FACTORS ASSOCIATED WITH SEVERITY OF COVID-19 DISEASE IN VACCINATED PATIENTS

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Abstract

Background*: Vaccines are considered the most promising approach for restraining the COVID-19 pandemic. We aimed to identify the disease profile and risk of severe disease despite vaccination.*

Methods: *A cross-sectional study was done from June 2021 to August 2021 in the COVID-19 dedicated hospitals in Dhaka. Total 169 RT-PCR positive adult patients were enrolled by a purposive sampling method who had completed two vaccine doses of COVID-19. Disease profile and severity was identified according to the national guideline of Bangladesh.*

Results: *Of the 169 patients, 19 (11%) had severe diseases. The mean age of the study participants was 50.46 (±14.03) year. The mean age of severely diseased patients was higher than that of non-severe disease 62.63 (±8.27) vs 48.91 (±13.86), p-value <0.0001. The overall mortality was 8 (4.7%). In univariate analyses, being elderly (e"60years) (cOR 6.14, 95% CI 2.09-18.03; p-value <0.0001) and male (cOR 5.06, 95% CI 1.13-2274; p-value <0.02 and having DM (cOR 32.94, 95% CI 4.28-253.69; p-value <0.0001, HTN (cOR 2.91, 95% CI 1.05-8.07; p-value < 0.034, OAD (cOR 3.47, 95% CI 1.09-11.07; p-value < 0.044, IHD (cOR 7.54, 95% CI 2.67-21.31; p-value <0.0001, and CKD (cOR 26.43, 95% CI 4.69-148.92; p-value <0.0001were identified as factors related to severe disease of COVID-19. In multivariate analyses, DM (aOR 13.9, 95% CI 1.5-130.1; p-value <0.021, OAD (aOR 7.9, 95% CI 1.2-50.1; p-value <0.03, IHD (aOR 7.4, 95% CI 1.6-34.4; p-value < 0.011, and CKD (aOR 41.9, 95% CI 2.6-667.4; p-value < 0.008 were independently associated with severe disease.*

Conclusion: *Vaccines against COVID-19 are showing a significant decrease in severity disease. Control of chronic diseases, exposure prevention and mass vaccination should be the main concern to mitigate the severity.*

Keywords: *COVID-19, vaccine, severity of disease.*

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Introduction:

Vaccine against COVID-19 was first introduced in UK[1], three vaccines were licensed in July 2021: BNT162b2 (Tozinameran; Pfizer–BioNTech), mRNA-1273 (Elasomeran; Moderna), and ChAdOx1 nCoV-19 (Oxford–AstraZeneca), each with satisfactory efficacy in phase 3 clinical trials.[2,3,4] Later on, Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson, Sinopharm COVID-19 vaccine, Sinovac-CoronaVac vaccine, Bharat Biotech BBV152 COVAXIN vaccine, Covovax (NVX-CoV2373) vaccine, Nuvaxovid (NVX-CoV2373) vaccine got approval for mass vaccination.[5] As a result, 220 countries are now under in vaccine coverage. The total dose given on 11.5 billion, among them fully vaccinated was 59.4% worldwide.[6] In Bangladesh, 71.1% got two

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doses of vaccine, at least one dose in 78.3% and a booster was given in 8.5% population.[7]

WHO recommended COVID-19 vaccines are safe for adults (18 or more) including those with pre-existing co-morbidities which included hypertension, diabetes, asthma, pulmonary, liver, kidney, neurological disease, as well as chronic infections that are stable and controlled.[6] The Pfizer vaccine can be safely administered to children from five years of age.[8]Both Moderna and Pfizer vaccines are licensed for use in children from 12 years of age.[6]

The COVID 19 vaccines are widely accepted worldwide for their role in reducing the spread of the disease and disease severity, mortality, and morbidity caused by COVID 19, however, some people are still infected with the virus even after being fully vaccinated.[9] According to a June 2022 study,it was found that COVID-19 vaccines had a significant impact in preventing many deaths.The study showed that between8 December 2020 to 8 December 2021 COVID-19 vaccines prevented an estimated 14.4 to 19.8 million deaths across 185 countries and territories.[10] Additionally ,various countries implemented phased distribution plans, prioritizing individuals at the most significant risk of complications, including the elderly, and those at high risk of exposure and transmission, such as healthcare workers.[11]

According to official reports from national public health agencies, 12.34 billion doses of COVID 19 vaccines have been administered worldwide up to 30 July 2022.[12] As of December 2020, countries had preordered over 10 billion vaccine doses, with approximately 50% of the doses bought by high income nations despite them only accounting for 14% of the global population.[13] Despite the rapid progress made in the development of practical mRNA and viral vector vaccines,thete is still a significant lack of global vaccine equity. To address this issue,experts have recommended the development whole inactivated virus (WIV) and protein-based vaccines have,which may be particularly useful for use in developing nations.[14]

