

The Other Side of the Coin of COVID-19: Development of Molecular and Genetic Sectors in Developing Countries as Exemplified by BANGAVAX® from Bangladesh

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Abstract

The world has been in pandemic situation after the outbreaks of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019. Relevant disease COVID-19 has devastated the world ever since, causing more than 5 million of deaths and still counting. The challenging epidemiology and pathogenesis of SARS-CoV-2 and COVID-19 along with emergence of new variants of the virus have jeopardized the entire health care delivery systems of almost all countries of the world. In the meantime, several drugs have been repurposed for treatment of COVID-19, however, the management of COVID-19 is still limited to a type of symptomatic management schedules, as no antiviral drug capable of eradicating SARS-CoV-2 could be established. In addition to conventional preventive measures to combat further propagation of SARS-CoV-2, several vaccine candidates have been developed. Billions of people have been vaccinated to protect from acquisition of SARS-CoV-2, however, the magic vaccine is yet to be explored that may provide effective HERD IMMUNITY to the society. In these circumstances, the major challenge of the mankind is to get real insights about the virus, SARS-CoV-2 and the disease, COVID-19 as well as initiate program for better management of future devastation. This review will provide a comprehensive outline regarding the virus and diseases that induced this pandemic with a new home-work to prevent such pandemic in future, especially in the context of developing and resource-constrained countries.

**Keyword:** SARS-CoV-2; COVID-19; Pandemic; Vaccine; BANGVAX®

### Kinetics of SARS-CoV-2 and COVID-19 in global perspectives

Coronaviruses (CoVs) represent a family of viruses that usually cause respiratory and intestinal illnesses both in humans and animals. Coronaviruses (family Coronaviridae, subfamily Coronavirinae) are pathogens of birds and mammals. Coronaviruses are positive-sense RNA viruses and are currently classified into four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. Seven different types of CoVs have been detected in human and two of them, viz., severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle-East respiratory syndrome coronavirus (MERS-CoV), have induced considerable turmoil in this century. In addition, 4 other CoVs, namely, HCoV-229E and HCoV-NL63 (alpha CoVs), and HCoV-OC43 and HCoV-HKU1 (beta CoVs) infect human as a common virus, have been detected in human. Evolutionary history indicates that the common ancestor of CoVs have been existed for millions of years; however, the recent ancestor may be about 10,000 years old [1]. Now, the world is struggling with the 7<sup>th</sup> CoV (a beta CoV), SARS-CoV-2. Initially, the virus was regarded as novel coronavirus and on 31<sup>st</sup> December 2019, the World Health organization (WHO) China Office was informed of cases of pneumonia of unknown etiology. Subsequently, a new type of virus was isolated as the cause of pneumonia on January 11 and 12, 2020, and the genome of the new virus was isolated within one week and on January 20, Republic of Korea declared novel coronavirus infection on January 2020. On January 30, 2020, the World Health organization (WHO) declared outbreaks of the novel virus constitutes Public Health Emergency of International Concern (PHEIC). On February 11, 2020, the International Committee on Taxonomy of Viruses, denoted the official name of "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease caused by SARS-CoV-2 has been termed as coronavirus disease 2019 (COVID-19) by WHO. On March 11<sup>th</sup> 2020, WHO declared COVID-19 a pandemic and 114 countries reported COVID-19 cases by that time. The numbers of COVID-19 patients were 118,465 with 4295 deaths on the day of declaration of pandemic of COVID-19 by WHO with highest number of cases deaths in China. Almost two years after outbreak of COVID-19 as of today (25<sup>th</sup> January 2022), the total numbers of confirmed COVID-19 patients have reached to 224 countries with more than 354 million patients and 5.62 million COVID-19-related deaths [2]. The main events regarding to nomenclature of this virus have been shown in table 1. The data of figure 1 indicates the sharp rise of COVID-19 cases during recent days.

