

Comparison of COVID-19 Infection Among Vaccinated and Unvaccinated Patients in Bangladesh During Second Wave: Single Centre Study

Fazila-Tun-Nesa Malik¹, Md. Kalimuddin², Mir Ishraquzzaman³, Ashok Dutta⁴, Md. Habibur Rahman⁴, Smita Kanungo⁵, Nazmun Laila⁵, Md. Shamim Chowdhury⁶, Sohel Reza Choudhury⁷ Mohammad Abdullah Al Mamun⁸.

Abstract:

Background: Vaccination may positively influence the clinical outcome of corona virus disease-19 (COVID-19) patients. But there is a lack of data regarding efficacy of vaccine against COVID-19 infection. This study aimed to compare the baseline characteristics, clinical profiles, and outcomes of COVID-19 infection in vaccinated and non-vaccinated patients in Bangladesh in the second wave.

Methods: This single centre prospective observational cohort study was carried out at National Heart Foundation Hospital & Research Institute from 27th February 2021 to 25th September, 2021 during the second wave. All COVID-19 positive patients & cardiac patients who became COVID-19 positive during the period of admission were included in this study for comparison.

Results: A total of 858 patients were included. Most patients in the second were unvaccinated (n= 691, 80.5%), while of the 167 individuals who were vaccinated, 125 (14.6%) patients were partially vaccinated while 42 (4.9%) were fully vaccinated. The mean age of the unvaccinated patients was 52.63±16.4 years, partially vaccinated

patients was 39.74±14.88 years, and fully vaccinated patients was 50.55 ± 12.48 years (p=0.001). Male were predominant in all groups. In the unvaccinated (98.4% vs 1.6%; p=0.001) and fully vaccinated (81% vs 19%; p=0.001) groups non healthcare personnel (non-HCP) were most commonly affected. Most of the patients (48.7%) in unvaccinated group had e³4 co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had <4 co-morbidities (p=0.001). In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group (table 3). Mortality rate was significantly higher in unvaccinated group than partially vaccinated group (6.2% vs 0.8%; p=0.001). There was no death in fully vaccinated group.

Conclusion: Unvaccinated individuals were more prone to COVID-19 infection. Most of the patients in unvaccinated group had e³4 co-morbidities. In unvaccinated group asymptomatic & severe disease were more prevalent than partially- and fully vaccinated group. Mortality rate was high in unvaccinated group.

Key wards: COVID-19, vaccine status, clinical features, in-hospital outcome.

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Introduction:

The novel severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) originated from Wuhan, China, in

2019 and struck the world like a tsunami. The healthcare system of the developing countries was paralyzed by

¹Professor & Head, ²Associate Professor, ³Consultant, ⁴Professor, ⁵Assistant Professor, ⁶Registrar, Department of Cardiology, National Heart Foundation Hospital & Research Institute, Mirpur, Dhaka. ⁷Professor & Head, ⁸Associate Professor, Department of Epidemiology & Research, National Heart Foundation Hospital & Research Institute, Mirpur, Dhaka.

Address of Correspondence: Prof. Fazila-Tun-Nesa Malik, Chief Consultant Cardiology, National Heart Foundation Hospital & Research Institute. Email : fazilamalik@yahoo.com

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this deadly virus. A country like Bangladesh, with limited resources and scarce healthcare facilities experienced major challenges while combating this transmission¹. There was an acute shortage of hospital beds, oxygen supply, medicines, and ventilators across the country for COVID-19 patients². Before availability of vaccine, the only way to prevent the spread of the virus was to wear masks in public places, wash hands diligently, cover mouth when coughing, maintain social distance, identify positive cases by large-scale testing and to isolate the infected^{3,4}. With time, several vaccines (Covishield, Pfizer–BioNTech, AstraZeneca, Covaxin) were invented to provide acquired immunity against the coronavirus⁵. Maintaining the necessary measures and proper dose of vaccines, several nations have succeeded in controlling the disease⁵. Bangladesh was one of the few countries that started vaccine rollouts timely⁶. As of April 19, 2021, 5.73 million people have received at least one dose of the Oxford-AstraZeneca vaccine and 1.51 million people are fully vaccinated with two doses (0.8% population fully vaccinated)⁷. However, a large fraction of people, mostly residing in villages and slums were hesitant toward vaccination, primarily due to lack of knowledge⁸. Anti-vaccine proponents, belief of being at a low risk of infection, concerns about adverse events, toxicity, and the overall efficacy of vaccines strongly discouraged many from the procedure of vaccination⁹. Some were also apprehensive about the long-term effects of the vaccines¹⁰.

