

Strategic Plan and Limitations in Tackling Delta Variant Outbreak in Bangladesh

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ABSTRACT

Since the early Covid-19 outbreak by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the topical Delta variant is currently taking over on a worldwide basis due to its high transmissibility and moderate resistance to vaccines. The variant showed its dominance in India, where it was first isolated and then, spread to neighboring Bangladesh along the porous border. Here, we aim to emphasize the actions taken by the government of Bangladesh to limit the potential for over ascendancy, with all its limitations. From time to time, a group of measures was taken by the government to keep the outbreak under control since its first isolation on March 8, 2020, like quarantine, local or nationwide lockdown, enforced social distancing, contact monitoring, restrictions on international travel, financial support, building awareness and vaccination, etc. However, due to the long-term nature of the outbreak, with the concomitant rise and fall characteristics of the outbreak, as well as the people's socioeconomic state, all efforts have recently been futile. To combat the highly transmissible Delta, the government implemented lockdown and vaccination coverage as the priority. Nevertheless, public unawareness, inadequate hospital beds, high flow oxygen, ICU, and uneven distributions of diagnostic centers and hospitals throughout the country are the major challenges in managing the Delta variant outbreak. The default nature of the Delta variant like high transmissibility, higher morbidity and mortality, less sensitivity to vaccines, and infection in any age group might be the curse to combating the outbreak.

Key Words: Covid-19, SARS-CoV-2, Delta, Bangladesh, Vaccination, Limitations.

INTRODUCTION

For more than 1.5 years, the world has been facing an undesirable situation caused by a microscopic organism named 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2). Corona viruses belong to a group of RNA viruses that can affect the respiratory tract and cause mild to severe respiratory illness in humans. SARS coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are two highly

pathogenic coronaviruses that caused outbreaks in 2002 and 2012, respectively, making coronaviruses a public health concern (1). Covid-19 is caused by a positive, single-stranded RNA enveloped virus first detected in China in 2019. By December 2019, China declared the outbreak as an epidemic when human-to-human transmission was undeniably obvious (2). By Jan 2020, WHO declared SARS-CoV2 as a matter of international concern when more than 80,000 confirmed

cases were reported worldwide (3). Bangladesh officially reported its first case on 8th March 2020 and its first official mortality case within 10 days from the detection of the first official case (4, 5).

Bangladesh has been facing the third wave of Covid-19 since July 2021, after an outbreak of a Delta variant from a nearby country, India. The ongoing pandemic poses a threat to public health, causing more than 4 million deaths and 233 million infections worldwide since 2019 (6). However, in Bangladesh, above 1.5 million people were infected and about 27 thousand people were died (7). It causes infection at a high rate not only in populated cities like Dhaka or Chittagong but also in other parts of Bangladesh, especially in Khulna district, which is the border area of the Indian state of West Bengal. In addition, about 98% of total Covid-19 infected samples contained the Delta variant (8).

To combat the fatal circumstances, it was thought that only a vaccine could be triumphant against the Covid-19. Among a good number of candidate vaccines, initially four types of vaccines overcome three phases are Pfizer/BioNTech's BNT162b2, Moderna's mRNA-1273, University of Oxford and AstraZeneca's AZD1222, and Gamaleya's Sputnik V vaccines (9). The efficiency of vaccines from Moderna, Pfizer/BioNTech, and AstraZeneca is 94.1%, 95%, and 70%, respectively (10). Vaccination against Covid-19 started in Bangladesh on 27 January 2021 in a pilot program. In developed countries, more than half of their populations are vaccinated while in Bangladesh, about 3.56% of the populations are fully vaccinated. People from South and Central Asia, however, showed less interest in taking the Covid-19 vaccine than other countries who have already developed economically (11, 12). It was noticed that vaccination can moderately stop the rate of mortality but can't reduce the rate of infection. In this deadly situation, there is no alternative way against proper vaccination, knowledge, and proper medical training on Covid-19. However, this review

is aimed at summarizing the current scenario of Covid-19 in Bangladesh. With the epidemiological characteristics like incidence, fatality, and vaccination at different times in comparison to some developed as well as some neighboring lower middle-income countries, to understand the limitations in public health preparedness are required to mitigate the gap in formulating a comprehensive control and prevention strategies.

Molecular basis of SARS-CoV-2

SARS-CoV-2 is a positive-sense single-stranded RNA virus (13). Its genome shares 79% sequence identity with SARS-associated *coronavirus* (SARS-CoV) and 50% with Middle East Respiratory Syndrome *coronavirus* (MERS-CoV), respectively (14). The genome contains six functional open reading frames (ORFs) arranged as replicase (ORF1a/ORF1b), spike (S), envelope (E), membrane (M) and nucleocapsid (N) in the 5'-3' orientation. Additionally, it contains seven putative ORFs which are interspersed within the structural genes and encode for accessory proteins. SARS-CoV-2 shares more than 90% amino acid identity with SARS-CoV, except for the S gene. The former encodes receptor binding spike protein and is highly divergent from other *coronaviruses*. Moreover, the S gene of SARS-CoV-2 has three short insertions in the N-terminal domain as well as changes in four out of five of the key residues in the receptor-binding motif (14, 15).

SARS-CoV-2 is transmitted into host cells through airborne routes and it uses the spike glycoprotein that stick tightly to glycans of mucins in the mucus lining of airway epithelial cells. It gets provision to lung epithelial cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor (Fig. 1). The spike glycoprotein is arranged in homotrimer on the surface of the virion. Glycoprotein, like other proteins, is subjected to post-translational modifications and glycosylations. Spike protein is cleaved into S1 and S2 subunits

by mammalian furin. The S1 subunit is comprised mostly of the amino-terminal domain and the receptor-binding domain (RBD). The receptor-binding motif residing

within the RBD domain of the S1 subunit of SARS-CoV is responsible for binding to the host cell surface receptor, ACE2 (15-17).