Important dates	Milestones/Major events
December 2019	Outbreaks of pneumonia in Wuhan, China by a novel virus
January 11 and 12 <sup>th</sup> 2020	Isolation of virus
January 20 <sup>th</sup> 2020	Republic of Korea declared infection by novel virus
January 30 <sup>th</sup> 2020	Declaration of "Public Health Emergency of International Concern (PHEIC)" by WHO
February 11 <sup>th</sup> 2020	Naming of SARS-CoV-2 and COVID-19
March 11 <sup>th</sup> 2020	Declaration of COVID pandemic by WHO
March 6 <sup>th</sup> 2020	COVID-19 cases: One million mark
January 25 <sup>th</sup> 2021	COVID cases: 100 Million mark
August 3 <sup>rd</sup> 2021	COVID-19 Cases: 200 Million mark
January 6 <sup>th</sup> 2022	COVID-19 cases: 300 Million marks
January 25 <sup>th</sup> 2022	COVID-19 cases: 354 Million

**Table 1:** Major events regarding SARS-CoV-2 and COVID-19 pandemic.

**Figure 1:** Cases of COVID-19 during last 2 years.

Source: <https://www.statista.com/topics/5994/the-coronavirus-disease-covid-19-outbreak/>

## Heterogenous pattern of epidemiology and pathogenesis of COVID-19 in different parts of the world

### Why fewer cases of COVID-19 in Asia and Africa compared to Europe and North America?

Millions of COVID-19 patients have been reported globally, however, all countries have not been affected in similar or compara-

tive manner. Even different parts of the same country have shown highly heterogeneous incidence of COVID-19. The numbers of COVID-19 cases and deaths in different continents are shown in table 2.

Geographical area	Population	Percentage of global population	Total COVID-19 Cases	COVID-19-related deaths
Asia	4641 million	59.5%	92 million (1.98%)	1.27 million
Europe	747 million	9.58%	109 million (14.59%)	1.58 million
Africa	1340 million	17.19%	10 million (0.746%)	0.235 million
North America	592 million	7.59%	82.6 million (13.95%)	1.28 million
South America	430 million	5.51%	44 million (10.23%)	1.2 million
Oceania	43 million	0.551%	2.2 million (5.11%)	5,222

**Table 2**

For example, Asia, Africa, Europe, North America, South America, Oceania have reported 92 million, 10 million, 109 million, 82.6 million, 44 million, and 2.2 million COVID-19 cases, respectively. If the proportions of COVID-19 cases are analyzed on the basis of total populations, data clearly indicates that Europe (14.9%), North America (13.95%), and South America (10.23%) have been harboring significantly higher proportions of COVID-19 patients compared to those of Asia (1.98%) and Africa (0.746%). Why these types of variability have been evident regarding COVID-19? The nutritional status of the population, power of health care delivery system, and economic strength of Western countries are usually considered better than those of Asian and African countries. The exact mechanisms underlying these disparities are not yet clear; however, several investigators have pointed out to the following factors:

The numbers of tests for SARS-CoV-2 has not been adequately accomplished in Asia and Africa as highly sophisticated diagnostic processes are required to confirm SARS-CoV-2 infection. This is a highly tempting conception, but lacks evidence. This might be the case at the beginning of pandemic when there has been minimum polymerase chain reaction (PCR) facilities in most countries of Asia and Africa. However, from the start of 2021, most of the countries of Asia and Africa, those reported considerable cases of COVID-19, developed the diagnostic system to a reasonable level. In addition, many countries of Asia and Africa had PCR facility from the

beginning of pandemic but did not register so many COVID-19 patients. Moreover, the deaths due to COVID-19 did not induce considerable panic in most Asian and African countries. It is also true that high load of COVID-19 cases and considerable mortality is a simple rule of all Asian and African countries. Being an Asian country, India has recorded 2<sup>nd</sup> highest cases (about 40 million) and 3<sup>rd</sup> highest mortality from COVID-19 (490,000). Also, Iran, Indonesia, Philippines, and Malaysia are within the top 25 countries recording massive numbers of COVID-19. South Africa is the only country of Africa that has ranked 19<sup>th</sup> regarding incidence of COVID-19 cases. Countries like Nigeria, Ethiopia and Egypt with considerable populations have registered considerably lower numbers of COVID-19 patients. Although we are not discarding that numbers of tests may be a factor but that does not explain the reality of COVID-19 epidemiology, almost 2 years after the pandemic started.