In randomized placebo-controlled Phase III trials, the BNT162b2 mRNA COVID-19 vaccine (Pfizer- BioNTech)¹¹, the mRNA-1273 vaccine (Moderna)¹², the ChAdOx1 nCoV-19 vaccine (AZD1222; Oxford-AstraZeneca)¹³, the absorbed COVID-19 (inactivated) vaccine (CoronaVac)¹⁴, and Ad26.COV2.S (Janssen) [15] vaccines showed 95%, 94.1%, 70.4%, 50.7% and 67% efficacy against symptomatic disease due to SARS-CoV-2. An interim analysis of four randomized control trials (RCTs) of Covishield vs control has reported an overall efficacy of 70.4% among 11,636 participants.¹³ In India, recent RCT of Covaxin vs placebo on 25,798 individuals reported vaccine efficacy of 93.4% against severe COVID 19 and 63% against asymptomatic COVID 19, with an overall vaccine efficacy of 77.8%.¹⁶ Studies in the real-world setting around the world have shown that the approved vaccines are highly protective against SARS- CoV-2¹⁷.

However, there is a lack of data regarding efficacy of vaccine against COVID-19 infection in Bangladeshi population. This study aimed to compare the baseline characteristics, clinical profiles, and clinical outcomes of fully vaccinated individuals with SARS CoV 2 infection with those of unvaccinated and partially vaccinated individuals in the second wave.

Material and Methods:

This single centre prospective observational cohort study was carried out at National Heart Foundation Hospital & Research Institute from 27th February, 2021 to 25th September, 2021 in the second wave. COVID-positive patients & all admitted cardiac patients who become COVID-19 positive during this period were included in this study for comparison. Based on the duration of having the symptoms from the date of vaccination, patients were classified into three groups: unvaccinated, partially vaccinated and fully vaccinated¹⁸. Unvaccinated patients were defined as those who had not received any vaccine or became symptomatic in <2 weeks of receiving the first dose. Partially vaccinated patients were defined as who got symptomatic two or more weeks after the first dose but not received the second dose or received the second dose <2 weeks before getting symptomatic. Participants who became symptomatic two or more weeks after the receipt of the second dose of the vaccine were defined as fully vaccinated¹⁸. The degrees of severity of COVID-19 were classified as mild, moderate, severe, and critical ill^{19,20}.

Continuous variables are described using the mean and standard deviation (SD), and compared using unpaired Student's 't' test. Discrete variables are expressed as number of cases and percentage. Comparison between variables was performed using the two-sided chi-square tests for discrete variables, or Fisher's exact tests (expected frequency <5). A two-sided p value <0.05 was considered statistically significant. All analyses were performed using SPSS statistical software version 16.0 (SPSS Inc., Chicago, IL, USA).

Results:

Most patients in the second wave were unvaccinated (n= 691, 80.5%), while of the 167 individuals who were vaccinated, 125 (14.6%) patients were partially vaccinated while 42 (4.9%) were fully vaccinated (Figure 1).

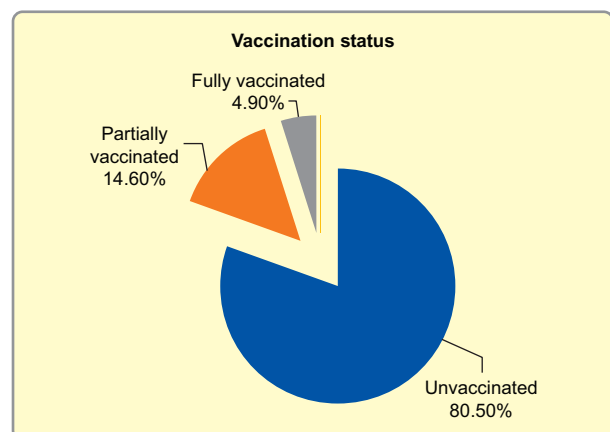


Fig.-1: Vaccine status of study cohort (n=858).

