manufacturer, distributor, retailer etc.) in the supply chain to restore full functionality after disruption. TTS is the maximum duration that supply chain can match supply with demand after facility disruption. TTS also estimate each measure under different scenarios of business and Identify its ability to recover from the disaster. Organizations need to have a backup plan when TTR of a stakeholder or facility is greater than its TTS. This helps the organization in quantifying the cost of disruptions and prepare mitigation plans for the most critical parts of the supply chain [25].

At macro level, the economic recovery requires actions such as government stimulus, digitalization, advance technologies like 3D printing, up-skilling/multiskilling of workforce, restructuring of supply chains with better resilience and response, collaboration/alliances, facilitating innovation by start-ups, strengthening research collaboration between government, industry and academia is also very critical for faster recovery.

7. Conclusions

There is a strong relationship between world trade, GDP and supply chain investments around the world during last more than two centuries starting from 1800. As globalization has increased, the world's supply chains have become substantially more interconnected. Moreover, as emerging market economies have steadily come to account for a greater proportion of global GDP, goods often have more stages to pass through before reaching the end consumer.

During last seven decades (starting from 1960s) the economic growth of the world is very significant and also seen many disruptions like Tsunamis, 911 Terrorist attacks, pandemics like COVID-19. Among all the COVID-19 crisis is more significant in terms of health and economy. COVID-19 has led to nearly 5% negative growth of world economy. From national lockdowns to closed airspace and borders, Covid-19 has resulted in unprecedented disruption to the mechanics of most economies, regardless of their size or stage of development. In particular, the erection of these barriers has placed a major strain on the world's supply chains, including essential linkages relating to food and medicines. COVID-19 also created tension between major economies of the world and disrupted global supply chains significantly. Supply chain leaders face pressure to rethink traditional distribution and supplier models. For example, Amazon looks to strengthen its healthcare influence through the expansion of services in the medical supply chain, industry stakeholders are reconsidering traditional hospital-supplier relationships. Data, analytics and technology are playing an increasingly important role in supply chain strategy. A 2018 Global Healthcare Exchange survey [28] showed roughly 60 percent of respondents indicated data and analytics were the highest priority areas for improvement. These changes and trends have pushed the role of supply chain

management into new territory. Now, supply chain leaders are positioned to help lead their organizations to higher levels of customer service with more efficient models [29, 30]. To ensure success amid this changing environment, business leaders including healthcare organizations should place an emphasis on technology, business practices and customer service.

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Chapter 7

Management of Blood Supply and Blood Demand to Ensure International Health Security

Amar Ibrahim Omer Yahia

Abstract

Maintaining international health security requires proactive and reactive activities and actions to minimise the negative impact of any health event that threatens public health. Blood transfusion services are a critical part of healthcare services, and blood and blood products can neither be synthesized nor stored for a long period. So, proper management of blood supply and blood demand is mandatory to preserve adequate safe blood. A failure to manage blood inventory and the resulting blood shortage are considered national and international health security threats because maintaining an adequate supply of safe blood is lifesaving for many patients. Blood shortages lead to the failure of blood transfusion services that ends with the collapse of the health system and health insecurity if health authorities do not take immediate corrective action. An imbalance between blood supply and blood demand is not only a threat to health security, but also poses some of the greatest threats to the national and international economy and security. The perception of health issues as an international health security threat is associated with benefits through attracting political and decision-makers' attention and support. The global health policies and international health regulations concerning the management of blood supply and blood demand should be implemented and updated regularly. The information provided by this chapter addresses the management of blood supply and blood demand as an international health security issue and provides guidance in planning for proper management of blood inventory to avoid a sudden blood shortage and its catastrophic consequences.

Keywords: international health security, management of blood supply, blood demand, adequate safe blood, blood inventory, blood shortage, blood transfusion services failure, health insecurity

1. Introduction

International (global) health security is defined by the World Health Organization (WHO) as the proactive and reactive activities and actions required to minimise the danger and impact of any health event that threatens people's health nationally and internationally. Management of blood supply and blood demand means close monitoring of blood supply and blood demand and appropriate responses to avoid sudden blood shortages, particularly for blood components with a short shelf life, such as platelets. Health problems and the collapse of health systems not only cost lives, but also pose some of the greatest threats to the global economy and security.

Many health issues have affected global health security and necessitated the United Nations Security Council announcing a risk to international security and stability [1–4]. Recently the coronavirus disease-2019 (COVID-19) pandemic has been considered a threat to the global economy, health and security. Maintaining blood supply is important for international health security since blood transfusions are lifesaving in many conditions. A failure to manage blood supply and blood demand and resulting blood shortages are threats that affect national and international health security. This is because maintaining an adequate supply of safe blood is lifesaving for many patients, such as those with blood diseases, cancer, trauma, and those who need emergency surgeries [5]. Blood shortages negatively affect blood transfusion services (BTS) and health services, and can end with the collapse of the health system and health insecurity. The latter starts nationally, but if national and international health authorities and organisations do not work together and manage national health insecurity, it will appear in other countries and become international in time. Furthermore, health insecurity can lead to societal insecurity, political insecurity, and ultimately national and international insecurity. This chapter discusses the management of blood supply and blood demand from the perspective of international health security and why and how it is an international health security threat.

2. Methods

2.1 Literature search strategy

The author has used a method that describes the process of developing a systematic search strategy. Databases were searched to identify relevant articles, policies, and guidelines using a Boolean combination of key terms around the management of blood supply and blood demand and its relations to international health security. To ensure inclusivity, the only search limits were English language and peer-reviewed publications or policies and guidelines approved by the international society up to mid-July 2000. Reference lists of identified articles and published reviews were also examined. A total of 1277 articles were identified (after duplicates were removed) and exported to an Endnote library for eligibility screening. The search terms used for extracting management of blood supply, blood demand, blood shortage, blood transfusion services, national health security, and international health security with Boolean combination of key words for abstract as (blood supply OR blood demand) AND (blood OR blood components) and for full text as (blood supply OR blood demand) AND (blood OR blood components) AND (international OR global OR worldwide OR universal.) AND (Health security OR health guarantee). The databases for search included ProQuest (ProQuest Central, Public Health Database, Social Science Database, ABI/INFORM, ProQuest Dissertations, and Theses Global), EBSCOhost (Academic Source Elite, Business Source Elite, PsycINFO, CINAHL, MEDLINE), and Wiley Online Library (specifying "blood supply and blood demand" in publication title).

3. Management of blood supply and blood demand to ensure international health security

3.1 Why and how improper management of blood supply and blood demand and the resulting blood shortages are an international health security threat

The recent conception of global health presents it as a security issue instead of only a humanitarian or health problem. To achieve national security, we need

to look beyond military dominance and take into account societal matters such as health, education and poverty as security threats [6]. When speaking about health issues related to health security, maintaining an adequate and stable supply of safe blood is the backbone, since blood shortages are a global threat to health security. The availability of an adequate supply of safe blood and blood components is crucial for managing many cases. BTS are an integral part of healthcare services, and blood and blood products can neither be synthesized nor stored for a long period. Platelets' shelf life is 5–7 days, while the shelf life of red blood cells is up to 42 days depending on the type of preservative solution used [7, 8]. Therefore, maintaining an adequate supply of safe blood by appropriately managing blood supply and blood demand is the only solution. To manage the blood inventory properly, the measures and strategies developed by the WHO should be implemented (**Table 1**). A failure to manage blood supply and blood demand and the resulting blood shortage will negatively affect blood transfusion and health services, and as a result, many patients may die or suffer unnecessarily. In addition, blood shortages have negative economic ramifications due to unpleasant consequences such as postponement of surgeries, prolongation of some diseases and increasing hospital stay duration. The subsequent failure and collapse of the health system will lead to health insecurity. The latter, adding to the adverse economic effects, will lead to societal insecurity, which leads to political insecurity and ultimately national and international insecurity. Thus, the improper management of blood supply and blood demand is not only an international health security threat, but can also extend beyond that, causing international insecurity (**Figure 1**). Health insecurity begins as a local problem, but if the problem is not well addressed and corrected, it will appear in other countries and become a global problem. In many countries, the health system's failure is one of the main factors leading to the government's failure. Consequences of the latter, such as violence and the appearance of refugees, will affect neighbouring countries and exacerbate national and international security problems. Therefore, governments should deal with any significant health problems as if they were threats to national security because the health system's stability is reflected in social and political stability. This can be done through regular and effective communication between the health authorities and politicians. The main advantage of considering health issues as international security threats is that countries will work together to develop policies, preventive measures, new vaccines and treatments, and support developing countries financially and scientifically. Thus, health crises will be adequately managed, resulting in a better outcome.

Key actions
• Building a supportive social, economic and political environment to reinforce national blood policies
• Building active cooperation and partnerships with complementary strategies and partners for harmonised actions in countries
• Responding to state requirements to achieve global access to safe blood transfusions
• Strengthening systems for observation and evaluation for better decisions by planners and policymakers
• Fulfilling 100% voluntary non-remunerated donation of blood through innovative methods to improve blood donation programmes
• Ensuring 100% testing of donated blood with high quality
• Fractionating the blood into blood products according to real needs
• Implementing national policies on the proper clinical use of blood and blood components
• Optimising blood usage for patient health

Table 1.
The WHO's global strategic plan for universal access to safe blood transfusions [10].

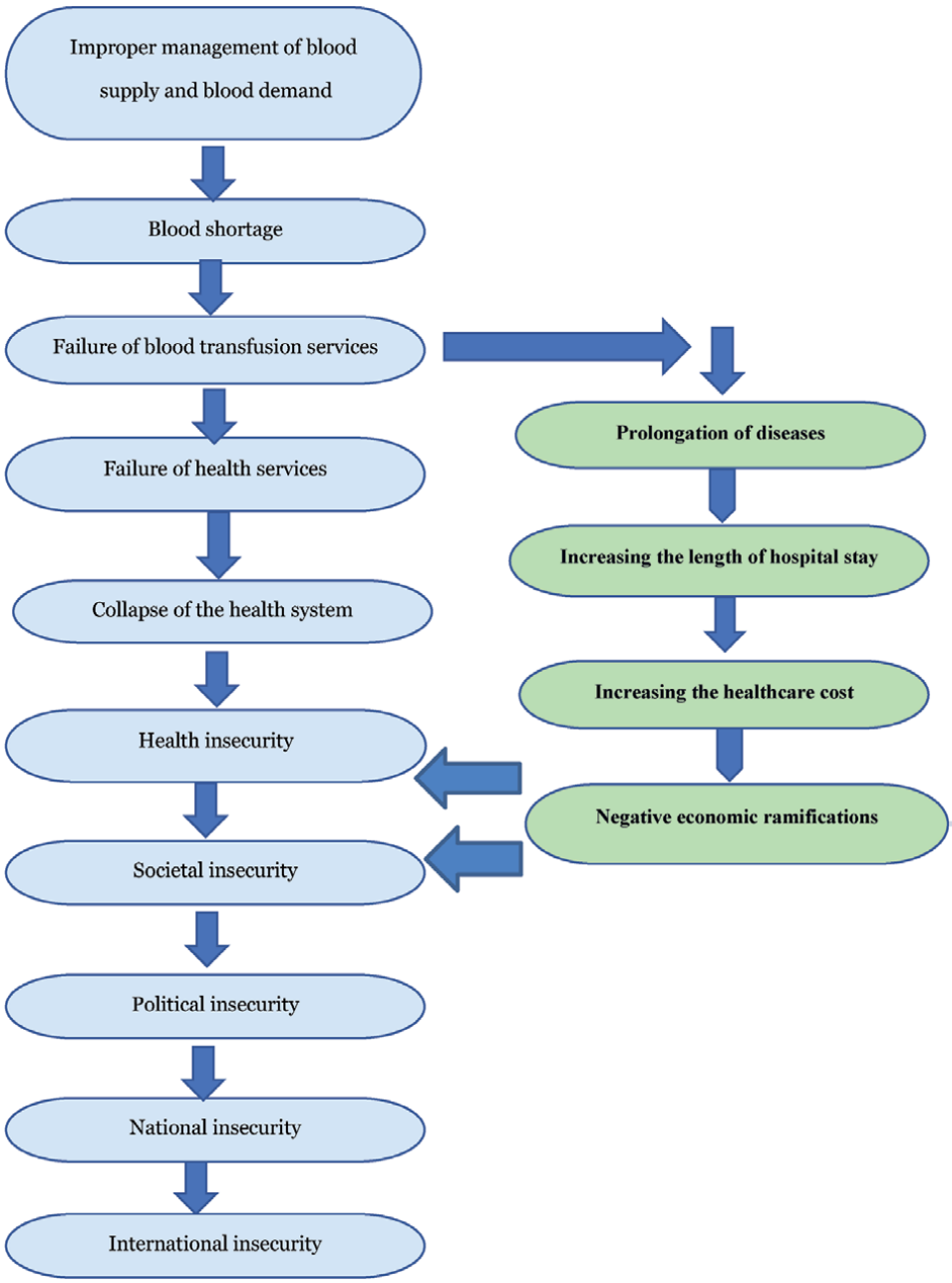

Figure 1.
Consequences of improper management of blood supply and blood demand.

Furthermore, linking health issues with global security is vital because it will bring more political attention and support, thus helping maintain global health security in favourable and stable situations [9]. In addition, this will help countries with poor health systems to benefit from international organizations such as the WHO.

3.2 Access to an adequate supply of safe blood

Globally, there is an increased need for blood and blood components to meet continuous demand. However, many patients requiring transfusion do not have

access to an adequate amount of safe blood at the proper time, and as a consequence, their health outcomes are negatively affected. The WHO recommends that 1–3% of the population should donate blood to meet a country's requirements. According to the WHO, each year, 80 million blood units are donated worldwide, mainly in developed countries. Rural and remote areas of countries have less access to safe blood than urban areas [10]. The prevalence of bloodborne infections has been reported as the lowest among voluntary non-remunerated blood donors; therefore, these blood donations are the safest option [10]. In some countries, a lack of blood supply forces healthcare professionals and patients' relatives to look for paid donors, increasing the risk of unsafe blood. Other factors that lead to an inadequate supply of safe blood include a shortage of trained blood bank staff or test kits, the use of low-quality reagents, a lack of appropriate cold chain facilities, and poor-quality assurance. Unfortunately, these issues are exacerbated by the globally increasing need for blood. To maintain an adequate supply of safe blood globally, the WHO developed evidenced-based strategies (**Table 1**). It is recommended that existing partnerships are maintained and new national and multinational partnerships are built to strengthen the global support for developing countries in terms of increasing access to safe blood. International collaboration in sharing excess supplies continues to grow at a remarkable rate and positively related to the impact on BTS.

3.3 Management of blood supply and blood demand

In response to this potential problem, the WHO and other organisations and societies approved global health policies and international health regulations to deal with all aspects of blood donations and transfusion. Collaboration between developed and developing countries is needed to ensure the transfer of novel technologies and updated scientific materials to implement the international health regulations and improve public health systems, thereby strengthening global public health [11]. This is called health diplomacy. Many measures should be implemented to manage blood supply and blood demand to avoid any sudden blood shortage. These measures may include monitoring blood supplies, using blood only in emergencies during crises, implementing patient blood management (PBM) [12–14] as an effective blood conservation method [15], educating and motivating people regarding blood donation through accessible and comfortable blood donation centres and using all available social media and other forms of advertising (**Table 2**). Among these methods of managing the blood inventory, the most effective one is PBM. The latter is defined as an evidence-based patient care strategy that optimises patients' outcomes using pharmacological medications and patients' blood [16]. In February 2020, the WHO called for the PBM strategy to be implemented after endorsing it in 2010 [17, 18]. PBM is a multidisciplinary approach that involves most healthcare staff, including haematologists, oncologists, surgeons, obstetricians, gynaecologists, anaesthesiologists, general practitioners and other clinical specialists. Many peer-reviewed studies indicated that PBM reduces hospital stay length and the chance of blood transmitted diseases, and improves care quality, morbidity and mortality at a reduced cost [19–22].

3.4 Recommendations to improve blood transfusion services and health security

To ensure proper management of BTS, it is necessary to recognise and fix the current systemic deficiencies affecting BTS in the national health system. These deficiencies include organisational difficulties, insufficient funds, unsafe blood

Key measures
• Raising awareness of the need for blood and blood components
• Increasing the knowledge about the blood donation process
• Optimising the donor experience
• Implementing effective strategies to convert voluntary non-remunerated donors into regular donors
• Organising a mobile blood drive
• Making timely appeals for blood donations before shortages through popular social media
• Regularly educating and training healthcare workers regarding clinical guidelines on transfusion, patient blood management and clinical audits
• Ensuring regular communication between blood bank specialists and clinicians regarding blood transfusion
• Implementing optimum patient blood management
• Creating an electronic blood monitoring system
• Close monitoring of blood inventory and blood demand
• Close monitoring of emergency blood supplies
• Establishing a commission for the responsible use of blood and blood components
• Saving the blood and blood components for the maximum permissible period by increasing blood storage facilities, especially in rural medical centres
• Improving the capacity of blood banks to produce maximum blood products
• Developing an evidence-based emergency plan for blood donations during disasters and crises
• Developing an evidence-based emergency blood management plan
• Adhering to all guidelines and plans regarding blood transfusion services

Table 2.
Specific measures for proper management of blood supply and demand to prevent blood shortages.

donation, outdated equipment, low quality blood test kits and an inadequate number of qualified personnel. Governments should implement strategies to increase their blood inventories and ensure the collection of safe blood. Countries require their governments' support for their health systems, including BTS, which is a political obligation to guard national health security.

The following are recommendations to help promote public health by ensuring an adequate supply of safe blood.

1. Promote a national blood transfusion services plan and strengthen its management

   Current laws, rules and standards that support a statutory structure for blood bank and BTS should be examined and adapted according to the international applications and the WHO's criteria and rules. Special care needs to be taken to ensure proper execution.

   - A blood transfusion service agency coordinated by the state should be established. The agency should have a combined management body and qualified staff. This will call for changes in organisational and management frames and procedures, together with strategies and plans to increase the central blood banks and minimise the hospital blood banks to attain reductions in costs.

   - An international system of voluntary non-remunerated blood donation should be established to minimise risky blood transfusion. Critical public health procedures need to be implemented to reduce paid blood donations to

a minimal level. It is also necessary to cooperate with the mass media to carry out targeted educational and promotional activities to encourage voluntary non-remunerated blood donation. Effective plans to foster voluntary non-remunerated blood donation include social recruitment at the national level. There is a need to enter into co-partnerships with communities, domestic institutions, and religious and community leaders.

- There needs to be appropriate use of productive donor screening strategies, containing direct questions for highest-risk attitudes.

- Support should also be delivered to assist each country in establishing a national blood donor register with the support of information technology systems that connect blood bank centres, reference laboratories and hospital users [23].

- Knowledge and awareness needs to be improved on two levels. First, the level of medical expertise must be increased through regular advanced training and continuous medical education. Second, there is a need to raise public awareness of the importance of voluntary non-remunerated blood donation and blood donation safety through appropriate information and publicity activities.

2. Solve the chronic shortage of BTS:

   The current budget allocated to the blood banks should be significantly raised to assist the performance of BTS.

3. Improve the quality of BTS and associated medical practices:

   - Blood transfusion service sites:

     ○ After reassigning tasks according to system reform, special attention must be paid to updating the existing BTS. This applies to the functional and safety requirements of donor selection, blood collection, test processing, and storing of the blood and blood components. Sufficient employee expertise is a prerequisite for BTS to function well.

     ○ Compulsory standard guidelines should be formulated and adopted to inform the purchasing of special requirements (such as blood collection bags, test kits and other consumables). Training support personnel should also be provided for blood transfusion service stations. These measures will assist in standardising collection procedures and ensuring safe service.

