Severity of SARS-CoV-2 infection among vaccinated individuals: A hospital-based study

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(Index words: COVID-19, SARS-CoV-2, Sinopharm vaccine, Covishield vaccine, breakthrough infections, severe disease)

Abstract

Introduction: Post-vaccination infections impart the need for real-world data on protection conferred by the vaccines against SARS-CoV-2. We aimed to evaluate the severity of post-vaccination COVID-19 and the predictors of severe disease.

Methods: This cross-sectional study analysed data from 307 patients admitted to the University Hospital KDU with confirmed COVID-19 from March 1st to November 1st, 2021, after receiving at least a single dose of a vaccine against SARS-CoV-2. Vaccination status and the disease severity were classified using standard definitions. A binary logistic regression model was fitted to investigate severe/critical disease predictors.

Results: Of the surveyed patients, 122 (39.7%) were fully vaccinated, 127 (41.4%) were partially vaccinated and 58 (18.9%) had developed the disease within 14 days of the first vaccine dose. Most were Sinopharm vaccine recipients (52.4 %). Non- severe disease was observed among 249 (81.1%) patients and 47 (15.3%) had severe disease, while 11 (3.6%) needed ICU care (critical illness). Severe/critical disease was reported among 32 (25.2%) partially vaccinated and 13 (22.4%) patients who developed the disease within 14 days of the first vaccine dose. Of the patients deemed to have vaccine breakthrough infections (122 fully vaccinated patients), 13 (10.6%) suffered severe/critical disease. Patients with comorbidity experienced more severe/critical illness (adjusted odds ratio [AOR]: 3.684, P=0.003) than those without pre-existing medical conditions. Disease progression to severe or critical illness was significantly higher among Sinopharm recipients than Covishield recipients (AOR:2.064, P=0.048).

Conclusions: Comorbidity was the most important predictor of severe COVID-19 irrespective of the vaccination status. Observed higher incidence of severe disease among Sinopharm recipients warrants more extensive population studies.

Introduction

The world was brought to a standstill by the COVID-19 pandemic for nearly two years, infecting 591 million people across the world and causing 6.4 million deaths [1]. As the implemented, social and public health mitigation measures were unable to curtail the pandemic, several vaccines against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) were developed at an unprecedented speed. By January 2021, mass vaccination programmes were commenced in multiple countries, including Sri Lanka [2-4]. Vaccination against SARS-CoV-2 has undoubtedly been effective in mitigating the COVID-19 pandemic. Even a single standard dose of the vaccines had been shown to confer protection against the disease in randomised control trials [5].

Initially, post-vaccination breakthrough infections were rare, accounting for less than 1% of COVID-19 cases in high-income countries [6,7]. However, the continued high global incidence of vaccine breakthrough infections has become a public health concern over time [8,9]. In the real world, severe disease among vaccine recipients had been higher than the incidence reported in clinical trials [10]. Incomplete adherence to the vaccine schedules, challenges in maintaining the cold chain and diversity in immune response among populations may have influenced the vaccine efficacy across the globe. Moreover, insuffi-

cient protection by the vaccines has resulted due to immunity waning and the emergence of variants [11]. The relatively high rates of vaccine breakthrough infections have arisen the need for post-vaccination surveillance. Although there is a broader consensus that vaccines protect against severe disease, the evidence is limited on the incidence of severe COVID-19 following vaccination in Sri Lanka.

This study evaluated the severity of COVID-19 among patients immunised with at least a single dose of a vaccine against SARS-CoV-2, presented to a University Hospital in Sri Lanka.

Methods

Study design and setting

This record-based cross-sectional study focused on patients with post-vaccination COVID-19 admitted to the University Hospital KDU (UHKDU) Covid Unit between 1st March 2021 and 1st November 2021.

The mass vaccination programme against SARS-CoV-2 was commenced in Sri Lanka by the end of January 2021 prioritising the health and front-line workers. Covishield was the first vaccine licensed to use in the country. The second phase of vaccination was initiated in late February 2021, targeting people above 30 years in the Western Province. This was rolled back in March 2021, limiting the vaccination to people above 60 years all around the country. By April 2021, the vaccination of persons above 30 years was resumed and extended beyond the Western province. Sinopharm has been the most used vaccine in Sri Lanka since its approval for emergency use in March 2021. The use of Sputnik V, Moderna and Pfizer-BioNTech as the prime vaccine was limited to a small proportion of the population [12].