Another factor may be related to reluctance of the people of Asia and Africa for not being interested to have a check for SARS-CoV-2. This does not seem to be the fact because lines of huge population have been formed in these countries to be checked for SARS-CoV-2. Data have shown that 16 countries of Asia have reported more than one million positive cases of COVID-19. Also, more than one million tests have been done in 20 African countries.

As the factors like capacity of testing and reluctance to test could not be substantiated in Asia and Africa compared to devel-

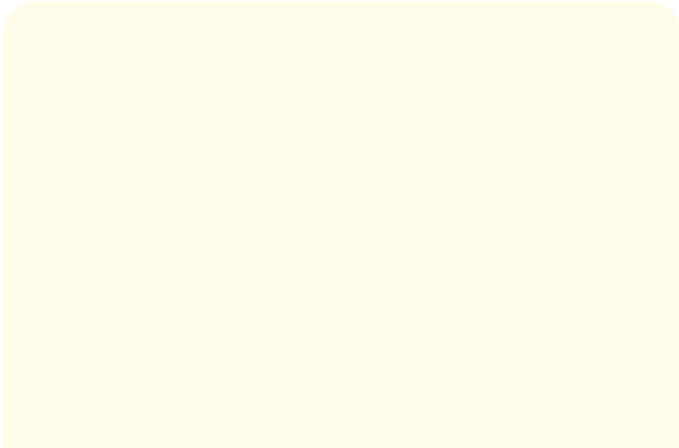
oped countries, the query remains as to why the proportion of positivity of SARS-CoV-2 is much higher in Europe and American continent than Asia and Africa. The factors like usage of spices, season facts, previous history of taking vaccine specially against tuberculosis, and food habits could not also be substantiated by scientific evidences. Countries like India, Iran, and Indonesia have shown very high numbers of COVID-19 patients at different points of pandemic and this was equally found in summer or winter. Usage of vaccine and chloroquine is a normal practice in Asia, Africa and South America. However, different pattern of prevalence of SARS-CoV-2 infection have been found over these areas. The implication of genetic factor and blood groups have been cited by some investigators, but those are yet to get a consensus.

If the entire period of pandemic is viewed as a whole, differences in population demography may be found as an indicator of diverse incidence and mortality between developed countries versus countries of Asia and Africa. SARS-CoV-2 spreads from hu-

man to human *via* droplet or personal contact. The pathogenesis of COVID-19 is also dependent on the localization of virus in lower respiratory tract and the lungs. The point of entry of virus is nasal and oral cavity. After the entry of the virus, it localizes in respiratory tracts, where it enters different cells mainly *via* ACE-2-receptor with the assistance of some co-factors. There may be other route of entry into pulmonary cells, but that is yet to be established. After entry into their target cells or organs, the infection may pass asymptomatic in most patients or it can induce mild or moderate COVID-19. The factor that would determine the nature of infection is dependent on the immunity and more specifically on the innate immunity of the infected persons [4]. Thus, Asia and Africa with considerably lower number of aged people were not severely attacked by COVID [5,6]. This is supported by the data that mention about 19.2% population of Europe is 65 years or older, where this is only 9.2% for Asia; whereas, only 4% people of Africa are 65 years or older (Figure 2).