     ○ The blood banks should use high-quality blood collection bags and optimal anti-coagulant additive solution to prolong the product shelf-life.

     ○ The quality management system should involve the entire blood chain from prospective donor to prospective recipient, including follow-up plans for monitoring and evaluating all relevant blood bank activities, consistent with WHO standards. Critical screening tests and obligatory quality assurance systems are crucial to ensure the safety of blood supply [24].

     ○ Current working situations and applications of BTS should be evaluated and improved. Special rules and procedures must be reviewed, focusing on blood handling, disinfection/decontamination and waste disposal procedures.

- Hospital sites:

  As the entry point for follow-up, assessing and discussing blood transfusion treatment indications, efficiency and associated side effects, the hospital blood transfusion committee is a vital structure of the blood alert system.

- Existing scientific evidence of blood transfusion treatment efficiency should be used, and international recommendations should be adjusted according to local conditions to revise and update outdated guidelines and practices. The standards and clinical guidelines should be formulated following the WHO's advice and applied to the national blood transfusion services.

4. Reinforce public health preventive medicine and primary healthcare plans to minimise blood demand and blood supply gaps:

   Develop an effective public health plan, focusing on correcting the causes of diseases that require blood transfusion treatment and strengthening the job of primary healthcare, which will reinforce prevention and early diagnosis.

5. Promote regional exchanges and cooperation arrangements between countries:

   Territorial integration and collaboration between countries for economic and social development is becoming increasingly important. Regional exchanges and cooperation arrangements should ease the sharing of information on experiences and best practices and allow for the horizontal spread of expertise and technical assistance.

However, unless these measures are systematically implemented and continue throughout the process, while progress is regularly monitored as a section of quality control, obtaining an adequate supply of safe blood and properly functioning blood transfusion services will remain out of reach.

4. Conclusions

Blood demand has increased worldwide; however, blood supply is insufficient to meet this need. Therefore, the proper management of blood supply and blood demand is crucial to avoid sudden blood shortages. The latter can result in the failure of BTS, national health insecurity and consequently, international health insecurity. Health insecurity ultimately leads to societal and political insecurity, so health security issues remain the priority in terms of national security. The perception of health difficulties through the global health security framework leads to international health securitisation, attracting the attention and support of governments, and pressuring decision-makers to act early. Evidence-based plans for blood safety and availability should be developed, implemented and updated regularly. Global health policies and international health regulations related to BTS should be ready to respond quickly to any challenges in delivering an adequate supply of safe blood, especially during disasters and emergencies. It is essential to implement guidelines and strategies that concern the management of blood supply and blood demand, particularly before any anticipated catastrophe or crisis, to avoid sudden blood shortages. The most essential and efficient method for managing blood inventory is PBM. The implementation of PBM not only reduces the chance of a blood shortage, but is also associated with a low risk

of blood transfusion complications, reduced hospital stays and healthcare costs, and most importantly, lower morbidity and mortality. The information provided by this chapter is linked to the management of blood supply and blood demand as an essential component of global health security. It helps in planning for the proper management of blood inventory and ensuring the availability of safe blood and blood components to avoid sudden blood shortages and the serious consequences of such shortages.

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Conflict of interest

The author declares that there is no conflict of interest.

Notes/thanks/other declarations

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Chapter 8

Timely Detection of SARS-CoV-2 in Limited Resource Settings: The Role of the Laboratory in Zimbabwe

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Abstract

The recommended approach for response to severe acute respiratory syndrome coronavirus 2, was to test to enable timely detection, isolation and contact tracing so as to reduce the rapid spread of the disease. This highlighted that the laboratory as one of the core capacities of the International Health Regulations and key technical area in the International Health Security was critical in curbing the spread of the virus. Zimbabwe embarked on testing for SARS-CoV-2 in February 2020 following the guidance and support from WHO leveraging the existing testing capacity. Testing was guided by a laboratory pillar which constituted members from different organizations partnering with the Ministry of Health and Child Care. SARS-CoV-2 testing expansion was based on a phased approach using a tiered system in which laboratory staff from lower tiers were seconded to test for coronavirus using RT-PCR with National Microbiology Reference Laboratory (NMRL) being the hub for centralized consolidation of all results. As the pandemic grew nationally, there was an increase in testing per day and reduction in turnaround time as five laboratories were fully capacitated to test using RT-PCR open platforms, thirty-three provincial and district laboratories to test using TB GeneXpert and 5 provincial laboratories to use Abbott platforms.

Keywords: pneumonia, detection, laboratory expansion, testing, partner coordination

1. Introduction

Coronavirus Disease 2019 (COVID-19) as it came to be known, was first reported as a novel pneumonia in Wuhan, China in December 2019 [1]. It was eventually shown to be caused by a coronavirus strain known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. This disease was

declared a Public Health Emergency of International Concern by the World Health Organization (WHO) on 30th January 2020 and eventually a pandemic on 11 March 2020. Africa experienced its first COVID-19 virus case on 14th February in Egypt [3]. This was an Italian citizen returning from Milan and had mild symptoms. South Africa a neighboring country to Zimbabwe had its first case confirmed on the 5th of March 2020 and this was also an Italian returning from Italy with mild symptoms identified on visiting a private general practitioner to consult for some symptoms [4]. Zimbabwe and other neighboring countries were at a high risk of importing cases and subsequent community spread of COVID-19 cases owing to the border trade activity with South Africa. SARS-CoV-2 presents differently among individuals in different population. The majority of cases in the African population present with asymptomatic to mild symptoms with few symptomatic cases [5]. People with severe forms of the disease mostly present with pneumonia and difficulty in breathing which may sometimes require mechanical ventilation [6]. SARS-CoV-2 infection is spread through contact and exposure to droplets and aerosols of viral particles from infected persons coughing, sneezing and talking [6, 7]. Therefore, the main prevention method for spread is by practicing hand hygiene through frequent hand washing with soap or alcohol based hand sanitizer [8, 9] and use of face masks as guided by WHO [10]. In order to control the rate of infection, it is important to put in place active disease surveillance for early identification, isolation and contact tracing [11, 12]. The detection of COVID-19 is largely based on the laboratory identification of SARS-CoV-2 virus [13, 14] hence the need to increase laboratory capacity for testing of suspected cases, in order to isolate cases and their contacts from the healthy population to reduce the spread.

The COVID -19 pandemic presented a huge demand on the laboratory compared to previous emergencies and at a time when most low-middle income countries were not well capacitated to respond to outbreaks/pandemics [14]. Laboratory being among the core capacities of the International Health Regulations, IHR (2005) plays a critical role in the timely response to emergencies [15]. Laboratory is a key technical area of International Health Security enabling countries and entities to detect infectious agents of human or animal origin, enhancing preparedness and response to infectious diseases of epidemic potential [16, 17]. Efficient diagnostic strategies and methods ensures timely detection of the virus [18].

Globally, SARS-COV-2 can be detected most reliably using Real-Time Polymerize Chain Reaction (RT- PCR), a highly sensitive molecular technique for viral nucleic acid detection using a number of different in-house as well as commercially available kits. Antigen and antibody based rapid diagnostic tests (RDTs) are less sensitive and also used as directed by testing strategies developed by the country's health regulatory authorities as recommended by WHO [19, 20].

The COVID-19 pandemic brought in a new dimension to international health security bringing new dimensions of solidarity [21] and selfishness in certain situations. These issues were more marked in the laboratory side of the preparedness and response efforts. First, to develop COVID-19 diagnostic testing, there was a need to share the viral material in line with the pandemic influenza preparedness plan [22] as well as the Nagoya Protocol [23]. This was done, according to WHO. Secondly, the development and distribution of diagnostics brought in a crunch with countries with capacity for development of these resources prioritizing themselves to the detriment of poorer countries with less capacity. This would then be improved with a solidarity movement spearheaded by WHO, which pooled organizations and entities involved in the response for centralized procurement and allocation of resources to countries in need. This saw the development of the online platform, COVID-19 supply portal [24] where countries could layout their requirements and have allocations from the global level according to their need and availability.

Like most of the Low to middle-income countries (LMIC), Zimbabwe started testing for SARS-COV-2 in February 2020 without a clear strategy for testing with support from WHO and Africa CDC. At this point, there was one laboratory staff at National Microbiology Reference Laboratory (NMRL) trained at NICD in South Africa (facilitated by Africa CDC) on testing for COVID-19 with only 5 tests being done a day. The available capacity for influenza surveillance in terms of staff and HIV surveillance in terms of equipment and laboratory consumables became the initial basis for COVID-19 testing. The first case of SARS-COV-2 was detected in Zimbabwe on 20th of March 2020 where a male traveler of 38 years of age traveling from UK to Victoria Falls, had mild symptoms and tested positive for SARS-COV-2. At this time, there was a great need to establish a strategy to expand testing to meet the country's needs before cases increased [25]. The speed at which WHO developed guidance document on the onset of the pandemic provided an opportunity for countries including Zimbabwe to ride on to develop their country testing strategies.

In this report, we showcase Zimbabwe's hands on experience in scaling up testing for COVID-19 using RT-PCR since the start of the response in February 2020 following a step by step tier-based approach and highlighting the major challenges identified along the process and key lessons learned from this experience.

2. Methodology

Zimbabwe employed a multisectoral approach through setting up dedicated expert committees to cover specific areas of the response based on the WHO guidelines on COVD-19 response preparedness [20]. In addition, a literature review of the available evidence was also done to understand the role of the laboratory in emergencies particularly of infectious diseases and how other countries have responded to the need to scale up laboratory capacity in order to meet the country needs in emergencies and outside emergencies [14, 26]. An operational plan was developed as well as guidelines and procedures for implementation. Coordination led by the MoHCC involved daily updates at the beginning reducing their frequency as implementation progressed. There were also weekly national coordination meetings for the national taskforce who reported to the inter-ministerial committee, cabinet and ultimately the presidium.

2.1 Expansion of laboratory testing

One of the Joint External Evaluation (JEE) focus areas in the laboratory technical area is the presence of an effective national diagnostic network [17]. Zimbabwe set out to scale up laboratory capacity to test for SARS-CoV-2 leveraging existing capacity from other programs like influenza, HIV and TB. This expansion was spearheaded by the laboratory pillar in a stepwise manner as explained in the following sections.

2.1.1 The laboratory pillar structure establishment

The journey in the COVID-19 laboratory response in Zimbabwe began with establishing of the Laboratory Pillar members mandated to support scale up of COVID-19 testing through developing a testing strategy and supporting its implementation. The laboratory pillar was one of the Zimbabwe modified Incident Management System (IMS) guided by WHO Emergency Response Framework (ERF) [27] in which the Laboratory was one of the pillars in addition to surveillance, case management and continuity of essential services, Infection

prevention and control, Risk Communication and Community Engagement, Logistics and Points of Entry. MoHCC and partners conducted a rapid assessment of the available capacity in country, leveraging existing investments in different programs and established a diagnostic network and infrastructure for COVID-19 testing. The Laboratory Pillar was led by the Directorate of Laboratory services (DLS) under the MoHCC and constituted of partners including United States Centers of Disease Control and Prevention (US. CDC), World Health Organization (WHO), Clinton Health Access Initiative (CHAI), African Society of Laboratory Medicine (ASLM), the leadership from the COVID-19 testing laboratories including the National Reference laboratories (NMRL) and institutions providing testing services on behalf of the MoHCC. With the pillar in place, a testing strategy, following the WHO guidance and recommendations for laboratory testing [20] was developed to guide the scale up process. The strategy employed a tier-based approach for expansion which activated higher tier laboratories followed by provincial then district. The pillar members were involved in the planning of this expansion which involved identifying through assessment and listing the laboratories with available capacity for COVID-19 molecular testing, drafting budgets and partner commitment to support in particular areas of the response.

2.1.2 The scale-up of testing: the tier-based system

In March, when the first case was detected, minimal testing was being done by the National Microbiology Reference Laboratory (NMRL) only with a few staff trained to perform testing for COVID-19 virus using RT-PCR. Tier-1 of the expansion involved assessment of the NMRL and training of extra staff who would support to test for COVID-19 virus using RT-PCR and further train other staff during the expansion process. After successful implementation of tier-1, tier-2 was initiated as shown in the scale up plan in **Figure 1**. This involved training of more laboratory cadres and capacitating five more national level laboratories to test for COVID-19 virus using RT-PCR on open PCR platforms to support the tier-1 laboratory. The cadres trained in tier-2 were from the laboratories listed during the initial planning process. The laboratories included tertiary, research and training laboratories namely, National Tuberculosis Reference Laboratory (NTBRL), National Virology Reference Laboratory (NVRL), African institute of Biomedical Research (AiBST), Biomedical Research Training Institute (BRTI) and University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC). The inclusion criterion was based on presence of existing testing capacity based on availability of RT-PCR equipment and resources as well as staff experienced in RT-PCR. This process took a total of 3 months to complete full rollout of tier-2 testing.

Leveraging existing TB GeneXpert platforms in the different provinces, university Bio-labs and Mobile trucks, tier-3 was implemented through capacitating thirty-three provincial and district laboratories to test for COVID-19 and 5 provincial laboratories to test using the Abbott platforms.

With the country experiencing a high influx of returnees from South Africa, there was increased risk of local transmission. This heightened the need for a robust surveillance strategy to minimize transmission. The country projected to test 33 000 tests in the month of April which target was not reached as planned. This saw the laboratory encouraging support from private laboratories which also joined forces increasing testing capacity. In this line, Lancet and CIMAS laboratories joined in supporting to test for SARS-CoV-2 using RT-PCR to complement government efforts to test for SARS-COV-2.

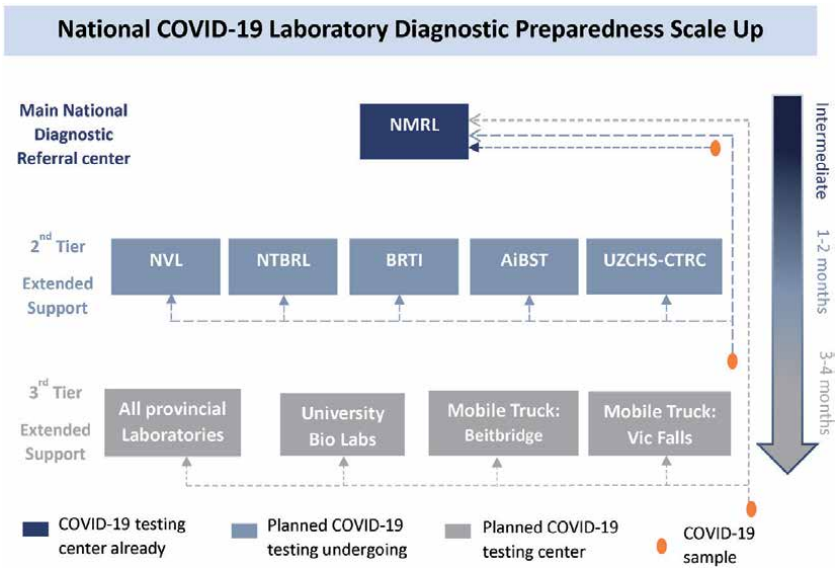

Figure 1.
National COVID-19 Laboratory Diagnostic Preparedness Scale Up plan. Tier 1; NMRL initially carried out all the testing, tier 2; expanded laboratory testing to National Virology Reference Laboratory (NVRL), Biomedical Research and Training Institute (BRTI), National Tuberculosis Reference Laboratory (NTBRL), African Institute of Biomedical Science and Technology (AiBST) and UZ Clinical Trials Research Centre, tier 3; capacitation of all provincial laboratories, University Biolabs and mobile trucks to test using GeneXpert.

2.1.3 Managing human resources

With the increase in samples being tested a day, it was pertinent to organize the flow of work to meet the workload demand. To do this, a two-shift duty system was introduced at every testing laboratory to increase daily throughput and reduce staff burnout. This extra shift system also involved separation of staff into cohorts such that in case of infection, quarantine and isolation procedures could be implemented without bringing the laboratories to a complete standstill. Additionally, locum staff were also hired in select laboratories to maintain adequate human resource for laboratory operations.

2.1.4 Quality assurance

Implementation of a new testing method for SARS-CoV-2 and use of a wide range of equipment, reagents, kits and consumables meant that a robust quality management system needed to be in place. The Laboratory services leveraged existing Quality Management Systems (QMS) to ensure key quality system essentials were adapted for the new testing requirements. Given that at least 7 laboratories had ISO 15189 accreditation, this process moved smoothly. Safety trainings were implemented together with waste management activities related to Guanidine thiocyanate (GITC) waste produced during RT-PCR testing using Abbott and GeneXpert machines.
In addition, thirty-two laboratories were enrolled for external quality assurance Proficiency Testing (PT) program with Thistle, a South African PT provider as an external means to objectively check and ensure reliable results are being produced.

2.1.5 Data management

A robust data management system is key in the response to enable timely identification of at-risk populations, timely contact tracing and resource mobilization

and response optimization [28]. With the increasing testing, there was a growing need for streamlining data management and flow to efficiently manage and report data. To achieve this, we leveraged on the HIV CDC-PEPFAR supported Laboratory Information Management System (LIMS) by introducing the COVID-19 module and training laboratory data staff for data entry. Fifteen testing laboratories were added on the LIMS allowing timely relay of results to requesting sites. To further reduce the data linked TAT, instant messaging system was added to the LIMS for automatic patient notification as soon as the results were released and published by the testing laboratory.

2.1.6 Resource mobilization

The beginning of the response was mostly supported through donations of testing kits and supplies from China Embassy, Jack Ma foundation, Africa CDC, World Health Organization (WHO), Clinton Health Access Initiative (CHAI), USAID and many other well-wishers. The laboratory pillar members also developed a budget projection that specified the test expansion requirements and partners in the pillar committed to specific items on the budget, making the process easier. Procurement requests were made through the WHO global procurement platform [22] which was established as a hub for laboratory to support the LMIC countries in procuring these resources with assured equitable distribution.

2.2 Data analysis

The outcomes of this response were measured through the increase in number of testing laboratories which was linked to the number of samples tested per day. The changes in sample testing per day was analyzed using R 3.62 software.