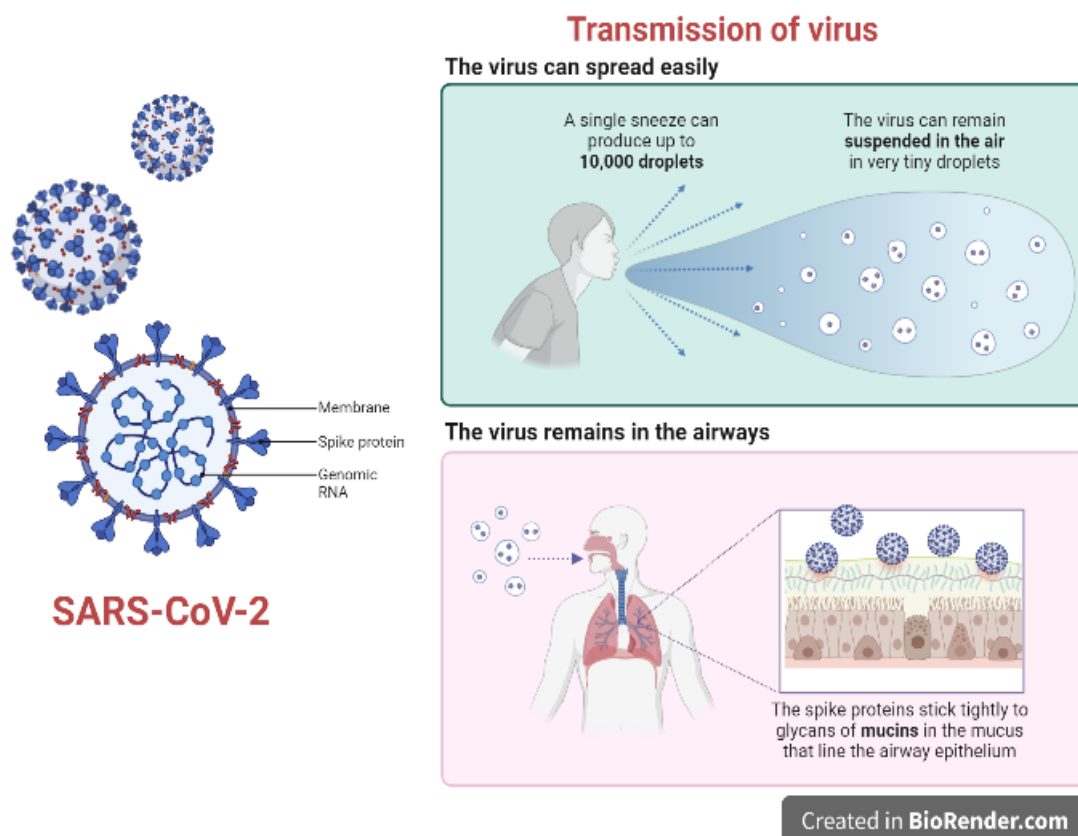


Figure 1: Schematic diagram of the SARS-CoV-2 structure and its transmission. Figure created with BioRender.com. Credit: Sanzida Jahan.

From the initial outbreak in 2019 till now, there have been several mutations of SARS-CoV-2 that contribute to different variants. According to the China National Centre for Bioinformation, a total of 15,018 mutations have been identified so far (15, 18). Among them, S protein contains substitutions of four amino acids, V483A, L455I, F456V, and G476S, located near the binding interface within the receptor binding domain (RBD) with no known function yet. Mutations to the D614G residue of the S1 subunit were found more frequently than in other S variants. However, variants containing G614 in the S protein replaced the original D614 around March 2020 and circulated as a dominant form worldwide (19).

The U.S. centers for disease control and prevention (CDC) regularly monitors the epidemiological distribution of various SARS-CoV-2 variants through sequence analysis. The U.S. government's SARS-CoV-2 Interagency Group (SIG) categorized SARS-CoV-2 into three classes of variants: Variant of Interest (VOI), Variant of Concern (VOC), and Variant of High Consequence (VHC) (20). These VOI and VOC emerged due to mutations in the spike protein and were reported to exhibit increasing transmissibility, disease severity, and infectivity of SARS-CoV-2. Recently, the Delta variant of the SARS-CoV-2, which first appeared in India, was detected globally due to its higher transmissibility and disease severity compared to other variants (21, 22).

Variants of Covid-19 in Bangladesh

Table 1: Monthly COVID-19 confirmed and death cases, case fatality rate (CFR) and vaccination percentage in high income countries (U.S., U.K., Canada and U.A.E.) from January 1, 2021 to August 31, 2021 (available from <https://ourworldindata.org/covid-vaccinations>).

Month-Year	Confirmed cases	Death	CFR (%)	Vaccination
		U.S.		
Jan-21	6150000	97185	1.58	7.45%
Feb-21	2400000	65619	2.73	14.88%
Mar-21	1800000	37503	2.08	29.18%
Apr-21	1880000	23786	1.27	43.32%
May-21	920000	18167	1.97	50.15%
Jun-21	390000	10319	2.65	54.02%
Jul-21	1320000	8702	0.66	55.10%
Aug-21	4220000	26862	0.63	60.96%
		U.K.		
Jan-21	1330000	32745	2.46	13.69%
Feb-21	360000	16716	4.64	29.87%
Mar-21	170000	3872	2.28	45.88%
Apr-21	70000	820	1.17	50.62%
May-21	70000	270	0.39	58.15%
Jun-21	320000	359	0.11	66.08%
Jul-21	1060000	1545	0.15	68.96%
Aug-21	940000	2910	0.30	70.50%
		Canada		
Jan-21	196306	4279	2.18	2.24%
Feb-21	87508	1949	2.23	3.61%
Mar-21	118250	970	0.82	13.26%
Apr-21	240507	1260	0.53	32.67%
May-21	160000	1308	0.82	57.72%
Jun-21	30000	745	2.49	68.15%
Jul-21	20000	287	1.44	71.49%
Aug-21	70000	388	0.55	73.36%
		U.A.E.		
Jan-21	95787	181	0.19	8.46%
Feb-21	87915	371	0.42	35.19%
Mar-21	69920	276	0.39	
Apr-21	58792	90	0.15	51.38%
May-21	50600	93	0.18	
Jun-21	62071	131	0.21	
Jul-21	47951	138	0.29	78.90%
Aug-21	37512	92	.24	86.93%

Table 2: Monthly COVID-19 confirmed and death cases, case fatality rate (CFR) and vaccination percentage in lower middle income group countries (Bangladesh, India, Nepal and Myanmar) from January 1, 2021 to August 31, 2021 (available from <https://ourworldindata.org/covid-vaccinations>).