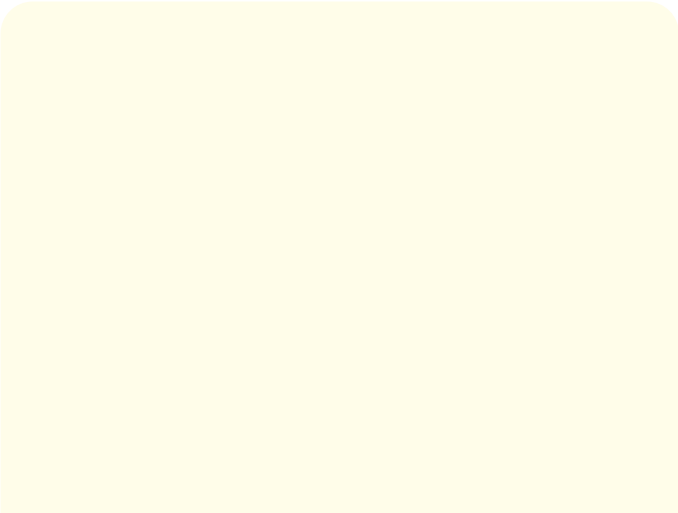


**Figure 2:** Age distribution of population of 5 continents.



**Figure 3:** The age distribution of deaths due to COVID in USA, the country that registered highest numbers of deaths.

Most of deaths were found in age group 50 years or older in USA. In India, 88% of all COVID-related deaths occurred in the age group of 45 years or older.



**Figure 4:** Diverse death due to COVID-19 in developing and developed countries.

Courtesy: IDB working paper series N<sup>o</sup> IDP-WP-1154.

However, considerably more deaths were recorded among young population in developing country compared to developed

country. Usually, patients with mild and moderate COVID-19 attend the testing centers. Thus, the bulk of SARS-CoV-2 infected patients remain out of screening as they are asymptomatic. The factor that determines whether one will be asymptomatic or may develop mild or moderate symptoms are dependent on the immunity of host and more specifically on the nature and magnitude of innate immunity in the upper respiratory tracts. It is well known that COVID-19 is prone to be symptomatic in patients with certain comorbidities. The comorbidities are usually prevalent in aged population. Thus, one tempting hypothesis regarding higher numbers of patients in Europe and America and lower numbers of patients in Asia and Africa may be explained by abundant younger population in Asia and Africa compared to Western countries (Figure 3,4).

Then, there is a natural query as to why so many patients of COVID-19 were detected in South America. In addition to the known comorbidities, there should be other relevant factors like usage of illicit drugs, HIV infection, and other relevant factors. It is understandable that there remains paucity of information during a pandemic, but these points should be considered in future in proper scientific manner.

Factors other than older age and presence of comorbidities:

The curative health service is well designed in Europe and America, but they had inherent limitation regarding public health delivery system in these developed countries. For example, there is provision of expanded program of immunization (EPI) in most developing countries of Asia and Africa and village level community health workers make a monthly house to house visit. These manpower and policy become a strong force during pandemic management in relevant countries.

Another important factor is related to vaccine hesitancy in developed countries of USA and Europe. This type of mentality is seldom present in developing and resource-constrained countries. Rather, these countries had the problem of procuring vaccines as they were not vaccine producer and depended on developed country for vaccine.

### Management of COVID-19 and its limitation

There are two spectrums of management of COVID-19 pandemic. All COVID-19 patients are endowed with variable symptoms related to pathogenesis of SARS-CoV-2 and they are living source of transmission of the virus to the society. Thus, the management of

COVID-19 is based on: (1) management of COVID-19 patients and (2) prevention of acquisition of SARS-CoV-2.

### Treatment of COVID-19

Irrespective of the nature of the SARS-CoV-2, studies of last 2 years, have shown that the (1) race of patients, (2) climatic condition of the region, (3) age of the patients, (4) presence and absence of comorbidities, the COVID-19 patients may be asymptomatic or they may develop mild, moderate or severe symptoms of COVID-19. However, proportions of pathological conditions may differ based on different co-factors of the patients and these have not been explored to sufficient extent.