3. Results

Through this response, Zimbabwe had an opportunity to strengthen systems regarding partner coordination, staff capacitation, resource mobilization, data management and laboratory testing output during this critical time. This response created and encouraged lasting coordination among the different partners on the laboratory pillar enabling a quick and successful scale up of testing. This coordinated approach enabled capacitation of staff to test for SARS-CoV-2 while observing the necessary biosafety measures and quality assurance. Besides the increased knowledge in using a wide range of testing platforms, a number of scientists gained the skills which can be used in other instances where testing is required. Data management platforms have been put in place and these have strengthened the data handling and dissemination system. Resource mobilization was enhanced through the response and timely stock replenishment measures put in place. Stock projections were developed and monitored strictly to avoid stock-outs using a stock availability tracing tool. In addition, the WHO global platform [24] was established to support procurement of COVID-19 commodities in an equitable way. This greatly reduced the delays in procurement and ensured timely and equitable supply of the required resources through a hub. In this line, over a period of 5 months, more than thirty-three laboratories could perform molecular testing for COVID-19 using available PCR platforms, capacity that can be used in case of any other emergency that requires extensive molecular testing. With this expansion, testing increased from five samples a day to more than 1000 samples a day over six months. As a result of this collaborative effort, the target of testing 1000 samples per day was surpassed

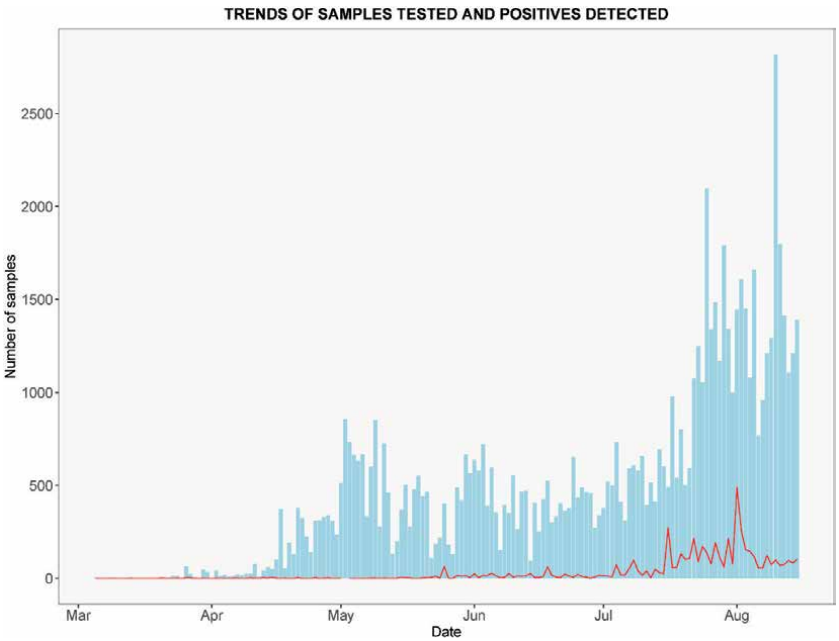

Figure 2.
Trends of samples tested and positives detected. Testing started in early March with one laboratory performing PCR testing. There was a marked increase in testing from April owing to the capacitation of five other labs to support the main reference laboratory to test using PCR. There were fluctuations owing to stock depletion due to the global challenge of timely delivery of reagents. Provincial laboratories were further capacitated to test using GeneXpert which further boosted the testing hence increasing the number of samples tested per day by early August.

in August and this exceeded the monthly projected target of 33,000 tests to 35,816 tests that month. The number of positive samples detected also increased with increase in testing as shown in **Figure 2**. There were notable fluctuations in testing as seen in **Figure 2** and these were due to intermittent stock outs which were due to the strain on the global supply that led to late delivery of commodities.

4. Discussion

The escalated and smooth scaling up of testing was made possible by leveraging existing capacity from other programs like Influenza Surveillance, HIV and TB work [29, 30]. The role of network optimsation exercises that had been done prior to the pandemic better placed the country to respond. The knowledge of locations and existing capacities and sample transport networks that had been mapped supported decision making in terms of activating new testing sites. However, like other countries, repurposing of testing laboratory facilities and consumables in Zimbabwe affected the HIV and TB programmes both in terms of human resources and consumables being repossessed for COVID-19 testing [31]. In addition, it was initially difficult to maintain quality management system for COVID-19 testing since everything operated as an emergency. At that time, there had not been proper planning and projecting of resources whether human resource or consumables which interfered with the processes. Partner coordination ensured the development of inter laboratory comparison panels and support sourcing of external quality assessment panels. Another challenge arose from the dependence on imports through external suppliers of all consumables which affected testing as supply chain

portals were overloaded with orders and could not meet the demand. Furthermore, competing with high income countries on these platforms to access *in vitro* diagnostics limited the projected rate of testing expansion. As a result like many other African countries [32], Zimbabwe faced a shortage in essential supply for use like GeneXpert supplies, PPE, molecular testing consumables and sample collecting kits which highly affected the testing capacity for over two months. Staff remuneration and motivation was also a setback throughout the participating pillars. In addition, some laboratory staff got infected in the course of the response which affected the work output and duty roster.

5. Conclusions

The laboratory is a key capacity area in International Health Security. Capacities to enable population access to testing of priority pathogens is key in enabling countries to respond to global health threats. More so the ability and agility of countries in finding solutions to respond to diagnostic needs of emerging novel infectious agents leveraging available capacities is a very important requirement in International Health Security. Collaboration of global and local stakeholders in responding to public health emergencies is key and this should be underpinned by a coordinated approach in addressing present and future challenges. This approach was key to successful implementation of processes to reduce the impact of COVID-19 pandemic in Zimbabwe. Working together with partners along with the country's Ministry of Health and Child Care made the process of expansion of testing easy as this facilitated leveraging off existing government and private infrastructure. Strengthening of laboratory systems is crucial in the timely detection of SARS-COV-2 virus and limiting its spread. It is also important to note that during emergencies, the population's need for other non-emergency laboratory tests remains important and should also be equally planned for in order to avoid unnecessary interruption of other lifesaving interventions.

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- Clinton Health Access Initiative (CHAI)
- Global Fund
- National Microbiology Reference Laboratory (NMRL)
- National Virology Reference Laboratory (NVRL)

- United Nations Children's Fund (UNICEF)
- United Nations Development Program (UNDP)
- US Center for Disease Control (CDC)
- World Bank
- World Health Organization (WHO)

Conflict of interest

There is no known conflict of interest.

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Chapter 9

Neurological Complications in COVID-19: Implications on International Health Security and Possible Interventions of Phytochemicals

Johnson Olaleye Oladele, Oluwaseun Titilope Oladele, Oyedotun M. Oyeleke and Adenike T. Oladiji

Abstract

Global health security or international health security (IHS) includes any natural or man-made phenomenon that challenged human health and well-being including emerging infectious diseases such as the current global pandemic: COVID-19. Since the sudden outburst of COVID-19 pandemic in 2019, many COVID-19 patients have exhibited neurological symptoms and signs. Till now, there is no known effective established drug against the highly contagious COVID-19 infection despite the frightening associated mortality rate. This chapter aims to present the mechanism of action of coronavirus-2 (SARS-CoV-2), the clinical neurological manifestations displayed by COVID-19 patients, impact on the global health system and present phytochemicals with neuroprotective ability that can offer beneficial effects against COVID-19 mediated neuropathology. Reports from COVID-19 clinical studies, case reports, and other related literature were evaluated. Neurological complications of COVID-19 include anosmia, acute cerebrovascular disease, acute disseminated post-infectious encephalomyelitis, encephalitis, etc. Also, SARS-CoV-2 could be a neurotropic virus due to its isolation from cerebrospinal fluid. Multiple neurological damage displayed by COVID-19 patients might be due to hyperinflammation associated with SARS-CoV-2 infections. Kolaviron, resveratrol, vernodalin, vernodalol, and apigenin are natural phytochemicals with proven anti-inflammatory and therapeutic properties that could extenuate the adverse effects of COVID-19. The phytochemicals have been documented to suppress JNK and MAPK pathways which are essential in the pathogenesis of COVID-19. They also showed significant inhibitory activities against SARS-CoV-2 main protease. Taken together, these phytochemicals may offer neuroprotective benefits against COVID-19 mediated neuropathology and suppress the burden of the pandemic on IHS.

Keywords: international health security, Neuropathology, COVID-19, Resveratrol, Kolaviron, Apigenin, Phytochemicals, SARS-CoV-2

1. Introduction

International health security (IHS) is a sum total of any natural, simulated or synthetic phenomenons that pose major threats on human health and well-being including emerging infectious diseases (EIDs) such as the current global pandemic: COVID-19. COVID-19, novel coronavirus pneumonia is ranked amidst the nine most deadly global pandemic ever occurred in the world. It was first recorded in 2019 at Wuhan, a Chinese city and since its first outbreak, the pandemic has dispersed wide to every region of the globe having critical negative impact on many countries both developed and developing nations. This severe acute respiratory disease is highly contagious and transmissible via a pathogenic virus called SARS-CoV-2 to humans and animals. Reports by the WHO team on COVID-19 pandemic as of 25th November 2020 showed that COVID-19 has really inflicted great havoc on human health and constitutes a major danger to global public health. It was reported that over 57.8 million cases of SARS-CoV-2 infections have been recorded with over 1.3 million deaths globally [1, 2]. In Nigeria, the most populous country in Africa, over 66,000 cases had been confirmed and more than 1,160 mortalities recorded [1, 2]. This statistic reveals the impact of this pandemic on the global health system capacity. The emergence of pathogens represents a significant threat to public health, including both high-income regions and low/middle-income regions [3–5].

COVID-19 has an average incubation period of 3 days [6]. The most prevalent medical manifestations of COVID-19 (such as cough, fever, shortness of breath, fatigue, and other complications) are nearly the same to those of other viral pneumonia; multiple organ failures and death were documented in critical and severe cases [7]. These indications are prominently expressed in aged persons perhaps owing to lingering and chronic underlying diseases such as diabetes, hypertension, neurodegenerative disorders, or heart diseases [8]. The spread of the virus (SARS-CoV-2) amid individuals happens when there is an infiltration of infected aerosols from cough, sneeze, or respiratory droplets into the lungs through inhalation in the nose or mouth.

Clinical case reports have documented a spectrum of neuropathological features displayed by COVID-19 patients. These neurological manifestations include anosmia, acute cerebrovascular disease, acute disseminated post-infectiousencephalomyelitis, Encephalitis, Guillain–Barré syndrome, acutedisseminated post-infectiousencephalitis, and viral meningitis [9]. Presence or confirmation of SARS-CoV-2 in cerebrospinal fluid suggest that it could invade and infect the central nervous system (CNS) as a neurotropic virus inducing multiple neurological impairments [9].

2. Methods

This chapter presents the pathogenic mechanism of SARS-CoV-2 and neurological complications of COVID-19. Furthermore, we present the possible intervention of potential anti-COVID-19 phytochemicals in the treatment of neuropathology associated with COVID-19. The literature search for this article was done on Medline, Google Scholar, and PubMed Central using keywords Clinical features, Coronavirus, SARSCOV-2, COVID-19, and complications.

2.1 Neurological damage associated with Covid-19

Several mechanisms have been projected for the neuropathology linked to SARS-CoV-2 in reference to clinical manifestations displayed by COVID-19 patients. Mao

et al. [10] documented hyposmia and anosmia in COVID-19 patients. This indicates that SARS-CoV-2 may be spread directly from the cribriform plate near the olfactory bulb to brain regions [11]. SARS-CoV-2 can diffuse to the CNS via enteric nerve and sympathetic afferent mediated by gastrointestinaltract infection [12]. Furthermore, anterograde and retrograde transmission can mediate neuro-invasion of SARS-CoV-2 through the sensory and motor nerve endings [13], coupled with involvement of motor proteins (dynein and kinesins), in particular through the vagus nerve from the lungs [14].

Brains are more vulnerable to oxidative and neuroinflammation insults due to the low level of cytoprotective endogenous enzymes. The cytokine storm syndrome (hyper-inflammation) accompanying SARS-CoV-2 infections may be one of the causes of the neurological impairments observed in COVID-19 patients. Viral infections have been documented as one of the chief agents that induces secondary haemophagocytic lymphohistiocytosis (sHLH) [15]. sHLH similarly referred to as Macrophage Activation Syndrome (MAS) is a severe health disorder which includes diverse group of hyper-inflammatory condition arisen after an infringement in the interaction between genetic predisposition and initiators such as infections. One of the features of sHLH is an abrupt and severe hyper-cytokinaemia due to inapt persistence of histiocytes and cytotoxic T-lymphocytes which eventually leads to multi-organ failure, haemophagocytosis, and mortality [16]. Other features of sHLH includes persistent fever, cytopenias, and hyper-ferritinaemia; pulmonary involvement occurs in approximately 50% of patients [17].

In the brain, activation of glial cells caused brain damage and severe inflammation with the secretion of pro-inflammatory cytokines including TNF-alpha, interleukin-2, and interleukin-5 [18]. Neuro-invasion of SARS-CoV-2 can activate macrophage via CD4+ cells to produce interleukin-6 which is a principal constituent of cytokine storm syndrome via granulocyte-macrophage colony-stimulating factor. Thus, causing damage to the neuronal cells.

2.2 Modes of action of SARS-CoV-2

Prospective EIDs which are major factor in IHS can emanate from vector-borne, vaccine-preventable, epidemic-prone, food-borne, zoonotic, and/or antibiotic-resistant pathogens or from a lack of access to safe water and sanitation. The experiences had and measures taken from prior outbreaks can enhance interventions and improve future responses to emerging infectious diseases [19, 20]. The genetic investigation on SARS-CoV-2 showed that the comprehensive genome sequence recognition rates of bat SARS coronavirus (SARSr-CoV-RaTG13) and SARS-CoV were 96.2% and 79.5%, respectively [21]. Comparing with other coronaviruses, SARS-CoV-2 proteins for viral replication, spikes formation, and nucleocapsid are initiated in specific genes in ORF1 [22]. The virus (SARS-CoV-2) gain entrance into the host cell and invade it via series of cellular alterations and modifications like other types of beta-coronaviruses. Subsequently, SARS-CoV-2 binds to the Angiotensin-Converting Enzyme 2 (ACE2) receptor in the human and/or host's alveoli of the lungs and respiratory epithelium via theRBM of the S protein [23, 24]. Similar type of receptors has been documented in the viral genome of SARS-CoV and SARS-CoV-2, particularly, the receptor binding motif (RBM) and the receptor binding domain (RBD) [25–27]. Attachment of SARS-CoV to the receptor leads to the recruitment of cellular proteases to split the S protein into S1 and S2 domains. Transmembrane protease serine 2 (TMPRSS2), human airway trypsin-like protease (HAT) and cathepsins are the cellular proteases that cleave the spike protein and enhance additional penetration modifications [28, 29]. The splitting of S protein facilitates the activation of S2 via a conformational modification

thereby allowing the insertion of the internal fusion protein (FP) into the membrane which facilitate the entry of the virus into the host.

There is a prospect that SARS-CoV-2 utilized mechanism similar to that of SARS-CoV as its receptor-binding domain (RBD) binding motif comprises the nucleotides connected to ACE2. Once SARS-CoV-2 enter into its host cell, ACE2 is shed and ADAM metallopeptidase domain 17 (ADAM17) exuviate it into the extra membrane space. This resulted into high concentration of angiotensin II from the transition of angiotensin I to angiotensin II by ACE2 and concomitant respiratory distress because angiotensin II negatively regulates the renin-angiotensin pathway consequently, damage the alveoli by increasing pulmonary vascular permeability [30]. Subsequent to SARS-CoV-2 proteins translation in the host, ORF3a protein is synthesized which codes for a SARS-CoV-2 related calcium (Ca^{2+}) ion channel. It reacts with TNF receptor associated factor 3 (TRAF3) and initiates the transcription of Nuclear Factor kappa-light-chain-enhancer of activated B-cells (NF-kB) pathway, resulting to the secretion of the pro-IL-1B gene [31], ORF3a together with TRAF3 can mobilize the inflammasome complex which includes caspase 1, Nod-like receptor protein 3 (NLRP3) and apoptosis-associated speck-like protein containing a CARD (ASC). Another signaling which include caspases activation, mitochondrial damage, ROS production, and Ca^{2+} influx activates pro-IL-1B to interleukin 1 beta (IL-1B) which enhance cytokine production. Furthermore, ORF8b protein through NLRP3 facilitates the inflammasome pathway. ORF8b protein is longer in SARS-CoV-2 [31]. Further studies are needful to ascertain the benefit or significance of the extra-nucleotides as contained in SARS-CoV-2. The E protein that forms an ion channel is also implicated in the cytokine's over-secretion (an occurrence referred to as cytokine storm syndromes which has been reported to be one of the major causes of respiratory distress in COVID-19) via NLRP3 inflammasome pathway (**Figure 1**) [32].

c-Jun N- terminal kinase (JNK) pathway is also one of the vital SARS-CoV pathogenic pathways. It is activated by ORF3a, ORF3b, and ORF7a. and results in pro-inflammatory cytokines over-secretion. These over-secretions of inflammatory cytokines have deleterious effects on lung and can accelerate lungs damage [33].

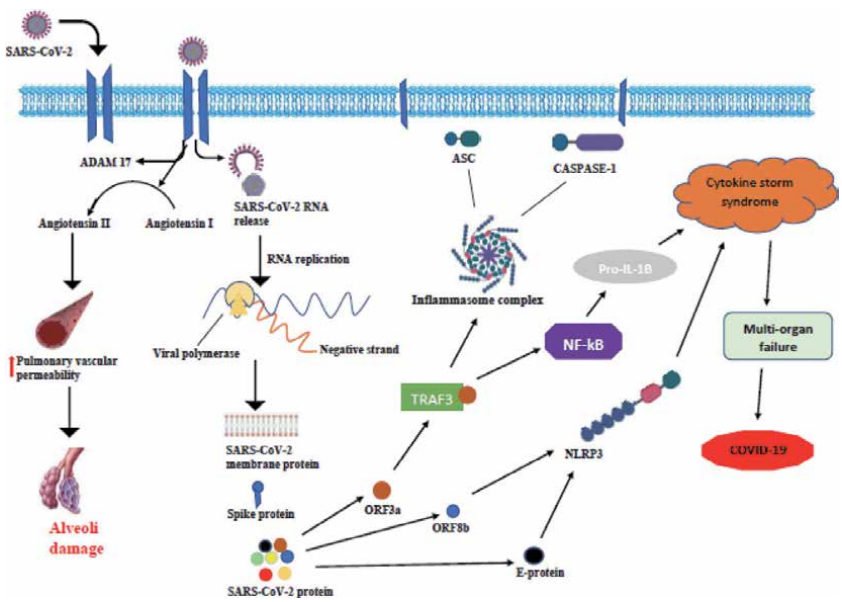

Figure 1.
Proposed mechanism of SARS-CoV-2.

Secondary haemophagocytic lymphohistiocytosis (sHLH) is a cytokine profile with a hyperinflammatory syndrome described by an abrupt hypercytokinaemia with multiorgan failure is related to COVID-19 severity. This also features increased granulocyte-colony stimulating factor, interferon-γ inducible protein 10, tumor necrosis factor-α, interleukin (IL)-2, macrophage inflammatory protein 1-α, IL-7, and monocyte chemoattractant protein 1 [33].

Additionally, SARS-CoV-2 exhibited higher infectivity and transmissibility but lower mortality rate when compared with other types of respiratory syndrome coronaviruses: severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). The noted increase in virulence of SARS-CoV-2 may be owing to great intensity and affinity at which SARS-CoV-2 attached to ACE2 and noted mutation in its genome sequence. The reported modifications on the SARS-CoV-2 gene include shorter 3b segments, alteration on Nsp 2 and 3 proteins, absent 8a, differences in orf8 and orf10 proteins, and longer 8b [34–37].

3. Phytochemicals with possible SARS-CoV-2 inhibitory and neuroprotective activities

Prevention is one of the predefined frameworks to effectively approach health security threats. To prevent the emergence or re-emergence of potentially life-threatening diseases, necessary measures must be initiated and these measures must be accessible, affordable and effective. Moreover, transmission of IHS threats was able to increase at an accelerating rate due to an overburdening of local health-care systems and widespread poverty where people lacked access to adequate water and waste management infrastructure. Therefore, the preventive and/or curative measures must be affordable by the populace. Furthermore, the remedy must be such that will be generally accepted by all; this will enhance the response and hasten the curb of the pandemic.

Different therapeutic approaches are being used since time immemorial for many health ailments apart from the pharmacological treatments. Approximately eighty percent of the World population still depends upon the use of herbal remedies for their health care. This traditional method of treating ailment is transferred from one generation to the other all over the world. Dependence on plants usage has been attributed to their affordability, effectiveness, safety, cultural preferences, and ample accessibility at all times and when it is needed. Globally, traditional healers are using various medicinal plants for the treatment of COVID-19. We therefore present some of the phytochemicals with therapeutic abilities which may serve as effective treatment for COVID-19 due to their antiviral, anti-inflammatory, antioxidant, antipyretic, immunomodulatory and cytoprotective properties.

