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ORIGINAL ARTICLE

COMPARISON OF DISEASE SEVERITY AND IN-HOSPITAL OUTCOME OF COVID-19 AMONG NON-VACCINATED VERSUS VACCINATED (1ST DOSE) HOSPITALIZED PATIENTS IN A TERTIARY CARE HOSPITAL: AN OBSERVATIONAL STUDY

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Abstract:

Background: *COVID-19 vaccines have a high rate of success in averting hospitalization and mortality. However, COVID-19 infection is still being detected among immunized patients, although with blunted severity. This study aimed to compare the severity and outcome of COVID-19 among immunized versus non-immunized individuals.* ***Methods:*** *This cross-sectional study was conducted over 179 COVID-19 patients in Popular Medical College Hospital, Dhaka. All the methods in the present study were carried out following the ethical guidelines of the 1975 Declaration of Helsinki. Data were collected from both hospital record and direct interview. Data were recorded in separated case record form and analyzed by STATA version 14.* ***Results:*** *Mean age of the study patients was 55.42±14.20 (SD) years wherein maximum were male (61.5%). Fever (88.8%), cough (81.6%), dyspnea (47.5%) and sore throat (30.2%) were most common symptoms. Maximum patients werehypertensive (60.9%) and diabetic (58.7%). About 35.8% of patients had mild severity, while 27.9% had moderate, 23.4% had severe, and 12.8% had critical stage. Maximum patients (n=122, 68.2%) were non-vaccinated and rest (n=57, 31.8%) had received 1st dose of vaccine. Vaccinated patients had significantly higher frequency of having mild COVID-19 (57.9% vs 31.1%, p<0.001) and getting discharge with full recovery (94.7% vs 76.2%, p=0.003) compared to non-vaccinated patients. Moreover, non-vaccinated patients were more prone to develop critical clinical syndrome (10.6% vs 1.8%, p=0.039) and had died or referred to higher center (11.4% vs 1.8%, p=0.029) than vaccinated individuals.* ***Conclusion:*** *COVID-19 vaccination was significantly associated with mild severity and lower rate of adverse outcome.*

Keywords: *COVID-19, Severity, Vaccination, Adverse outcome*

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Introduction:

Since the beginning of COVID-19 infections, and its proclamation as a pandemic on March 11, 2020, the total 5,84,395 cases have been confirmed and 8,797 deaths have been recorded in Bangladesh, as of March 25, 2021.[1] The infection rate and death toll had gradually climbed since the last week of March 2021, indicating the onset of the second wave of COVID-19.[2]The sudden surge of cases might be caused by the newly identified SARS-CoV-2 double mutant Delta variant (B.1.617.2), which was wreaking havoc in India, UK, and other countries around the globe in recent months.[3]

The main strategy to combat the COVID-19 infection is to stop the transmission in the community with preventive measures. Maintaining health protocols like frequent washing of hands, wearing a mask, maintaining social distance remains the main preventive attitude towards this disease. Yet, the vaccine has no alternative to mitigate the current pandemic situation.Worldwide, it is being taken seriously and responded to this rapidly for the development of vaccines against SARS-CoV-2, which have led to an unprecedented number of candidate vaccines starting clinical trials during 2020.[4]Bangladesh received the Oxford AstraZeneca vaccine from Serum Institute of India, and started the mass vaccination program on 7 February 2021, with a focus primarily on high-risk groups such as the elderly, those with comorbidities, or front-line workers. Till March 25, 2021, total51,39,456 people had received at least one dose of vaccine.[5]

Unfortunately, several studies have reported the development of COVID-19 despite prior full vaccination throughout the world.[6]Moreover, the delta version was shown to reduce the effectiveness of Oxford-AstraZeneca vaccinations by 6.2 times when compared to the alpha variant.[7] However, evaluations of COVID-19 vaccines have primarily focused on prevention of symptomatic infection and hospitalizations till date [8–11], though effectiveness against progression of COVID-19 severity following breakthrough infection, must be taken into account when interpreting the protective benefits of COVID-19 vaccinations.[12] SARS-CoV-2 infection in vaccinatedpersons is expected to triggermemory antibody and cellular responses owing to prior vaccination; these immune responses couldmitigate disease progression, possibly-preventinglife-threateningorgan failure and death.[13] Surprisingly, there is still paucity of data regarding the association of prior vaccination and clinical outcome ofCOVID-19. Hence, this study was conducted to compare the disease severity and in-hospital outcome of COVID-19 among immunized versus non-immunized individuals.