Month-Year	Confirmed cases	Death	CFR (%)	Vaccination
		Bangladesh		
Jan-21	21629	568	2.63	0.00%
Feb-21	11077	281	2.54	1.89%
Mar-21	65079	638	0.98	3.26%
Apr-21	147837	2404	1.63	3.53%
May-21	41408	1169	2.82	3.54%
Jun-21	112718	1884	1.67	3.54%
Jul-21	336226	6182	1.84	5.17%
Aug-21	250000	5510	2.20	11.17%
		India		
Jan-21	470000	5398	1.15	0.27%
Feb-21	350000	2765	0.79	0.86%
Mar-21	1110000	5770	0.52	4.04%
Apr-21	6940000	48926	0.71	9.09%
May-21	9020000	120042	1.33	12.12%
Jun-21	2230000	67564	3.03	19.67%
Jul-21	1250000	24892	1.99	26.07%
Aug-21	1150000	14669	1.27	36.67%
		Nepal		
Jan-21	10366	173	1.67	
Feb-21	3184	745	23.39	1.38%
Mar-21	3166	256	8.09	5.49%
Apr-21	45878	249	0.55	7.18%

Table 2 Continued...

May-21	238115	4107	1.73	7.25%
Jun-21	77503	1726	2.23	8.93%
Jul-21	56584	745	1.32	13.51%
Aug-21	67258	893	1.32	17.99%
		Myanmar		
Jan-21	15515	449	2.89	0.01%
Feb-21	1751	68	3.89	0.70%
Mar-21	538	7	1.03	1.84%
Apr-21	383	3	0.79	2.76%
May-21	812	8	0.99	3.26%
Jun-21	13648	117	0.86	3.38%
Jul-21	141908	6000	4.23	
Aug-21	100097	6055	6.04	8.13%

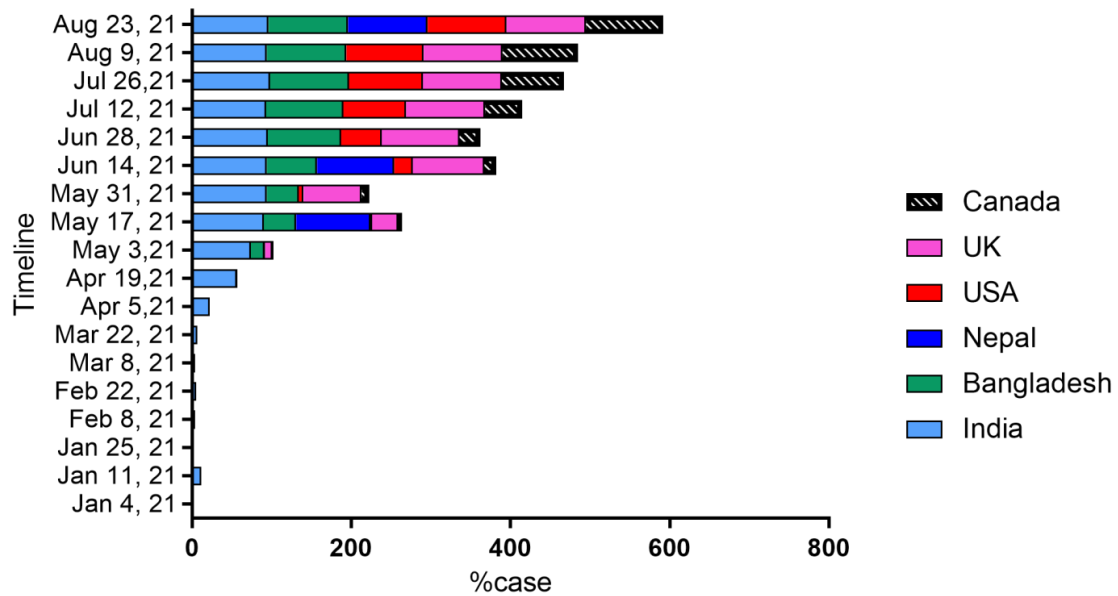


Figure 2: Delta variant's share of total analyzed sequences in the last two weeks. This share may not reflect the complete breakdown of cases, since only a fraction of all cases are sequenced (available from <https://ourworldindata.org/covid-vaccinations>). Not all the data was available at the given time point.