The mean age of the unvaccinated patients was 52.63±16.4 years, partially vaccinated patients was 39.74±14.88 years, and fully vaccinated patients was 50.55 ± 12.48 years (p=0.001). Among unvaccinated cases, the number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years were 3.8%, 16.6%, 47.8%, 29.6%, and 2.2%, respectively. Among partially vaccinated cases, the number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years were 0.0%, 58.4%, 28.0%, 13.6%, and 0.0%, respectively. The number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years among fully vaccinated cases were 0.0%, 21.5%, 59.5%, 19.0%, and 0.0%, respectively.

Male were predominant in all groups. In the unvaccinated (98.4% vs 1.6%; p=0.001) and fully vaccinated (81% vs 19%; p=0.001) groups, non healthcare personnel (non-

HCP) were more infected. Cardiovascular disease (80.5%), hypertension (69.3%), chronic kidney disease (45.3%) and diabetes mellitus (DM) (43.1%) were more prevalent in unvaccinated group; while Hypertension (32.8%), obesity (31.2%), cardiovascular disease (29.6%) and DM (24%) were more prevalent in partially vaccinated group & cardiovascular disease (71.4%), HTN (66.7%), smoking (40.5%) and DM (35.7%) in fully vaccinated group (p=0.001). Comparison of demographic profile of study cohort is outlined in table 1. Most of the patients (48.7%) in unvaccinated group had e⁴ co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had <4 co-morbidities (p=0.001).

Abbreviation: COVID-19: coronavirus disease 2019; HCP: healthcare personnel; non-HCP: non-healthcare personnel; SD: standard deviation; HTN: hypertension;

Table-I
Demographic profile of study cohort

Variables	Vaccination status (n=858)			P value
	Unvaccinated (n=691)	Partially vaccinated (n=125)	Fully vaccinated (n=42)	
Age (Mean age ±SD)	52.63 ±16.4	39.74 ±	50.55 ±	0.001 [#]
years	14.88years	12.48years		
<20 years	26(3.8%)	0(0.0%)	0(0.0%)	0.001
21-40 years	115(16.6%)	73(58.4%)	9(21.5%)	
41-60 years	330(47.8%)	35(28.0%)	25(59.5%)	
61-80 years	205(29.6%)	17(13.6%)	8(19.0%)	
>80 years	15(2.2%)	0(0.0%)	0(0.0%)	
Gender				
Male	462(66.9%)	64(51.2%)	31(73.8%)	0.002 [*]
Female	229(33.1%)	61(48.8%)	11(26.2%)	
HCP	11(1.6%)	83(66.4%)	08(19.0%)	0.001 [*]
Non-HCP	680(98.4%)	42(33.6%)	34(81.0%)	
Risk factors & co-morbidities				
HTN	479(69.3%)	41(32.8%)	28(66.7%)	0.001 [*]
DM	298(43.1%)	30(24.0%)	15(35.7%)	0.001 [*]
Smoking	257(37.2%)	19(15.2%)	17(40.5%)	0.001 [*]
Dyslipidemia	150(21.7%)	16(12.8%)	10(23.8%)	0.06 [*]
Cardiovascular disease	556(80.5%)	37(29.6%)	30(71.4%)	0.001 [*]
COPD/BA	53(7.3%)	46(5.4%)	46(5.4%)	0.114 [*]
Obesity	176(25.5%)	39(31.2%)	15(35.7%)	0.19 [*]
CKD	313(45.3%)	28(22.4%)	11(26.2%)	0.001 [*]
Number of co-morbidities				
0	47(6.8%)	39(31.2%)	3(7.2%)	0.0001 [*]
<4	307(44.5%)	64(51.2%)	23(54.7%)	
≥4	337(48.7%)	22(17.6%)	16(38.1%)	

DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; BA: Bronchial asthma; CKD: chronic kidney disease. *Chi square test was done to find out the significance; #Student's 't' test was done to find out the significance.