3.1 Kolaviron from *Garcinia kola* (Guttiferae)

Since time immemorial, medicinal plants have become a source of novel and affordable drug compounds as plant-derived medicines have made significant impacts to human health and well-being [38, 39]. Garcinia kola (bitter kola) is a medicinal plant and a member of the Guttiferae family. It is an evergreen tree largely cultivated and highly esteemed for its edible nuts in West and Central Africa. Garcinia kola is commonly used by the people due to its ability to improve mouth odour and cause nervous alertness. In African traditional medicine, bitter kola is employed in the treatment and management of laryngitis, throat infections, bronchitis, inflammatory disorders, and as an antibacterial, antiparasitic, and

antipurgative. The seeds have also been used in the treatment of chronic hepatitis and cholangitis with significant improvement of liver functions. Similarly, *Garcinia kola* seeds are used a general tonic to boost the immune system [40, 41].

Many experimental findings have established the traditional medicinal uses of Garcinia kola. Kolaviron, the biflavanone of Garcinia kola (**Figure 2**) have been documented to protect against oxidative stress and hepatotoxicity induced by many xenobiotics which includes aflatoxin, 2-acetylaminofluorene, carbon tetrachloride, dimethylnitrosamine, paracetamol, phalloidin in animal studies [42–45]. Futhermore, the pharmacologically activities of biflavanone of Garcinia kola have been shown with many pharmacokinetic preferences over basic monomeric flavonoids as they pull through first-pass metabolism which incapacitates most flavonoids [40].

Neuroprotective abilities of kolaviron has been reported in many neuronal cell lines. Abarikwu *et al.* [46] documented the protective roles of kolaviron against atrazine induced toxic insult in human dopaminergic SH-SY5Y cells. The findings revealed that the antiapoptotic and antioxidative properties of Kolaviron make it effective to prevent against atrazine-induced toxicities. Similarly, kolaviron was reported to protect against apoptotic cell death in pheochromocytoma derived (PC12) cells exposed to Atrazine [47]. Igado *et al.* [48] reported the biochemical and morphological examination on the potential protective effects of kolaviron in vanadium-induced neuronal damage in rats. Kolaviron has been shown to suppress neuroinflammation in BV2 microglia via the Nrf2/ARE antioxidant protective mechanism [49]. Also, Olajide *et al.* [50] reported multidirectional suppression of cortico-hippocampal neurodegeneration by kolaviron. In another study, Omotoso *et al.* [51] reported that kolaviron ameliorated cuprizone-induced multiple sclerosis in the brain of experimental animals.

In a recent study, we reported the neuroprotective effects of kolaviron in striatal oxidative stress and neuroinflammation associated with rotenone model of neurodegenerative disease [52]. In the study, we showed that kolaviron restored rotenone-associated exploratory deficits, motor/neuromuscular incompetence and locomotor impairment. Also, kolaviron effectively ameliorated the neurobiochemical imbalance, striatal neurodegeneration, neuroinflammation and altered antioxidant defence system in the brain of the neurodegenerative rats. Kolaviron displayed a potential capacity to enhance efficient gait with minimal severity and improved coordination. This shows that kolaviron could be a prospective drug for the effective management and/or treatment of Parkinson's disease.

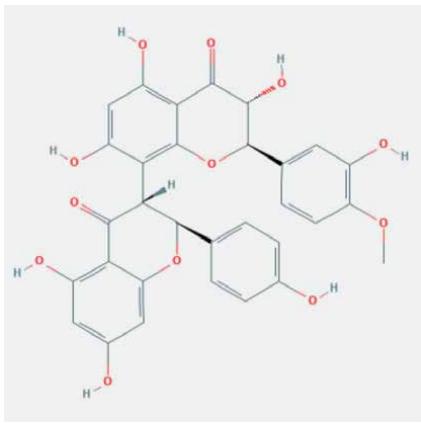

Figure 2.
2D structure of kolaviron (Kolaflavanone).

Kolaviron has been noted to be a potential anti-COVID-19 drug candidate in a computational experimental study aimed to screen phytochemicals in drug repurposing approach to combat COVID-19 [53]. The study employed USCF Chimera in virtual screening and molecular docking for possible inhibitors of SARS-CoV-2. Kolaviron was observed to exhibited a higher docked score with the SARS-CoV-2 major protease (6 LU7) above remdesivir, a recommended drug for the treatment of COVID-19. This showed that kolaviron could offer a better inhibitory effect on SARS-CoV-2 and be a more effective drug candidate in the treatment of COVID-19.

3.2 Apigenin

Apigenin (4′,5,7-trihydroxyflavone) is one of the most explored phenolics and the most commonly disseminated flavonoids in many plant species (**Figure 3**). It is predominantly present in herbs (oregano, thyme, basil, chamomile), phytochemical-based beverages (tea, beer, and wine), in vegetables (parsley, celery, onions), and fruits (oranges). It is also found extensively in Matricaria, Achillea, Artemisia, and Tanacetum [54]. Apigenin has been documented to have anticancer activities as well as theurapeutic effects on depression, Alzheimer's disease, amnesia, and insomnia treatment [54]. The dietary availability of apigenin could facilitate an efficacious intervention to inhibit activation of microglial and prevent onset of Alzheimer's disease.

After absorption, apigenin can easily be transported through the circulatory system, crossing to the blood-brain barrier to the brain, where it acts on the CNS and exhibits interaction with the GABAA-receptor [55, 56]. Sloley *et al.* [57] reported the inhibitory activity of apigenin on neuronal monoamine oxidases. Unregulated activities of monoamine oxidases may be one of the causes of some psychiatric cases and neurological disorders. However, monoamine oxidases inhibitors such as apigenin showed efficacy as antidepressant and anxiolytic agents.

The protective roles of apigenin in the amyloid precursor protein double transgenic Alzheimer's disease mouse has been reported by Zhao *et al.* [58]. Apigenin is also a potent cognition-enhancing, anti-amyloidogenic, antioxidant, neuroprotective, and anti-inflammatory agent with efficacy in the prevention and/or treatment of neurodegenerative diseases [58]. Nabavi et al. [59] in a review article emphasised the therapeutic potentials of apigenin in some human clinical trials and experimental animal models. Furthermore, apigenin's chemical structure, metabolism of action, and pharmacokinetics were elucidated in relation to its medicinal usefulness in depression, Parkinson's and Alzheimer's diseases [59].

Apigenin has also demonstrated strong anti-inflammatory property in lipopolysaccharide -induced macrophages by reducing the level of interleukin 6 (IL-6) {a pro-inflammatory cytokine}. It also inhibited tumour necrosis factor (TNF-α), interleukin 6, and cluster of differentiation 40 (CD40) production via suppression of

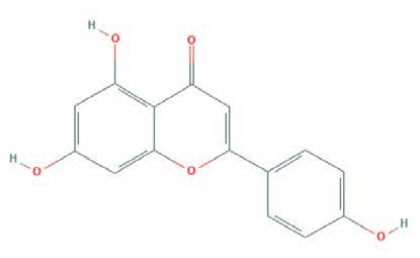

Figure 3.
2D structure of apigenin.

interferon gamma-mediated STAT1 (signal transducers and activators of transcription 1) phosphorylation in microglia [60]. An experimental study has established the inhibitory ability of apigenin on nuclear factor kappa-light-chain-enhancer (NF-kB), facilitated by inhibition of lipopolysaccharide-mediated phosphorylation of the p65 subunit [61]. Apigenin also suppressed the activities of adhesion molecules which is very essential to mitigate oxidative stress and prevent oxidative damage [62].

Apigenin promotes the release of cytoprotective enzymes such as glutathione-s-transferase, superoxide dismutase, and catalase to inhibit and neutralize cellular oxidative. Similarly, apigenin enhances activation of Nrf-2 signaling pathway leading to increase in phase II enzymes production [63, 64]. Anticancer property of apigenin in human cell culture models has been reported to be via suppression of angiogenesis and metastasis by interfering with the main signaling molecules in mitogen-activated protein kinase (MAPK) pathways which include c-Jun N-terminal kinases (JNK), extracellular-signal-regulated kinase (ERK), and p38 [65].

Apigenin has been documented to interact with both S 1 and S2 domains of the spike protein of SARS-COV-2 with substantial binding energies thus unsettling viral attachment and internalization into the host [66]. Similarly, *in silico* study in our laboratory revealed that apigenin displayed a significant binding affinity with the SARS-CoV-2 major protease (6 LU7). The result also suggested that apigenin could be a potential inhibitor of SARS-COV-2 [53].

3.3 Phytochemicals from *Vernonia amygdalina*

Bitter leaf (*Vernonia amygdalina*) is an indigenous African plant with a number of scientific proven medicinal importance [67–70]. Recent study from our laboratory has examined the possible inhibitory activity of selected phytochemical constituents of the leaf extract of *Vernonia amygdalina* (hydroxyvernolide, vernodalin, vernodalol, vernolide, and veronicoside) (**Figure 4**) against SARS-COV2 major protease (6 LU7) [71]. The phytochemicals exhibited significant binding affinity to the binding pocket of SARS-COV2 major protease suggesting them as potential molecules that could mitigate/inhibit SARS-COV2. Binding of these phytochemicalsto SARS-COV2 could inhibit or interfere the pathogenesis of COVID-19 thereby preventing its cellular entryand proliferation.

Veronicoside has been reported to have radical scavenging and antioxidant activities. It has also been documented to have cytotoxicity activities againstHep-2 (human larynx epidermoidcarcinoma), RD (humanrhabdomyosarcoma), andL-20B (transgenic murine cells) cell lines [72]. Severalspecies of plants containing veronicoside are being used in traditional medicine to treat influenza, respiratory diseases, hernia, cough, laryngopharyngitis, cancer, hemoptysis, and are also used as an antiscorbutic and expectorant [73].

Vernodalinandvernolidehave been reported to exhibit antiproliferativeactivities [74] against lung A549 (adenocarcinomic human alveolar basal epithelial cells), HeLa, and MDA-MB-23 (human breast cancer) celllines and induced apoptosis on HepG2 cells with G2/Mphase cell cycle arrest [75]. They have potential to be usedas lead compounds in the development of a therapeutic natural product for treatment of cancers in the lungs, breast or liver. These phytochemicals may also offer help in inhibiting the proliferative activities of SARS-COV2 in the host thereby mitigate the pathogenesis of COVID-19.

Sinisi *et al* [76] has reported vernodalol has a good activator of Nrf2. NF-E2-related factor-2 (NRF2) is a transcriptional factor that bindsto and facilitates the activation of the ARE-dependent gene. Under basal conditions, NRF2 is sequestered in the cytoplasmand its expression is maintained to be low due to constantpolyubiquitination. In response to different kinds of stress, NRF2is significantly induced

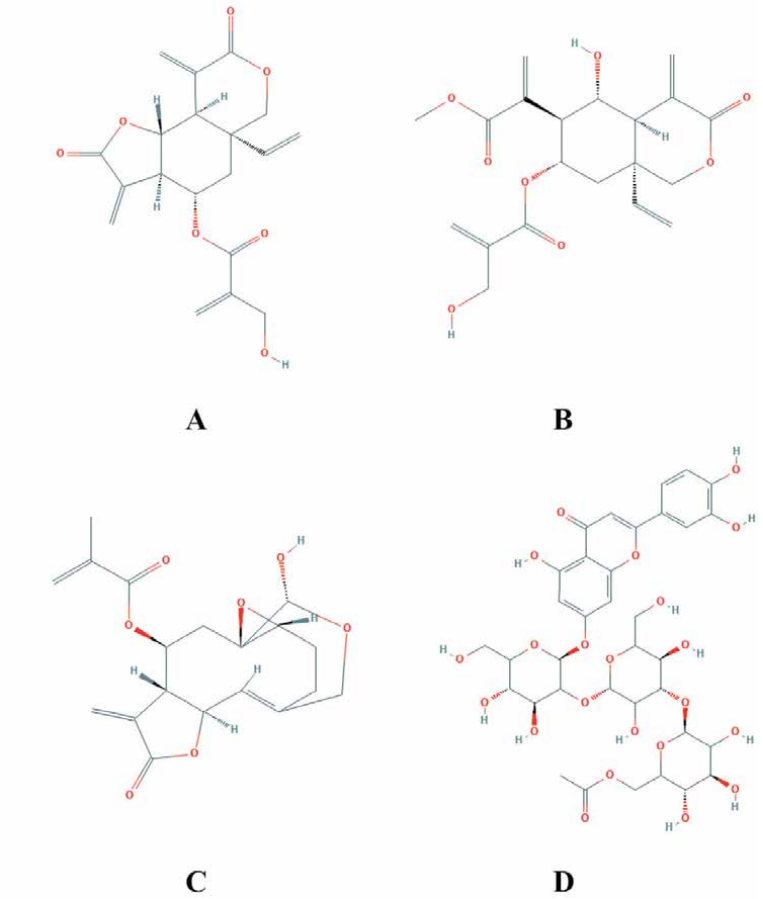

Figure 4.
2D structures of (A) Vernodalin, (B) Vernodalol, (C) Vernolide, (D) Veronicoside A.

andtranslocates into the nucleus, where it activates the antioxidant responseelement (ARE)-dependent gene expression in association with small Maf proteins and other coactivators. Thus, causing the release of phase IIcytoprotective enzymes such as γ-glutamylcysteine ligase (γ-GCS), NAD[P]H:quinone oxidoreductase-1 (NQO1), heme oxygenase-1 (HO-1), and glutathioneS-transferase (GST) which protect the cells against the attack of the stress. Since oxidative stress has been reported as one of the features of COVID-19, vernodalol can help to extenuate it by activation of NRF2.

Nuclear Factor kappa-light-chain-enhancer of activated B-cells (NF-kB) pathway has been implicated in the mode of actions of SARS-COV2 [77, 78] leading to a cytokine profile resembling secondary haemophagocyticlymphohistiocytosis (sHLH) with a hyperinflammatory syndrome characterized by a fulminant and severe hypercytokinaemia with multiorgan failure. This is characterized by increased tumor necrosis factor-α, interleukin (IL)-2, IL-7, interferon-γ inducible protein 10, granulocyte-colony stimulating factor, macrophage inflammatory protein 1-α, and monocyte chemoattractant protein 1 [79]. However, vernolide and vernodalol have been documented to show marked inhibitory activity onSTAT3/NF-κB [76]. Therefore, vernolide and vernodalol could protect against COVID-19-induced multiorgan failure by suppressing the hyperinflammatory syndrome via inhibition of NF-kB.

3.4 Resveratrol

Resveratrol (3,5,4′-trihydroxystilbene) is a naturally occurring lipophilic and phenolic phytochemical found abundantly in edible plants and easily cross the plasma membrane after oral absorption [80–82]. it is a polyphenolic phytoalexin which comprises two aromatic rings linked by a styrene double bond which permit its trans- and cis-isomers formation (**Figure 5**) [83, 84]. Resveratrol has been reported as a possible reason accountable for the French paradox [85, 86], a phenomenon described by an epidemiological study that the French population displayed a comparatively low rate of coronary heart disease, in spite of their high consumption of saturated fat diet [87, 88]. A number of preclinical studies proposes that resveratrol has the capability to influence a variety of human diseases, this is due to its cardioprotective [89, 90] antiviral [91, 92], antiapoptotic [93, 94], anti-inflammatory [95, 96] antidiabetic [97, 98], and antioxidative [97, 99] properties.

Evidences from experimental studies has established the neuroprotective properties of resveratrol which may be beneficial in combating neurological disorders showed in COVID-19 patients. Resveratrol enhances enzymes that are responsible in stress response, for instance quinone reductase 2 (QR2), a cytosolic enzyme which influences the release of destructive activated quinone and ROS, thus, exhibiting a pivotal role in the cellular response [100]. Previous report has showed that QR2 is overproduced in the hippocampus of rat's brain in a model of learning deficits. Hippocampus is a brain region which is seriously affected in Alzheimer disease and it is primarily responsible for memory and learning. This indicates that the overproduction of this enzyme initiates memory impairments [101]. Similarly, neuroprotective effect of resveratrol has been documented to includes inhibition of microglia-mediated neuroinflammation [102]. Resveratrol has been demonstrated to inhibit the activation of NF-κB signaling pathways and mitogen-activated protein kinases (MAPKs) in lipopolysaccharides-induced dopaminergic neuronal death [102].

Activation of microglia is the hallmark of neuroinflammation and play a critical role in the pathogenesis of neurological diseases [103, 104]. Microglia is the neuronal immune cells that perform a vital role in the homeostasis in the central nervous system, and act as the first line of defense during cellular assaults, oxidative damage or progression of neurological diseases in the brain [105]. During microglial activation (microgliosis), different kinds of proinflammatory markers such as chemokines, prostaglandins, reactive nitrogen species, and cytokines are release. The overproduction and accumulation of these proinflammatory factors leads to

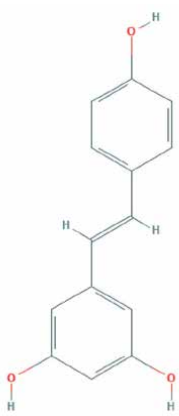

Figure 5.
2D structure of resveratrol.

damage of the neuronal cells and ultimately cause release of soluble factors and debris [106]. Many experimental studies have demonstrated the neuroprotective ability of resveratrol to inhibit the activation microglia [107–109]. Resveratrol has been reported to suppress upsurge expression of IL-1β, nitric oxide and TNFα that accompanied activation of microglia which mediate phosphorylation of p38 and NF-κB signaling [109, 110]. Resveratrol inhibited secretion of TNFα, IL-1β and reactive nitrogen species, and activation of microglia in the ischemic cortex [111].

Anti-covid-19 potentials of resveratrol has been reported in an *in-silico* study designed for drug development targeting SARS-CoV-2 Spike Protein of COVID-19 [66]. The study reported that resveratrol displayed a strong binding ability with the S2 domain of SARS-CoV-2spike protein. This spike glycoprotein, located on the surface of the virus (SARS-CoV-2), is a class I fusion protein which enhance the initial attachment of the virus with ACE2 receptor and itsconsecutive fusion with the host cells [112]. The ability of resveratrol to bind to this spike protein indicates that resveratrol may inhibit or alter the mechanism by which the virus gain entrance into its host. Furthermore, since resveratrol has been reported to modulate phosphoinositide3-kinase (PI3-k), NF-κB signaling and mitogen-activated protein kinases pathways whose end products release cytokines; It may provide beneficial effects in COVID-19 via these pathways to inhibit the over-secretion of inflammatory cytokines which resulted to cytokine storm syndromes that accelerate lungs damage and multiorgan failure is related to COVID-19.

3.5 Quercetin

Quercetin, 3,3′,4′5,7-pentahydroxyflavone (**Figure 6**), is a broadly disseminated plant polyphenol, found as conjugates with residualsugars (quercetin glycosides) in many grains, fruits, seeds, leaves, and vegetables (capers, onions, berries, and apples) [113]. The highest levels of quercetin among vegetables were found in red leaf lettuce, asparagus (*Asparagus officinalis* L.), and onions (*Allium cepa* L.), while peas, green peppers, broccoli, and tomatoes contained lower levels. Quercetin arabinoside, quercetin galactoside, and quercetin glucoside are examples of quercetin glycosides present in vegetables, fruits and other food items. They are first are deglycosylated by gut microbiota-derived betaglucosidase or lactase phlorizin hydrolaseto quercetin aglycone before passive absorption in the small intestine [114]. The quercetin aglycone produced then go through series of metabolic reactions to form methylated, sulphated, and glucuronidated metabolites, signifying participation of the phase II enzymes COMT (catechol-O-methyltransferase), SULT

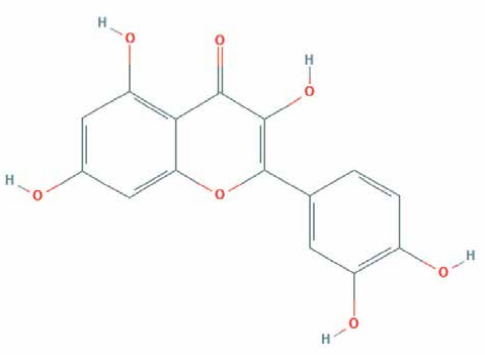

Figure 6.
2D structure of quercetin.