Covid-19 was identified in Bangladesh at the start of March 2020, which was first identified in Wuhan city, China in 2019. Due to different geographical locations, weather and lifestyles, the virus has been changing its characteristics, and as a result, different variants have been originating. There are six variants identified in Bangladesh, including Alpha (formerly UK variant, officially as B.1.1.7), Beta (formerly South African variant, officially as B.1.351), Gamma (formerly Brazilian variant, officially as P1), Delta (formerly Indian variant, officially as B.1.617.2), Eta (formerly Nigerian variant, officially as B.1.525) and Lambda (formerly Peru variant, officially as C.37) (23, 24). The very first patient with

the UK variant was identified in Bangladesh on January 6, 2021 which increased gradually until in March 2021 it accounted for 52% of positive patients (25). After the outbreak of the UK variant, South African variant was identified in March 2021 which was made up of 81% of variants in the fourth week of March (25). Six patients with the Nigerian variant were found in Bangladesh in April 2021 which was first identified in Nigeria in December 2020 (26). The Institute of Epidemiology, Disease Control and Research (IEDCR) identified an Indian variant known as the Delta variant on May 8, 2021 (27). In June 2021, 80% of the total positive samples contained the Delta variant while 16% of samples contained the Beta variant (28). The percentage of Delta

variants increased to 98% in July, with a negligible scale of Beta and Eta variants (8). Delta variants are spread all over the country. It was shown that people in the age range of 30 to 39 are prone to the Delta variant and the mortality rate is higher in patients with cancer, breathing problems, and diabetics (29). The bi-weekly data presented in figure 2 showed that a rapid increase in Delta variant outbreak was observed in the listed countries from sequencing data of a fraction of samples (Fig. 2). However, the sequencing data was not available for the UAE, Myanmar, and partly available for Nepal. With the rise of Delta variant cases, the number of death cases also increased in India and Bangladesh from April to August. Nevertheless, with the increase of Delta variant infections, mortality cases did not simultaneously increase as much in the countries like U.S., U.K., and Canada when compared with the lower middle income countries (Table 1 and 2). High vaccination coverage might work here as a shield to keep the case fatality rate (CFR) under control. Moreover, in the mid of August, another type of variant named Lambda variant was identified in Bangladesh which was declared as the variant of interest as the cases were increasing noticeably (24).

Features of the Delta variant

Evidence-based analysis shows that the Delta variant presents different symptoms not only in severity but also in type of symptoms in partially versus fully vaccinated and vaccinated versus unvaccinated population (30). Moreover, Delta-associated symptoms can vary compared to those of the other variants (31). The efficacy of vaccines also varies between Delta and other variants, like the efficacy of Pfizer and AstraZeneca vaccines dropped from 94 to 64% and 73 to 60%, respectively, in symptomatic infection caused by Delta compared to the Alpha variant (32, 33). The neutralizing titer, even in fully vaccinated individuals, is two-to-five-fold lower against Delta variant

compared to Alpha variant. This might be associated with the mechanism by which this variant escapes the immune system of the patient. Moreover, the Delta variant seems to have the potential to evade the immune system in patients who have been vaccinated (34). Nevertheless, partial and full vaccinations did reduce the requirement of hospitalization as well as mortality caused by the Delta variant (35). Furthermore, the Delta variant load of vaccinated patients decreases faster than that of unvaccinated patients within a week (35, 36).

The Delta variant is estimated to be 60% more transmissible, translating to an approximate basic reproduction number (R_0) of 7.0 compared to other strains, which had an R_0 of around 2.79 (37, 38). Patients infected with the Delta variant seem to have a 1,260 times higher viral load in nasopharyngeal samples at diagnosis and a longer shedding interval compared to those infected with parental strains of Covid-19 (39, 40). This variant is associated with a higher risk of hospitalization, longer hospital stays, ICU admission, oxygen requirement, and mortality compared to the original strains (40-42).

Lockdown and shutdown to prevent recent transmission

Bangladesh is facing the deadliest 3rd wave of Covid-19. The Government of Bangladesh (GoB) imposed lockdowns and shutdowns at different times to prevent the transmission of the virus. The first lockdown was declared in Shibchar, Madaripur local area on 19th March 2020 after confirmation of the first three cases on 8th March in Bangladesh. Moreover, the GoB declared 10 days of shutdown as a general holiday from the 26th of March to 4th of April, which was later extended seven times and ended up on May 30th (43). The GoB decided not to extend the lockdown to ensure the sustainability of the nation but set strict measures on public movement (44). The lowest rate of transmission was observed from December 2020 to the end of

February 2021 when the infection rate was below 5% (45). A second wave approached from March, 2021 to May, 2021 with an increased positivity rate to over 23% in the early April (46). A timely lockdown was declared by GoB from April 5th, but it was not effective due to the protests from various groups of the population including merchant groups (47). However, to restrict transmission, GoB again imposed a lockdown on all but some emergency services from 14th to 21st April 2021 (48). At the end of April, the death rates became some of the lowest in the world, which prioritizes the government's reopening of everything with hygienic guidelines (49).

The third wave of Covid-19 started from May 2021 in Bangladesh after the transmission of the Delta variant from India. According to IEDCR, more than 30% of positive cases were identified where the majority of the samples that were tested contained Delta variants, which are very transmissible. This variant, however, was found in almost every district of the country (50). Initially, to reduce transmission, a localized lockdown was declared in the district, Chapainawabganj, where the infection rate rapidly increased due to the permeable border with India. The *Directorate General of Health Services (DGHS)* recommended a strict lockdown among eight districts where the average positivity rate was over 30%. Besides, IEDCR confirmed community transmission of Delta variants among seven districts. In June 2021, a steep rise was observed in the border districts like Khulna and Rajshahi where the positivity rate was increased to 50 or 60% (51). Therefore, districts like Khulna, Chapainawabganj, Satkhira, Bagerhat, and Noakhali were subjected to strict restrictions on transportation, and a lockdown was declared in the districts surrounding Dhaka to restrict transmission in the capital (52). On July 1st, national lockdown for 7 days was declared to curb the transmission of Delta variant (53). All kinds of offices, shops, and transportations were shut down except for some emergency

cases, like local food markets for essential goods, which were allowed to open for few hours with the deployment of the Army and Border Guard Bangladesh to enforce the actions. Due to continued high infections and death cases, an additional 7-day lockdown was announced that lasted until July 14th (54). However, although the rate of infection was at its peak, GoB relieved the restrictions to allow economic activities to continue to accommodate the second largest festival, Eid-ul-Azha. Just after the festival, another strict lockdown from 23rd July to 5th August was declared to control the probable widespread transmission following the Eid festival (54). Moreover, a huge rush of buses, ferries, launches, and trains was observed just after the declaration of lockdown several times, which is assumed to increase the transmission further due to incoordination and chaos in taking decisions by the supreme authority.