Methods:

Descriptive observational study was performed in the COVID dedicated isolation wards/ cabins/ICU of Popular Medical College Hospital, a tertiary care center located in Dhaka, Bangladesh. The study data were collected between 1st April to 30th May 2021.All admitted COVID-19 patients diagnosed by reverse transcription polymerase chain reaction (RT-PCR) positivity were approached for this study. Patients who were not willing to include and had incomplete data were excluded from the study. Finally, a total of 179 patients were enrolled for data analysis. Data were collected from direct interview. A detailed history of clinical presentations, physical examinations, co-morbidities, along with relevant investigations was also collected. Details ofCOVID-19 vaccination, including dates and location, vaccine product were ascertained. The severity assessment and management of the COVID-19 was done as per updated national guideline on clinical management of COVID-19.[14]Patients were treated by the respective doctors of isolation wards/ cabins/ICU without any interference by the study physician for study purpose. The patients were followed up daily until discharge (with full recovery or on risk bond) and death. Adverse events were defined as death or referred to higher center due to disease deterioration. Study variables were demographic (age, gender, occupation, contact history, smoking history), clinical profile (symptom duration, clinical symptoms and comorbidities like hypertension, diabetes mellitus, obesity, asthma, chronic obstructive pulmonary disease, cardiac disease and renal disease), COVID-19 vaccination history, disease severity (mild, moderate, severe and critical) and in-hospital outcome (discharge with full recovery, referred to higher center, discharge on risk bond and death. The quality of the data was ensured by properly designing the tool and the questionnaire was pre-tested in randomly selected 20 cases before actual data collection, and some minor modifications were made accordingly. The principal investigator throughout the data collection process was in close contact and under close supervision. Data was collected in separated case record form. After collection of all the required data, data were checked, verified for consistency and entered into the STATA version 14. Association of vaccination status with disease severity and outcome was assessed by applying chi-square test taking a level of significance of <0.05 [Table-IV].

Results:

The average age of study population was 55.42±14.20 (SD) years wherein maximum (40.2%) were >60 years of age. Male was the predominant gender (61.5%) with a male:female ratio 1.6:1. Fifty-six (31.3%) patients had positive contact history with COVID-19 patients within last 14 days .Almost 1/3rd patients (n=57, 31.8%) had received at least one dose of vaccine and rest 122 (78.2%) patients were non-vaccinated. [Table-1]

Table-I

Socio-demographic profile of study population. (n=179)

Variables	n (%) Mean±SD
Age (in years)	
21-30	10 (5.6)
31-40	19 (12.8)
41-50	30 (17.3)
51-60	46 (24.0)
>60	74 (40.2)
Mean±SD	55.42±14.20
Gender	
Male	110 (61.5)
Female	69 (38.5)
Occupation	
Business	58 (32.4)
Service holder	8 (4.5)
Doctor	2 (1.1)
Not employed	45 (25.1)
House wife	66 (36.9)
Positive smoking history	12 (6.7)
Positive COVID-19 contact history within last 14 days	56 (31.3)
Vaccinated status	
Vaccinated (1st dose)	57 (31.8)
Non-vaccinated	122 (68.2)

SD= Standard deviation

Maximum study patients (51.4%) admitted within 5 days of symptoms onset. The most common symptoms were fever (88.8%), cough (81.6%), dyspnea (47.5%) and sore throat (30.2%). Of all comorbidities, hypertension was on top (60.9%) followed by diabetes mellitus (58.7%), bronchial asthma (15.1%), chronic heart disease (8.9%), chronic kidney disease (7.3%) and chronic obstructive pulmonary disease (1.1%). Maximum study patients had mild COVID-19 illness (35.8%), while 27.9% had moderate, 23.4% had severe and 12.8% had critical clinical syndrome. [Table-II]

Majority COVID-19 patients were discharged with full recovery (n=149, 83.2%). Fifteen patients (8.4%) had adverse outcome, wherein 7 patients were referred to higher center and 8 patients had been expired. [Table-III]

Table-II

Disease profile of the study patients. (n=179)

Variables	n (%)
Day of admission after symptom onset	
1-5 days	92 (51.4)
6-10 days	73 (40.8)
>10 days	14 (7.9)
Clinical symptoms*	
Fever	159 (88.8)
Cough	146 (81.6)
Dyspnea	85 (47.5)
Sore throat	54 (30.2)
Diarrhoea	25 (14.0)
Fatigue	21 (11.2)
Altered taste	21 (11.2)
Chest pain	17 (9.5)
Headache	13 (7.3)
Vomiting	11 (6.1)
Conjunctivitis	11 (6.1)
Anorexia	10 (5.6)
Confusion	10 (5.6)
Nasal congestion	3 (1.7)
Co-morbidities*	
DM	105 (58.7)
HTN	109 (60.9)
Bronchial asthma	27 (15.1)
COPD	2 (1.1)
CHD	16 (8.9)
CKD	13 (7.3)
Clinical severity	
Mild	64 (35.8)
Moderate	50 (27.9)
Severe	42 (23.4)
Critical	23 (12.8)

*multiple response

DM= Diabetes mellitus, HTN=Hypertension, COPD= Chronic obstructive pulmonary disease, CHD= Chronic heart diseases, CKD= Chronic kidney disease

Table-III

In-hospital outcome of COVID-19 patients. (n=179)

In-hospital outcome	n (%)
Discharge	
Discharged with full recovery	149 (83.2)
Discharge on risk bond	15 (7.8)
Adverse events	
Reference to higher center	7 (3.9)
Death	8 (4.5)

Table-IV

Association of clinical severity and in-hospital outcome of COVID-19 with vaccination status. (n=179)

Clinical outcome	Vaccination Status		p-value
	Vaccinated (n=57) n (%)	Non-vaccinated (n=122) n (%)	
Clinical severity			
Mild	33 (57.9)	38 (31.1)	<0.001
Moderate	11 (19.2)	39 (31.9)	0.078
Severe	12 (19.3)	32 (26.2)	0.454
Critical	1 (1.8)	13 (10.6)	0.039
In-hospital outcome			
Discharged with full recovery	54 (94.7)	93 (76.2)	0.003
Adverse events	1 (1.8)	14 (11.4)	0.029

p-value was determined by Pearson chi-square test. p-value<0.05 was considered as significant.

