Hit hard in golden hours: thoughts on preventing the next pandemic

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Dear Editor,

We are submitting manuscript titled “Hit hard in golden hours: Thoughts on preventing next pandemic” for your kind consideration and publication in your esteemed journal.

The crisis due to COVID-19 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has been the largest and biggest catastrophe of our lifetimes. Its devastating impact included every aspect of human life. Like, so many other pandemics in the past, this too shall pass, but it has undoubtedly changed the world.

There were several high-impact pathogens over the past two decades including three new coronaviruses, several highly pathogenic influenza A viruses, more recent pandemics like the Zika virus in 2016 and the continuing rise and spread of Ebola in West and Central Africa since 2013 [1]. According to UN, WHO and WWF International, pandemics such as coronavirus are the results of humanity’s destruction of nature. There is an increasing number of diseases leaping from wildlife to humans due to unsustainable and illegal wildlife trade as well as the devastation of forests [2]. A WWF report warns: “The risk of a new [wildlife-to-human spillover] disease emerging in the future is higher than ever, with the potential to wreak havoc on global security, economy, and health.” [2] Similar warnings were raised by experts on various occasions in the past also before the current pandemic. Now the question emerges, can we prevent the next pandemic?

To prevent pandemics, there have been global health security initiatives to increase current capacities, processes, and institutional arrangements over the past decade. It consisted of international health regulations on the global health security agenda; however, none of them proved sufficient in stopping the emergence and spread of SARS-CoV-2 [3]. The current pandemic has exposed failures to act appropriately and adequately. According to Andrew PD et al. (2020), the costs of preventing future zoonotic outbreaks—by controlling the trade of wildlife and curbing deforestation—are as little as $22 billion a year, 2% of the economic and mortality costs of tackling COVID-19, which some economists predict could reach $10-20 trillion [4].

The frequency of epidemics and pandemics is likely to increase in future, mainly fueled by climate change, globalized travel and trade, environmental degradation, urbanization, and persistent social and economic inequalities [3]. There is an unmet need to create global strategies, policies, and regulatory frameworks that adequately address all aspects of disease emergence [5]. According to Dennis C et al. (2021), one of the very important aspects of these efforts is to build surveillance for early detection of any microbe transfer into humans and livestock and disrupt that transmission pre-emptively, particularly in geographical hotspots [3]. We believe there are two clear stages where the emphasis should be focused. Firstly, how can we prevent the emergence of such diseases? Notably, the current focus is mainly on this stage. Secondly, how can we prevent the local disease conversion into a pandemic if the disease emerges? So, there is a simultaneous need to address that if a similar situation, as of COVID-19, arises then how to deal with it differently and effectively based on the lessons learnt during this pandemic given the ongoing threat of more pandemics in the future.

To understand what can be done next time, let’s have a look at the chronology of the current pandemic. The first known case of COVID-19 was identified in Wuhan, (Hubei province) China, on December 1, 2019. On December 27, a Chinese lab assembled a near-complete sequence of the virus, showing it to be like the coronavirus that caused the 2002-03 SARS outbreak. The WHO office in China was informed of pneumonia patients of unknown aetiology in Wuhan City, on 31 December 2019. Cases of pneumonia with unknown aetiology, a total of 44 in
number were reported by national authorities of China to WHO from 31 December through 3 January 2020. The Chinese Centre for Disease Control and Prevention (CDC) obtained a full sequence of the virus on January 3rd. CDC issued a “Watch Level 1 Alert” for Wuhan and advised travelers’ to Wuhan to avoid animals, animal markets, and animal products on January 6. On 7 January, a novel coronavirus was identified by the Chinese authorities as to the cause and was named “2019-nCoV” [6–8]. The first case outside China was identified in Thailand on January 13th. Based on clustered cases, there is a possibility of human-to-human transmission was conveyed in an internal meeting by Chinese health officials on January 14. As of January 20 January 2020, 282 confirmed cases of 2019-nCoV were reported from four countries including China (278 cases), Thailand (2 cases), Japan (1 case) and the Republic of Korea (1 case). Cases found outside China were exported from Wuhan City. Among the 278 cases confirmed in China, 258 cases were reported from Hubei Province, 14 from Guangdong Province, 5 from Beijing Municipality and one from Shanghai Municipality. CDC announced the first novel coronavirus case in the United States, in a patient who returned from Wuhan on January 15, 2020. The Wuhan lockdown began on 23rd January 2020. On 30 January 2020, WHO declared the novel coronavirus outbreak a public health emergency of international concern (PHEIC), WHO’s highest level of alarm. Till then only 98 cases without any death were documented outside China. On January 30 January, President Trump suspended entry into the United States of most foreigners who were physically present in mainland China during the preceding 14-day period, effective February 2. WHO announced the outbreak as a pandemic on 11th March 2020, because of the rapid rise in cases outside China. The reported figures in total 114 countries were more than 118,000 cases, and the number of deaths was 4,291 on the same day [6–8]. Thereafter, restrictions and lockdowns were placed widely across the globe. International flights were suspended along with domestic flights and borders were closed. The work-from-home orders were issued and many industries were temporarily shut down. Everything was done to prevent the spread of the organism and control the pandemic. But by that time the disease moved way beyond an easier control and out of golden hours. Can we prevent the next pandemic (emergence of disease) when such warnings of increasing prevalence are there? Or should we hit hard if disease emerges? An unusual cluster of severe cases or deaths in humans was the main factor leading to the identification of past epidemics or pandemics [3]. In December 2019, it was identified that some unknown disease has emerged, and cases are clustering in Wuhan city. It took almost 44 days from the identification of the first case in China to the identification of the first case outside China on 13th January 2020. We believe the period of December 2019 was a crucial one and it was a period of golden hours in terms of controlling local disease and preventing its conversion into an epidemic or a pandemic. In December 2019, the disease was restricted in and around its source. Later, it spread to neighboring provinces in China, nearby countries, a large portion of Europe, the USA, and Asia and eventually grappled the rest of the world. The level of measures/precautions/notifications was rising as the disease was progressing. Essentially, measures to control the disease were being escalated stepwise.

