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Editorial

SARS-CoV-2 Pandemic: Public Health Prevention Strategies

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Public health strategies aimed at the primary prevention of infectious disease, starts with tracking of possible outbreaks, tracing the modes of transmission, seeking to prevent new cases of infection from occurring by interrupting the transmission of pathogens to susceptible hosts, increasing their resistance to infection. SARS-CoV-2, the most potent killer virus has caused unprecedented pandemic worldwide. At the time of this writing, according to the Johns Hopkins COVID-19 tracker (coronavirus.jhu.edu), global reported cases exceed 23.6 million, with over 800,000 deaths. In the most advanced country, the USA, there are 5.5 million infected individuals, and over 174,000 deaths. Brazil (3.4 mil) and India (2.8 mil) are ranked 2nd and 3rd in terms of number of infected individuals reported. In the absence of a cure, this pandemic has become a public health providers nightmare. Early preparation, messaging, and social distancing interventions during this first phase of the pandemic, have accomplished the goal of flattening the curve in some of the countries. In an unprecedented effort, hundreds of scientists, clinicians, public health workers as well as laymen worldwide, are in race against time, to answer myriad questions raised by individuals who are under a panic, to develop better diagnostic tools (preservatives, reactants and characterization technologies), novel drugs, interventions (pharmacological and nonpharmacological), vaccines and neutralizing antibodies [1-4].

After 6 months of the first reported case of coronavirus infection, epidemiologists, research scientists, and clinicians are analyzing the global data, to find out more about the origin of this killer virus, genomics, mutation, mode of transmission, infectivity, acquired immunity, clinical symptoms, severity of the disease, innate immune response, and ways and means of containment, management and prevention. According to an article in the recent MIT Review, titled, "The Virus That Split the World," the author says, that by late July, most rich countries had brought their Covid-19 infection rates down far below their initial numbers [5]. In the US. However, the number of daily new cases and deaths are still climbing as of this writing. This crisis has badly damaged global opinion about American Competence. Only future will tell us, as to which country did better than the rest, and how did they achieve such success. This brings us to the big question, -why have some countries fared so much better than the others, in preventing, flattening the curve, or containment of this unprecedented pandemic? In the same issue of MIT Review, Varagur Krithika has discussed how the following six countries handled the SARS-CoV-2 pandemic: Mongolia, Germany, Liberia, Uruguay, Sweden and Vietnam. The one that stands out amongst these six countries is Vietnam, with population of 97 million, with zero coronavirus deaths. In a short guest editorial, it is hard to cover all aspects of this unprecedented pandemic, readers are urged to refer to original articles and comprehensive reviews on this topic [6-9].

The main route of SARS-CoV-2 transmission is through respiratory droplets and close contact. Angiotensin enzyme 2 (ACE2) the major receptor for the transmission of this virus, is a type 1 integral membrane protein that is expressed on many cell types, including, nasal epithelial cells, cardiovascular system, gut kidneys and lungs. In the cardiovascular system, ACE2 is expressed in cardiomyocytes, epicardial adipose tissues, cardiac fibroblasts, vascular smooth muscle cells and endothelial cells. Recent studies have demonstrated, that ACE2 receptors are expressed 100-fold more in the upper and lower gastrointestinal tract than respiratory organs. Hence covid-19 patients suffer from diarrhea, diminished appetite, nausea, vomiting, and abdominal pain. Both the S-glycoprotein of the

SARS-CoV-2 and ACE2 receptors are highly glycosylated. The spike protein of the virus consists of two functional units, S1 and S2 and the receptor binding domain (RBD), resides within the S1 subunit. Spike proteins that protrude from the viral envelope, constitute main target of neutralizing antibodies, as well as for possible pharmacological interventions. In the absence of any cure for the coronavirus disease, currently, best public health practices, such as wearing facial masks, frequent hand washing, social distancing, contact tracing of infected individuals and self or mandated quarantine are the only choice. Having said that, I would like to remind the readers that there is a great challenge and an opportunity to develop designer drugs and designer antibodies for combating this killer virus.

The US Centers for Disease Control (CDC) and Prevention has posted an updated (July 2020) Pandemic Planning Scenario, which includes information on viral transmissibility, disease severity, pre-symptomatic and asymptomatic contribution to the disease transmission. Viral transmissibility (Ro) is defined as the average number of people that one person with COVID-19 is likely to infect in a population, without any immunity (from previous infection) or any interventions. It is important to understand, that Ro is an average number of people an infected host can infect and can therefore, change according to different scenarios. At the time of this writing, Ro value is more than 1 in many states in the USA, Brazil and India, indicating that in these localities, exponential growth in the number of positive cases can be expected. Disease severity is defined as infection fatality rate (IFR), which denotes the number of individuals who die of the disease among all infected individuals. Pre-symptomatic case is an individual infected with SARS-CoV-2 who has not exhibited any symptoms at the time of testing, but who later exhibits symptoms during infection. An asymptomatic case is an individual infected with SARS-CoV-2 who does not exhibit any symptoms during infection [3].

World Health Organization in their April 24, 2020 report reviewed the evidence on antibody response to SARS-CoV-2 infection. According to their views, most of the studies show that people who have recovered from infection have antibodies to the virus. However, some of these people have very low levels of neutralizing antibodies in their blood [1]. This finding suggests that cellular immunity may also be critical for recovery. No study, yet, has demonstrated that the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by this virus in humans. According to the researchers at the University of Pennsylvania Perlman School of Medicine, acute SARS-CoV-2 infection in humans, results in broad changes in the circulating immune cell populations, including CD8T cell activation in a subset of patients. They also noted, that infection results in heterogenous CD4T cell response and activation of CD4T cell subsets. The authors concluded - "Our data suggest that the immune response in hospitalized COVID-19 patients may fall across this spectrum of immune response patterns, presenting as distinct immunotypes linked to clinical features, disease severity and temporal changes in response and pathogenesis." In view of these findings, there is a great opportunity to develop indigenous drugs that modulate the innate immune response. For instance, China has been conducting several clinical trials with Chinese traditional medicines for managing immune response in Covid-19 patients.