Asymptomatic patients were more predominant in unvaccinated group than in partially- and fully vaccinated group (30.1% vs 12.8% vs 16.7%; p= 0.001). In unvaccinated group, fever, shortness of breath, cough and fatigue were the predominant symptoms. In partially vaccinated group fever, cough, fatigue and headache

were the predominant symptoms & fever, cough, fatigue, shortness of breath in fully vaccinated group. Comparison of baseline clinical profile of study cohort is depicted in table 2.

In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group (table 3). Mortality rate was significantly higher in unvaccinated group than partially vaccinated group (6.2% vs 0.8%; p=0.001). There was no death in fully vaccinated group. Comparison of in-hospital outcome of study cohort COVID-19 patients is shown in table 3.

Table-II
Baseline clinical profile of study cohort

Variables	Vaccination status (n=858)			P value*
	Unvaccinated (n=691)	Partially vaccinated (n=125)	Fully vaccinated (n=42)	
Clinical presentation				
Symptomatic	483(69.9%)	109(87.2%)	35(83.3%)	0.001
Asymptomatic	208(30.1%)	16(12.8%)	7(16.7%)	
Presenting symptoms				
Fever	316(45.7%)	83(66.4%)	26(61.9%)	0.001
Fatigue	155(22.4%)	59(47.2%)	17(40.5%)	0.001
Cough	221(32.0%)	69(55.2%)	23(54.8%)	0.001
Body ache	71(10.3%)	40(32.0%)	10(23.8%)	0.001
Headache	35(5.1%)	49(39.2%)	9(21.4%)	0.001
Anosmia	15(2.2%)	42(33.6%)	5(11.9%)	0.001
Sore throat	9(1.3%)	33(26.4%)	3(7.1%)	0.001
Shortness of breath	314(45.4%)	40(32.0%)	15(35.7%)	0.013
Diarrhea	6(0.9%)	22(17.6%)	2(4.8%)	0.001
Generalized itching	15(2.2%)	7(5.6%)	1(2.4%)	0.09

Abbreviation: COVID-19: coronavirus disease 2019. *Chi square test was done to find out the significance.

Table-III
In-Hospital outcome of study cohort

Variables	Vaccination status (n=858)			P value*
	Unvaccinated (n=691)	Partially vaccinated (n=125)	Fully vaccinated (n=42)	
Disease severity				
Asymptomatic	208(30.1%)	16(12.8%)	7(16.7%)	0.001
Mild	400(57.9%)	98(78.4%)	34(81.0%)	0.001
Moderate	1(0.1%)	2(1.6%)	0(0.0%)	0.0370.041
Severe	79(11.4%)	9(7.2%)	1(2.4%)	
Critical ill	3(0.4%)	0(0.0%)	0(0.0%)	0.695
Mortality	43 (6.2%)	1(0.8%)	0(0.0%)	

Abbreviation: COVID-19: coronavirus disease 2019. *Chi square test was done to find out the significance.

Discussion

Important findings of this study are: 1) Most of the infected persons were unvaccinated (80.5% vs 19.5%; $p=0.001$); 2) Unvaccinated patients were older than fully vaccinated and partially vaccinated patients (52.63 ± 16.4 yrs vs 50.55 ± 12.48 years vs 39.74 ± 14.88 years; $p=0.001$); 3) Vaccinated people were less affected by COVID-19; 4) Most of the patients (48.7%) in unvaccinated group had ≥ 4 co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had < 4 co-morbidities ($p=0.001$); 5) Asymptomatic patients were more predominant in unvaccinated group than in partially- and fully vaccinated group (30.1% vs 12.8% vs 16.7% ; $p=0.001$); 6) In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4% ; $p=0.001$) were more prevalent than partially- and fully vaccinated group; and, 7) Mortality rate was high in unvaccinated group (6.2% vs 0.8% vs 0.0% ; $p=0.001$).