(sulfotransferase) and UGT (uridine 5-diphosphoglucuronosyltransferase) respectively.

Similar toother polyphenols, Studies have reported that quercetin exhibited anti-inflammatory, and immunoprotective [115], antioxidant [116], and antiviral [117], effects. It's medicinal effects on cancer, nervous system disorders, gastrointestinal tract function, infections, inflammatory processes, diabetes, and cardiovascular diseases has been documented [118–120]). Previous findings have documented the inhibitory activities of quercetin against reverse transcriptase [121], proteases [122], and polymerases [123]. Also, it has been studied in modelsof viral infection to bind to viral capsidproteins and inhibit DNA gyrase [124, 125].

During viral infection, entrance of virus into the host cell is a vital step and has been targeted as a possible point of intervention in antiviral treatments [126–128]. Quercetin has been reported to inhibit H1N1 and H3N2 influenza infection ofMDCK cells through binding to hemagglutinin proteins which is accountablefor membrane fusion during virus entry and virus-mediatedhaemolysis [129]. Furthermore, quercetin has been studied to interfere with DNA and RNA polymerases in viral infections. During adenoviruses (ADV-3,−8,−11) and herpesviruses (HSV-1, 2) infections, quercetin was reported to suppress viral DNA and RNA polymerase [123, 130, 131] and inhibit the early stage of viral replication [125, 132]. Li et al. [133] also reported antiviral activities of quercetin against HIV via its ability to suppress protease, integrase and reversetranscriptase. Quercetin upregulated IL-13 and suppressed the levels of Long Terminal Repeat (LTR) gene expression, TNF-α, p24 in HIV infection [115].

Possible antiviral effect of quercetin on many types of Coronaviruses has been described by Yi et al. [134]. Quercetin metabolite have been documented to bind to SARS-Cov 3CL protease and suppressed itsproteolytic activity [135]. Quercetin has been studied through computational studies to interact with the S2 domain of spike protein of SARS-CoV-2, thus altering the virus entry process [66]. The obstruction of virus entrance into the host cell signifies a vital approach in antiviral therapy and quercetin hinders viral membrane fusion for SARS-Cov and influenza in vitro [134].

4. Conclusion

International health security is multifaceted phenomenon that threatened the peace existence of man including emerging infectious diseases such as the current global pandemic: COVID-19. COVID-19 is a highly infectious and severe acute respiratory disorder induced by a morbific virus referred to as SARS-CoV-2. Many COVID-19 patients have displayed neurological symptoms and signs which include anosmia, acute cerebrovascular disease, acute disseminated post-infectiousencephalomyelitis, encephalitis, etc. The underlying mechanisms of pathogenic actions of SARS-CoV-2 includes activated by ORF3a, ORF3b, and ORF7a via the JNK pathway which induces lung damage; reduction of ACE2 to enhance pulmonary vascular permeability and damage the alveoli; immunosuppression; hyper-inflammation characterized by a fulminant and fatal hyper-cytokinaemia with multi-organ failure. Prevention is one of the predefined frameworks to effectively approach health security threats. To prevent the emergence IHS threats, effective measures must be initiated. Moreover, transmission of IHS threats was able to increase at an accelerating rate due to an overburdening of local health-care systems. Therefore, the preventive and/or curative measures must be affordable by the populace. Dependence on plants usage has been attributed to their affordability, effectiveness, safety, cultural preferences, and ample accessibility at all times and

when it is needed. Kolaviron, hydroxyvernolide, vernodalin, vernodalol, vernolide, and veronicoside, resveratrol, quercetin and apigenin are phytochemicals and natural products from medicinal plants with proven antiviral, antipyretic, anti-inflammatory, cytoprotective, antioxidant, immunomodulatory, and pharmacological activities that can inhibit SARS-CoV-2 and mitigate COVID-19. The phytochemicals have been documented to suppress JNK and MAPK pathways which are essential in the pathogenesis of COVID-19. Taken together, these phytochemicals could be potential drug candidates in the treatment/management of COVID-19 mediated neuropathology.

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Chapter 10

Autistic Spectrum Disorder in the Context of Pandemic by Covid-19: Caring for Children and Caregivers

José Vilelas

Abstract

The COVID-19 pandemic has brought important challenges to society and families, with repercussions on child behavior and development with special importance for children with neurodevelopmental disorders that affect and impair the child's functionality: Autism spectrum disorder. Thus, we set as objective to Identify and analyze the scientific evidence of interventions performed on children with Autism Spectrum Disorder in the context of a Covid-19 pandemic. A search was conducted in the MEDLINE, PubMed, CINHAL databases and gray literature. Children with Autism Spectrum Disorders (EAP) may become more anxious, agitated and unregulated with the change in routines to which they are subjected in this phase of the Covid 19 pandemic. Autism disorders affect communication, social interaction and behavior, usually with a tendency to be repetitive and routine, but in a scenario of pandemic and social isolation, anxiety and agitation may be more pronounced and, in more severe cases, there may be less capacity to function. It is important that the family of the child with ASD propose cooperative activities or resources that they have at home and that can be adapted. The insertion of some tasks contributes to the establishment of the ability to play independently. In it, the child gets involved independently. And so it prevents negative behaviors from occurring due to leisure and the need for attention, also favoring concentration.

Keywords: Autism spectrum disorder, children, COVID-19, parents, support

1. Introduction

Autistic spectrum disorder (ASD) is a psychiatric problem that used to be identified in childhood, between 1 and a half years and 3 years, although the initial signs sometimes appear in the first months of life. The disorder affects the level of communication, interaction with others and learning capacity, the child's adaptation to new situations and the display of stereotyped and restricted behavior. This description is reinforced by Leo Kanner, in 1943 who defines autism for the first time as a disorder in children that was manifested by the inability in the relationship and in the acceptance and adaptation to changes. They are children with physical development equal to that of other children but have great limitations in social or affective relationships, causing social isolation. In 2013, the Diagnostic

and Statistical Manual of Mental Disorders (DSM-5), aggregates as four separate previous categories: autism disorder, Asperger's syndrome, childhood disintegration disorder and generalized undefined development disorder, in a single concept of Autism [1]. Although it appeared to be a rare disease, the prevalence of ASD has steadily increased. In this context and in the face of the pandemic, children and families needed to reorganize themselves. The World Health Organization said the new coronavirus (COVID-19) was a global pandemic on March 11th, 2020 [2]. In Portugal, children were forced to stay at home with the closure of schools on 13th March. Some of them received daily tasks from their teachers, while others attended classes by videoconference. In addition, the portuguese government started broadcasting classes on television [3]. Despite the attempt to maintain access to universal education, some children who needed special education were hampered by the absence. In addition, with the adaptation of the health system, children with neurodevelopmental diseases, such as ASD, their therapies were suspended.

The child with ASD does not have a physical disability, looking perfectly normal. Therefore, understanding autism becomes more complex. Even to try to understand a child with autism it is necessary to consider their individual needs. However, these children have some genetic diseases associated with autism. This situation is due to the existence of a multifactorial genetic factor and several organic causes related to its origin. Thus, reinforcing the previous idea of children with autism spectrum disorders, the prevalence of associated diseases is about 2.5 times higher than in the general population [4]. The repercussions of the pandemic may be of more concern to children suffering from mental illness and development. Sudden changes in daily routine have consequences and can potentiate existing symptoms, increasing the risk of emotional, behavioral and relationship complications. With such special and peculiar characteristics, these children need help, specialized and continuous support in their most affected areas. In this way and due to the times in which we live due to the public health situation by Covid-19 and for reasons of quick action to prevent and minimize a major outbreak of infection and contagion, these children are more susceptible to the development of serious forms of COVID- 19 [3].

COVID-19 is caused by a coronavirus that can induce SARS in humans: SARS-CoV-2 [5] first reported in Central China in December 2019 [6]. Due to person-to-person transmission, it quickly spread across Europe [4], with northern Italy becoming the epicenter of Europe [7] and the USA [8]. As of May 1st, 2020, more than 3 million cases have been reported worldwide, affecting more than 200 countries. Currently, in October 2020, the USA has approximately 9,500,000 cases, followed by China with around 8,500,000 cases, Brazil with 6,000,000 cases, Russia with 1,700,000 cases, and Portugal in Portugal with 142,000 [9].

Since the beginning of the pandemic, most clinical and research efforts have been devoted to understanding the properties of the virus and its pathogenicity to treat the infection and prevent its spread [10].

However, according to some research evidence, the COVID-19 pandemic has revealed a worsening of the mental health of citizens in general [11]. The repercussions of the pandemic can be even more worrying in children suffering from mental illnesses and development. Sudden changes in daily routine have consequences and can potentiate existing symptoms, increasing the risk of emotional, behavioral and relationship complications [12]. The COVID-19 pandemic has brought important challenges to society and families, with repercussions on child behavior and development, the dimension of which we do not yet fully understand. The effects on children's mental health derive from several factors: concerns about the disease itself and uncertainties about contagion [13] and lethality, as well as measures taken to minimize its impacts, such as isolation and social distance [14]. In addition to the threat to the physical health of the general population, the pandemic has boosted a

plurality of psychological responses by the progressive increase in confirmed and suspected cases such as compulsory confinement at home or in health facilities, the decrease in the availability of personal protective equipment and/or the exhaustive coverage of the media capable of causing our alert and fear system to be constantly activated [14]. It is important to note that the pandemic required unprecedented measures by governments, including imposing quarantine on citizens [15].

The search for innovative approaches and the need to ensure continuity of care for children and young people with chronic health problems, should not be underestimated during the pandemic. A specific response is needed to minimize the mental suffering of children and young people who are quarantined.

Specialist Nurses in Child and Pediatric Health Nursing in partnership with Specialist Nurses in Mental Health and Psychiatric Nursing must design and develop socio-culturally appropriate programs to define strategies that facilitate the way to intervene in mental suffering and provide psychosocial support nursing care. to mitigate the adverse effects of prolonged isolation in children and young people [16].

The COVID-19 pandemic led families to adapt their lives, including social isolation and work from their parents' homes. The consequences of this confinement on mental health are still unknown [17].

Among vulnerable populations, children and young people with autism spectrum disorders are a group of special concern for the impact that the outbreak of COVID-19 may have on their well-being, as well as the specific support they may need to preserve their mental health during the pandemic [18].

Children and young people with autism spectrum disorders have problems with social communication, difficulties in maintaining social interactions and unusual patterns of repetitive behavior. These characteristics are associated with a preference for highly predictable environments, while children and young people may feel stressed, anxious or confused if unpredictable or complex changes occur [19]. The outbreak of COVID-19 has undoubtedly led to a fast-paced and rapidly changing social situation, which can increase the difficulties of children with autism spectrum disorders.

In view of the above, we intend to respond to the following objective: Identify and analyze the scientific evidence of interventions performed on children with Autism Spectrum Disorder in the context of a Covid-19 pandemic.

2. Methods

A search was conducted in the MEDLINE, PubMed, CINHAL databases, using a search strategy to identify studies published between January 2019 and December 2020, in Portuguese, English and Spanish. Studies that described interventions in children with autism spectrum disorders in the context of a pandemic by Covid-19 were included. 21 articles were selected using the PRISMA method. Gray literature and other articles researched in the Google Scholar, were also included.

3. The impact of environmental changes and disrupted routines during the COVID-19 pandemic

Children and young people with autism spectrum disorder are vulnerable to the effects of prolonged isolation or quarantine, and may have difficulties adapting to this new routine, especially since inflexibility and a great reluctance to change are hallmarks of this disorder [20]. All of these practices leading to decreased

transmission of the coronavirus (SARS-CoV-2) negatively affect children and young people with autism spectrum disorder, but also their families, including siblings. Prolonged isolation increases the risk of losing daily practical skills; in the case of children with Autism Spectrum Disorder, it can also lead to an increased risk of disruptive behaviors such as depression and anxiety, and difficulty in relationships with peers, manifested by isolation, anger and aggression [20]. It is known that physical contact and socialization are fundamental to the well-being of all human beings, but children with ASD are particularly vulnerable because harmful changes in the environment can negatively affect their social, cognitive and emotional development. Children with special educational needs may need additional support to adapt to new routines and to understand changes. The most susceptible youth may develop symptoms of anxiety, depression and, in some cases, obsessive–compulsive behaviors.

Some authors recommend that you can combat the adverse effects of isolation through [7, 20, 21]:

- Do everything possible to keep children/young people active, reprogramming their daily routines in a way that incorporates activities that can be performed at home, including occupational, motor and recreational activities (for example, self-care and personal hygiene, house cleaning, care for a pet and exercise). Using a "visual agenda" can be a great help, with the inclusion of sequences of images, drawings, or written messages that illustrate, in advance, what will happen during the day. To plan the entire week, other visual aids can be used, such as personalized calendars.

- Maintain, as far as possible, the same daily routines (for example, getting up at the same time, having breakfast, doing intellectual and physical activities, relaxing, eating, doing new tasks, leisure and dining).

- Maintain contact, by phone or computer, with teachers, with health professionals, as well as with other people who are important to them.

- Use social networks, such as Facebook or Instagram, moderately, to keep in touch with other people.

- Carry out occupational, recreational and sport activities at home, in order to maintain a similar routine that previously existed.

- Consider that the fact that the child/young person with autism spectrum disorder is in constant contact with other people during the isolation period may lead to the need for some time alone, time for themselves. In these circumstances, a space and time appropriate to their privacy needs should be promoted.

- To increase the likelihood of children/young people feeling motivated to be active, they must be involved in the planning process for their days.

In a study of 527 parents of children with autism spectrum disorder, with the aim of investigating the impact of the COVID-19 outbreak on these children, carried out in northern Italy, one of the most affected European regions, concluded that the majority of children who had 13 years old showed a decrease in autonomy and in the ability to carry out structured activities. After COVID-19, parents reported that their children had more intense (35.5%) and more frequent (41.5%) behavior problems, with about 20% having to go to health institutions [22].

During the COVID-19 pandemic, strong attention should be paid to the potential and resources existing in the communities and not to their weaknesses and vulnerabilities. In this regard, efforts should be made to create or maintain safe and protected environments for children/young people with autism spectrum disorders. One of the measures is the use of masks; DGS recommends its use from the age of 10 [23]. These children may have difficulty accepting and/or using masks appropriately and continuously, which are a fundamental health and hygiene rule for outings and activities carried out outside the home. To get used to its use, it may be useful to adopt a gradual approach to the use of these articles, progressively increasing the time of use and resorting to positive and motivating reinforcements for their use. As for the masks, if a person does not accept to use anything strange on the face, it is suggested to introduce the use of it in regular activities, applying it gently over the nose and mouth without squeezing. When the child/young person accepts its use, their behavior should be reinforced, for example, praising. As time goes by and the child/young person feels more familiar with the use of the mask, it can adjust to the proper position of total protection of the nose and mouth. It is recommended that the intention to use the mask be repeated several times a day, explaining in advance the need for its use (for example, communicating that it is a new way of preparing to leave) or creating a situation in which you remember when it is necessary to wear the mask outside the home. The forms of communication should be adjusted as closely as possible to the person's support needs (pictograms, objectives, verbal information, ...). It is also essential that professionals and teachers use their own mask to show the child/youth how it should be used, acting as a reference and motivating element [24]. As for hand washing and respiratory etiquette, the child/young person with autism spectrum disorder should be advised on specific actions and behaviors for controlling the pandemic. Visual support can be used to complement the parents' explanations. It is important to develop a routine with the child/young person and make hand washing a priority. Parents need to be aware that this activity will take some time to make it an habit, but children/young people learn when taught by example. This measure should be considered a family activity and the parents' participation in this routine is very important. The norm of hand washing can be difficult for children/young people with autism spectrum disorder, because the process generates some confusion, either due to the increase in the time it takes, as the steps involved in the technique, result in increased stress in children/young people and the desire to avoid the process [25].

4. Caregivers of children with autism spectrum disorder in the context of COVID-19

As for the family of the child/young person with autism spectrum disorder in the context of COVID-19, parental stress is greater in parents of children/young people with autism spectrum disorder when compared to parents with children who show typical development [26].

In a study by Colizzi, Sironi and Antonini in 2020 it was concluded that parents' stress was still related to the risk of job loss, economic uncertainty, lack of adequate health resources, and increased time to access intervention programs could impair the ability of the caregiver or parents to deal with the child/young person in the context of Pandemic [22].

Parents face several challenges generated by COVID-19. One is the transitions in lifestyle changes caused by social isolation and the adoption of new routines that the child/young person with autism spectrum disorder was not used to. These transitions and changes in routine can be very disturbing, aggravating the behavior

of children/young people, such as the increased frequency of crying and aggressive behaviors such as reactive strategies and even the refusal to transition [27]. While some parents reported that their children adapted without major problems, thinking of this period of the pandemic as a break from school or vacation, other parents reported that their children were uncomfortable with the transition. Other parents also reported that their children immediately felt the effects of the interruption in their routine as an impossibility to go to school, to see teachers and friends. The mood and behavior of children/young people changed immediately, showing anger, confusion, sadness and exhibiting more hyperactivity [26].

While we can predict that parents' stress will be greater during the pandemic, we also recognize that there are ways for parents to combat and deal positively with daily stressors. Pottie and Ingram in 2008, identified coping responses that can elevate the parents' mood: social support, positive restraint, focus on the problem, emotional regulation and making a commitment. Simultaneously, the authors identified four coping responses that reduced positive mood: escape, guilt, inhibition and lack of support [28].

In Italy, parents, due to the suspension of educational and rehabilitation services during confinement caused by the pandemic and the consequent isolation, expressed having experienced some challenging situations, namely problems with Internet connection (19%), ignorance about the use of the web (17%) and difficulties in following the instructions given by health professionals (22%). The emotional burden faced by parents during the pandemic involved mainly the fear of being alone and caring for children with special health needs without the support of an expert [29].

In the study by Parenteau, Bent and Hossain in 2020, parents reported positive and negative techniques for dealing with COVID-19. To face the transitions that the pandemic caused in their family routines in a healthy way, parents resorted to: exercise (walking, cycling, yoga), meditation, prayer, reading the newspaper, participating in virtual groups to connect with the community, friends and therapists. For families who had more than one caregiver at home, some parents suggested the idea of alternating between rest intervals so as not to get too overwhelmed [26].

Finding positive ways to cope with illness and isolation can be beneficial for parents and children/young people with autism spectrum disorder.

With the challenges that arise for children/young people with autism spectrum disorder and that they have online support/classes, many families have decided to concentrate their efforts to work on the skills of daily living. With more time at home, families can start or deepen the development of self-care activities in children/young people, be present to reinforce and clarify doubts and provide reminders [27].

In an observational, cross-sectional and analytical study carried out in Portugal by Amorim, Catarino and Miragaia in 2020 to a total of 99 parents of school-age children, two groups were formed: one of parents of children with ASD and the other of parents of children without neurodevelopmental problems. The average age of the children participating in the study was 10.75 ± 3.13 years and 68.7% male. Most fathers had university degrees (62.9% of mothers and 61.1% of fathers). Emotional dysregulation was also a common problem experienced by children with ASD and was associated with problems of inadequate adaptation. In addition, anxiety and depression were the most prevalent affective disorders in these children. It is also known that school demands and social commitment are stressors for children with ASD. So you can imagine that staying at home during quarantine, away from these challenges, can comfort these children. However, in that period, these children had to live with a great stressor for them: the change of routines [30].