As the third wave of the COVID-19 pandemic unfolded in April 2021, only 4.2% of people had received at least a single dose of a vaccine and none were fully vaccinated in the country. The vaccine rollout accelerated with the third wave, and by the end of October 2021, more than two-thirds (69.6%) of the population were partially vaccinated, while 60.8% were fully vaccinated [13].

Participants

All patients who had received at least a single dose of a vaccine against SARS-CoV-2 admitted with a confirmed diagnosis of COVID-19 during the study period were eligible for inclusion. Pregnant females and children under 14 years were excluded. The diagnosis of COVID-19 was confirmed by real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) or rapid antigen test performed on a nasopharyngeal throat swab or nasal swab and the vaccination status was recorded as per their immunisation certificate. Patients were recruited consecutively without applying any random selection methods. The admission book maintained at the COVID Unit was used as the sampling frame.

During the study period, high-risk patients and patients with moderate to severe COVID-19 were recommended for hospital-based care, while asymptomatic and mildly symptomatic patients were managed in intermediate care centres [14]. As the UHKDU COVID Unit functioned in both these capacities, our study population represents the full spectrum of disease severity (Asymptomatic – severe/critical disease). The study population consisted of asymptomatic staff members who had become positive on post-exposure screening, symptomatic staff members with a confirmed diagnosis, patients admitted for other reasons (non-covid related diagnosis, surgery, chemotherapy, procedures or investigations) and became positive on routine screening, asymptomatic and mildly symptomatic patients who requested admission following confirmation of the diagnosis, high risk patients irrespective of disease severity on presentation, and patients with moderate to severe disease who visited the hospital for treatment.

Data collection

Data were collected retrospectively by a trained pre-intern medical officer using a structured data extraction form. Data extraction was done manually from medical records (daily clinical status reports, laboratory and radiological investigation reports) of all patients fulfilling the inclusion criteria. Data regarding basic demographics, the previous diagnosis of COVID-19, comorbidity, vaccination status, the clinical spectrum of the disease, respiratory support required, investigation results and the clinical outcome were collected and compiled in a computerised database.

Operational definitions

Per the WHO AFRO guidelines, the participants were deemed partially vaccinated and fully vaccinated 14 days after the first and second doses, respectively [15]. Infection among fully vaccinated individuals was considered a vaccine breakthrough infection [7]. The severity of infection among participants was categorised according to the NIH disease severity classification [16]. For the purpose of further analysis, the disease severity was categorised as a non-severe disease (asymptomatic, mild and moderate illness) and severe/critical disease (severe or critical illness).

Asymptomatic infection

Individuals who test positive for SARS-CoV-2 using a virologic test (i.e. a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms consistent with COVID-19.

Mild illness

Individuals who have any of the various signs and symptoms of COVID-19 (e.g. fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting,

diarrhoea, loss of taste and smell) but who do not have shortness of breath, dyspnoea, or abnormal chest imaging.

Moderate illness:

Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO$_2$) ≥94% on room air at sea level.

Severe illness:

Individuals who have SpO$_2$ <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO$_2$/FiO$_2$) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%.

Critical illness:

Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Statistical analysis

Data were analysed using Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics were executed for participant characteristics, vaccine status and disease severity. Categorical variables were presented as frequencies and percentages. The Shapiro-Wilk test was used to assess the distribution normality of data. Median and interquartile range were used to describe continuous data with a skewed distribution. Association between severe disease and vaccination status and patient characteristics were determined using the Chi-square test. Binary logistic regression analysis was conducted to calculate the odds ratio of severe disease according to age, gender, co-morbidities, vaccine type and vaccination status with a confidence level of 95% and a significance value of < 0.05.

Ethical considerations

Ethics clearance for this study was obtained from the Ethics Review Committee of the Faculty of Medicine, General Sir John Kotelawala Defence University, Sri Lanka (RP/2022/06).