In our study, 4.9% (42) patients were fully vaccinated which is also defined as vaccine breakthrough infection. It could be due to emergence of newer mutant strains capable of escaping the host immune response²¹, ineffectiveness of the vaccine secondary to various factors including a break in the cold chain, etc, faulty techniques of vaccination, and host factors leading to ineffective antibody production^{22,23}.

Unvaccinated patients were older than fully vaccinated and partially vaccinated patients (52.63 ± 16.4 yrs vs 50.55 ± 12.48 years vs 39.74 ± 14.88 years; $p=0.001$). This may be due to targeting of vaccination program from frontline fighters and people aged >40 years in the first phase in Bangladesh (combination of young and older age). Later people >18 years were included in vaccination program so younger age was predominant in partially vaccinated group. Elderly patients were more prone to COVID-19 infection and they afraid of vaccination. In contrast to our study, the fully vaccinated individuals were older than the partially vaccinated and the unvaccinated patients (66 vs 59 vs 55 years, p -value <0.001)²⁴.

Fatima et al. [24] from Pakistan recruited 434 COVID-19 patients. Of them, 37.7% ($n = 164$), 6.6% ($n = 29$) and 55.5% ($n = 241$) were fully vaccinated, partially vaccinated, and unvaccinated, respectively. Majority (35.7%) of the patients had received Sinopharm vaccination and the median time interval from the last dose of vaccination to symptom onset was 74 (42-114) days. The severe (33.2% vs 34.5% vs 30.5%) and critical disease (44.8% vs 48.3% vs 34.8%) was significantly higher in the unvaccinated and partially vaccinated group as compared to the vaccinated group (p -value 0.04). Comparatively higher

number of unvaccinated and partially vaccinated patients required invasive ventilation than the fully vaccinated cohort (7.9% vs 3.4% vs 1.8%, p -value 0.025). Unvaccinated patients had significantly higher rate of sepsis (19.5% vs 6.7% p -value <0.001), septic shock (7.5% vs 0.6% p -value 0.002) and multi-organ dysfunction (9.1% vs 1.2% p -value 0.002) as compared to fully vaccinated patients. Overall, mortality rate was also significantly higher in unvaccinated patients (16.2%, $n = 39$) as compared to 6.1% ($n = 10$) in fully vaccinated patients (p -value 0.006). Age, gender, and presence of ≥ 2 co-morbid conditions, vaccination status was an independent predictor of mortality and unvaccinated patients had statistically significant mortality risk with p -value <0.001 (OR 5.04, CI 2.04-10.55).

Balachandran et al.²⁵ analyzed 1446 COVID-19 patients. Most patients were non-vaccinated ($n = 1100$, 76.1%), while of the 346 individuals who were vaccinated, 189 were partially vaccinated while 157 were fully vaccinated. Comparing between the vaccinated and the unvaccinated COVID-19 patients, ICU admissions (3.5% vs 7.1%), gastrointestinal symptoms (9.5% vs 6.9%), non-invasive ventilation use (10% vs 4.3%), death (5.8% vs 1.4%), mechanical ventilation (5.9% vs 5.2%), oxygen use (9% vs 7.5%), antibiotics (19% vs 12.4%), use of steroids (12.8% vs 9.2%), antivirals (16% vs 11.5%) and length of stay in hospital 11.33 ± 9.9 days for the unvaccinated and 8.06 ± 4.18 days in the vaccinated group were all favourable for the vaccinated cohort with ICU admissions, need for non-invasive ventilation and death reaching statistical significance. Mechanical Ventilation (5.9% vs 5.2%), non-invasive ventilation (8% vs 4.3%) and moderate-severe symptoms (9% vs 7.5%) were all more favourable for the vaccinated as compared to the unvaccinated patients. Deaths occurred in 0.63% of the fully vaccinated, 2.1% of the partially vaccinated, and in 5.8% of the unvaccinated patients. Thangaraj et al.²⁶ enrolled 539 COVID-19 patients (241 partially vaccinated patients, 113 fully vaccinated patients, and 185 unvaccinated individuals) in the study. The median age of the individuals who were unvaccinated, partially vaccinated and fully vaccinated were 47 years (IQR; 33–57), 53 years (IQR; 46–60) and 54 years (IQR: 42–64), respectively. The proportion of patients with moderate/severe illness was significantly lower in the fully vaccinated group (7/104, 6.7%) than in the unvaccinated (34/176, 19.3%) group ($p = 0.003$). No deaths were reported in the fully vaccinated group, whereas 3 partially vaccinated group (1.3%) and seven unvaccinated (4%) COVID-19 patients died. The proportion of COVID-19 deaths was significantly lower in the partially vaccinated