As lockdown and shut down cannot limit the transmission of viruses and it also hampers the economic wheel of our country, the health minister is emphasizing vaccination to become available for all.

Vaccination strategies in Bangladesh

It is thought to be the most rapid and effective way to combat the Covid-19 pandemic by ensuring effective vaccination among the maximum population within the shortest time possible. Another importance of vaccination is that it reduces the replication of viruses, which may in turn reduce the risk of generating novel strains with high transmissibility or pathologic features. Therefore, governments from all countries have prioritized vaccination programs as their primary accountability to save their own citizens (55). Pre-existing knowledge about SARS and MERS aided in the rapid development of vaccines against SARS-CoV-2 (56). The worldwide first vaccination program started in December 2020 and by this month, 1.47%, 0.83%, and 0.10% of population were vaccinated in the U.K., the U.S.A. and the European Union (E.U.), respectively (57). However, the

uneven distribution of vaccines due to economic disparities leaves the developing nations behind, as warned by the International Monetary Fund (IMF). As of 31st August 2021, approximately, 40.1% of the population received at least one dose of the Covid-19 vaccine and 27.4% obtained complete doses of vaccines globally (57). Although 100 vaccines are in clinical trial, according to the WHO EUL/PQ evaluation process, around 22 types of Covid-19

vaccines were approved, which were developed by 18 companies. Among them, Pfizer-BioNTech, Moderna, AstraZeneca, Sinopharm, Sinovac, NOVAVAX, GAMALEYA, Bharat Biotech and Johnson & Johnson's Janssen are the most widely used vaccines (57). The types of vaccines that were accepted for administration in high and lower middle income countries including Bangladesh (Table 3)

Table 3: Types of vaccines administered in high income (U.S., U.K., Canada and U.A.E.) and lower middle income (Bangladesh, India, Nepal and Myanmar) countries against Covid-19 up to July 31, 2021 (available from <https://ourworldindata.org/covid-vaccinations>).

Vaccine	Type	U.S.	U.K.	Canada	U.A.E.	Bangladesh	India	Nepal	Myanmar
Johnson&Johnson	Adenovirus vector (recombinant Ad26)	√	-	-	-	-	-	-	-
Oxford/AstraZeneca	Adenovirus vector (ChAdOx1)	-	√	√	√	√	√	√	√
Pfizer/BioNTech	RNA (modRNA in lipid nanoparticles)	√	√	√	√	√	-	-	-
Moderna	RNA (modRNA in lipid nanoparticles)	√	√	√	-	√	-	-	-
Sinopharm/Beijing	Inactivated SARS-CoV-2 (vero cells)	-	-	-	√	√	-	√	√
Covaxin	Inactivated SARS-CoV-2 (vero cells)	-	-	-	-	-	√	-	-
Sputnik V	Adenovirus vector (recombinant Ad5 and Ad26)	-	-	-	√	-	√	-	-
Sinopharm/Wuhan	Inactivated SARS-CoV-2 (vero cells)	-	-	-	√	-	-	-	-

In Bangladesh, the first pilot vaccination program began on January 27, 2021, but massive administration started using the AstraZeneca-Oxford vaccine from the Serum Institute of India on February 7, 2021, with the plan of giving 30 million doses over the next few months. In February, approximately, 1.89% of the population received at least first dose of vaccine (Table 2) (58). To accelerate the vaccination program, the Prime Minister instructed the authorities to reduce the age limit from 55 to 40 on February 8, 2021 (59). Among the 30 million doses ordered from the Serum Institute of India, only 7 million doses were received, with 3.2 million as a gift. Due to the worst Covid-19 situation, India failed to provide complete doses of vaccines, which led to the approval of Russian Sputnik V and Chinese BBIBP-CorV in late April, 2021. Consequently, the first dose of the vaccination program was halted on April 26th and 5.78% of the population got at least one dose of vaccine as of April 23rd (60).

The 2nd phase of vaccination started after two months' break in July 2021 (61), and due to the rising number of confirmed cases, the age limit for Covid-19 vaccination was reduced to 35 years on July 5th and 30 years on July 9th 2021 (62, 63). By this time, several vaccines came from different countries. Among them, USA sent 1,06,000 doses of Pfizer's vaccine on 2nd June (64), 1.8 million doses of AstraZeneca vaccines on 11th June (65), 6,00,000 doses of Sinopharm vaccines as a gift from China on 13th June (66), 1.25 and 3 million doses of Moderna Covid-19 vaccines from U.S. on 2nd and 19th July, respectively (67, 68), 1 million Sinopharm vaccines on 3rd July (69), 2,45,000 Astra-Zeneca vaccines on 24th July from Japan, second and third shipments of 7,81,000 and 6,16,780 doses of Astra-Zeneca came from Japan on 31st July and 2nd August, respectively (70-72), 1.77 million Sinopharm on 11th August and 1 million more Sinopharm from China as a gift on 13th August (73, 74), 7.81 and 6.34 lakh doses of Astra-Zeneca vaccines from

Japan on 21st and 28th August (75, 76) were received in 2021.

As of 31st August 2021, Bangladesh administrated approximately, 26 million doses of vaccines wherein 18 million people (11.3%) got at least one dose of vaccine and 7 million people (4.8%) were fully vaccinated (The Daily Star 2021j)(76). More males were vaccinated among 8 divisions in Bangladesh than females in terms of 1st or 2nd doses of vaccination (Fig. 3a and 3b). Here, the male and female population constitutes 50.6% and 49.4% of the total population, respectively (77). The highest number of vaccines was administered in Dhaka, followed by Chittagong, Rajshahi, Khulna, Rangpur,

Mymensingh, Sylhet, and Barisal divisions (Figure 3a and 3b), as the highest number of people reside in Dhaka (78).

