Prospects for controlling future pandemics of SARS in highlights of SARS-CoV-2

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Abstract Throughout human history infectious diseases have emerged to become global threats once in a while. Sometimes the previously established infections surfaced due to geographical extension or by increasing their transmissibility or pathogenicity while in other instances new infections have periodically emerged by transmitting from animals to humans. A proper strengthening of the existing health care system, disease surveillance, advancement in medical technology and healthy lifestyle is a must for controlling the future re-emergence of pandemics. Similarly, a deeper understanding of (1) key medical and social elements; (2) treatment and prevention options; (3) epidemic preparedness of the health care system; and (4) investing in ethno medicine research is necessary to prevent the future devastating pandemic emergencies.

Keywords SARS · COVID-19 · Pandemic preparedness · Ethomedicine research · Surveillance

Introduction

Pandemic diseases are frequently emerging and posing greater global health threats resulting in the breakdown of socio-economic network. The miniscule architecture and hasty mode of transmission, the causative agent of pandemic disease spread speedily to damage any population at any time [1]. With the ever-increasing human population and environmental changes along with the adoption of maximum safety measures and surveillance system, there has been a steady rise in pandemics and other human health crises ever since. Pandemic and epidemic diseases such as influenza, malaria, Ebola, human immunodeficiency viruses (HIV)/Acquired immunodeficiency syndrome (AIDS) and severe acute respiratory syndrome (SARS) pose various threats to human health. Even the twenty-first century has already experienced the emergence and global spread of one of the coronaviruses i.e. severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has been causing severe human infections. Besides these, the influenza virus pandemic of 2009 claimed thousands of human lives [4]. Given the history of pandemics, there can be a speculation that a highly sophisticated disease pandemic will hit humankind in the future. Hence, there is a necessity of enough preparedness to mitigate or lessen the impact of upcoming pandemics. Such preparedness should be driven by the progress made in the medical sector, advancement in science and technology, and the experiences gained from past outbreaks. Though we must first deal with the ongoing coronavirus disease 2019 (COVID-19) pandemic for the foreseeable future using all of the available preventive and therapeutic measures, we should start envisioning the readiness for future threats that will be posed by emerging and reemerging infectious pathogens.

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Identification of the key medical and social elements

One of the key determinants of COVID-19 morbidity and mortality in people is the social and economic status [13]. Animal trafficking, poor sanitation and hygiene at animal facilities, and increased human-wildlife conflicts could increase the risk of emergence of zoonotic diseases as wild and domestic animals can act as the intermediate hosts for several infectious pathogens [8]. Anti-smuggling operations, close monitoring of the rearing of wild and domestic animals and associated workers' hygienic status, and effective use of disease surveillance and control in wild and domestic animals are important to break the transmission link of infectious agents from animals to humans. A multidisciplinary one health approach, that brings environmental, animal, and human health sectors together for a common goal of reducing the risk of emerging and reemerging pathogens, would be appropriate to tackle the COVID-19 and any future pandemics. Cross country open borders such as between Nepal and India have also made it difficult to contain the spread of disease across countries. The connection between socio-cultures, climate change, humidity, and seasonal variability assumes that the risk of transmission of SARS-CoV-2 does appear to be the greatest [12]. Further, availability of a balanced diet and having a good food habit might help in boosting the immune responses and provide a positive impact on nullifying the severity of infections including that of SARS-CoV-2 [6]. Assessments of global changes introduced by the current COVID-19 pandemic are crucial to speculate possible impacts for the future endemic/pandemic and get prepared for their mitigation and management. Likewise, development of appropriate technologies and devices for effective tracking and tracing, as well as rapid screening of infections are important not only to deal with current pandemic but also to eliminate future outbreaks [9]. The higher adverse outcomes such as hospitalizations, intensive care unit (ICU) admissions and deaths due to SARS-CoV-2 in non-communicable disease conditions including obesity, high blood pressure, chronic obstructive pulmonary disease, diabetes mellitus, cardiovascular diseases, and cancer indicates the vulnerability of people with comorbidities, which should also be a consideration for future epidemic/pandemic preparedness [3]. Social awareness, contact tracing of infected people, social distancing and collaborative implementation of medical facilities between the government and private medical institutes, along with technical and financial support from the international organizations and nations would have a profound role in preventing the future pandemics.

