First-Generation SARS-CoV-2 Vaccines: A Comparative Analysis between Vaccinated and Unvaccinated Hospitalized Patients Infected with SARS-CoV-2

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ABSTRACT

Background

Severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) variants, which have emerged due to several mutations in spike protein, have a potential to escape immune protection provided by the first-generation vaccines, thereby resulting in breakthrough infections.

Objective

To identify the socio-demographic factors, clinical features, and outcomes in both vaccinated and unvaccinated hospitalized patients infected with SARS-CoV-2.

Method

Socio-demographic details, clinical features, and the outcomes among fully vaccinated (double for Covishield/AstraZeneca and BBIBP-CorV and single for Janssen), partially vaccinated, and unvaccinated hospitalized patients with coronavirus disease of 2019 (COVID-19) were collected and analyzed using SPSS version 17.

Result

Among the hospitalized COVID-19 patients (n=299), 175 (58.5%) patients received a single-dose, 82 (27.4%) double-dose, and 124 (41.5%) did not receive any dose of the COVID-19 vaccines. The risk of SARS-CoV-2 infection when compared between vaccinated and unvaccinated patients was found to be associated among professional degree holders (23.4% versus 9.7%) ($p<0.05$), professional workers (43.4% vs. 25.0%) ($p<0.05$), hospitalization to general ward (76.6% vs. 72.6%) ($p<0.05$), and presence of multiple symptoms (≥3) (86.8% vs. 75.0%) ($p>0.05$) and comorbidities (≥2) (15.5% vs. 13.7%) ($p>0.05$). Despite such approximate incidences, the risk of in-hospital mortality among the vaccinated patients was reduced (0.6% vs. 3.2%) ($p>0.05$), when compared to the unvaccinated patients. The risk of in-hospital mortality was associated with the older age and the presence of multiple comorbidities including bronchial asthma, diabetes, and hypertension.

Conclusion

Full or partial vaccination against the SARS-CoV-2 variants of concerns might be effective in preventing in-hospital mortality among COVID-19 patients.

KEY WORDS

COVID-19, Clinical features, SARS-CoV-2, Socio-demographic factors, Vaccine, Variants

INTRODUCTION

The presence of empirical therapies having mostly a supportive role resulted in the need and development of an effective vaccine that can generate enough immunity and protective efficacy. In addition protection against vaccine-resistant variants has now become the ultimate strategy to overcome the COVID-19 pandemic.[1] Based on the interim recommendations of the WHO Strategic Advisory Group of Experts on Immunization (SAGE), Ministry of Health and Population (MoHP), the Government of Nepal approved Covishield/AstraZeneca (Oxford/AstraZeneca) (Serum Institute of India), BBIBP-CorV (Vero cell) (Sinopharm), and Janssen (Johnson and Johnson) on January 15, 2021, February 17, 2021, and July 12, 2021, respectively for a mass vaccination campaign, from January 27, 2021.[2-6]

Over time, the SARS-CoV-2 genome has undergone numerous mutations, resulting in the emergence of variants of concern (VOC).[1] VOCs such as B.1.427 and B.1.429 with S gene mutations, B.1.351 and B.1.1.28 with RBD mutations, B.1.617.2 with E484Q and L452R mutations showed increased virus transmissibility, binding affinity of the virus to the ACE2 receptor as well as an increased risk of hospitalization.[1] These dominant mutations have reduced susceptibility to neutralizing antibodies generated by the first-generation SARS-CoV-2 vaccines as evidenced by several studies, mentioning a decline in effectiveness (89.3-21.9%) of the SARS-CoV-2 vaccine against the VOCs.[1,7-10]

Hence, for a better understanding on the significance of first-generation SARS-CoV-2 vaccines against COVID-19, a comprehensive analysis of the most prevalent comorbidities, clinical symptoms, and outcomes amongst vaccinated and unvaccinated COVID-19 patients has been provided.

METHODS

This qualitative cross-sectional study was conducted at COVID-dedicated Nepal Armed Police Force Hospital, Kathmandu, Nepal, between June 2021 to December 2021.

The sample size was calculated using the following formula.