Older adults, males, and people with underlying medical co-morbidities such as hypertension (HTN), diabetes mellitus (DM) and chronic kidney disease (CKD) have shown the worst prognosis especially diabetic patients have increased morbidity and mortality rates and have been linked to more hospitalization and intensive care unit (ICU) admissions than that of the other people.In addition People with obstructive airway disease (OAD), ischemic heart disease (IHD), cancer, and neurological disease are also at higher risk for severe illness from COVID-19. The risk of exposure to COVID-19 in patients with OAD is found to be 4-fold higher than in patients without OAD.[15]

Among the Bangladesh people, Bronchial asthma, Hypertension, Chronic kidney disease are identified as risk factors COVID-19 in various studies.[16] A study from caner patient who affected with COVID-19 has shown a mortality about 19 % which is quite high in comparison to general population.[17]

In the present study, we aimed to describe the risk factor causing severity in disease patterns irrespective of vaccination.

Materials and methods

A cross-sectional, hospital-based study was done from June 2021 to August 2021 in COVID-19 dedicated hospitals in Dhaka city. Total 169 RT-PCR positive COVID-19 adult patients (e”18 years) were enrolled by a purposive sampling method who had completed two doses of vaccine, COVID-19 positive by RT-PCR after at least seven days of the second dose, attending inpatient and outpatient departments. Patients with incomplete information, and unwilling to participate were excluded from the study.

After taking written informed consent demographic parameters, baseline comorbidities, the outcome such as recovery and death were collected from individual patients or relatives on a structured questionnaire.

The severity of disease was categorized as either adolescent as adolescent or adult with clinical indications of pneumonia such as fever, cough, dyspnea,rapid breathing , in addition to at least one of the following: respiratory rate exceeding 30 breaths per minute; severe respiratory distress; or an oxygen saturation level below 90% on room air. Although the diagnosis can

be established based on clinical evidence, chest imaging technique like radiography , CT scan or ultrasound can help diagnose and determine the presence or absence of pulmonary complications.[18]

The definition of COVID-19 death, particularly for surveillance purposes, refers to a death that occurs as a result of clinically consistent illness in a porbable or confirmed case of COVID-19 unless there eits an evident alternative cause of death is not related to COVID-19 disease (such as trauma).It is also necessary to note that there should be no interval of complete recovery between the onset of illness and death.[18]

The study's participants baseline characteristics were reported in terms of frequency and percentage for categorical variables. Mean & standard deviation (SD) were used to express continuous variables with normal distribution . Independent sample t-test were employed to compare of parametric data between groups,wheres differences between two categorical data were analyzed using the Chi-square test/ Fisher's exact test as appropriate. Logistic regression was conducted via enter method to identify risk factors for developing severe/critical disease. The Data were expressed as odds ratio (OR) and 95% confidence interval (CI). SPSS Statistics 25.0 software ,located in Armonk, New York, USA was used for all statistical analysis.

Result:

Of the 169 patients, 19 (11%) had severe disease. The mean age of the study participants was 50.46 (±14.03) years. (Table I)

Table-I

Demographic and clinical characteristics of post-vaccinated COVID-19 patients

Total patients n (%)

Demographic characteristics of patients	
Age, years ± SD	50.46 (±14.03)
Male	111 (66)
Clinical characteristics	
Co-morbidities	
HTN	77 (46)
DM	71 (42)
IHD	25 (15)
OAD	19 (11)
CKD	7 (4)
Severity	
Non-severe	150 (89)
Severe/critical	19 (11)
Outcome	
Recovery	161 (95)
Death	8 (5)

The mean age of severely diseased patients was higher than that of non-severe disease 62.63 (±8.27) vs 48.91 (±13.86), p-value <0.0001. The overall mortality was 8 (4.7%). (Table II)

Table II

Comparison of baseline characteristics of non-severe and severe disease the post-vaccinated COVID-19 patients

Variables	Total patients (n=169)	Non-severe disease (n=150)	Severe/critical disease (n=19)	p-value
Age (Mean ± SD)	50.46 (14.03)	48.91 (13.86)	62.63 (8.27)	<0.0001
Elderly (≥60 years), n (%)	61 (36.1%)	47 (31.3)	14 (73.7)	<0.0001
Male gender	111 (65.7)	94 (62.7)	17 (89.5)	0.02
Co-morbidities, n (%)				
DM	71 (42)	53 (35.3)	18 (94.7)	<0.0001
HTN	77 (45.6)	64 (42.7)	13 (68.4)	0.034
OAD	19 (11.2)	14 (9.3)	5 (26.3)	0.044
IHD	25 (14.8)	16 (10.7)	9 (47.4)	<0.0001
CKD	71 (4.1)	2 (1.3)	5 (26.3)	<0.0001