Regarding management of COVID-19, there remain diverse strategies in all countries of the world. In case of COVID-19, the asymptomatic patients are not usually given any sorts of specific treatment; however, based on local conditions, they are given treatment of symptomatic management strategies. These include antipyretic agents, anti-histamin drugs and other symptomatic medications. On the other hand, patients with mild COVID-19 patients are given the drugs for symptoms along with some other medications. The patients with moderate COVID-19 receive a variety of medications, and in most cases, these are not so ethical. The drugs those have been used in moderate COVID-19 patients include drugs for symptoms, as well as drugs related to antibacterial drugs and antiviral drugs. Some non-approved drugs have also been used in many countries. Finally, patients with moderate and severe COVID-19 have been provided oxygen and management in intensive care units. Patients with severe COVID-19 also received immunomodulators or serum therapy and steroids [7,8]. Taken together, it is apparent that there is no specific anti-COVID drug and all treatments were targeted to minimize the symptoms.

### Prevention of SARS-CoV-2

During COVID-19 pandemic, the most important fact related to containment of spread of SARS-CoV-2 is multivariate. After the outbreak of COVID-19 and declaration of pandemic, WHO provided 3T conception that describes "Test", "Treatment" and "Tracing" as fundamental pillars required for containment of SARS-CoV-2. The 3T approaches have been followed differently in different countries. To implement 3T approaches, different countries have adopted partial and total lockdown, different restrictions involving educational institutions and business activities. Some countries have adopted some unique approaches as national policy. Japan has adopt-

ed 3C policy which represents “policy of avoidance”. 3C indicates avoidance of “Closed spaces”, “Crowded places”, and “Close-contact settings”. In fact, the hall mark of prevention approaches includes “usage of mask” and “hand sanitizers”.

Finally, preventive vaccines have been developed to contain SARS-CoV-2 propagation. Several types of vaccines have been developed. These include (1) nucleic acid-based, (2) whole virus-based, (3) protein subunit-based, and (4) viral vector-based. Among several prophylactic vaccines, the following vaccines have received Emergency Use Listing (EUL) by WHO.

- The Pfizer/BioNTech Comirnaty vaccine, 31 December 2020.
- The SII/COVISHIELD and AstraZeneca/AZD1222 vaccines, 16 February 2021.
- The Janssen/Ad26.COV 2.S vaccine developed by Johnson and Johnson, 12 March 2021.
- The Moderna COVID-19 vaccine (mRNA 1273), 30 April 2021.
- The Sinopharm COVID-19 vaccine, 7 May 2021.
- The Sinovac-CoronaVac vaccine, 1 June 2021.
- The Bharat Biotech BBV152 COVAXIN vaccine, 3 November 2021.
- The Covovax (NVX-CoV2373) vaccine, 17 December 2021.
- The Nuvaxovid (NVX-CoV2373) vaccine, 20 December 2021.

Comparative evaluation of different vaccines regarding safety and efficacy are not in the scope of this review. Generally speaking, vaccines against COVID-19 is differentially effective with considerable safety if properly used as per recommendation of the manufacturer. However, the waning of antibody responses of these vaccines, need of boosting vaccination, and nature of efficacy on different variants have exposed considerable discussions. Credible evidences to support or discard these speculations are yet to emerge. However, it seems that the vaccines are effective to contain transmission of SARs-CoV-2 for different duration, and booster doses may provide extended efficacy. Considerable numbers of vaccinated population develop a milder infection after they are infected by SARS-CoV-2. As COVID-19 is just in its 3<sup>rd</sup> year, and prophylactic vaccine has stepped into 2<sup>nd</sup> year, we have to wait more to get credible responses regarding these issues. The role of vaccination against different variants of SARS-CoV-2 is another controversial issue.