$n= Z^2 \times p \times q / e^2$

$= (1.96)^2 \times 0.183 (1-0.183) / (0.05)^2$

$= 229.62$

Where,

n= required sample size

Z= 1.96 at 95% of Confidence Interval (CI)

p= prevalence taken as 18.3% as per the data from MoHP[11]

q= 1-p

e= margin of error, 5%

The calculated sample size was 229. Considering a 30% non – respondent rate among the participants, the sample size was calculated as 298. A total of 299 Nepalese patients with COVID-19 were included in the study.

The details include socio-economic and demographic identifiers (age, gender, occupation, academic qualification), pre-existing conditions, clinical signs and symptoms, prior exposure to the virus and hospitalization, SARS-CoV-2 vaccination status (date and location, administered dose, manufacturer, vaccine card information, post-effect after administrations) were collected from each of the SARS-CoV-2 infected patients. The individuals who had been administered two doses of Covishield or BBIBP-CorV or a single dose of Janssen were considered fully vaccinated. Similarly, the individuals who had been administered one dose of Covishield or BBIBP-CorV were considered partially vaccinated. Individuals who had not received any dose of Covishield, BBIBP-CorV, or Janssen were referred to as unvaccinated.

Pneumonia was diagnosed on clinical and radiological evaluation by the treating physician. The data and the nature of hospital admission (ward, high dependency unit, or intensive care unit), and clinical outcomes (discharge or death) were obtained and verified by the attending clinical staff.

The inclusion criteria for the study population were defined as (1) patients with confirmative reverse transcriptase-polymerase chain reaction (RT-PCR) result for SARS-CoV-2 infection (nasopharyngeal or oropharyngeal swab) and (2) patients willing to give informed consent. Exclusion criteria for patients were defined as (1) patients unwilling to give informed consent, (2) patients who had been administered vaccines other than Covishield, BBIBP-CorV, and Janssen, and (3) patients who failed to show the vaccination card as a reference of their vaccination status.

A survey was conducted by taking bedside interview of every admitted patient diagnosed with COVID-19, using a set of pre-tested semi-structured questionnaires. For patients who were unable to respond to the interview independently, information was obtained from responsible healthcare personnel in charge of the patient or the patients' relative/guardian.

Household transmission of SARS-CoV-2 infection referred to the cases where multiple individuals of the same or different families shared the same residence which included dining, working, and living space and/or traveled together. These individuals also seeked medical consultation anytime between 4 days before the onset of symptoms of the confirmed patients or 4 days before sampling of asymptomatic patients.[10]

Education status was characterized as per the modified Kuppuswamy's socioeconomic status scale.[12] Similarly, the classification of occupation were as per the Nepal Standard Classification of Occupation.[13]

Data were analyzed by using SPSS Statistical Software version 17. Descriptive statistics [median (interquartile range), number (n), and percentage (%)] were used to characterize the study variables. Binary logistic regression analysis was performed at a 95% confidence interval. A p-value of less than 0.05 was considered statistically significant.

The study was approved by the Institutional Review Committee (Reference number: 06/20/2021) of the Shi-Gan Health foundation, Shankha marg, Chakrapath, Kathmandu, Nepal. All data were anonymized when received from the patients. Written informed consent was obtained from the study participants.

RESULTS

Among a total of 299 patients diagnosed and admitted cases of COVID-19, 175 (58.5%) patients belonged to the vaccinated group and 124 (41.5%) to the unvaccinated group. The median (Q1-Q3) ages of the vaccinated and unvaccinated patients were 43 (31-58) years and 37 (24.3-55) years, respectively. There were 183 male patients [vaccinated: 105 (60.0%); unvaccinated: 78 (62.9%)] (p=0.612). University graduates [n=76, 25.4%; vaccinated: 45 (25.7%); unvaccinated: 31 (25.0%)] (p=0.539) predominated the study group. There were 107 [vaccinated: 76 (43.4%); unvaccinated: 31 (25.0%)] (p=0.006) professional workers (Table 1).

Among the total COVID-19 cases, there were 22 [vaccinated: 16 (9.1%); unvaccinated: 6 (4.8%)] (p=0.505) cases of household transmission. Most of the patients were admitted to general ward [n=224, 74.9%; vaccinated: 134 (76.6%); unvaccinated: 90 (72.6%)] (p=0.003), followed by intensive care unit [n=37, 12.4%; vaccinated: 21(12.0%); unvaccinated: 16 (12.9%)] (p=0.725) of the hospital. Among the total infected patients, 5 [vaccinated: 1 (0.6%); unvaccinated: 4 (3.2%)] (p=0.226) patients were deceased (Table 2).