For parents with children/young people with ASD, quarantine means not only serving as their child's teacher, but also serving as a special educator, social skills trainer, speech therapist or behavioral/mental therapist, sometimes with little support from professionals [31]. Children with ASD generally require more intensive services and support than children with typical development, which can intensify parents' tension during the pandemic.

The pandemic is changing several factors closely associated with person-environment suitability. These factors include balancing the needs of children/young people with autism for routine and environmental predictability versus the unpredictability associated with the pandemic; learning or working styles of autistic individuals versus opportunities available at this time; and the living environment or activity schedules among family members.

As we have seen, changes in daily routines and restrictions on the regular environment interrupt a number of domains as physical health, mental health and family factors. For example, sleep dysregulation, reduced access to specific foods will impact selective feeding by children/young people with ASD, which may lead to reduced food intake, poor nutrition or worsening problems of elimination and constipation. Restricted access to regular programming, activities and preferred locations contributes to the decrease in physical activity, which is already a concern among children/youth/family, as well as higher rates of obesity [32].

Maintaining typical routines as it has already been demonstrated is impossible during the COVID-19 pandemic. However, the impact of changes in routines can be mitigated by the joint creation and implementation of alternative routines, incorporating regular bedtime and morning hours, attention to sensory stimulation, adequate but limited exposure to the media, regulated times of watching TV and game viewing and attention to regular hygiene, food and water intake, daily exercise and sleep. Maintaining social networks (even if the only viable option to do this is online) is essential for children/young people/autistic and their families [33].

COVID-19 has become a pandemic and many governments have declared restrictive measures to prevent its spread. For parents and children, staying at home is one of those measures. In this situation, the treatment of young children with special needs, such as autism can be a challenge for families and caregivers.

Autism is increasingly among us and close to all of us; at home, in schools, in families, in society and in the world in general. What is extraordinary about the times in which we live due to the public health situation by Covid-19 and because of quick action to prevent and minimize a major outbreak of infection and contagion, leads us to rethink the school, the reality, our actions, our priorities, the different ways of acting in order to minimize a worsening at the psycho-emotional level and behavioral responses in children and young people and other population that are part of a group, which is no longer as a minority, as was initially believed by the statistical data, for the researches presented of the significant increase of children with Autism Spectrum Disorder, in the current world.

Families with children with autism spectrum disorder face a number of challenges with the rise of the COVID-19 pandemic, including the explanation of the pandemic and the need to ensure and monitor safety measures for children in an understandable way, building a structure at home to minimize social isolation. These children usually have to undergo specific interventions by health professionals. However, at this moment, due to contention measures, both families and children with autism are limited in face-to-face professional support.

These routine changes can cause them profound suffering. For this reason, all of us (parents, nurses, other health professionals and researchers) must be united and quickly establish new methods and functional routines to enable children with autism spectrum disorder to be safe and at peace.

5. Maintain the safety of children with autism spectrum disorder in a pandemic situation

Currently, we all live in a time of uncertainty related to the covid-19 pandemic situation. These are particularly challenging times for all of us and for children with autism spectrum disorders, this is no exception. Children with characteristics of the autism spectrum have greater difficulty in dealing with uncertainty and changes, as previously mentioned. In this phase in which your routines have changed profoundly and in which therapies, support and consultations have been suspended or are taking place in a different way than usual, it will be important to pay special attention and respond to your needs.

Thus, the pandemic caused by the new coronavirus poses numerous challenges in guaranteeing the fundamental rights of children. In order to prevent the overload of health systems and to protect those who are most vulnerable, States must establish policies to combat Covid-19 in an agile way to minimize the contagion as much as possible, a fact that is unfeasible based on the general population, but also based on the peculiarities and rights of children with autism spectrum disorder.

Some of these measures can be adapted to reconcile the fight against coronavirus with the rights of children. The best way to fight the disease has been through preventive actions, following some control and protection measures such as hand washing and hygiene, wearing masks and social isolation as a way to prevent the spread of the disease. These measures are currently widespread [34].

The COVID-19 pandemic has generated a series of changes in the lives of families and society in general, which may impact not only on physical and biological health, but also on mental health. As an example, social isolation and other recommendations, necessary for the prevention and reduction of disease transmission, end up significantly modifying daily life, which may result in tension, fear, stress and anxiety, both for caregivers and children with TEA [35].

For this specific population, it may be difficult to understand the pandemic scenario and all the ramifications resulting from COVID-19, especially when it comes to young children and/or those who have intellectual and sensory disabilities concomitant to the condition [36].

It is important to note that autism is not a risk factor for COVID-19. Thus, children with ASD have symptoms similar to those of other young people without the disorder. However, the characteristics of autism can create difficulties in adopting preventive measures. An example is changes in sensory functions. An autistic child may have a great interest in the smell, taste and texture of objects, and it is common to observe him passing his hand over everything and bringing the utensils to his mouth. This practice increases the possibility of contamination and parents must be aware of hygiene issues, keeping the environments ventilated and avoiding sharing objects [34].

Thus, children and adolescents with ASD can be considered more vulnerable to COVID19, not because they are susceptible to the complications of the virus, but due to the characteristics of the clinical picture that weaken the understanding of the pandemic scenario as well as the control and protection measures, exposing them to greater risks of contamination. In this sense, considering the particularities present in this picture, all the existing complexity and the current pandemic scenario, it is essential to reflect on the impacts of this global health crisis on the daily lives of this population, since they naturally already experience very difficult and challenging situations.

The control and protection measures adopted by countries to contain the spread of the virus and contagion of the population need to be carefully managed to avoid

the intensification of psychological distress in families and behavioral difficulties in children with ASD. In this direction, the text presents ten tips that aim to help families deal with these children during the pandemic, such as explaining children about what the disease is, organizing daily activities, having time for play activities, using games for teaching, online therapy, among others [18]. Another author says that the process of social isolation and its implications in the lives of children with ASD, depend on personal, contextual, political aspects and mainly on the current health systems. Children with autism may show strong resistance to change. The closure of kindergartens, schools and other facilities that children with autism attend daily can create additional tension. In addition, the author points out that the current moment has mobilized the community to develop solidarity actions and to deal with the invisibilities of the most vulnerable populations [36].

Safety measures must be enforced by parents. These are the example for the child with ASD. This technique is called live modeling. If the child is interested in videos, this is a resource that can also be used. Hand washing as we have seen is extremely important and therefore parents should wash their hands as recommended by specialists and record each step of this activity. The process list is a guide to start learning the child with ASD. Recording the video of the child performing the process can be a way to improve their learning. The child's help should be gradual and little by little it should promote the child's autonomy. It is very important to provide these children with compensation for the goals achieved, this motivates the child to do more and better [37].

It is reinforced that adopting these measures is fundamental not only for the protection of these individuals, but also of the family and community. However, due to the difficulty of understanding and, in some cases, the presence of important sensory issues, some children and adolescents with autism will not be able to use the mask and/or remain in social isolation for a long time.

In Portugal, people with intellectual, developmental or autism spectrum, with a degree of disability equal to or greater than 60%, as evidenced by a multi-use certificate, are exempt from the use of a mask or visor in places that generally require it [37].

In addition to these sensory challenges, masks also create new social communication challenges. Autism spectrum disorder can include impaired visual perception skills, making the chances of accurately reading another person's facial expression under a mask, from a socially appropriate distance, more difficult than normal. In addition, when seeing another person's face while they are wearing a face mask, the eyes are the main area of the face that is visible. Individuals with ASD often have difficulty making eye contact, adding yet another obstacle for them in the realm of social communication. These factors can cause communication problems and frustration. As masks drown out voices, verbal communication also becomes more difficult. Fortunately, there are several strategies that can make using a face mask more bearable.

As we have seen, the impact of the pandemic can be even more worrisome in children suffering from autism spectrum disorders. Sudden changes in daily routine have consequences and can potentiate existing symptoms, increasing the risk of emotional, behavioral and relationship complications.

Children with special health needs may need additional support to adapt to new routines and to understand changes.

In the future, with the opening of schools and the return to routine, it is essential to create a balance between the public health measures necessary to minimize the impact of the pandemic and the gradual resumption of interpersonal relationships and school, professional and leisure activities, maintaining the child safety.

6. Conclusions

The child with ASD in Covid-19 is experiencing an extremely difficult situation with their families. Everything that we as health professionals believe is important and emerging to be worked towards in order to better adapt their functionality, we now have enormous restrictions in enhancing their capabilities, in removing them from rigid patterns of behavior, stereotypes, rituals and isolation. It is not easy, however it is important not to forget, that even though it is not ideal, it is possible to work with them, through strengthening the parental potential, enabling parents for the tasks, promoting cooperation between family, school and professionals, by digital platforms, and by the technologies and social networks to which we have access, or even by telephone and by mail, to get closer, to guide parents and together, we reduced some of the inherent difficulties, making it possible to be close, thus continuing to develop activities and tasks that, if they were in a school context, they would possibly be carrying out, so as not to lose the essential routines, such as, for example, parents establishing waking times, cleaning times, structured task times, promoting playful and relationship moments and broader, if the nuclear family allows it, without calling into question public health guidelines. The pandemic risks widening inequalities for children, particularly in vulnerable groups. As such, this presents an opportunity to redress the imbalance and support children and families' wellbeing as we emerge into the 'new normal' world.

As we have seen, the impact of the pandemic can be even more worrisome in children suffering from autism spectrum disorders. Sudden changes in daily routine have consequences and can potentiate existing symptoms, increasing the risk of emotional, behavioral and relationship complications.

Children with special health needs may need additional support to adapt to new routines and to understand changes.

In the future, with the opening of schools and the return to routine, it is essential to create a balance between the public health measures necessary to minimize the impact of the pandemic and the gradual resumption of interpersonal relationships and school, professional and leisure activities, maintaining the child safely.

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Chapter 11

COVID-19 Pandemic and Mental Health of Nurses: Impact on International Health Security

Gonca Ustun

Abstract

COVID-19 was first detected in Wuhan, China, in December 2019 and spread rapidly in many other countries. This situation, defined now as a pandemic, has turned into a worldwide public health problem that threatens health security, especially that of healthcare professionals. Nurses, particularly those at the forefront of healthcare and directly involved in COVID-19 patient care, have been affected not only physically but also mentally. Because nurses have longer communication and interaction times with patients, they are more concerned about becoming infected or infecting others. Nurses have the highest level of occupational stress compared to other groups and are accordingly subjected to anxiety and depression. For many reasons such as intense working hours, working in a shift system, an insufficient number of personnel, severe conditions of the unit, being in constant contact with patients and their relatives and showing intense empathy for them, nurses experience primary and secondary traumatic stress, job burnout, compassion fatigue, and moral injuries. For this reason, conducting appropriate prevention activities and planning prevention strategies for future pandemic situations is important to support nurses psychologically and to protect their mental health.

Keywords: COVID-19, health security, mental health, mental problems, nurse, pandemic, psychological empowerment, resilience

1. Introduction

Coronavirus disease (COVID-19) is an infectious respiratory tract infection with common symptoms including high fever, dry cough, and fatigue; it is caused by a newly discovered coronavirus (SARS-CoV-2). The novel coronavirus was first detected in Wuhan, China's Hubei province in December 2019 and spread rapidly in China, and then, worldwide. The World Health Organization (WHO) declared the COVID-19 epidemic a pandemic on March 11, 2020 [1]. A total of 70,829,855 confirmed cases of COVID-19 and 1,605,091 deaths had been reported worldwide as of 10:25 AM, December 14, 2020, with cases continuing to increase [2].

The COVID-19 epidemic is unprecedented in modern times and has become a major public health problem, not only for China but worldwide [3–6]. The increasing number of cases posed a major challenge to hospitals treating individuals with

COVID-19 symptoms and has resulted in a serious shortage of medical supplies and health personnel, especially in intensive care units [7–9]. During the COVID-19 pandemic, healthcare workers were infected and forced to fight against a deadly virus while lacking personal protective equipment [9–11]. The International Council of Nurses (ICN) reported that approximately 10% of worldwide cases are healthcare workers and that more than 20,000 healthcare workers were infected. It was reported that the epidemic cost the lives of at least 1,500 nurses and many other healthcare workers [12].

This fatal situation has caused all healthcare professionals, especially nurses who work directly with sick or quarantined individuals, to face serious physical and psychological problems. Working with protective equipment that restricts breathing and movement makes it difficult to meet basic physiological needs such as eating, drinking, going to the toilet, and sleeping [13–15]. In addition, conditions such as limited hospital resources, long working hours, physical fatigue, infection risk, lack of protective equipment, disruption of sleep patterns, loneliness, and being separated from their families cause nurses' mental health also to be at risk [4, 8, 16]. All these stressors cause noticeable psychological changes for nurses working closely with patients [6, 8, 15]. It has been reported that nurses experience major mental problems such as primary and secondary traumatic stress, job burnout, compassion fatigue, and moral injury during this process [4, 17–26].

Although it is difficult to provide both safe physical environmental conditions and mental security, having a safe work environment is the right of every health worker. Nevertheless, although physical security measures are prioritized for nurses serving in difficult conditions, mental security measures are either insufficient or ignored completely, despite nurses' mental health being very important for controlling an epidemic [15, 16, 27]. For this reason, conducting appropriate prevention activities and planning prevention strategies for future pandemic situations is important to support nurses psychologically and to protect their mental health. This study discusses the mental problems of nurses caring for COVID-19 patients and psychological empowerment studies for nurses; it will make an important contribution to the health security of nurses.

2. Methods

This chapter deals with the mental problems faced by nurses during the COVID-19 pandemic at an international level. Academic literature and other public databases for the year 2020, when COVID-19 cases started to appear and studies on the subject were carried out all over the world, were examined. Articles published in electronic databases including CINAHL, Cochrane Library, PubMed, Web of Science, Science Direct and Google Scholar, Scopus and related internet websites (WHO, ICN and APA) were used. Firstly, a comprehensive search of peer-reviewed journals were completed based on a wide range of key terms including "COVID-19", "health security", "mental health", "mental problems", "nurse", "pandemic", "psychological empowerment", "psychological resilience", "primary traumatic stress", "secondary traumatic stress", "burnout", "compassion fatigue", and "moral injury".

The literature search was carried out between November–December 2020 and 140 academic studies were reached as a result of the searching. The data were obtained from 53 international papers and 3 different websites (WHO, ICN and APA) that address the mental problems of COVID-19 nurses and contain prevention and strengthening studies on this issue that threatens international health

safety were included in the study. In line with the results obtained from the studies, the mental problems experienced by COVID-19 nurses were grouped under five headings, and some suggestions about protect and strengthen mental health at international level were presented.

3. Nursing in the COVID-19 pandemic

Nurses are anonymous heroes, playing critical roles in disease prevention and diagnosis, and providing primary health care services including prevention, treatment, and rehabilitation [28]. They have been and continue to be at the forefront of combating infectious diseases such as COVID-19, leading the way in developing best practices in disease management and clinical security [13, 29, 30]. However, despite this obvious situation, for centuries nurses have found themselves trying to explain the importance of their profession, the reason for its existence, and its indispensability.

The World Health Assembly has announced the year 2020 as the "International Year of Nurses and Midwives" [31]. Because of the COVID-19 pandemic, the nursing profession is on the world agenda, just as it suits the name of the year, and nurses have started to show that they are "A Pioneering Voice in World Health" [32]. This year, which created a global awareness for nurses, once again emphasized the importance of necessary health security measures in harmony with the changing roles of nurses.

3.1 Changing roles of nurses in the pandemic

The high prevalence, highly contagious nature, and associated morbidity and mortality rates of COVID-19 in the general population of many countries create an unprecedented demand for health and social care services worldwide [13, 14]. This demand has transformed the role of nurses beyond patient care, which is regarded as a security boat that integrates different professions and communities to reduce the risk of the COVID-19 pandemic and ensure effective communication [13]. The addition of new ways of nursing, which is already demanding in terms of attention and care, has made working in the COVID-19 environment extremely stressful. Nurses try to adapt to new protocols to the "new normal", beyond just experiencing an increase in the intensity of their work in this process. Concomitantly, due to the increasing number of patients, the need for more nurses in clinics, emergency rooms and intensive care units where care is provided for COVID-19, and the interruption of work due to the infection of health personnel in this process, has constituted an extra workload for all healthcare professionals [14].

Nurses who work at maximum capacity also experience various problems such as deciding which critically ill patients may be allocated to the intensive care unit and which patients can be provided with a respiratory device; they accompany the end-of-life journey of both the patient and the family in the face of deterioration faster than they are accustomed to [33–35]. At the same time, because of isolation precautions and rules, patient relatives are not able to be with the patients, which results in nurses' providing the necessary support and establishing remote communication between the patient and relatives, giving nurses additional responsibilities [36]. Protective measures such as masks, visors, and social distancing applied in this process make interaction difficult and patients, and nurses suffer from communication problems such as not being able to see each other's faces or hear what they are saying [5, 14].

In addition, factors such as limited resources of hospitals, lack of protective equipment, longer shifts, increased workload, new tasks and procedures, exposure to COVID-19 and risk of transmitting the infection, inadequate access to COVID-19 testing if symptoms develop, uncertainty as to whether their organization will support their needs if infection develops, support for additional needs (such as food, accommodation, transportation) as working hours increase, obligation to work in new units (such as those who are not intensive care nurses to serve in the intensive care unit), dilemmas with teammates, prioritizing care for specific patients, watching patients die alone, different pathologies seen in addition to COVID-19, neglect of personal and family needs, social distancing from loved ones, inadequate communication, and exposure to insufficient information make nurses' compliance even more difficult [8, 11, 37]. Nurses experience many complications at the same time in this process, such as inadequacy, uncertainty, fear, and change, and not only need physical but also mental support.

3.2 International health security of nurses in the pandemic

When determining innovative ways to provide an adequate workforce during the pandemic period, it is important that everything applied is safe for staff and patients [30]. The WHO called on governments and healthcare leaders to address persistent threats to the health and security of healthcare workers and patients in the COVID-19 pandemic and emphasized that no country, hospital, or clinic can keep their patients safe unless they first keep healthcare workers safe [38]. In this regard, the importance of mental security as well as physical security has been emphasized. The psychological effects of the infection itself should not be neglected for healthcare professionals.

While the COVID-19 crisis continues, situations such as the dismissal of nurses in some areas, reducing workforce and granting leaves, calling back retired nurses for help due to the growing demand for nursing services to combat the COVID-19 outbreak, or suspension of leave has made health care even more difficult [13, 35, 39]. Most of the nurses were not allowed to go home due to lack of staff: to meet their staffing needs many organizations have asked healthcare professionals treating COVID-19 patients to continue working until they show symptoms of the disease [13].

Although these different regulations made by governments are important for the protection of groups and society at risk of COVID-19 infection, it supports the stigmatization and exclusion of nurses [24, 40, 41]. Being able to report difficulties without worrying about being stigmatized or blamed is very important for both nurses and others to dare seek help [5, 14, 42]. Nurses' mental problems should be detected early, and their access to mental health services should be provided for the security of the entire society, not just nurses or healthcare professionals [35].

4. Mental problems of COVID-19 nurses

Nurses are not only exposed to physical risks, but have also faced concerns over the impact of COVID-19 on their own lives and families, as well as long working hours and work environment security [13, 19]. The susceptibility to psychiatric disorders has increased, especially in nurses who directly care for infectious patients in critical and intensive care units [7, 30]. Studies conducted in centers and units providing COVID-19 care in different parts of the world have reported that the mental health of nurses has been significantly affected and that nurses experience psychological problems [6, 15, 43–45].