#### Development of vaccines against SARS-CoV-2 in different parts of the world

Vaccine development for SARS-CoV-2 is a complex interplay among health, science, economy, diplomacy, drug imperialism, and what not. Although WHO has given EUL to 9 vaccines, at least 19 vaccines have been used in the world to contain SARS-CoV-2. The numbers of vaccines used in different countries have raised to 30 as national emergency authority have provided permission to these vaccines. Some countries could not procure vaccines recommended for EUL by WHO and they solely used their home-grown vaccine.

#### Limitations of vaccine availability in most of the countries

The 9 vaccines those have been provided EUL recommendation by WHO have been produced by USA, UK along with EU, China, and India. Vaccine is an important tool to counter COVID-19. At the height of pandemic, the first vaccine of Pfizer was approved in UK and then in USA. As USA has more than 330 million population, the Pfizer vaccine reached outside USA after several days and months. The next, the cost of the vaccine, condition of temperature maintenance, and transport was highly specialized and thus, the vaccines made in USA was a dream for people of resource-constrained countries of Asia and Africa for several months after the entry of vaccine for prevention of SARS-CoV-2 in world arena. Legal procedure inhibited India to export vaccine to other countries until

**Figure 5:** Different types of vaccine against SARS-CoV-2.

Courtesy: List of COVID-19 vaccine authorizations.

[https://en.wikipedia.org/wiki/List\\_of\\_COVID-19\\_vaccine\\_authorizations](https://en.wikipedia.org/wiki/List_of_COVID-19_vaccine_authorizations)

their national demand are met. Thus, vaccine availability in most countries were dependent on many factors inclu foreign policy of relevant countries

#### Approach of other countries under constrained situations

Thus, USA, EU, and India had imposed several limitations to transport their vaccine to other countries. It is also true that the production capacity of vaccine was not adequate in these countries to cover the entire world. The limitation of maintenance of temperature, cost of vaccine and transport from one country to other remained as dark matter. Moscow's Gamaleya Institute developed a Russian vaccine, SPUTNIK, and in fact this is the first vaccine developed against SARS-CoV-2 in August 2020. The vaccine has been used in some countries, but it did not get the EUL of WHO.

Another notable example is Cuba. As we all know that collection of COVID vaccine from Western countries may not be accessible for Cuba, therefore, Cuba developed its own vaccine against COVID-19. The impact of SPUTNIK on containment of SARS-CoV-2 would remain as a controversial issue, as Russia has been registered 11 million cases of COVID-19 with 326,00 death with a population of only 144 million. On the other hand, the deaths due to COVID-19 has reduced tremendously after October 2021 in Cuba, the time when the effects of COVID-19 vaccine were expected.

#### BANGAVAX®, the home-grown COVID-19 vaccine of Bangladesh

Bangladesh is the 8<sup>th</sup> most populous country of the world. Till now, Bangladesh has recorded 1.68 million COVID-19 patients with more than 28,000 deaths. At the start of the pandemic, different foreign countries proposed to have phase III clinical trial with novel vaccine against COVID-19 in Bangladesh. However, nothing finally happened. Thus, the country is completely dependent on the vaccine coming from abroad. As of today, 35% Bangladeshi has been fully vaccinated and 56% had received at least one dose of vaccine. Containment of SARS-CoV-2 infection by vaccination is a complex and mostly elusive reality. Millions of people with two doses of WHO-approved vaccines have shown reinfection with SARS-CoV-2, irrespective of their variants. Thus, the concept of booster doses of vaccination was internationally accepted. However, people with one booster has also been infected by SARS-CoV-2. In this context, Israel planned to introduce 4<sup>th</sup> dose of COVID vaccine for the susceptible population group. These factors indicate that COVID vaccine may be required for decades and there may be necessity of 3

or 4 doses of COVID vaccine per year. In this context, there is no option but to develop home-grown COVID vaccine for Bangladesh to save millions of their population.