Out of 299 patients enrolled in the study, 294 patients (98.3%) were symptomatic and 5 patients (1.7%) were asymptomatic. Most of the symptomatic COVID-19 patients showed presence of multiple symptoms (≥3) [n=245, 81.9%; vaccinated: 152 (86.8%); unvaccinated: 93 (75.0%)] (p=0.926). Among the total patients, fever was the most common symptom [n=237, 79.3%; vaccinated: 131 (74.9%); unvaccinated: 106 (85.5%)] (p=0.518), followed by dry cough [n=183, 61.2%; vaccinated: 108 (61.7%); unvaccinated: 75 (60.5%)] (p=0.608), myalgia [n=157, 52.5%; vaccinated: 97 (55.4%); unvaccinated: 60 (48.4%)] (p=0.258), anosmia [n=140, 46.8%; vaccinated: 84 (48.0%); unvaccinated: 56 (45.2%)] (p=0.323), ageusia [n=135, 45.2%; vaccinated: 88 (47.4%); unvaccinated: 52 (41.9%)] (p=0.272), dyspnea [n=126, 42.1%; vaccinated: 80 (45.7%); unvaccinated: 46 (37.1%)] (p=0.211), pharyngitis [n=99, 33.1%; vaccinated: 65 (37.1%); unvaccinated: 34 (27.4%)]

Table 1. Socio-demographic factors of patients

Demographics	Total patients (n=299)	Vaccinated (n=175)		Unvaccinated (n=124)		p-value
		n	%	n	%	
	Median age (IQR) (years)	43 (31-58)		37 (24.3-55)		
Age	≤ 15: Children (n=8)	-	-	8	6.5	0.999
	16-59: Adult (n=228)	134	76.6	94	75.8	0.999
	≥ 60: Elderly (n=63)	41	23.4	22	17.7	0.999
Gender	Male (n=183)	105	60.0	78	62.9	0.612
	Female (n=116)	70	40.0	46	37.1	0.027
Academics	University graduate (n=76)	45	25.7	31	25.0	0.539
	High school (n=70)	40	22.9	30	24.2	0.686
	Middle school (n=25)	11	6.3	14	11.3	0.498
	Primary school (n=41)	20	11.4	21	16.9	0.720
	Professional degree (n=53)	41	23.4	12	9.7	0.019
	Illiterate (n=34)	18	10.3	16	12.9	0.732
Occupation	Agricultural workers (n=23)	16	9.1	7	5.7	0.133
	Armed forces (n=28)	9	5.1	19	15.3	0.067
	Government officials (n=11)	9	5.1	2	1.6	0.078
	Professionals (n=107)	76	43.4	31	25.0	0.006
	Student (n=21)	11	6.3	10	8.1	0.977
	Unemployed (n=98)	51	29.1	47	37.9	0.686
	Others* (n=11)	3	1.7	8	6.4	0.133

*Laborers (n=6), technicians/associate professionals (n=4) and foreign return (n=1).

Table 2. Outcomes upon hospitalization of COVID-19 patients

Parameters	Total patients (n=299)	Vaccinated (n=175)		Unvaccinated (n=124)		p-value
		n	%	n	%	
Household Transmission	Yes (n=22)	16	9.1	6	4.8	0.505
	No (n=277)	159	90.9	118	95.2	0.742
Hospitalized Ward	General ward (n=224)	134	76.6	90	72.6	0.003
	High dependency unit (n=38)	20	11.4	18	14.5	0.406
	Intensive care unit (n=37)	21	12.0	16	12.9	0.725
Mortality	Yes (n=5)	1	0.6	4	3.2	0.226
	No (n=294)	174	99.4	120	96.8	0.226