When compared to non-vaccinated patients, vaccinated patients had a significantly higher rate of mildseverity (57.9% vs 31.1%, p<0.001) and discharge with full recovery (94.7% vs 76.2%, p=0.003). Furthermore, non-vaccinated patients were more likely to develop critical clinical syndrome (10.6% vs 1.8%, p=0.039) and to die or be referred to a higher center (11.4% vs 1.8%, p=0.029) than vaccinated patients. [Table-IV]

Discussion:

Coronavirus disease 2019 (COVID-19) can present with a variety of symptoms. The severity of the disease may be associated with several factors.[15] Clinical trials of COVID-19 vaccines currently authorized for emergency use in the United States (Pfizer-BioNTech, Moderna, and Janssen-Johnson & Johnson) indicate that these vaccines have high efficacy against symptomatic disease, including moderate to severe illness.[16] In the recently encountered second wave of COVID-19 from the last week of March 2021, we observed that people coming to the hospital as a case of Covid-19 even after getting the first shot of vaccination. Hence, this study was designed to compare the clinical outcome of COVID-19 among vaccinated (1st dose) and non-vaccinated hospitalized patients.

In this study, out of 179 COVID-19 patients, almost 1/3rd (n=57) patients were vaccinated (1st dose). This high rate is plausible as mass vaccination program started in Bangladesh on 7 February, less than two months earlier from our study period. Hence, maximum study patients hospitalized within less than 21 days of their vaccination. Studies proposed that during the first two to three weeks after the first dose of vaccination, efficacy is much lower than afterwards, as spike immunoglobulins G (IgG) begin to appear around this period.[17] Besides, vaccine efficacy may be attenuated by antigen mutation (12), and it was during the study period that new variants (Delta variant) – possibly with antigen mutation – started to appear worldwide.[18]

This study found that vaccination has significant association with COVID-19 severity as vaccinated patients had significantly higher frequency of having mild disease, while non-vaccinated patients were more prone to develop critical clinical syndrome. Previous studies also illustrated that vaccinated individuals experienced a less severe form of the COVID-19 infection and less frequent hospitalization.[1911182021] In addition, a prospective cohort study by Thompson et al. concluded that COVID-19 vaccinated cases suffer lower duration of illness, and have lower risk of febrile symptoms.[8] The mechanism, however; by which partial immunization attenuates the disease remains mostly unknown. This is possibly achieved through the vaccines' ability to produce immunological memory responses, that hasten the removal of infected cells, while reducing viral replication.[22] Indeed, several other studies also reported that influenza vaccination can lower COVID-19 severity. [23–25]

Our study also revealed that vaccinated patients had significantly lower rate of adverse outcome (death or disease deterioration to refer in higher center). Besides, vaccinated individuals had higher frequency of getting discharge with full recovery compared to non-vaccinated patients. These results are also in accordance with the previous studies [201826,27] Similar

to our research design, Mhawish et al. observed that at least one dose of immunization lowers the adjusted odds of in-hospital mortality by 55%.[18]

The main baseline characteristics of our study were in accordance with studies from previous COVID-19 waves, as maximum study patients were older aged [28–32],male [33–35], hypertensive and diabetic[36–38].

However, our study suffers numerous limitations. This was an observational study lacking the advantages of randomization. The sample size is relatively small and may have affected the power of the study. This was a single center study, reflecting the management of only one hospital. Also data on variants and impact on disease severity is lacking. And finally, our analysis lacks subdivision of immunized patients by duration since vaccination, which could have produced more informative results.On the other hand, the strengths of our work include the novelty of the topic, and identification of the under-reported problem pertinent to the population subjected to vaccination.

Conclusion:

In our study, the majority of COVID-19 patients were non-immunized, older aged, male, hypertensive and diabetic. Receiving at least one dose of immunization significantly decreases severity of the disease. Furthermore, at least one dose of immunization is significantly associated with lower adverse in-hospital outcome. Policy makers and clinicians may need to take the immunization status in consideration during management of COVID-19 patients.

Supplementary Materials: Available on request

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Conflict of Interests: None

Ethical consideration: Ethical measures were taken throughout the study period to maintain a high standard of confidentiality and anonymity of the participants. Formal approval was taken from the ethical review committee of Popular Medical College.

Consent for Publication: The authors agreed to publish the article by written consent.

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