The Government of Bangladesh is taking all possible approaches to save every single precious life. The age limit for Covid-19 vaccination has been further reduced to 25 years, in which case, students whose age is 18 can register for vaccination (79). A deal was signed among GoB, China's Sinopharm and Bangladesh's Incepta vaccine Ltd. for the collaboration in terms of bottling, labeling and dispensing China's Sinopharm vaccine (80). According to official data, more vaccines will come in the next few months (79).

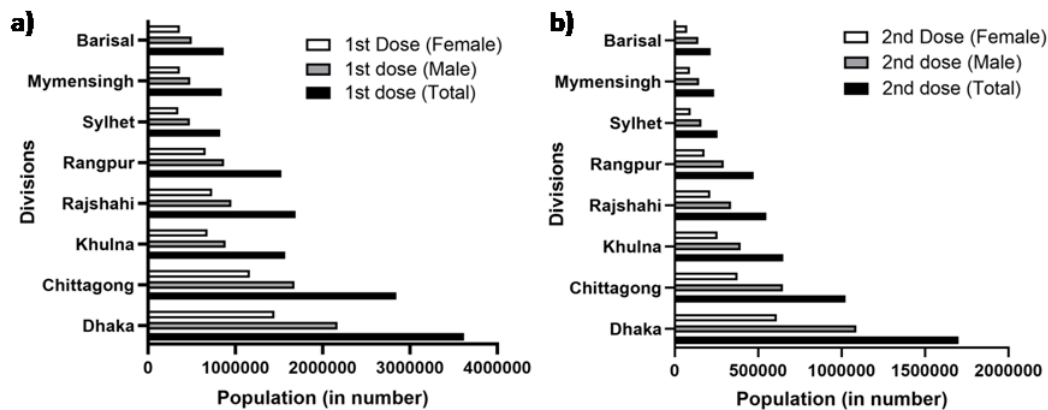


Figure 3a and 3b

Fig. 3: Division- and gender-wise administration of the 1st dose (a) and 2nd dose (b) of Covid-19 vaccines in Bangladesh (Available from <http://103.247.238.92/webportal/pages/covid19-vaccination-update.php>).

Effect of vaccines against Covid-19

In this pandemic situation, vaccination has great significance on infection and death rates. In response to vaccines, the body's immune system produces long-lasting memory cells and antibodies which protect the body from future infections (81). Initially, the vaccination program started in high-income countries, where people got vaccines at the earliest convenience. It took some time to reach vaccines in lower middle-income countries like Bangladesh (57). By December 2020, many countries pre-ordered over 10 billion doses of vaccines, in which almost half the amount was bought by high-income nations, accounting for 14%

of the world population (82). Higher percentages of vaccines were administrated in high-income countries by January 2021 (Table 1) whereas, in lower middle-income countries, the vaccination programs were not started or if started, the percentages were very low (Table 2). It is expected that Covid-19 vaccines will reduce transmission of the virus, serious outcomes of the disease, hospitalization and death. Like all other vaccines, Covid-19 is not 100% effective as well, but trials have shown high efficiency with several Covid-19 vaccines. A recent publication on August 18 showed that as of May 9, the Covid-19 immunization program in the U.S. has resulted in a projected decrease of 1,39,393

pandemic fatalities. Due to vaccination, the decreased Covid-19 fatalities have led to a statistical life benefit worth \$625 billion to \$1.4 trillion (83). Another study held in Israel showed that two doses of Pfizer-BioNTech mRNA Covid-19 vaccine BNT162b2 showed a high degree of efficiency against any age group, symptomatic and asymptomatic SARS-CoV-2 infections, hospitalizations, severe disease, and death (84). A growing body of research has shown the high efficiency of most of the available Covid-19 vaccines against most of the variants by stimulating a broad range of immunity. Mutations are unlikely to make the vaccines completely ineffective, but if any of the variants surpass the vaccine efficiency, it may require developing vaccines with new compositions. Ongoing research on continuous monitoring of new variants and their effect on Covid-19 vaccines will update us to deal with any novel situation (85). One study published on July 14th, 2021, suggested that to control the spread of the virus, the success of vaccination is not only dependent on effectiveness and coverage but also, on concomitant nonpharmaceutical interventions (86). Nevertheless, a new variant named C.1.2 was first isolated from South Africa in May, 2021, and occupied only around 3% of the country in July, 2021, but it is increasing consistently. Although WHO has yet to declare it as a variant of interest or a variant of concern, it is suspected that the variant can evade the immune system partially and the effectiveness of vaccines (87, 88). However, a population can be protected from a disease by hard immunity, which can be achieved through vaccination against Covid-19, but it is difficult to achieve due to vaccine hesitancy, how long the vaccine can protect, and varied vaccine roll-out among regions (89).

Limitations in combating the Delta variant outbreak

Bangladesh is home to 164 million people. Around 60% of the population is

aged 15–64 years, and 7% of its population is senior citizens who suffer from non-communicable diseases like chronic obstructive pulmonary disease, cardiac disorders, diabetes, cancer, and asthma (90). In addition, the prevalence of smoking is the highest in Bangladesh among South Asian countries (90). Research has shown an association between pollution and Covid-19 disease severity (91). In 2019, Bangladesh was said to be the world's most polluted country for fine particulate matter 2.5 (PM2.5) (92). It is possible that dwellers in polluted cities already have pre-existing respiratory issues that make them vulnerable when it comes to Covid-19. This would make people in Bangladesh more prone to Covid-19. These morbidities and risk factors undoubtedly put a vast majority of the population in the vulnerable groups for Covid-19. The outbreaks of dengue, chikungunya, and malaria (93) further complicate the management of the Covid-19 pandemic in Bangladesh every year. Moreover, the overlapping clinical manifestations of Covid-19 and dengue can mislead health practitioners into misdiagnosis due to possible serological cross-reactivity between Covid-19 and dengue, and might further complicate the already disastrous situation in management of Covid-19 in Bangladesh. Cross-reactivity between Covid-19 and dengue has already been reported in Singapore (94).