Results

A total of 1609 patients were admitted to the UHKDU COVID Unit during the study period and 315 of them had received at least a single dose of a vaccine against SARS-CoV-2. Five patients were excluded due to incomplete data and three patients who received mRNA vaccines were not included in the study as their representation is negligible for analysis. The study included 307 patients with a median age of 50 years (IQR 31-64). The majority were males (53.1%), and pre-existing medical conditions were present in 54.1% of participants. Exposure to a suspected or confirmed COVID-19 patient was reported by 165 (53.7%)

participants. Considering the vaccination status, 122 (39.7%) were fully vaccinated, 127 (41.4%) were partially vaccinated, and 58 (18.9%) had developed the disease within 14 days of receiving a single dose of the vaccine. More than half of the participants (52.4%) were Sinopharm recipients and 47.6 % had received the Covishield vaccine (Table 1).

In the studied population, 249 (81.1%) suffered non-severe disease, where 59 (19.2%) were asymptomatic, 179 (58.3%) had mild disease and moderate disease was seen in 11 (3.6%). Forty-seven patients (15.3%) had severe disease requiring oxygen/ NIV support, while 11 (3.6%) patients with critical illness required ICU care. Severe or critical disease was reported among 13 (10.6%) fully vaccinated and 32 (25.2%) partially vaccinated patients (Table 2).

Vaccine breakthrough infections

Of the 122 patients deemed to have vaccine breakthrough infections (patients who developed the disease after being fully vaccinated) the median age was 41 years (IQR 29-58.5) and 53.3% were females. Nearly half (48.4%) of them had comorbidity. Twenty-eight (23.0%) were asymptomatic (admitted for a non-covid related diagnosis and PCR became positive on routine screening), 80 (65.6%) suffered mild disease, one (0.8%) had moderate disease and 12 (9.8%) developed severe illness. Only one patient (0.8%) suffered critical illness and died following admission to the ICU. Among those with severe or critical illness eight were Sinopharm recipients and five had received Covishield vaccine.

Predictors of severe disease

Severe/critical illness was more frequently observed among patients > 40 years (26.5%) compared to younger participants (5.4%). Similarly, patients with comorbidity had a higher incidence of severe/critical illness than their counterparts. Concerning the type of vaccine, severe/ critical disease was more prevalent among Sinopharm recipients (27.5%) than those who were vaccinated with Covishield (9.6%). Progression to severe or critical disease after hospitalization was less among fully vaccinated patients compared to those who had not completed the vaccination (10.6% vs. 24.7%).

Nonetheless, after adjusting for the confounding factors in the binary logistic regression analysis, comorbidity and vaccine type were the only statistically significant predictors of severe/ critical disease. Patients with pre-existing medical conditions had an adjusted odds ratio (AOR) to develop severe or critical illness of 3.68 times (CI: 1.549- 8.764) higher than the patients without comorbidity (P=0.003). In addition, the likelihood of developing the severe disease was higher among Sinopharm recipients compared to patients who were immunised with Covishield vaccine (AOR: 2.064, P=0.048) (Table 3).

Table 1. Demographic characteristics and vaccination status of the participants (n=307)

Variable	Within first 14 days of the first dose	Partially vaccinated	Fully vaccinated	Total
Age				
<40	20 (18.0%)	33 (29.7%)	58 (52.3%)	111
≥40	38 (19.4%)	94 (48.0%)	64(32.7%)	196
Gender				
Male	36 (22.1%)	70 (42.9%)	57 (35.0%)	163
Female	22 (15.3%)	57 (39.6%)	65 (45.1%)	144
Profession				
HCW	09 (12.7%)	22 (31.0%)	40 (56.3%)	71
Non-HCW	49 (20.8%)	105 (44.5%)	82 (34.7%)	236
Co-morbidities				
Yes	29 (17.5%)	78 (47.0%)	59 (35.5%)	166
No	29 (20.6%)	49 (34.8%)	63 (44.7%)	141
On immunosuppressants				
Yes	2 (28.6%)	1 (14.3%)	4 (57.1%)	7
No	56 (18.7%)	126 (42.0%)	118 (39.3%)	300
Exposure history				
Yes	32 (19.4%)	53 (32.1%)	80 (48.5%)	165
No	26 (18.3%)	74 (52.1%)	42 (29.6%)	142
Vaccine type				
Sinopharm	39 (24.2%)	76 (47.2%)	46 (28.6%)	161
Covishield	19 (13.0%)	51 (34.9%)	76 (52.1%)	146