#### BANGAVAX®: Update and future projections

GBPD060, trade name BANGAVAX®, is an mRNA-based vaccine and this has been developed by GLOBE BIOTECH LIMITED, Dhaka, Bangladesh [9]. The vaccine has systematically developed. After its development, the vaccine has been tested for safety and efficacy in small animal. Subsequently, the vaccine has been checked in resus monkeys and the study has shown safety and efficacy in monkeys. Now, the vaccine is waiting for phase I/II/ and III clinical trials before being used in human. Now, there remain queries about the necessity of developing a new vaccine for Bangladesh at this time when the pandemic may come to an end.

#### Rationality of development of BNAGAVAX®

This can be discussed from multivariate perspectives. There may be several outcomes of present pandemic. The pathological involvements of SARS-CoV-2 may also have persistent effect on the infecting host. The following points would provide insights as we why we need to develop a home-grown vaccine against SARS-CoV-2 even in 2023 for Bangladesh.

#### Transition from pandemic to endemic

Evolutionary aspects of virology of SARS-CoV-2 indicate that the ongoing pandemic of COVID-19 pandemic will be reverted to a status of endemic within a reasonable time that may expand from some months to one year. Although this depends on various factors, the emergence of new variants of SARS-CoV-2, their infectivity and pathogenesis, and coverage of vaccines would be important determinant. However, it is extremely difficult to assess if SARS-CoV-2 would similar or comparable path like SARS and MERS or this will take a different course of viral evolution.

#### Therapeutic effect of vaccine/pandemic of non-vaccinated persons

Vaccination with the presently-available vaccines with boosters would be determining factor for finding the exit from the ongoing pandemic. It is a challenge of entire humanity as to how we can vaccinate the entire world population and the speed of vaccination would also be important. Development of new and more effective vaccines would also alter the picture of pandemic drastically.



### Herd Immunity and Tissue expression of SARS-CoV-2

The nature of virus and its localization at different tissues deserves credible re-thinking about HERD IMMUNITY against SARS-CoV-2. The virus has been localized in most of the tissues months after being negative for SARS-CoV-2 in nasal specimens. Also, it is still unclear regarding the mechanism of post-COVID syndrome. It is yet to be clarified about the replication properties of tissue-localized SARS-CoV-2, their role in post-COVID syndrome is also yet to be explored.

### Effect of SARS-CoV-2-induced immunity

The pathological features of COVID-19 is not attributable completely or mostly to the cytopathic effect of the virus. Alteration of host immunity and events like cytokine storms have been accounted for the massive organ injury in severe COVID-19. If the immunological events are completely reversed after recovery, the effect can be minimized. However, if there is any sustained effect of aberrant immunity induced SARS-CoV-2, the entire clinical picture may be different. The 5 points those have been described indicate that SARS-CoV-2-related concerns will prevail for decades. Thus, if the pandemic reverts to an endemic, if there is no or compromised HERD IMMUNITY against SARS-CoV-2, if we shall have to handle considerable proportions of post COVID syndrome, we persistently need vaccine to counter SARS-CoV-2 infection.

### Role of BANGVAX® in this perspective

BANGVAX® [9] that is waiting to enter into phase I study soon may be visible by the middle of 2022 as a commercial product. This will be cheaper than other commercially-available mRNA vaccines, easy to preserve and transport, and huge amounts may be produced in Bangladesh. If its safety and efficacy can be shown and the vaccine is registered in Bangladesh, it will be the first endeavor of vaccine development in Bangladesh from Bench to Bedsides.

The following points regarding ensuing BANGAVAX® may be considered at this moment;

- The vaccine can be used for booster doses for millions of our population in late 2022 and onward.
- BANGAVAX® has used a technique of mRNA vaccine development, the entire system is the new and novel for Bangladesh. In fact, mRNA vaccine received approval only because COVID-19 pandemic and exposed sky-rocketing chances for drug development. We developed DNA vaccine as early as 2000 but could not received permission of the ethical committee to use DNA vaccine in human [10].

Use of mRNA-based drug development will facilitate development of numerous vaccines and drugs for many intractable viruses and diseases. For example, a vaccine against hepatitis C virus is now visible, also novel vaccine against human immune deficiency virus is within our sight.