Table 3. Distribution of symptoms among patients with COVID-19

Clinical Characteristics		Total patients (n=299)	Vaccinated (n=175)		Unvaccinated (n=124)		p-value
			n	%	n	%	
Patients	with asymptomatic condition (n=5)	3	1.7	2	1.62	0.657	
	with 1 symptom (n=13)	5	2.9	8	6.45	0.416	
	with 2 symptoms (n=36)	15	8.6	21	16.93	0.446	
	with ≥ 3 symptoms (n=245)	152	86.8	93	75.0	0.926	
Symptoms	Ageusia (n=135)	83	47.4	52	41.9	0.272	
	Anosmia (n=140)	84	48.0	56	45.2	0.323	
	Arthralgia (n=62)	41	23.4	21	16.9	0.169	
	Asthenia (n=20)	11	6.3	9	7.3	0.626	
	Chest Pain (n=14)	9	5.1	5	4.0	0.343	
	Diarrhea (n=17)	12	6.9	5	4.0	0.174	
	Dry Cough (n=183)	108	61.7	75	60.5	0.608	
	Dyspnea (n=126)	80	45.7	46	37.1	0.211	
	Fever (n=237)	131	74.9	106	85.5	0.518	
	Headache (n=74)	45	25.7	29	23.4	0.315	
	Myalgia (n=157)	97	55.4	60	48.4	0.258	
	Nausea (n=12)	9	5.1	3	2.4	0.144	
	Pharyngitis (n=99)	65	37.1	34	27.4	0.162	
	Rhinorrhea (n=21)	14	8.0	7	5.6	0.234	
	Sweating (n=8)	3	1.7	5	4.0	0.673	
	Vomiting (n=18)	9	5.1	9	7.3	0.849	
	Others* (n=18)	7	4.0	8	6.5	0.796	

*Retroorbital pain (n=4), anorexia (n=3), gastritis (n=2), haemoptysis (n=2), tonsillitis (n=2), and vertigo (n=2)

(p=0.162), headache [n=74, 24.7%; vaccinated: 45 (25.7%); unvaccinated: 29 (23.4%)] (p=0.315), and arthralgia [n=62, 20.7%; vaccinated: 41 (23.4%); unvaccinated: 21 (16.9%)] (p=0.169). Symptoms such as, rhinorrhea (n=21, 7.0%), asthenia (n=20, 6.7%), vomiting (n=18, 6.0%), diarrhea (n=17, 5.7%), chest pain (n=14, 4.7%), and nausea (n=12, 4.0%) were present in fewer number of patients (Table 3).

Among the total patients, 122 (40.8%) patients had comorbidities, of whom 44 (14.7%) (p=0.433) had ≥2 comorbidities. Hypertension [n=64, 21.4%; vaccinated: 45 (25.7%); unvaccinated: 19 (15.3%)] (p=0.548) was the most common comorbidity followed by diabetes [n=36, 12.0%; vaccinated: 25 (14.3%); unvaccinated: 11 (8.9%)] (p=0.623),

Table 4. Distribution of comorbidities among patients with COVID-19

Clinical Characteristics		Total patients (n=299)	Vaccinated (n=175)		Unvaccinated (n=124)		p-value
			n	%	n	%	
Patients	without comorbidities (n=177)	97	55.4	80	64.5	0.202	
	with 1 comorbidity (n=78)	51	29.1	27	21.8	0.116	
	≥ 2 comorbidities (n=44)	27	15.5	17	13.7	0.433	
Comorbidities	Benign prostatic hyperplasia (n=3)	3	1.7	-	-	0.999	
	Valvular heart disease (n=3)	2	1.1	1	1.8	0.891	
	Coronary heart disease (n=7)	4	2.28	3	2.4	0.809	
	Bronchial asthma (n=16)	6	3.4	10	8.1	0.162	
	Hypertension (n=64)	45	25.7	19	15.3	0.548	
	Hyperthyroidism (n=14)	8	4.6	6	4.8	0.765	
	Hypercholesterolemia (n=5)	3	1.7	2	1.6	0.920	
	Diabetes (n=36)	25	14.3	11	8.9	0.623	
	Osteoarthritis (n=10)	4	2.3	6	4.8	0.268	
	Neurological disorders (n=3)	2	1.2	1	1.8	0.891	
	Others* (n=16)	10	5.7	6	4.8	0.323	
Clinical diagnosis of pneumonia	Yes (n=14)	11	6.3	3	2.4	0.133	
	No (n=285)	164	93.7	121	97.6	0.011	