Table 2. Clinical spectrum of the disease among participants stratified by vaccination status (n=307)

Vaccination status	Asymptomatic	Mild disease	Moderate disease	Severe disease	Critical disease
Within 14 days of first vaccine dose	6 (10.3%)	35 (60.3%)	4 (6.9%)	10 (17.2%)	3 (5.2%)
Partially vaccinated	25 (19.7%)	64 (50.4%)	6 (4.7%)	25 (19.7%)	7 (5.5%)
Fully vaccinated	28 (23.0%)	80 (65.6%)	1 (0.8%)	12 (9.8%)	1 (0.8%)

Table 3. Predictors of severe disease among study participants (n=307)

Variable	Non-severe disease	Severe/critical disease	P value	Binary logistic regression analysis AOR (95%CI)	P value
Age					
<40	105 (94.6%)	6 (5.4%)	**0.001***	Reference	
≥40	114 (73.5%)	52 (26.5%)		1.550 (0.52-4.58)	0.428
Gender					
Female	116 (73.5%)	28 (26.5%)	0.816	Reference	
Male	133 (81.6%)	30 (18.4%)		0.868 (0.46-1.62)	0.659
Co-morbidities					
No	132 (93.6%)	09 (6.4%)	**<0.001***	Reference	
Yes	117 (70.5%)	49 (29.5%)		3.684 (1.55-8.76)	**0.003**
Occupation					
HCW	69 (97.2%)	2 (2.8%)	**<0.001***	Reference	
Non-HCW	180 (76.3%)	56 (23.7%)		2.785 (0.56-13.94)	0.213
Vaccine type					
Covishield	132 (90.4%)	14 (9.6%)	**<0.001***	Reference	
Sinopharm	117 (72.7%)	44 (27.3%)		2.064 (1.00-4.24)	**0.048**
Vaccination status					
Within 14 days of first dose	45 (77.6%)	13 (22.4%)	**0.010***	Reference	0.817
Partially vaccinated	95 (74.8%)	32 (25.2%)		1.099 (0.49-2.44)	0.185
Fully vaccinated	109 (89.3%)	13 (10.7%)		0.53 (0.213-1.35)	

*Chi square test

Discussion

In this study, we describe the impact of vaccination on severity of COVID-19 among 307 patients admitted to a university hospital with confirmed SARS-CoV- 2 infection.

We observed that most patients admitted during the studied period were unvaccinated or had not completed the full vaccine course. The susceptibility to SARS-CoV-2 infection persists in the early post-vaccination period as the immunity takes time to develop. Hence, individuals within the first 14 days of receiving a single dose of vaccine are considered unvaccinated [15]. Many previous studies, including randomised controlled trials, had shown protection with one standard dose of

Covishield vaccine against SARS-CoV- 2 infections after 14-21 days of vaccination. The vaccine efficacy was further enhanced after 14 days of the second dose [5,17,18]. The data on the efficacy of a single dose of Sinopharm vaccine are sparse. However, the Sinopharm vaccine had shown 60.8% and 98.6% efficacy in reducing the risk of hospitalisation and mortality among recipients two weeks after the second dose [19].

Overall, the incidence of severe or critical illness was 18.9% in our study population. Occurrence of non-severe, severe or critical illness showed no significant difference between partially immunised patients (14 days after receiving the first dose) and patients who developed the disease within 14 days of receiving the first vaccine dose. Nearly

one-quarter (25.1%) of partially vaccinated patients developed severe/critical disease. A marked reduction in the incidence of severe/critical illness was observed among fully vaccinated patients compared to the participants who had not completed the vaccination (10.6% vs. 24.7%). Nonetheless, the vaccination status was not shown to be a significant predictor of the severe/critical disease on binary logistic regression analysis (P=0.185). The real-world data on vaccination status and protection against severe disease are incongruous. Some studies observed higher protection against severe disease with complete vaccination compared to partial vaccination among Covishield recipients [20-22]. However, a survey among Indian medical officers following Covishield vaccination revealed no significant difference in hospitalisation and the requirement for ventilatory support between fully and partially vaccinated individuals [23].

