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Review article

A brief overview on the threat of zoonotic viruses

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ABSTRACT

Background: Microbial agents such as viruses, bacteria or parasites are linked to zoonotic outbreaks. Zoonotic diseases transmitted from animals to humans pose a major global burden on public health. Worryingly, recent decades have seen an increase in viral zoonotic outbreaks. Zoonotic viruses have the potential to cause pandemics leading to substantial morbidity and mortality globally. The intrinsic factors contributing to the pandemic potential of these viruses are manifold and interconnect in complex ways. Accelerating rates of globalization, urbanization and deforestation have led to the increased contact between humans and wild animals, creating fertile ground for zoonotic spillover events. In addition, climate change, behavior of vector species and intermittent host also had a pivotal role in the emergence and reemergence of viruses. Further, these viruses undergo rapid genetic changes and adapt to the new host which presents a dreadful challenge for surveillance process and detection. In addition, wildlife hunting and trade contributing to the virus spill over cannot be understated. Understanding the nature of zoonotic viruses and identifying the reservoir hosts is critical for predicting the risk of outbreak and evaluating the potential impact on human health. To lessen the likelihood of zoonotic virus-related epidemics/pandemics in the future, it is imperative to address this complex web of social, economic, and cultural elements. Further, proper surveillance mechanisms, active research, and promoting interdisciplinary collaboration, data sharing, and coordinated action are vital for effectively managing the challenges posed by zoonotic agents and reducing their burden on global health.

Introduction

For centuries, emerging and re-emerging zoonotic viruses have been responsible for various disease outbreaks at unpredictable intervals with varying severity, epidemiology, and pose serious public health, social and economic threat worldwide. Zoonotic viruses can infect animal hosts and have the potential to infect humans causing enormous burden. Few examples of zoonotic diseases are anthrax, salmonellosis, tuberculosis, lyme disease, plague (Bacterial zoonoses), rabies, ebola, avian influenza, severe acute respiratory syndrome (SARS-CoV), middle east respiratory syndrome (MERS-CoV) and coronavirus disease (viral zoonoses). These viruses have the potential to cause epidemics or pandemics if not properly controlled and managed. Most of the recently emerged human pathogens are zoonotic in nature [1,2]. Zoonotic outbreaks in the recent years including coronaviruses, chikungunya, nipah, ebola, influenza and others have expanded geographical spread resulting in high mortality and caused significant disruption to economy and human lives that shows the dangers associated with zoonotic outbreaks. Further, morbidity and mortality burdens associated with zoonotic viral infections are

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enormous leading to significant loss in human and animal population [3-6]. The integrated intervention strategy involving the world health organization, national and international government organizations, research community, pharma companies, health professions, regulatory authorities, funding agencies have made significant efforts in controlling several infectious diseases. This article review the overview of zoonotic infections and its pandemic potential.

Zoonoses

Zoonotic viruses affecting humans can either originate in domestic or wild animals [7-9]. Zoonotic viruses comprise a wide range of pathogens each with unique characteristics and have a ranging impact on public health. The emergence and spread of zoonotic diseases with pandemic potential occurred at regular intervals throughout history. The diversity of circulating zoonotic viruses in animals expands every year. Although several infectious diseases have been controlled or eradicated in the past, the emergence and pandemic spread of SARS-CoV-2 [10], the most recent example of zoonotic outbreak highlight the threats associated with novel pathogens that could be transmitted to humans from animals.

Coronavirus disease 2019 (COVID-19) demonstrated that the newly emerging pathogens can spread dramatically and are capable of being transmitted globally in short time, if it is not identified and controlled in a timely manner. Even though vaccination is effective against SARS-CoV-2, still many countries continue to report cases and the frequent emergence of mutated variants with high infectivity, transmissibility, and severity is causing a significant health concern globally [11,12]. The recent emergence of SARS-CoV-2 variants JN.1, KP.2, and KP.3 has sparked concerns globally, particularly due to the increasing number of cases in many countries. These variants have demonstrated enhanced transmissibility and in some cases, resistance to existing vaccines. Of particular concern is the dominance of these variants in certain regions, such as the United States, where they have become prevalent strains, leading to heightened vigilance and public health measures to mitigate their spread and impact. Efforts to monitor and understand the characteristics of these variants remain critical in the ongoing battle against the COVID-19 pandemic [13]. COVID-19 has exposed the shortcomings and vulnerabilities in the human healthcare system both at the national and international level. This pandemic is a wake-up call for the need to implement relevant policies and countermeasures to prevent future disease outbreaks [14]. Further, the recent identification of monkeypox infections in non-endemic countries such as USA, UK, Spain, Portugal and Canada [15-17] showed our continual susceptibility to emerging and reemerging infectious diseases. The major challenge is to develop the vaccines, therapeutics and ensuring its uniform accessibility. The timely administration of vaccines or antivirals could control the viral spread and reduce the disease severity.