Treatment and prevention options for a future pandemic

SARS-CoV-2 is an enveloped positive-sense, single-stranded ribonucleic acid (RNA) virus with 50–200 nm in diameter with four major structural proteins; spike, membrane, envelope, and nucleocapsid protein; together with other accessory proteins [10]. Also, the close genomic relationship (> 75% nucleotide identity) of SARS-CoV-2 with severe acute respiratory syndrome-coronavirus (SARS-CoV) and middle East respiratory syndrome-coronavirus (MERS-CoV) has been a good playground for exploring similar therapeutic insights. Despite that, effective treatment options are not available with the exception of certain hopes with the drugs like remdesivir, hydroquinone, and dexamethasone which could lessen the severity of COVID-19-associated complications and deaths. Antiviral agents could be discovered and developed by targeting various stages of the life cycle of virus, like entry, attachment, replication, transcription, translation, maturation, and release. More investment and efforts are required into the research in drug discoveries targeting SARS-CoV-2 and other emerging and reemerging pathogens by using traditional and more recent computational methods. For instance, molecular targets such as ACE2 of human, 3CL^{pro} protease, and Nsp13 helicase of SARS-CoV-2 can be targeted [11]. Discovery and/or testing of existing broad-spectrum antiviral drugs, screening of all available molecular databases, and using the knowledge on the genomics, signaling cascades, and pathological information could lead to the discovery of more effective therapeutics for future use. Thus, identification, discovery, and development of stockpiles of antivirals, and developing standard operating procedures for their rapid deployment should also be considered to cope with the disastrous impact of the future outbreaks.

The next powerful weapon to combat SARS-CoV-2 at present and for the future outbreak is vaccination, which has worked spectacularly, well against different diseases. The availability of structural and genomic information could provide a basis for discovery, development and distribution of vaccine production strategy. Technical support, capacity building, and technology transfer for the development of SARS-CoV-2 vaccines to developing countries are necessary to prepare stockpiles of vaccines. Since the genome sequence of SARS-CoV-2 displayed nucleotide similarity (> 75%) to the previously identified coronaviruses SARS-CoV and MERS-CoV, developing broad-spectrum monoclonal antibodies against the plethora of coronavirus strains could be very useful [2].

Epidemic preparedness of the health care system

Besides non-pharmaceutical interventions, healthcare facilities and their staffs are key players in epidemic preparedness for outbreak response. The lack of progress in controlling the current pandemic of SARS-CoV-2 revealed poor settings of public health systems and services together with limited contact tracing, a poor setting of quarantine, disobeying physical distancing rules, and so on. Inspiring statements about bold policy changes for health system strengthening must be urgently translated into action with efficient collaboration and coordination among state, local, and territorial national and international public health agencies for full protection against the evolving catastrophic direct and indirect cost of illness [7]. Addressing all barriers (Fig. 1) is a tall order and will require political will on the highest level, stimulated by forceful grassroots demands.

Investing in ethno medicine research

Calamitous outbreaks have been recorded from ancient periods in the history of human civilization, including Spanish Flu, Hong Kong Flu, SARS, H7N9, Ebola, Zika, to name a few. These viruses explode informally as an endemic, epidemic, and pandemic, in some cases

remaining as the seasonal flu and infecting millions of people and leading to thousands of deaths each year. Herbal drugs have been used historically in traditional medicine for the treatment of different diseases and even against COVID-19 at present. *Astragali Radix*, *Glycyrrhizae Radix Et Rhizoma*, *Lonicerae Japonicae Flos*, and *Fructus Forsythia*, are the examples of few traditional herbal drugs explored in COVID-19 treatment [14]. The era of antiviral therapy can be traced back to the 1960s and since then over 60 clinically efficacious antiviral compounds have been discovered. However, mostly if not all have some limitations, ranging from poor bioavailability to toxic side effects and drug resistance with some virus where no effective drugs or vaccines exist. After some period (1990–2010s) of pace dawn of discovery of drugs from plant origin, there is again a resurgence of research in ethno medicine-based drug discovery. In the current era, in many developed countries research institutes, universities, and pharmaceutical laboratories as well as in the clinics thereof priorities have been given to scientific research on medicinal plants. In the present scenario, about 35 percent of western medicines originated directly from natural products or their derivatives {plants (approx. 25%), microorganisms (approx. 13%), animals (approx. 3%) and derived from natural products (approx. 14%)} [5]. Therefore, medicinal plants and their bioactive metabolites are the main focus of interest and have several advantages over

Fig. 1 Potential preventive actions in the health care setting in pandemics

synthetic drugs due to their broad therapeutic potency, limited side effects, and their ongoing human trial for a long time. Thus, the research on ethno medicine is a key step for transferring antiviral agents from the impatient to the patient. To catalyze this transformation and pave the way for future research scientific investment is necessary in ethno medicine. SARS-CoV-2 and the currently existing technologies should be used as an opportunity to explore the antiviral potential of various natural products.

Conclusions

With the addition of SARS-CoV-2 in the long list of pandemics, it can be assured that we will be facing off with increasingly aggressive microbial threats in the future too. Sure, science will fight back with better sensitive diagnostics, vaccines and lifesaving drugs; however, these might not be enough to overcome the threats. Rather a holistic approach to the pandemic control needs to be applied which the recent COVID-19 pandemic clearly demonstrated the humankind's most vulnerable side. The study highlighted the medical and social determinants, the discovery of broad-spectrum vaccines or/and antiviral drugs, empowerment, and upgrading of health care systems and re-investigation of pre-approved ethno medicine and search for new herbal and/or medicinal plants. All the aforementioned findings could be necessary and important for public health policymakers to promote strategies for not only the COVID-19 control but also against future pandemics.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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