Compared to the lower incidence rate (10.6%) of severe/critical vaccine breakthrough infections observed in the present study, more than a quarter of fully vaccinated patients admitted to Yale New Haven Health System were severely or critically ill with COVID-19. Of note, the studied population was immunised with different types of vaccines (mRNA-1273, BNT162b2, Ad.26.COV2. S). In the same study occurrence of severe or critical COVID-19 illness had been higher in those who received the BNT162b2 vaccine than mRNA-1273 or Ad.26.COV2. S recipients [24]. The observed variations in the protection conferred by vaccines could be reflective of numerous factors, including the type of vaccine, differences in immunogenicity, waning of immunity and insufficient protection against variants.

The emergence of the delta variant posed a substantial challenge on protective efficacy of vaccines, triggering a new wave of pandemic in many countries [25]. In Sri Lanka, the alpha variant, which caused the second major outbreak of COVID-19 from April to June 2021, was replaced by the delta variant causing the largest SARS-CoV-2 outbreak in the country from July to October 2021 [26]. Although the information on strains is not available, this study represents both outbreaks. Of the identified variants of SARS-CoV-2, the delta variant was associated with more severe disease compared to other strains [27]. The reported protective efficacy of Covishield vaccine against the delta variant was substantially lower with a single dose, but the difference was modest following two doses as compared with the alpha variant. Noteworthy Covisheid vaccine had shown higher protection for severe illness than the moderate disease caused by the delta variant [28]. The effectiveness of Sinopharm vaccine on the delta variant is not well established yet. Hence, broader population studies are required to understand the extent and the time taken to confer protection by each vaccine.

We studied the predictors of severe/critical disease (Table 3). Corroborating the data from previous studies, comorbidity was the most important predictor of severe/critical disease in our study population [22, 23, 29-31]. Moreover, disease progression to severe or critical illness after hospital admission was significantly higher among Sinopharm recipients than patients immunised with the Covishield vaccine (P=0.048). This strengthens the previous study findings where the incidence of severe disease varied according to the vaccine type [26]. Although severe/critical illness was more frequent among older patients (age>40 years), age was not a statistically significant predictor of severe disease in the studied population. Previous studies reported contrasting findings where increasing age was associated with severe disease and high mortality irrespective of vaccination status [21, 22].

There are several limitations of this study, including the cross-sectional study design. Although we provide extensive documentation of the severity of COVID-19 among a vaccinated population, the study sample is relatively small and included only hospitalised patients with post-vaccination SARS- CoV- 2 infections. Thus, it may have resulted in an underestimation of protection conferred by the vaccines and limits the generalizability of the results. Ideally, a larger cohort of vaccinated individuals needs to be followed up to determine the incidence and severity of post-vaccination infections. Moreover, analysis of all possible risk factors for severe disease, including the impact of the different variants on disease severity, could not be undertaken. Despite these limitations, our study provides significant evidence on incidence and predictors of severe or critical illness among hospitalised patients with post-vaccination COVID-19.

Conclusions

The incidence of severe or critical illness was less among fully vaccinated patients than in those who had not completed the vaccination course. Irrespective of the vaccination status, comorbidity was associated with an increased risk of developing severe disease. Thus, people with comorbidity should practice preventive strategies, including wearing masks and physical distancing, despite being vaccinated. The observed higher number of severe/critical illness among Sinopharm recipients than those who received the Covishield vaccine imparts the need for broader population studies. The findings of this study could help inform future decisions on booster vaccination.

Declarations

Availability of data and material

Conflict of interests

Ethics approval and consent to participate

Funding

Author contributions

Conceptualization: DG

Design of research study: DG, NS, MPJ

Data acquisition: DG, MPJ, RR

Data analysis: DG, NS, RR

Interpretation of results: DG, NS

Writing the manuscript: DG, NS, RR, MPJ

All authors contributed and approved the final draft of the manuscript.

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