Virus Spill Over

Zoonotic viruses are a concerning issue due to their ability to jump from animals to humans and potentially cause widespread outbreaks across the globe [Figure 1]. The circumstances under which zoonotic disease outbreak lead to the pandemics are complex and multifaceted [18]. Proper identification and surveillance of these viruses in animal populations could prevent these viruses from causing pandemics. The animal-to-human spillover of new viruses and microbial evolution are seemingly unpredictable and is the most important factor contributing to the zoonotic outbreaks and pandemic risk. Increasing proximity, dynamic human and animal interface has increased the probability of encountering zoonotic viruses[19]. Several other external factors such as climate change, hunting, deforestation, intensive livestock farming, urbanization, biodiversity loss, international trading, anthropogenic activities and travel are also potential drivers of zoonotic infections [20,21]. The drivers of novel virus emergence are likely to continue and intensify over time [22]. Even now, many of the viruses harbor undiscovered diversity and the reservoirs are still unidentified. Although it is hard to precisely evaluate the pandemic risk of individual virus, more intensive and effective infectious disease surveillance systems, better understanding of virus replication, transmission route, persistence in the environment, rapid diagnosis, and an effective treatment are the core factors to protect against epidemic or pandemic potential of the infectious diseases. Further, establishing and implementing systematic and multisectoral action plans with standard approaches to effectively prepare for detecting, investigating, and responding to zoonotic infections could mitigate the impact of future

infections arising from new or reemerging pathogens [23,24]. In addition, detailed study of the ecological and epidemiological factors that facilitate the spillover of zoonotic viruses is crucial for early detection and containment [25,26]. Moreover, the implementation of effective public health interventions and policies to lessen the risks associated with zoonotic viruses is crucial for pandemic preparedness.

Given the interconnected nature of zoonotic virus transmission, a complete and interdisciplinary approach that involves the collaboration between public health professionals, veterinary agencies, environmental organizations, and international health authorities is vital. To protect global public health, governments, international organizations, and research institutions must collaborate to strengthen monitoring systems, foster a deeper comprehension of viral ecology, and put evidence-based solutions into practice. Only through sustained and collective action, we can effectively reduce the threat posed by zoonotic viruses and prevent future pandemics.

Challenges and lessons

Zoonotic virus epidemics and pandemics have twisted human history, with major outbreaks (Table 1) [27] causing significant morbidity, mortality, societal disruption, economic damage and political impacts. In human history, black death, also known as the great Plague, was one of the most devastating pandemics in the 14th century with lasting impacts on societies across the globe. The Spanish flu of 1918 caused widespread devastation, claiming millions of lives globally and subsequent years, including the H1N1 swine flu in 2009, highlighted the rapid spread and mutation potential of influenza viruses and underscored the importance of global cooperation in surveillance, prevention, and control efforts. Recently, COVID-19 resulted in millions of deaths and had a great impact on human life [28]. These pandemics serve as reminders of the fragility of human existence and the need for collective efforts to mitigate future outbreaks. Mitigating zoonotic virus pandemics presents a multitude of challenges, stemming from the intricate interactions of biological, ecological, socio-economic, and governance factors. Some of the key challenges are cross-species transmission dynamics, human encroachment into wildlife habitats, deforestation, climate change, alterations in biodiversity, increased global travel, trade networks, limited surveillance infrastructure, lack of robust healthcare systems and diagnostic capabilities, scientific and logistical challenges associated in developing new vaccines against newly emerging zoonotic viruses, vaccine hesitancy and challenge associated with intersectoral coordination and governance [29].

Historical pandemics, from Spanish Flu till COVID-19 [30] have underscored the importance of robust surveillance systems, investment in laboratory infrastructure for rapid diagnosis, and the utilization of digital surveillance tools for real-time data collection and analysis. In order to prevent and control the zoonotic virus outbreak, deep understanding on the characteristics and behavior of these viruses is essential in developing effective prevention and control strategies. Additionally, a broad understanding of the host species, virus reservoirs, and transmission mechanism of these viruses is a key in implementing targeted control measures [31]. Although mortality and morbidity associated with several diseases are reduced in recent years due to the access to therapeutics, better sanitation and the development of vaccines, still inequalities in the access to these advances within the countries and between the countries presents a major challenge [32,33]. Vaccine equity and addressing vaccine disparities is crucial in managing the future virus outbreaks.