Jon Cohen in a recent article in Science (2020), argues that designer antibodies could battle COVID-19 before vaccines arrive [10]. There are over hundred studies, trying to develop a vaccine to SARS-CoV-2 virus. According to experts, there is an equal competition to produce targeted designer antibodies, that could provide an instant immunity boost against the virus. The World-renowned Infectious Disease expert Dr Anthony Fauci, head of NIAID of the National Institutes of Health, USA says, "If you were going to put your money down, you would bet that you get the answer with the monoclonals, before you get the answer with a vaccine." The author concludes, that "Regardless of cost, evidence that monoclonals work as preventives could benefit everyone, by giving vaccine makers a clear sign, that antibodies against the surface protein of SARS-CoV-2 are enough to protect a person." In my opinion, this should also encourage the development of designer drugs, against the spike protein interaction with SARS-CoV-2 receptors. Indeed, in vitro studies with Vero E6 cells have demonstrated, that when exposed to chloroquine or hydroxychloroquine prior to infection, these drugs effectively prevent the subsequent viral infection [11,12]. Hoffman and associates in a recent article, report that although chloroquine has been shown to inhibit SARS- CoV-2 infection in vitro in some cell lines, it does not inhibit infection of human lung cells by coronavirus-2019 (Nature: July 22, 2020) (https://doi.org/10.1038/s41586-020-2575-3). That poses a challenge to the pharma industry, to come up with a drug that can prevent the virus-host receptor interaction in any cell lines.

When faced with an unprecedented challenge by a new and a novel killer virus, we have just few options. First and the foremost will be, to anticipate the worst and prepare the country and the population for aggressive quarantine measures. At the individual level, to follow the best public health policies such as face covering, hand washing, social distancing, contact tracing and containment. Once the infection is detected, best option is to triage the infected and provide the best treatment to manage the symptoms. In terms of interventions, encourage, drug, biologics, and vaccine development projects. In the USA, Food and Drug Administration (FDA), has created a special emergency program for developing coronavirus therapies, the Coronavirus Treatment Acceleration Program (CTAP). The international Clinical Trials Registry Platform of the WHO, has recorded 536 clinical studies for the development of post-infection therapies. At the time of this writing, potential drugs of importance include, those that are in the final stages of human trials (phase 111-1V), favipiravir, remedesivir, and lopinavir. The WHO has initiated the "SOLIDARITY Trial" in 10 countries, enrolling thousands of people. Seventeen vaccine candidates are in the second or third stage of human safety and efficacy testing (Phase 11 and Phase 111). Indian Pharma Industry is only second to the Chinese Pharma, in terms of drug discovery and development. Coronavirus has opened a new opportunity in the areas of biotechnology and pharmacology, for the development of cost-effective test kits, designer drugs, designer antibodies, and mass production of potent vaccines.

In the midst of all these activities, some researchers are wondering about "herd immunity." In a recent issue of New York Times (August 17, 2020), Apoorva Mandavilli discusses about this topic under the title, "What if 'Herd Immunity' is Closer Than Scientists Thought? It was thought that to attain herd immunity at the population level, perhaps 70 percent of a given population must be immune. It appears there is quite a debate, as to at what lower number can such herd immunity be achieved. The author speculates, that in parts of New York, London and Mumbai, it is conceivable, that there is already substantial immunity to the coronavirus. The author discusses a study in Mumbai, where researchers conducted a door to door survey and took blood samples for antibody testing. They found that 51 to 58% percent of residents in poor areas had antibodies, versus 11 to 17 percent elsewhere in the city. Similar findings have been reported from the city of New York in poor neighbor hoods versus posh communities. In an article in the New York Times dated July 9, 2020, Goldstein reports, that in a working-class neighborhood, a clinic in Queens, 68% of people tested positive for antibodies to the CoV-2, and in another similar neighborhood in Jackson Heights, the number was 56%. Whereas, in a wealthy suburban clinic in Cobble Hill, only 13% of people were positive for antibodies. According to Sunetra Gupta, a theoretical epidemiologist at Oxford University, -London and New York may already have reached herd immunity. Although it is a welcome news, we still do not have data to support such hypothesis.

The famous epidemiologist from Midwest, Michael T. Osterholm, Regents Professor University of Minnesota, says, that only viable endgame for coronavirus is to play 'whack-a-mole' with the virus, -meaning if the virus cannot find you, you will not get the disease. He also predicted that SARS-CoV-2 may not eventually burn out. It may just stay with us like the HIV, only a full 'lockdown' would save more lives. He further emphasizes that, "We need to bring everyone together and say, 'This is us versus the virus". Therefore, based on the global experience, the final 'Mantra' for public health workers for the prevention of SARS-CoV-2 spreading should be, to repeat the following advice: Mass testing, social distancing, use of facial masks in public or crowded places, rapid quarantines, contact tracing, and when necessary, strict lockdowns.

As the MIT reviewer Feldstein wrote, "The SARS-CoV-2 has split the World"- the unprecedented pandemic has split the countries as well. In the US 2020 presidential election, 'to lockdown or not to lockdown,' has become a contentious issue, This is a burning issue not only in the USA, but also in many other countries, whether to have a total lockdown to suppress the surge of the virus or keep it open and face the consequences. Only time will tell as to which country did better in handling this unprecedented pandemic of SARS-CoV-2 virus.

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