It has been determined that the most common psychological effects in nurses were fear, despair, anxiety, depression, and post-traumatic stress symptoms [19–21, 37, 46, 47]. Worldwide studies on mental problems that occur as a cause or consequence of these psychiatric disorders showed that nurses are facing primary and secondary traumatic stress, job burnout, compassion fatigue and moral injury [4, 17–26]. To better understand the mental problems seen in nurses in the pandemic it is necessary to define these concepts and carry out studies within the scope of combating these problems.

4.1 Primary traumatic stress

Primary (direct) traumatic stress, stress that is directly perceived by the individual, is a threat to health security, along with time constraints, patient expectations, lack of social support, and inadequate coping [25]. Among the factors that directly lead to stress for nurses in the COVID-19 pandemic are staff shortages, lack of personal protective equipment, being in an unfamiliar environment or care system, and concerns about lack of organizational support. In addition, the psychological conflict between health care workers' responsibility to care for patients and their behavior to protect themselves from a potentially deadly virus can also lead to stress [14].

Nurses who are at bedside 24 hours a day, seven days a week, have the highest occupational stress compared to other groups [14]. Studies on COVID-19 show that work-related stress is especially prominent in nurses [4, 20, 21, 24]. Work-related stress in nurses leads to decreased physical function, emotional exhaustion, desensitization, decreased personal success, low job satisfaction, and personnel transfer [25]. Although nurses seem to function in this process, they also experience accompanying physical and psychological symptoms due to background long-term stress exposure.

4.2 Secondary traumatic stress

Secondary (indirect) traumatic stress, defined as the stress of helping people who are in pain or who were traumatized and recovered, develops without direct sensory traces because of long-term exposure of the helping individual to the traumatic event and the continuous repetition of an event with unpleasant details [25, 48]. The more traumatic the event and the greater the contact with the patient, the greater the risk of secondary traumatic stress formation [24]. It emerges due to risk factors such as the unpredictability and increased infection rate during the COVID-19 emergency, repeated exposure to trauma, and witnessing patients suffering. In addition, a more intense empathic approach to patients that causes greater vulnerability of healthcare workers also leads to secondary traumatic stress [10, 24, 40].

Secondary traumatic stress, which is considered an occupational hazard, is very common in nurses, especially those working in emergency, oncology, psychiatry, and pediatrics departments [25]. Healthcare workers who directly encountered COVID-19 patients intensive care units and in critical centers reserved for COVID-19, experienced higher secondary traumatic stress than others. [17, 18, 25]. Secondary trauma has been studied more than primary trauma. Its prevalence brings with it other serious problems such as anorexia, insomnia, fatigue, anger, apathy, unwillingness, hopelessness and depression.

4.3 Job burnout

Burnout is a psychological syndrome characterized by emotional exhaustion associated with prolonged exposure to occupational stress (depletion of emotional

resources), desensitization (developing cynical attitudes about patients), and decreased professional success (a sense of negative self-evaluation) [18, 49, 50]. The deadly and uncontrollable nature of COVID-19 with currently no known effective cure and the relatively high infection and mortality rate among healthcare workers trigger feelings of anxiety and stress. Problems such as social stigma, lack of personal protective equipment, and heavy workload pave the way for burnout in healthcare workers [49].

Recent studies report that nurses caring for COVID-19 patients experience more burnout than others [18, 19, 23, 25]. Burnout can have serious consequences for patients, healthcare professionals, and institutions. This not only results in poor physical and mental health consequences, lack of motivation, absenteeism, and low morale, but also in deterioration of the quality of care provided by the staff affected, decrease in patients' satisfaction levels, an increase in health-related infections, and high mortality among patients [18, 49].

4.4 Compassion fatigue

Compassion fatigue is seen as contextually interchangeable with secondary traumatic stress; it is generally known as a combination of secondary traumatic stress and burnout symptoms [8]. Compassion fatigue is a job-related stress response that is considered a "maintenance cost" in healthcare workers. It is closely related to professional satisfaction, personnel transfer rate, and nursing quality [7, 25]. During pandemics such as COVID-19, intensive care nurses witness patient suffering and death more frequently than before, and in addition are responsible for decisions regarding allocation and use of resources, which is why they carry a high risk of compassion fatigue [7].

Studies report that among all healthcare professionals, nurses who provide uninterrupted care to patients and who show an approach with empathy are at risk for compassion fatigue and that their health status, job performance, and professional satisfaction levels are affected [8, 25]. It was seen that nurses, who have been in contact and interacting with COVID-19 patients for a long time, also experience compassion fatigue [19, 23, 25]. Nurses experiencing compassion fatigue may use harmful coping methods such as absenteeism, leaving work, despondency, social isolation, alcohol-substance use, and overeating [7].

4.5 Moral injury

Moral injury is a concept used to describe psychological distress caused by acts that violate a person's ethical or moral rules or acts that lack said rules [8, 51]. The pandemic is a difficult time during which healthcare professionals experience dilemmas in the triage of COVID-19 patients, for instance where they must decide which of two patients will get the emergency room's only remaining ventilator. As a result of this decision the nurse may experience feelings such as guilt, shame, or remorse, which will negatively affect all aspects of life. Although the health worker tells himself/herself that he/she is following the protocol and doing his/her best, he/she will think that he/she has violated moral values [14, 52].

All healthcare workers and all frontline workers such as emergency first responders are subject to moral injury during this time [51, 52]. However, the measurement tools and studies to diagnose the painful and powerful internal struggles experienced by healthcare workers during the COVID-19 pandemic and the resulting moral injury are insufficient [52, 53], although some scales have been developed to describe this process [22, 26]. Moral injury negatively affects ability to

function and performance; it can also lead to depression and post-traumatic stress disorder [5, 52]. In addition, nurses are prone to quit their jobs if they feel that they are not sufficiently supported by organizations and the government [14].

5. Protecting and strengthening the mental health of COVID-19 nurses

The topic of focusing on the mental health of health professionals has been brought to the agenda during the COVID-19 pandemic [54]. It is necessary to have spiritual endurance to overcome this unprecedented situation: nurses have the need be supported by the employer, the team, and professional and community resources. During this time, the applause given to healthcare professionals every day of the week across Europe has been a morale boost for healthcare professionals. However, this is not a satisfactory solution. In addition to that, healthcare professionals need to feel that their needs are met and that they are safe in all environments [14]. In this regard, the development of psychological resilience of nurses through both individual, social, and organizational studies comes to the fore.

Resilience (psychological resilience) is defined as the process and result of successfully adapting to difficult life experiences through mental, emotional, and behavioral flexibility and adaptation to internal and external demands. The ways individuals see and relate to the world in the face of problems, the availability and quality of social resources, and certain coping strategies contribute to adaptation [55]. Psychological resilience, which increases the ability to cope with and resist difficulties, ensures that healthcare workers are less affected by the consequences of the stress they face and are more successful in crisis management, and it helps them recover more easily after the pandemic [56]. At the same time, resilience plays a role as a protective factor so that mental problems might not develop in all individuals exposed to high adverse effects or crisis situations [37, 57].

When all these factors are considered, it is seen that high levels of psychological resilience are important for healthcare workers to effectively combat COVID-19 infection and maintain mental health. To increase nurses' psychological resilience, needs should be determined early, initiatives should be made to reduce or eliminate factors that have negative effects on mental health, and approaches to increase mental health protective factors should be determined [15, 25, 48, 56, 58]. Taking effective psychological support measures, and removing and balancing the fear, anxiety or sadness caused by the epidemic will help healthcare professionals to feel psychologically safe. This may also improve crisis resistance, adaptation, and prevent mental disorders [43].

Studies have shown that nurses battling against the COVID-19 epidemic need mental support [4, 17–26]. It is necessary to determine and implement appropriate and effective strategies for the development of psychological resilience and mental health protection of nurses. For future epidemics like COVID-19, protective and supportive measures to protect health professionals' mental health should be taken in addition to measures to protect their physical health. Organizational, managerial, physiological, social, and psychological protective measures are needed in this regard.

5.1 Organizational support

Organizational support, or the degree to which an organization provides resources, empowerment, encouragement, and communication for an individual

to perform their functions effectively, is a vital factor that also contributes to organizational success. There is a positive relationship between higher organizational support levels, patient satisfaction in nurses, and positive outcomes [59]. Resilience intervention implemented in response to the COVID-19 epidemic, focuses on self-care, self-efficacy, and social relationships, as well as providing quick access to mental health consultation and support when needed [60]. Nine evidence-based organizational strategies are recommended to encourage participation of health system leaders and managers and to reduce burnout: acknowledging and evaluating the problem; harnessing the power of effective leadership; developing, and implementing targeted interventions; improving the community at work; using rewards and incentives wisely; aligning values and strengthening culture; promoting flexibility and work-life integration; providing resources to promote endurance and self-care; and facilitating and financing organizational science [61].

5.2 Managerial support

Providing managerial support in this period is of critical importance. Strategies must be developed so that health system leaders and managers may stay well in these turbulent and sad times, and so that organizations become able to lead the repair and revitalization of a post-COVID-19 world [61]. Nurse managers play a vital role in providing evidence-based measures, supportive organizational policies, and a safe and secure work environment to support the mental, psychological, and emotional health of nurses, thereby relieving their fears or anxieties [4, 59]. Managers should also assess the mental state of nurses and identify high risk individuals, provide psychological support and counseling, and collaborate with expert teams to provide professional psychological services when needed [43]. In this regard, managers need to adopt the issue of mental security of nurses with a holistic approach that recognizes the broader impact of the emotional distress caused by COVID-19. This will lead nurses to feel safe psychologically and will encourage them to communicate security concerns and problem-solving strategies to managers [11].

5.3 Physiological support

To eliminate psychological stress responses to the COVID-19 pandemic and to create personal resilience, it is important to implement physical measures. The working environment and daily life should be optimized to support proper nutrition, rest, sleep, and security requirements [5, 14, 60]. Also, hospitals should be careful about physical security issues in addition to meeting basic physiological needs, such as busy working times and provide protective equipment against infections [8, 61]. Ensuring physical security will help prevent symptoms such as fear, anxiety, fatigue, and exhaustion, and thereby protect mental health.

5.4 Social support

There is good evidence that social support has a stronger effect than material support and that it is often protective for mental health [48, 51]. Social and peer support has been identified as an important protective factor against trauma effect and general mental well-being [8]. Start and end of shifts create natural opportunities for interactions to develop friendship and teamwork. Social support should be developed within the team, and friend relationships of potential shift colleagues should be strengthened for them to monitor each other's

well-being [5, 14]. Social support has a positive effect on nurses' professional satisfaction, commitment to work, health, and well-being. Sufficient social support is needed for healthcare professionals for them to effectively manage stressful events, including emergencies, disasters, and infectious disease outbreaks [59]. The social isolation measures taken to minimize the transmission in the COVID-19 pandemic forces nurses to stay away from family, social circles, and team colleagues, which makes it difficult for nurses to reach the adequate support system that is very important.

5.5 Psychological support

With a few exceptions, hospitals all around the world are generally not designed or adaptable to provide continued emotional support to its staff. Despite that, there are many services that a healthcare worker can use when he or she feels in distress. However, these systems are rarely used [54]. In many countries, consultancy teams that include psychiatrists have been established to reduce the effects of COVID-19, and healthcare professionals have been provided with counseling and psychotherapy services; various mental support programs have also been developed to address the mental health problems among health professionals [33, 50].

Wuhan University RenMin Hospital and the Mental Health Center in Wuhan formed psychological intervention teams that included four groups of healthcare personnel. The first, the psychosocial response team (consisting of hospital directors and press officers), is the team that coordinates the work and promotional tasks of the management team. The second, the psychological intervention technical support team (consisting of senior psychological intervention professionals), is responsible for formulating psychological intervention materials and guidelines and providing technical guidance and supervision. The third, psychological intervention medical team, consisting mostly of psychiatrists, participate in clinical psychological intervention for healthcare professionals and patients. The fourth group, the psychological helpline team (consisting of volunteers trained in psychological assistance to cope with the COVID-19 pandemic), provides telephone guidance for dealing with mental health problems [16].

Psychiatrists have published various guidelines to prevent the development of mental problems worldwide and promote social and peer support, psychological support and resilience programs have been developed, and online and telephone mental support lines have been established [5, 14, 33, 39, 54]. In addition, consultation liaison psychiatric support was emphasized concerning the necessity for awareness studies, nutritional and exercise supplement, communication skills, stress management and relaxation skills, psychoeducational interventions, small group therapies, cognitive restructuring, yoga, music and art therapy, grief counseling, pharmacological treatment, and suicide protocols for severe cases. [41, 42].

As a result, the COVID-19 pandemic has shown us that there are numerous resilience initiatives in various forms, both those specific to COVID-19 and those more general. Digital interventions common in recent years are increasingly used to improve healthcare and outcomes. Within the scope of COVID-19 measures, it has been discovered that it is not always possible to work elbow to elbow, and the best applications can be carried out without contact are possible through online environments. It is very important to develop studies in this regard, considering their positive effect on nurses.

In **Table 1**, the causes and results of the mental problems experienced by nurses in the COVID-19 pandemic are stated, and attempts to protect and strengthen the mental health of nurses are summarized.

Mental problems	Causes	Effects	Interventions
Primary traumatic stress	• 24 h/7d bedside presence • Staff shortage • Lack of personal protective equipment • An unusual environment • Change of maintenance system • Lack of organizational support	• Decreased physical functions • Emotional exhaustion • Desensitization • Decline in personal success • Low job satisfaction • Personnel transfer	• Organizational support should be provided for the effective use of resources in personal and professional terms • The mental status of nurses should be evaluated by the managers and if necessary, they should be provided with professional support • Nutrition, rest, sleep and security needs should be supported • Intensive working periods should be planned in accordance with the health safety of nurses • Adequate protective equipment should be provided • Social support within the team should be developed and friendships should be strengthened • Counseling and psychotherapy services should be provided to nurses • Social support, peer support, psychological support and resilience programs should be developed • Online and telephone mental support lines should be established • Awareness studies should be done • Communication skills, stress management and relaxation skills should be developed • Psychoeducational interventions, small group therapies, cognitive restructuring programs should be implemented • Yoga, music and art therapy should be applied
Secondary traumatic stress	• Uncertainty about COVID-19 • Increasing number of cases • Repeated exposure to trauma • Witnessing patients suffering • Intense empathic approach to patients	• Anorexia • Insomnia • Fatigue • Anger • Apathy • Unwillingness • Hopelessness • Depression	
Job burnout	• The deadly and uncontrollable nature of COVID-19 • Increasing infection and mortality rates among healthcare workers • Lack of personal protective equipment • Heavy workload • Social stigma	• Poor physical and mental health problems • Lack of motivation • Absenteeism • Low morale • Deterioration of the quality of care service • Decrease in patients' satisfaction levels. • Increase in infections • High mortality among patients	
Compassion fatigue	• Witnessing the suffering and death of the patient • Responsibility for decisions regarding the allocation and use of resources among patients • Providing uninterrupted care to patients • Intense empathic approach to patients • Prolonged communication and interaction with patients	• Absenteeism • Quit job • Low morale • Social isolation • Harmful coping behaviors such as alcohol-substance use and binge eating	
Moral injury	• Dilemmas in the triage of COVID-19 patients, responsibility for decisions regarding the allocation and use of resources among patients	• Feelings of guilt, shame, or remorse. • Violate moral values • Decreased ability to function and performance • Quit job • Depression • Post-traumatic stress disorder	

Table 1.
Mental problems of COVID-19 nurses and prevention strategies.

6. Conclusion

Combating epidemics is an important responsibility that both affects all layers of society deeply and increases the physical and psychological burden of healthcare workers. Nurses caring for COVID-19 patients experience serious mental problems because they must help individuals in pain, stay with them, provide help for relatives, and perhaps witness a patient's death. Although physical security measures such as maintaining adequate protective equipment are prioritized in this process, it is observed that mental security measures are mostly ignored.

Ensuring and maintaining nurses' security is an important indicator of the effective management of the pandemic process. For this reason, it is necessary to determine the factors that may cause mental problems in nurses, diagnose these problems, provide appropriate physical and working conditions, and maintain psychosocial support. For this to happen, it is necessary to provide both emergency psychological first aid and long-term psychological assistance services and carry out follow-up studies. It is suggested that institutions and leaders follow policies on professional mental health support, initiate appropriate studies for services to be provided in the context of future crises, and create an action plan.

Focusing on supporting nurses during and after the pandemic is of great importance for the future of nursing and the security of society. It is also expected that this support for the welfare of nurses will continue when the health care system returns to pre-pandemic condition. To protect and maintain the well-being of nurses will enable them to assume their caring roles and responsibilities wherever they are located practice more effectively and competently. In this regard, that the role of nurses in the universal healthcare system involves a very important key role in meeting the care needs of the society and ensuring security, should not be forgotten.

Conflict of interest

There is no conflict of interest.

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Chapter 12

Significance of Diet and Behavior During Pandemic Situation According to Ayurveda

Gaurav Sawarkar and Punam Sawarkar

Abstract

Ayurveda is the oldest science of health care, explaining both the perspectives, i.e., prevention and cure of diseases. The fundamental principles of Ayurveda explore life's philosophy, including the entire cosmos having five significant elements (Akash, Vayu, Agni, Jala, and Prithvi) establishing the Prakruti, i.e., a unique combination of physiological and psychological characteristics in a human being. In Ayurveda, Ahara (Diet), and Vihar (Exercise/Movements), fundamental pillars are thoroughly explained according to a specific Prakruti, which denotes personalized medicine in the present era. Diet is the essential factor that comprises the five significant elements with six rasas (Sweet, Sour, Saline, Pungent, Bitter, Astringent). Each Rasa has its specific nutritional properties helpful for the maintenance of health. Moreover, it also prevents diseases and plays a vital role in the restoration of health from disease conditions. The appropriate diet plan is essential in the pandemic situation because the digestive power (Agni) becomes hampered due to faulty lifestyle and unwholesome food habits that result in vitiation of three bio-humors (Vata, Pitta, Kapha) in the body. According to Ayurveda's basic principles, weakened digestive power is the main culprit for forming various diseases. Therefore, it is highly imperative to select a suitable diet and behavioral regimes during pandemic situations.

Keywords: Ayurveda, diet, behaviour, pandemic, health

1. Introduction

Ayurveda is a science, aims to heal and maintain the quality of life with its longevity. It is a simple art of living comprising of practical knowledge, philosophical and spiritual illumination. Ayurveda medicine is an ancient legacy that resides in the Indian subcontinent. Millions of people in India are presently applying Ayurveda in daily life. Nowadays, it is in practice for health care in European countries. The literary meaning of the word "Ayurveda" is a compound of the word 'Ayush' (life principle) and 'Veda' (knowledge). Life itself is defined as the body's combination, sense organs, mind and soul, the preventing factor for decay and death. With this perspective, Ayurveda includes healthy living and therapeutic measures like purification (Panchakarma) and palliative medicine related to physical, mental, social, and spiritual harmony [1]. Thus, Ayurveda is motivating to preserve a healthy person's health and treat causative factors of pathogenesis.

2. Methods

A comprehensive literature search related to Diet and Behavior and description related basic principles of Ayurveda using all available Ayurvedic compendium, research articles from the various database such as Google Scholar, PubMed, Shodhganga was performed. The reference list of research articles identified and were screened for the diet and behavior in health security.