The most important aspects of BANGAVAX® development may be an urgent need of the global population about other coronaviruses (COVs). There are seven types of COVs those have been described till now. Prior to COVID-19 pandemic, two CoV, SARS-CoV and MERS-CoV shattered the world with severe infections and considerable mortality. Figure 6 shows the present status of MERS-CoV. During the month of August 2021, four laboratory-confirmed cases of MERS and 2 deaths were reported to WHO from Saudi Arabia. One of the deaths was of a case reported in March 2021. The four reported cases are all male, non-healthcare workers and with co-morbidities. All cases were primary cases with history of contact with dromedaries and consumption of their raw milk in the 14 days prior to the onset of symptoms (Figure 6) [11].

The principle of vaccine developing for SARS-CoV-2 as exemplified by BANGAVAX® can be applied to develop vaccine for MERS and SARS. These two vaccines may be required in any future time point due to their breakout as epidemic or pandemic as they are prevailing in sporadic forms. Among these 7 COVs, prior to pandemic of COVID, two CoVs induced outbreaks.

**Figure 6:** Recent cases of MERS in Saudi Arabia.

### BANGVAX® and cuban strategy

Cuba is a small country with only 11 million people. However, the country is highly developed technologically that it prepares

several vaccines and medicines, which are used by Americans in large numbers, although Cuba and USA are not in harmonious relation. Due to prevailing development of Cuban drug industry in respect to biotechnology, genetic and molecular biology, Cuba soon developed 5 vaccines against SARS-CoV-2 in their country. It is to be mentioned that Cuba is the only country that prepared vaccines that can given to children 2 years onward. If BANGAVAX® can be produced in Bangladesh after passing the road blocks of vaccine development, Bangladesh would lead the Asian and African countries regarding new and novel drug developments.

### Conclusion

Natural disaster, pandemic, sufferings of humanity always comes with several PINCHES. The challenge is how to convert these PINCHES to Chances. The pandemic of COVID-19 has induced 5.61 million of human deaths. There have been tremendous sufferings associated with economy. High inflation and social unrest have followed as collateral damages. However, most of the biomedical companies of the developed countries have earned billions of dollars from this pandemic. Now, time has come in front of Bangladesh and other developing countries to develop their drug industry, vaccine producing capacity, genetic engineering, and molecular biology to stand side by side with developed country. BANGAVAX® is at the entry point of this endeavor and the sky is the limit.

### Bibliography

1. Mcintosh K., *et al.* "Coronaviruses". UpToDate (2022)
2. "COVID Live-Coronavirus Statistics". Worldometer (2022).
3. Number of cumulative cases of coronavirus (COVID-19) worldwide from January 22, 2020 to January 23, 2022, by day (2022).
4. Shaw AC., *et al.* "Age-dependent dysregulation of innate immunity". *Nature Reviews Immunology* 13 (2014): 875-887.
5. "Times of India".
6. Chauvin JP., *et al.* "The younger age profile of COVID-19 deaths in developing countries" (2022).
7. WHO Solidarity Trial Consortium, Pan H., *et al.* "Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results". *The New England Journal of Medicine* 384.6 (2021): 497-511.
8. Huq AKMF., *et al.* "Real-life Management Strategy of COVID-19 Patients in Bangladesh with No Death: An Observational and Cohort Study". *Euroasian Journal of Hepato-Gastroenterology* 10 (2020): 31-35.
9. Nag K., *et al.* "An mRNA-based vaccine candidate against SARS-CoV-2 elicits stable immuno-response with single dose". *Vaccine* 39 (2021): 3745-3755.
10. Oka Y., *et al.* "Mechanism and therapeutic potential of DNA-based immunization against the envelope proteins of hepatitis B virus in normal and transgenic mice". *Immunology* 103 (2001): 90-97.
11. MERS. Situation update (2022).

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