Table III

Associated factors analyses for severe COVID-19 in the study population in the regression model (n=169)

Variables	Univariate analyses			Multivariate analyses		
	cOR	95%CI	p-value	aOR	95%CI	p-value
Elderly (≥60 years)	6.14	2.09-18.03	0.0001			
Male gender	5.06	1.13-22.74	0.02			
DM	32.94	4.28-253.69	0.0001	13.9	1.5-130.1	0.021*
HTN	2.91	1.05-8.07	0.034			
OAD	3.47	1.09-11.07	0.044	7.9	1.2-50.1	0.03*
IHD	7.54	2.67-21.31	0.0001	7.4	1.6-34.4	0.011*
CKD	26.43	4.69-148.92	0.0001	41.9	2.6-667.4	0.008*

Data are reported as odd's ratio and 95% CI. cOR=crude odd's ratio; aOR= adjusted odd's ratio; CI (Confidence interval). *significant. All variables showing a p <0.2 in the univariate analysis were presented to a multivariate model by using the forward method. Variables were retained in the model if a Wald test revealed a significance of <0.05.

In univariate analyses, being elderly (≥60years) (cOR 6.14, 95% CI 2.09-18.03; p-value <0.0001) and male (cOR 5.06, 95% CI 1.13-22.74; p-value <0.02) and having DM (cOR 32.94, 95% CI 4.28-253.69; p-value <0.0001), HTN (cOR 2.91, 95% CI 1.05-8.07; p-value < 0.034), OAD (cOR 3.47, 95% CI 1.09-11.07; p-value < 0.044), IHD (cOR 7.54, 95% CI 2.67-21.31; p-value <0.0001), and CKD (cOR 26.43, 95% CI 4.69-148.92; p-value <0.0001) were identified as risk factors for severe disease of COVID-19. In multivariate analyses, DM (aOR 13.9, 95% CI 1.5-130.1; p-value <0.021), OAD (aOR 7.9, 95% CI 1.2-50.1; p-value <0.03), IHD (aOR 7.4, 95% CI 1.6-34.4; p-value < 0.011), and CKD (aOR 41.9, 95% CI 2.6-667.4; p-value < 0.008) were independently associated with severe disease. (Table III)

Discussion:

We presented data from 169 RT-PCR positive COVID-19 patients who completed two doses of vaccine and symptoms of COVID-19 appeared after seven days of the second dose of vaccine as immunity developed by this time and infection was unlikely to be due to exposure around the time of vaccination (eg when travelling to the vaccination centre).[19]

Disease severity significantly reduced after COVID-19 vaccination. Our study found that severe disease occurred in only 11% of patients significantly lower than that of non-vaccinated people which was found a study from the Bangladeshi population where severity of 48% in hospitalized non-vaccinated COVID -19 patients.[20] A population-based study from China found a 90% reduction in the disease severity in vaccinated people compared to non-vaccinated ones.[21] Another study from the UK found an 85-90% reduction in the disease severity after vaccination.[22]

In this study, we observed 5% death which was slightly higher than that of China[21] and UK [22], as data were collected from the patients who visited the hospital with certain co-morbidities.

Male gender and increasing age were found to be higher in severe disease than non-severe in the present study similar to a study from the UK highlighting the need for ongoing caution in this clinically vulnerable groups.[23] This result concerns altered immune function (immunosenescence), a well-established feature of physiological aging. The increased risk for males reflects increased exposure than in the female in the perspective of the Bangladeshi population.

The higher Odd's ratio was found in specific co-morbidities, especially CKD, DM, IHD, OAD,

and HTN which was quite similar to the study from the UK and China.[21,22,23] where they found kidney disease, heart, and respiratory disease associated with increased severity, hospitalization, increased risk of mechanical ventilation and mortality.[24]

A nationwide study from the UK found that among all other co-morbidities kidney disease showed a higher Odd's ratio which may reflect increased exposure (eg, when attending dialysis appointments) or impaired immunogenicity, and is supported by a study looking at humoral and B-cell responses in vaccinated, immunosuppressed kidney transplant recipients and patients having dialysis.[24]

This study had some limitations. Data were collected only from the patients visiting the hospital. So a nationwide community-based study will be more appropriate for this particular concern. This study could not compare the different groups of vaccines to see their efficacy. However, the concern of the severity of COVID-19 disease was found to be related to elderly people and co-morbidities, and particular strategies need to be taken to mitigate the problem through mass vaccination including booster dose, early referral, and prevention of exposure.

Conclusion

Vaccines against COVID-19 are showing a significant decrease in severe disease. However, vaccinated persons who are elderly and have underlying co-morbidity should receive intervention to control the chronic disease, prevent exposure, additional booster dose and effective pharmaceutical therapy to mitigate morbidity & mortality.

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