3. Fundamental principles of Ayurveda

3.1 Theory of Panchamahabhut

The basic principle of Ayurveda denotes that everything in the external universe also appears in the human body's internal cosmos. The human body consists of millions of cells, having a self-disseminating and self -correcting system to maintain harmony in the body as similar to the universe. Human is the essence of the universe, there is as much diversity in the world, and the same is observed in human beings themselves. In other words, human beings are a living microcosm of the universe, and the universe is a living macrocosm of human beings. The Panchamahabhut are the five significant elements present in both the form as a microcosm in the human body and cosmos in the universe, namely Prithvi (Earth), Jala (Water), Agni (Fire), Vayu (Air), and Akasha (Aether). Panchamahabhut is taking part in the formation of an embryo and shelter a development of the origin with its different peculiarities, gives appropriate shape to the body and various organs with the help of Prithvi (Earth). Formation of multiple types of fluids (like blood, serum, lymph, etc.) and gives elasticity, moistness to the body with the help of Jala (Water). Bodily temperature, digestive fire, various enzymes, metabolism symbolizes Agni (Fire). The various activities inside the body (circulation, digestion, filtration, transportation, respiration, etc.), multiple movements, and body functions represent Vayu (Air). The numerous spaces in the body (blood vessels, capillaries, gastrointestinal space, lungs lobules, ear, eyes, nostrils, skin pores, etc.) symbolizes Akasha (Aether). Panchamahabhuta also helps in the formation of Dosha, three fundamental bodily humors; Vata, Pitta, and Kapha. The related elements are Air and Ether, Fire and Water, Water and Earth take part in the formation of Vata, Pitta, and Kapha, respectively. Thus, Panchamahabhuta is the utmost important factor that describes the fundamental principles of Ayurveda [2].

3.2 Theory of Triguna

The concept of Guna is thoroughly explained in scientific literature since Bhagwat Gita, Sankhya Darshana, and Atharva Veda. Triguna theory has been utilized to explain the perception of personality in modern era as well. Triguna is Sattva, Rajas, and Tamas, featured with stability, activation, and inertia, respectively. All three exist in human beings, representing the predominance of one or other feature, providing unique quality to humankind. The manifestation of Triguna is attributed to the mental function and mental processes of human beings and all living beings, including the food, surrounding animals, and other elements in the environment [3]. Each individual behaves or lives based on the dominance of Triguna they have and project their personality as well in the mode of worship, the type of food consumed, and everyday activities, having specific qualities (**Table 1**).

SN	Triguna	Qualities
1	Sattva	Spiritual qualities, mental strength, respect for teachers and elders, non-violence, kindness, silent demeanor, self-control, meditative, etc.
2	Rajas	Passionate, enthusiasm, interest, activity & work-driven, restlessness, desire, greed, etc.
3	Tamas	Cautiousness, apprehension, revengeful, hardworking, materialistic, ambiguity, idleness, etc.

Table 1.
The qualities of Triguna are described as follows.

3.3 Theory of Tridosha

The fundamental concept of health is a balanced state between three bodily humours, i.e., Tridosha (Vata, Pitta, and Kapha). Vata is the air principle necessary for every movement and function of various systems. Pitta is the fire principle useful for digestion, energy level, and metabolism in the system. Kapha is the water principle related to mucous, lubrication, nutrient, serous fluid in the system. The five significant elements (Panchamahabhut) combine in pairs to form three dynamic forces: Vata, Pitta, and Kapha, continually moving in emotional balance with the others, required for healthy life normalcy in human behavior.

Every person comprises all three Doshas. However, the proportion varies according to the individual and is predominant [4]. That is why people can have many standard features and have an endless variety of nature, which decides the Prakrit of each individual. Each Dosha has its characteristics of governing principles (**Table 2**).

3.4 Theory of Sapta Dhatu

Dhatus are the primary supporter to structure and function of the body as like a tissue, seven in number known as Rasa (final metabolic juice and plasma-derived from the digestive system), Rakta (blood and related circulatory system), Mamsa (musculature, tendons, muscular system), Meda (fat, fat-like structures, adipose tissues), Ashti (bones, bony part, and skeleton), Majja (marrow, bone marrow) and Shukra (structurally and functionally related to the male and female reproductive system). These all structures that make the body, an integral part of it, imbalance causes fatigue and diseases. It is imperative to understand the normal and abnormal functioning of all Dhatus to recognize the exact pathophysiology in the body during disease condition. The formation of Dhatus is consecutively, and nourishments of each Dhatus depends upon the previous one. During this tissue formation process, some metabolic waste is produced as tissue excreta is known as Dhatumala, also having a unique identity in structural and functional processes in the body. If some abnormality is molded in Rasa Dhatus, the sequential nourishment will be affected, resulting in improper microcirculation and developing deformity in the next tissue [5].

3.5 Theory of Srotasa

Srotasa is the passages or channels through with Dhatus (various tissues) are transported for their transformation and metabolism. Srotasa comprises multiple systems in the body, described under the physiological heading, the structures from which the contents move out, ooze out, or transude out. The nutrient substances are provided to various tissues through these channels, related to their corresponding

Dosha	Vata	Pitta	Kapha
Predominant stage in life	Old age	Teen and Adult.	Childhood years.
Function	Body movement, respiration, natural urges, the transformation of the tissues, motor and sensory functions, secretions, anxiety, emptiness, nerve impulses, etc.	Body temperature, digestion, eyesight, understanding, hunger, thirst, intelligence, anger, hatred, jealousy, etc.	Steadiness, energy, lubrication, compassion, greediness, attachment, build-up, holding, etc.
Characteristics	Cold, light, irregular mobility, dry, rough, etc.	Hot, light, liquid, delicate, sharp, smelly, soft, strong, etc.	Fatty, cold, heavy, stable, dense, smooth, etc.
Stage of Vitiation	nerve irritation, high blood pressure, gas, confusion, nerve loss, congestion, constipation, thoughtlessness, etc.	Ulceration, hormonal imbalance, irritable skin, emotions, anger, faulty digestion, inability to understand, slow metabolism, etc.	Sinusitis and cough and cold, obesity, lethargy, experiences a dry respiratory tract, burning stomach, etc.

Table 2.
The characteristics of the governing principles of life are as follows.

tissues' metabolic state through different mechanisms. They are of different shapes like circular, elongated, and reticular. Channels are microscopically innumerable in numbers, but they are thirteen in number or eleven in pairs as per other ancient authors in a macroscopic manner. Each channel has its roots organs; an entire track is governed given its physiology, pathology, and treatment [6].

3.6 Concept of Prakriti

Prakriti is the crucial concept, and the fundamental constitution of the body decides at the time of conception, fixed throughout the lifetime. It is the genetically determined physical and mental constitution of the individual. It is a combination of Vata, Pitta, and Kapha. Different persons have different varieties known to be their basic Prakriti as per the predominance of bodily humor. According to Ayurveda, it is the unique feature of human beings that every individual reacts differently when exposed to the same environment as once fingerprint or DNA. Thus, it is necessary to determine the person's exact Prakriti to assess a person properly for their diet, behavior, pathology, and treatment. Every person has their own unique identity, which constitutionally defines body physiology, stimuli to environmental factors, the reaction towards various drugs, and susceptibility to multiple diseases. However, in the current scenario, it is considered as a concept of preventive and personalized medicine. The knowledge of Prakriti is a unique specialty and essential tool to understand the mental and physical nature of the person, predict disease susceptibility, helps in diagnosis of the disease, and even break the pathophysiology of the disease [7]. There are many recognizable phenotypic features described for each type of Prakriti (**Table 3**).

3.7 Concept of Koshta

In Ayurveda, the term Koshta is explained in two senses; first is regarding anatomical ground viz. space and hollowness of the body and second in terms of physiological way viz. bowel movement according to the fundamental constitution of the person. There are three types of Koshta explained in the Ayurveda context viz. Kura (hard

Vata	Pitta	Kapha
Body frame is thin, does not gain weight. Skin is dry rough with dark complexion. Hairs are dry and splitting. Activities are quick. Appetite is variable. Working capacity is less. Poor immunity. Required warm food and climate. Perspiration is quite scanty. Frequent constipation, having disturbed sleep. Anxious, depression, unpredictable in nature.	Body frame is medium. Skin is delicate, pinkish complexion, warm in touch. Hairs are soft, having premature graying and tendency to baldness. Increased appetite. Having sharp vision. Feels internally warm and hot. Required cold food, and climate. Hot food and climate can not be tolerated. Having frequent loose motion, excessive thirst and smelly perspiration. Brilliant, having sharp memory, brave, jealous, aggressive and commanding in nature.	Body frame is broad and large, tendency to gain the weight. Complexion is fair, glossy and skin is thick, soft and smooth. Hairs are thick, oily and dark. Having good working stamina, but less physical activity. Voice is deep and pleasant. Perspiration is moderate and having low thirst. Sleep is deep and sound. Eyes are large calm and stable. Having calm, joyful and polite nature.

Table 3.
Key distinguishing features for Prakriti determination.

bowel), Mrudu (soft bowel), Madhyam (moderate bowel), having their features with specific Prakriti and Dosha (**Table 4**). It can be assessed with bowel habits frequency, consistency, straining, or efforts, and time is taken for proper defecation [8].

3.8 Concept of Agni

Agni has an integral role in digestion and metabolism, that ingested food is digested, absorbed, and assimilated, make available as a final metabolic juice with the help of this rest of the tissue (Dhatu) nourished sequentially. As per modern medicine, metabolic processes, division, and multiplication are a continuous process from birth to death. As biological energy, Agni essential to be constant for the body's survival, provided strength to every cell till the end of life. Agni is also classified into four heads, viz. Vishama (Irregular Metabolism), Tikshna (Hypermetabolism), Manda (Hypometabolism), Sama Agni (balanced state) correlated concerning Koshta as in **Table 4**. The balanced Agni featured happiness, perfect health, calm and clear state of mind. Individuals can digest a reasonable quantity of food in any season without any problem and can easily tolerate changes in the environment and changes in the seasons. A person can enjoy balanced digestion, absorption, and elimination [9].

3.9 Concept of Ahar and Vihar

Ahar means taking in, swallowed through the throat, esophagus, and process in the gastrointestinal tract. Food is the best thing that endures life and provides strength, color, complexion, vigor, and body development, hence called superior medicine. The great scholar Lolimbaraj said that when the diet is wrong, medication is of no use; when the diet is correct, there is no need for medicine. Most of the time, the cause of numerous diseases is improper diet. Food also contains five great elements, i.e., Panchamahabhutas; if one consumes food in proper proportion, it will help balance similar elements in the body. Light food comprises Vayu, Agni, and Akasha Mahabhuta, whereas heavy food contains Prithvi and Jala Mahabhuta predominance. Based on Agni and Koshta, individuals have to consume their diet concerning the saturation point to maintain proper body strength [10].

SN	Koshta	Meaning	Dosha relation	Agni relation	Feature
1	Kura	Hard bowel	Vata	Vishama	Poorly secretive and absorptive, hard feces with the difficulty of elimination or even non-elimination. Appetite Irregular, variability in digestion, abdominal distension or gas, tendency of constipation, etc.
2	Mrudu	Soft bowel	Pitta	Tikshna	Stool is soft, lubricated and slippery, watery or semi-solid, nature of hyperacidity, prone to gastritis, heartburn, hot flashes, acidic saliva, and fever. Tendency of loose motion etc.
3	Medium	Moderate bowel	Kapha	Manda	Stool with more lubrication, but less slippery, having optimum secretion and absorption, metabolism is slow and feel heaviness in the stomach, the body, and the mind, etc.

Table 4.
Characteristics of the Koshta.

The word Vihar means transportation, distribution, wandering, which includes daily and seasonal activities. According to individual Prakriti, Agni, and Kosta, great scholars have described their importance, usefulness, and harmfulness. The great ancient scientist prescribed daily schedule and behavioral changes in terms of daily routine, yoga and exercise, nighttime routine, seasonal routine, regarding basic instinct, suppressible or non-suppressible natural urges, code of conducts related to ethics, social, mental, moral, and physical category, sidestepping of excessive and incorrect use of sense organs, governing on speech and thoughts. With this regime, a person remains healthy and can prevent disease conditions related to lifestyle disorders [10].

4. Importance of Agni

The Agni, biological energy, in a balanced state, keeps the body healthy and leads to long life. The imbalance or stoppage of this energy's functioning, the whole metabolism would be disturbed, and the individual may ill, diseased, or dies in a short duration. It plays a vital role in nutrition. Most of the diseases, physical-physiological and psychological, are the byproducts of the Agni's malfunctioning, hence called the key root of health. It coordinates physiological processes like digestion, reabsorption, sensations, and the formation of energy. Due to the malfunctioning of Agni, food is not digested correctly and formed a toxic substance in the body that is referred to as 'Ama' in Ayurveda. This poisonous substance is solely responsible for poor digestion, improper blood circulation, low energy level, poor complexion, poor immunity leads to disease conditions according to Prakriti, and Dosha-Dhatu balance [11, 12].

5. Importance of Ahar and Vihar

Ayurveda, Ahar (Diet), and Vihar (Behaviour) are advised as per seasonal and diurnal regimes based on Prakriti. The individual should adopt these regimes as per

their Prakriti and keeps equilibrium in Dosha (three bodily humours). Ayurveda offers extensive preventive measures considering Prakriti types to maintain health with favourable foods and behavioral, physical activities. And at the same time, restrict and advised to avoid unfavorable diet and physical activities that may create disease and illness in the body. The healthy state of the body and disease condition depends entirely on Agni concerning diet and behavior [13].

6. Role of diet and behavior during a pandemic situation

The basics of Ayurveda suggested the state of equilibrium of Dosha (three body humors), Dhatu (seven types of tissues), and Trimala (Sweat, Urine, Stool) for the healthy living being. The ingested food gets digested well with the help of balanced biological energy and form productive nutrients for the nourishment of the bodily tissues. It sequentially takes place with the metabolic energy of each tissue and nourishes dependent tissues also. A healthy diet is essential for good health, which protects the body from many diseases. A healthy diet means a variety of foods, with less salt and sugar, the saturated and trans essential fats, including cereals, starchy roots, lentils and beans, fruits and vegetables, animal source foods (as per need), a preferably fibrous diet with sprouts, salad, leafy vegetables which keeps the body fit and fine. The intake of diet at the appropriate time and with due interval is essential. A person should consume food which is suitable to him as per his Prakriti and which digested quickly. Keep three-four hours interval between breakfast and lunch. Please keep in mind the gap between dinner and next morning breakfast should be eleven-twelve hours. With proper diet, quality of sleep is of utmost importance for good health. For good digestion and sleep, keep a minimum two hours interval between dinner and bed time [14]. Adequate sleep is as equally important as eating healthy and exercising. Nowadays, people sleeping less than the required duration are connected with higher body weight, poor nutrition, greater risk of heart disease and stroke, affected glucose mechanism, risk of diabetes, and low immunity. In a pandemic situation, body physiology gets changes according to the external environment that will affect the person's overall health. In that situation, everyone has to make a diet plan as per the suitability of the person. Proper diet planning includes good food habits, nutritional food, a wholesome diet, an easily digested diet, low calory healthy diet, and a timetable of breakfast, lunch, and dinner. Dietary and behavioral measures include the type of diet, time of consumption, the interval between intake of food, the quantity of intake (should be one-third of stomach capacity), and nutrition values. The central concept of diet in Ayurveda includes three types of diet Satvik, Rajas, and Tamas; a person should consume a diet accordingly to keep equilibrium for sustenance and good health management strong relation between gut health and mind. Whole things are interconnected; scheduling and management play a significant role in the pandemic situation for good health. Perhaps Ayurveda teaches us an important lesson that our health is up to us, how to live every day and every hour, choose either health or illness, opt for sound options, and think-rethink our choices [15].

7. Role of diet and behavior in health security

The awareness regarding diet and behavior is essential for health security, which is excellently elaborated in the Ayurveda context. The dietary pattern related to various ages is also explained in the literature. The adolescent age group is very vulnerable to food choices responsible for growing age health related problems.

Consciousness and knowledge about recommended food and nutrition may reduce the risk in growth and development. There should be a feedback system in adolescent age for nutrition knowledge and healthy behavior. Simultaneously, the pregnant woman is the weaker part of society. She needs the intervention of more nutritious diets and healthy habits that improve her health and reflections on a healthy baby. There should be one unique health plan related to pregnant women, which should be developed and validated regularly for the part of the government's health care mechanism. The dietary interventions affect the gut microflora composition and their function, reducing the risk of various diseases. Another concept related to the drug delivery system of bioactive components through nanotechnology plays a vital role in health promotion, health security, and disease prevention. In this method, one can increase bioactive compounds' bio-availability at various stages of digestion, absorption, and assimilation. In old age people, the most significant risk factor is neurodegenerative diseases due to calorie restrictions and intermittent fasting. According to age and Prakriti and behavioral guidelines, a health regulatory body should unanimously frame a comprehensive diet plan [16–21].

8. Initiatives for international health security

The health streams like Ayurveda, Modern medicine, Homeopathy, Siddha, Unani, etc., are solutions to health-related problems. The global health community has to determine health crisis problems and strategic level integrated models with disaster defender system which can enhance global capacities and capabilities for infectious diseases. The complementary sciences can help community-based contextual issues effectively and maybe the part of more decisive strategic planning in the outbreak of contagious diseases for strengthening the immune system of the society. The global health leadership, WHO must formulate strong international health regulations treaty and country-wise administration, considering bottom line community no longer been deprived of health providers in disaster situations. WHO should develop a global response system for crisis response and risk reduction worldwide to collaboratively take opinion of practitioners and health care decision-makers in various fields irrespective of the health care system [22–25].

9. Conclusion

The Ayurveda plays a significant role in managing diet and behavior, advised ingesting, according to Prakruti, Koshta, and Agni, considering the daily and seasonal changes for health security. A person has to take the proper diet recommended to their Prakriti in a pandemic situation and ensured activities with exercise are suggested in the prescribed period.

Conflict of interest

The authors declare no conflict of interest.

Appendices and nomenclature

Aakash	Aether
Agni	Digestive power, biological energy

Agni	Fire principle
Ahara	Diet
Ashti	bones, bony part, and skeleton
Ayush	life principle
Bio-humors	Tridosha (Vata, Pitta, Kapha)
Dhatus	body tissue
Jala	Water principle
Koshta	bowel movement type
Kura koshta	hard bowel
Madhyam koshta	moderate bowel
Majja	marrow, bone marrow
Mamsa	musculature, tendons, muscular system
Manda Agni	Hypometabolism
Meda	fat, fat-like structures, adipose tissues,
Mrudu koshta	soft bowel
Panchamahabhut	five elements - (Akash, Vayu, Agni, Jala, and Prithvi)
Prithvi	Earth principle
Rakta	blood and related circulatory system
Rasa	final metabolic juice and plasma-derived from the digestive system
Sama Agni	balanced state of metabolism
Shukra	structurally and functionally related to the male and female reproductive system
Tikshna Agni	Hypermetabolism
Vayu	Air principle
Veda	Knowledge
Vihar	Exercise/Movements/behaviour
Vishama Agni	Irregular Metabolism

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Since the publication of the first volume of *Contemporary Developments and Perspectives in International Health Security*, a lot has happened in this rapidly evolving area. Perhaps the most dominant global event of the past eighteen months is the COVID-19 pandemic. Within this general context, the importance of the multiple and diverse international health security (IHS) subdomains is becoming evident, especially when one begins to appreciate the interconnectedness of the modern world and the interdependence of various existing societal systems. Moreover, this complexity presents our civilization with both dangers and opportunities, and among the most pronounced opportunities is our ability to effectively "work together and coordinate" as humanity. With a goal to summarize and synthesize our collective experiences from the COVID-19 pandemic, this second tome of *Contemporary Developments and Perspectives in International Health Security* is a repository of knowledge and a practical resource for those who seek to learn about the current pandemic as well as for those who may already be preparing for the "next pandemic" or as yet unforeseen IHS threats. In addition to the COVID-19 global response, topics discussed in this book include climate change, mental health, supply chain management, and clinical diagnostics, among others.

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