While 50% of adults in neighboring India have had at least one dose of the vaccine, less than 5.0% of the population in Bangladesh has been vaccinated (95). The supply of Covishield/AstraZeneca vaccine has been restricted to Bangladesh due to the worst Covid-19 conditions in India, resulting in an alarming situation. The GoB has currently relied on donations of doses from Moderna, which have quickly run out, and is waiting to receive doses of Pfizer/COVAX for the coming months. The government was paying to get supplies of vaccine doses from Sputnik and Sinopharm (95) which were not as effective as the aforementioned vaccines. The current rate

of vaccination was not in line with the massive need to vaccinate all the vulnerable groups of the remaining 95% unvaccinated population in Bangladesh.

A vast majority of the Bangladeshi population is very unlikely to know that almost half of the adults and up to 90% of the Covid-19 cases in babies and children can be asymptomatic (96). Another report showed children as young as 2 days old have been positive for Covid-19 (97), while another finding revealed babies of the same age have died from Covid in South Africa (98). In addition, there is scarce knowledge about the fact that babies, infants, and young children can also be positive for Covid-19 and that shedding of the viral particles can extend to more than months after infection. Others are in self-denial of contracting Covid-19 and appear to associate their symptoms with flu in fear of being discriminated and isolated from the community. Many people do not consider the possibility of a reinfection with Covid-19, although reports of a second episode or reinfection of Covid-19 are evident after a span of as little as 70 days free of any symptoms from the first episode of infection (99). A recent study reported that 73.5% of the study population believed Covid-19 did not transmit from human to human, 57.5% believed that Covid-19 could not be transmitted by sexual intimacy, and 36.4% believed that the virus would be active only for 4 hours, despite the fact that the virus can be detected for up to 3 days on surfaces (100). To add more to that, many people are unaware of the concept of waning immunity after vaccination and therein, undo all protective measures once they have been vaccinated. It is beyond the knowledge of the vast majority that those who are already immune-compromised may not develop an adequate level of immunity despite the fact that they have had two doses of vaccination. Likewise, many people are unaware that almost 66% of Covid-19 mortality cases caused by the Delta variant had at least one dose and 54% had both doses of the vaccine, according to a new report (101).

The lack of knowledge misleads people into relaxing protective measures for themselves right after vaccination without allowing a window of a few weeks for the vaccine immunity to develop. All these factors, collectively, might be affecting the social behavior that is driving the transmission of Covid-19 at a surmounting rate throughout the pandemic in this densely populated country.

According to a recent report, there are only 0.7 beds for every 1,00,000 people distributed amongst the 432 government and 737 private hospitals in the country (91). According to the official figures from the government, there are only 582 ICU beds and 620 ventilators for critically ill Covid-19 patients in Dhaka and Chittagong. The remaining 240 ICU beds are disproportionately scattered among the remaining 135 million people in different parts of the country (91). Most of the rural and divisional cities do not have any ICU facilities for critically ill Covid-19 patients. It is important to highlight that Bangladesh ranks the lowest in terms of the number of ICU beds per 1,00,000 population among almost all of the Asian countries (102).

Reports indicate that 79% of Covid-19 patients remain at home to manage their symptoms and seek medical advice over the phone (102). Those who recover from Covid-19 are by and large unfamiliar with the post-Covid-19 syndrome and acute or chronic Covid-19, which can extend between 3 to 12 weeks from the onset of symptoms after initial recovery (103). They are, therefore, unlikely to seek medical attention in a timely manner for the management of complications arising from post-Covid-19 syndrome. As far as the critically ill Covid-19 patients are concerned, family members have been rushing to Dhaka after failing to find medical care in local and regional hospitals. Even beds with general oxygen supply are now unavailable in all hospitals dedicated to Covid-19, i.e., Dhaka North City hospital and Dhaka Medical College Covid hospital (104). Moreover, a vast majority of ICU

beds are owned by private hospitals. In Dhaka alone, more than 60% of ICU beds are owned by private hospitals, which are not accessible to middle- and low-income families (91). Even when patients have made it to the hospital, reports indicate that 65.3% healthcare professionals seem reluctant to attend suspected or confirmed cases of Covid-19. Besides, 45% of healthcare professionals keep at least 1 meter away from Covid-19 patients, and 6% refuse to serve any suspected case of Covid-19 (105).

The risk of exposure to biohazards, contributed by the poor management of biomedical wastes by hospitals and testing services, is also very high in the absence of the implementation of a proper management plan. In April 2020, a month after the first official case was declared in Bangladesh, up to 1.99 kg of medical wastes were produced per bed, and 14,500 tons of biomedical wastes were generated in the month of April 2020 alone (91). Many rural, urban and semi-urban hospitals are completely devoid of disposal facilities. The used personal protective equipment (PPE), masks, gloves and other Covid-19 biomedical wastes were disposed in common bins used for household disposal containers. The biomedical waste is a grave health hazard for Covid-19 transmissions. Around 40,000 untrained as well as unprotected cleaners are routinely being put at risk of their own lives to collect and dispose of Covid-19 as well as other infectious biowastes in the country (91). Improvised infrastructure and training of staff for management of biohazards are undoubtedly needed to control the transmission of these sources.