(1.3%, p value (1-tail) = 0.046) and fully vaccinated (0%, p value (1-tail) = 0.018) than the unvaccinated (4.0%).

Sagiraju et al.¹⁸ from India, compared the differences in clinical, biochemical parameters and the hospitalization outcomes of 53 (35) fully vaccinated individuals with those of 1464 (83.8%) unvaccinated and 231 (13.2%) partially vaccinated individuals. Vaccination status of their patients was similar to our study. They showed that completing the course of vaccination protected individuals from developing severe COVID 19 as evidenced by lower proportions of those with hypoxia, abnormal levels of inflammatory markers, requiring ventilatory support, and death compared to unvaccinated and partially vaccinated individuals. In our study, in unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; $p=0.001$) were more prevalent than partially- and fully vaccinated group.

Completing the vaccination schedule for COVID 19 significantly decreased the inflammatory response caused by the SARS CoV 2 virus, thereby reducing the risk of developing serious complications during illness¹⁸. Even receiving a single shot of the COVID 19 vaccine seemed to reduce the inflammatory response after 14 days of receiving the vaccine, making the individual less prone to severe COVID 19¹⁸. More individuals in the unvaccinated and partially vaccinated groups had a hyper inflammatory response as evidenced by high d Dimer, IL 6 and CRP levels as compared to fully vaccinated individuals¹⁸. This may indicate that vaccination reduces the risk of developing hypoxia and cytokine storm, but once the patient develops hypoxia and ARDS, the odds of developing critical illness and death are similar to those of unvaccinated individuals^{18,27,28}.

In our study, mortality rate was 6.2% in unvaccinated group, 0.8% in partially vaccinated group and no death in fully vaccinated group ($p=0.001$). Almost similar death rate was observed in study by Thangaraj at al.²⁶ (4.0% vs 1.3% vs 0.0%; $p=0.001$), and by Balachandran et al.²⁵ (5.8% vs 2.1% vs 0.63%). But in other studies mortality rate was higher than our studies: (22.8% vs 19.48% vs 5.66%)¹⁸, and (16.2% vs 13.8% vs 6.1%; $p=0.006$)²⁴. Muthukrishnan et al.²⁹ in their hospital-based cross-sectional study reported a higher mortality rate of 31.45% vs 12.5% among unvaccinated as compared to those fully vaccinated. Moreover 70% lower risks of mortality were reported in the fully vaccinated cohort.

There have several limitations to our study. Firstly, study conducted in non-COVID-dedicated hospital. Secondly, the genomic variants were not considered. Thirdly, COVID

variants were not determined and fourthly. Fourthly, the brand name of vaccine was not included. Fifthly, COVID-19 antibodies tests were not done to see the effectiveness of the vaccine.

Conclusion:

Unvaccinated individuals were more prone to COVID-19 infection. Most of the patients in unvaccinated group had ≥ 4 co-morbidities, while in partially- and fully vaccinated groups most of the patients had < 4 co-morbidities. In unvaccinated group asymptomatic & severe disease were more prevalent than partially- and fully vaccinated group. Mortality rate was high in unvaccinated group. The vaccine offers strong protection against the most serious outcomes of COVID-19, increasing vaccination rates is key to limiting severe COVID-19 cases and saving lives.

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