In this context, artificial intelligence (AI) serves as a powerful tool in managing zoonotic diseases by providing insights into disease dynamics, enhancing surveillance capabilities, supporting diagnostic efforts, and facilitating rapid response and control measures [34]. AI enables computers, algorithms, software and data to perform tasks by mimicking human intelligence and cognitive abilities. AI and data science are innovative, technology-driven solutions nowadays in projecting the virus spread, cases, mortality, contact tracing of individuals, early detection/diagnosis, treatment monitoring, data compilation and training of healthcare workers. AI algorithms analyze diverse datasets to predict and detect outbreaks early, facilitating timely interventions. AI accelerates drug discovery and vaccine development processes, supports epidemiological modeling, and promotes a one health approach by integrating data across disciplines. AI also enhances wildlife surveillance efforts, enabling proactive interventions to prevent zoonotic spillover and bolstering global preparedness for future pandemics [35]. AI has the

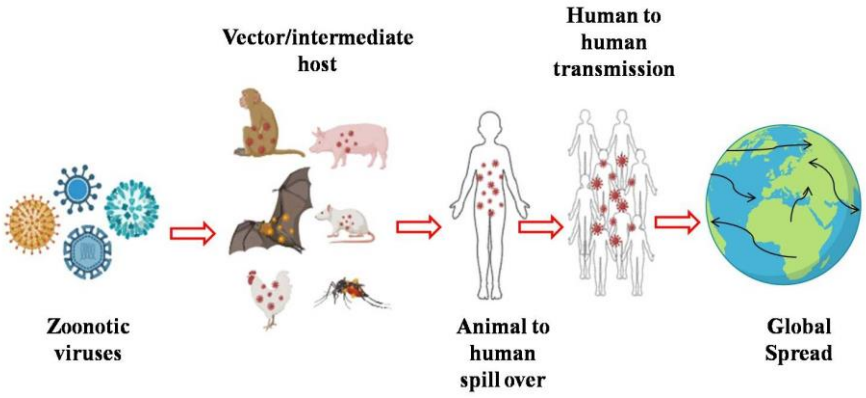
potential to change medical practices. The integration of AI in the healthcare sector has great potential in enhancing the accessibility of healthcare services [36-38]. AI can quickly identify the red flags and alert the healthcare authorities about any abnormal symptoms and helps in providing faster decision making. In addition, AI-based medical chatbots help to avoid crowding in the clinics, hospitals by providing online consultation on disease symptoms, infection, self-screening and care [39]. Telehealth has become a powerful communication tool during global health emergencies which can be adopted either synchronous or asynchronous. This allows patients and provider to communicate thereby improving the access and while reducing the risk of infection and disease transmission [40-42]. These technologies have proven to be powerful in the fight against the pandemic, which was evidenced in counteracting the COVID-19 as they provide strong support in pandemic prevention and control [43-45].

The lesson from the past zoonotic virus pandemics is crucial for present-day pandemic preparedness and response efforts. Past zoonotic virus pandemics provide valuable insights into the complex dynamics of virus emergence, transmission, and control [46]. By analyzing the similarities and differences between different epidemics or pandemics, the recurring patterns could be identified that could shed light on the effectiveness of various containment and mitigation strategies.

Table 1. List of some of the major virus outbreaks in history

Disease	Pathogen	Family	Year
Spanish Flu	H1N1 virus	Orthomyxoviridae	1918-1919
Asian flu	H2N2 virus	Orthomyxoviridae	1957–1958
Hong Kong flu	H3N2 virus	Orthomyxoviridae	1968 – 1970
HIV/AIDS	HIV	Retroviridae	1981
SARS	SARS-CoV	Coronaviridae	2002-2003
Zika	Zika virus	Flaviviridae	2007
Swine Flu	H1N1 virus	Orthomyxoviridae	2009-2010
Ebola	Ebola virus	Filoviridae	2014-2016
MERS	MERS-CoV	Coronaviridae	2015
COVID-19	SARS-CoV-2	Coronaviridae	2019

Figure 1. Zoonotic viruses spill over from different animal species to humans and spread globally.



Conclusion

The virus outbreak and the responsible pathogen that will cause the next epidemic or pandemic are unpredictable. Hundreds of unidentified viruses that are circulating among the wildlife, likely are responsible for the next epidemic or pandemic unless the zoonotic "spill-over" or "evolutionary jump" events are not defined. The zoonotic virus once it establishes human-human transmission can spread to most of the countries within days in the globalized world. However, not all zoonotic pathogens are capable of establishing sustained animal-human or human to human transmissibility due to the hierarchical series of genetic, immunological, ecological and epidemiological barriers. By gaining a systematic understanding of these viruses and their associated risks, proactive measures to prevent and control future outbreaks can be implemented. Outbreak preparedness and response plans should be in place in each country, so that viral outbreaks can be detected as soon as possible and proper control measures can be implemented thereby minimizing the societal and economic disruption. In addition, pharmaceutical interventions such as rapid diagnostic assays and new systems for rapid vaccine development, production and distribution should be developed to improve the worldwide response to the pandemic. The race between the continually evolving zoonotic viruses and humans aiming at understanding their origins and epidemiology is never going to cease. The viral threats will not reduce; the challenge lies in our ability to control and prevent them.

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Conflicts of interest

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Ethics statement

Not applicable.

Data availability statement

Not applicable.

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