The testing rate of Bangladesh is the second lowest amongst South Asian countries, ranking only above the worn-out Afghanistan (102). As of March, this year, the country is home to only 118 Covid-19 testing laboratories. Among them, 68 are present in Dhaka and the remaining 50 serve the rest of the country (106). Several rural and remotely located areas have limited or no access to testing laboratories at all. This

is leading to a sharp rise in Covid-19 cases in remote areas of the country since cases are not detected in time to prevent transmission in the community. There are facilities for only 0.013 tests per 1,000 people (13 tests per million) (107). At present, only 10,000-15,000 testing facilities are there for a country of 164 million people. Of these, 5000-8000 tests are performed as a pre-requisite for people traveling abroad (91). This leaves the official testing numbers at only 2,000-7,000 tests for the 164 million people. There are 64 districts across the eight divisions in Bangladesh. Only 30 of the 64 districts have testing facilities. Although cases have been reported in all districts, some districts do not have any testing facilities, and some, like Barisal, Khulna, and Kushtia, have just a solitary facility. Districts like Netrokona, Nilphamari, Naogaon, Natore, Panchagarh, Thakurgaon and Sunamgonj have no testing facility at all (108). Hence, an extremely low capacity of testing is leaving the vast majority of cases undetected in Bangladesh. Thus, often times, the test results are not delivered to districts from the divisional cities within acceptable time frames. It takes around 24 hours to collect and deliver samples to testing facilities from rural areas, and more than 5 days to have the test results delivered (108). The vast majority of rural, poor, and disadvantaged people remain undetected even if they have been suffering from Covid-19. Many patients die without having been tested or before test results have been received. The mortality rate from Covid-19 is at least four times higher than the official figures reported in the media (109). Either in the absence of testing or due to delays in delivery of test results, Bangladesh has become one of the hotspots for Covid-19 transmission. It is of utmost importance that Bangladesh urgently adopts the 'trace, test, and treat' strategy to allow policy makers to take timely decisions to implement and relax lockdown at the height of each peak. However, the breach of privacy in the name of Covid-19 surveillance and the fact that only 18.5% of

the population are smartphone users will only complicate the 'test, trace, and treat' strategy in the country (110). In light of these issues, GoB needs to approach a non-app-based strategy for contact tracing, like that of South Korea, with the aid of multiple stakeholders to form another integrated system based on advanced information technology (110).

The premature lifting of lockdown restrictions is bringing in unimaginably devastating outcomes to the already suffocating circumstances in Bangladesh. Much of the population, like in neighboring India, abuses the closure of offices as an opportunity for leisure in resorts and vacations to distant cities and even to India, where the cases of the Delta variant have been souring. A vast majority of the people defied Covid-19 related personal measures not only for shopping but also to attend large gatherings like weddings and birthdays, amongst others. The relaxation of a lockdown, for instance, just before Eid in July 2021 might transmit the Delta variant across the whole country as people abused this opportunity to travel from one zone to another and from one city to another.

Bangladesh is a poverty-stricken country. According to Bangladesh Bureau Statistics dated 5 years back, Bangladesh was home to 40 million poor people (111). The economic situation has only aggravated the Covid-19 pandemic in 2020. Around 1 million people became jobless during the early phase of the pandemic last year (111). Export earnings have fallen from 3.2 billion to 520 million in Bangladesh. It is, thus, not surprising that 2 million garment workers have been laid off without prior notice and, by and large, without pay (4). Those who have still managed to stay in the garment sector are forced to work under very cramped conditions with poor aeration, which is essential in the strategic management of Covid-19. There has been a 60% rise in the number of people who are extremely poor (111). At least 1 in 6 poor citizens do not have any food at home (111). In the absence of an appropriate support

system to deliver food reserves to this extremely vulnerable class of citizens, the poorest citizens are often bound to be transient and mobile dwellers. They often live in the streets or temporarily in slums. In fact, around 55% of the urban population in Bangladesh lives in the urban slums (112). Moreover, 82% of the slum dwellers live in single rooms with their entire families and have a space of barely 26-50 square feet per person (105). Besides, 90% of the slum residents share toilets with 10 or more households (4, 105) and one hand washing station amongst 10-16 families, making it difficult for them to commit to using soap and running water for cleansing (4). It is, therefore, extremely difficult to control Covid-19 transmission under these overtly crowded living conditions. A government strategy must be implemented to test, trace, and treat and protect this class of citizens who continue to serve the garment sector and have largely contributed to its revenue over many decades.

While it has been extremely difficult for Bangladesh to manage the first two waves, due to its highly porous border with India, it became beyond manageable in the wake of the third wave, led by the Delta variant, which was officially identified in the Indian state of Maharashtra in October 2020. The Delta variant is more than twice as contagious and infectious compared to previous variants of Covid-19. Studies from Canada and Scotland indicate that patients infected with the Delta variant are more likely to be hospitalized compared to those infected with Alpha or other variants (113). The first official report of a case linked to the Delta variant was confirmed in May 2021 (114). The first mortality case due to black fungus was confirmed in BIRDEM in a span of a few days after the first case of Delta variant. It is highly possible that the Delta variant has been circulating in Bangladesh long before May 2021 as people have been recklessly crossing the borders to India for leisure trips (115). By July 2021, all the genomes sequenced from a fraction

of samples in different parts of Bangladesh were Delta variants (96).

Supplies of medical oxygen in areas of Bangladesh bordering India were out of supply. In Bangladesh, on 2nd July 2021, seven people died at the Bogura government Covid hospital by 12 hours (116). Bangladesh relies on its neighboring country for supplies of liquefied oxygen. It was of utmost importance to present the actual number of casualties and mortality associated with Covid-19 to the media so that they could put the gravity of the Covid-19 crisis in Bangladesh in front of the global platform. This might help the government in seeking assistance either in the form of medical, oxygen, and vaccine supplies or funds towards training staff and building testing centers, as well as much needed improvisation as well as expansion of government hospitals across the country.

CONCLUSION

Covid-19 is not a curse. It is a natural phenomenon. In the past, infectious diseases took many lives during preceding outbreaks and no one can say when another deadly outbreak can arise. From the confines to control the recent outbreak by Delta variant, the GoB might prepare the health sector in a shape to quickly adapt to diagnose, treat, and survey any novel infectious cases, progress research sector with cutting-edge technology, improve and increase medical facilities, and above all, with proper knowledge and training develop the human resources to fight against any new variant of SARS-CoV-2 or any potential infectious agent. Government and non-government organizations may complement each other to achieve sustainable development in the health sector in near future.

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