This situation is analogous to the concept of antibiotic therapy during golden hours in the management of sepsis in critical care (early, adequate, and appropriate therapy). Over the years the strategy of antibiotic prescription has changed from escalating therapy to de-escalating therapy in critically ill septic patients. On encountering critically ill septic patients in hospital, empirical therapy is started, and it covers the broadest spectrum. It usually consists of multidrug and/or combination therapy [9]. Not only does it covers the broadest spectrum but also must be given as early as possible, preferably within one hour of sepsis recognition. This is a strategy of hitting hard. For such therapy to be planned more specifically in context to each patient, there is a need to answer a few questions and based on responses to these questions, an antibiotic prescription is individualized. These questions consist of the most likely site of infection, likely pathogens, any history of previous hospitalization or antibiotic intake, any comorbid illness or chronic organ dysfunction and local culture and sensitivity pattern [Table 1]. During the management of such patients as more information becomes available, antibiotic is changed from broad-spectrum empiric antibiotic therapy to more specific and targeted therapy and its spectrum is narrowed down (de-escalation) based on the clinical response and available culture and sensitivity report. This is based on the evidence that early, appropriate,
and adequate antibiotic therapy in critically ill septic patients improves morbidity and mortality while ensuring simultaneously that antibiotics are not being used unnecessarily thus avoiding extra cost, toxicity, and the emergence of resistant organisms [9].

When a new virus emerges there’s a chance that its true extent and impact will initially be under-reported or cannot be assessed fully, and this is the first potential delay. Then, there’s likely to be a time lag while scientists try to identify the virus, its infectivity rate and potential along with its mode of transmission, its effect on health and how best it can be contained. We believe rather than escalating preventive measures, the strategy of de-escalating measures (Hit Hard) should be used, and it can be started right from the day when there is the first suspicion of an unusual cluster of similar illnesses due to undiagnosed disease in a particular geographical area in a large number. This situation is a prerequisite and then, there is a need to answer a few questions, about the way it is done while prescribing antibiotic therapy. It includes the most likely source of infection, most likely organism, how it spreads, what are the symptoms, whether there is an asymptomatic stage in the disease or an asymptomatic disease state and then implements the most effective measures from the very beginning including rapid detection of the disease, availability and access of basic care facilities, tracing of contacts, surveillance, quarantine, isolation procedures and curfew/lockdowns in that geographical area [Table 1]. The idea is to contain the spread and to restrict the disease to its source of origin by doing everything required (hit hard). Over the period with more understanding of the disease process, the measures can be de-escalated according to the information accumulated based on available data from research. While answers to these questions remain under research, it should be assumed that the disease spreads from person to person, has an asymptomatic stage in the disease/asymptomatic disease and has the pandemic potential. This is a strategy of preventing a local disease from converting into a more widespread epidemic or pandemic by hitting hard initially. This is feasible provided appropriate measures are in place at the international and national levels, including the regulatory and legislative framework.

Though the best strategy is the prevention of emergence, it is easier said than done. It is true that health systems typically prefer responding to illnesses rather than preventing them. As the current pandemic has shown us that unknown diseases can emerge and spread rapidly in this globalized world. It is likely that in future more such pandemics become the reality since it is difficult to control factors leading to emergence. So, it becomes more important to create a strategy where the disease should not be allowed to spread by responding early, adequately, and appropriately (hitting hard in golden hours) as we do with antibiotic therapy in critically ill septic patients.

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