*Gastric ulcer (n=2), hemorrhoid (n=2), hypercreatinemia (n=2), gout (n=2), cholelithiasis (n=2), myocardial infarction (n=2), hypothyroidism (n=1), prostate cancer (n=1), endometrial cancer (n=1), and chronic obstructive pulmonary disease (n=1).

and bronchial asthma [n=16, 5.4%; vaccinated: 6 (3.4%); unvaccinated: 10 (8.1%)] (p=0.162). Comorbidities such as, hyperthyroidism (n=14, 4.7%), osteoarthritis (n=10, 3.3%), and coronary heart disease (n=7, 2.3%) were infrequent (Table 4). Additionally, there were, 14 [vaccinated: n=11 (6.3%); unvaccinated: 3 (2.4%)] (p=0.133) patients, who were clinically diagnosed with pneumonia (Table 4).

Prior SARS-CoV-2 infection

Among the total patients, 22 patients [vaccinated: 17 (9.7%); unvaccinated: 5 (4.0%)] (p=0.072) had prior SARS-CoV-2 infection (Table 5).

Perception concerning the necessity of the vaccine

Concerning the urgency of vaccines, 281 [vaccinated: 170 (97.2%); unvaccinated: 111 (89.5%)] (p=0.024) patients realized the necessity of vaccines as urgent for the mitigation of SARS-CoV-2 infections (Table 5).

Table 5. Vaccine details of study participants

Parameters	Total subjects (n=299)	Vaccinated (n=175)		Unvaccinated (n=124)		p-value
		n	%	n	%	
Prior SARS-CoV-2 infection	Yes (n=22)	17	9.7	5	4.0	0.072
	No (n=277)	158	90.3	119	96.0	0.072
Perception concerning the necessity of vaccine	Yes (n=281)	170	97.2	111	89.5	0.024
	No (n=12)	3	1.7	9	7.3	0.711
	Unsure (n=6)	2	1.1	4	3.2	0.099

Vaccine types and side effects

Among the vaccinated patients (n=175), 50 (28.6%) patients were recipients of the first dose of Covishield, and 118 (67.4%) patients were recipients of the first dose of BBIBP-CorV. Out of 175 patients recipient of the first dose, 34 (19.4%) patients administered the second dose of Covishield, and 48 (27.4%) patients administered the second dose of BBIBP-CorV. A single dose (complete dose, as instructed by the manufacturer) of Janssen was administered to 7 (4.0%) patients only (Table 6).

The most common side effects observed in vaccinated patients after the administration of first dose was myalgia (n=27, 15.4%), followed by fever (n=26, 14.9%), nausea (n=15, 8.6%), and headache (n=11, 6.3%). Similarly, fever (n=9, 11.0%) was the most common side effect observed in patients after the administration of the second dose of the vaccine, which was followed by myalgia (n=6, 7.3%) (Table 6).

Table 6. Vaccines and their associated side effects in study participants

Variables	Vaccinated (n=175)	First dose only (n=175)		Both doses (n=82)	
		n	%	n	%
Vaccine type	Covishield (n=50)	50	28.6	34	19.4
	BBIBP-CorV (n=118)	118	67.4	48	27.4
	Janseen (n=7)	7	4.0	NA	NA
Side effects	Allergy at the site of injection (n=5)	5	2.9	-	-
	Diarrhea (n=3)	2	1.1	1	1.2
	Fever (n=35)	26	14.9	9	11.0
	Headache (n=13)	11	6.3	2	2.4
	Myalgia (n=33)	27	15.4	6	7.3
	Nausea (n=17)	15	8.6	2	2.4
	Pain at the site of injection (n=34)	30	17.1	4	4.9
	Others* (n=5)	4	2.3	1	1.2

*Abdominal pain (n=1), chills (n=1), stomach ache (n=1), vertigo (n=1), and swollen face (n=1).

Deceased vaccinated and unvaccinated patients

The vaccinated yet deceased COVID-19 patient had higher age (84 years) and possessed multiple comorbidities including bronchial asthma, diabetes, and hypertension. On the other hand, unvaccinated yet deceased COVID-19 patients were of lower median age (64.5 years) and were without (1 patient) or mostly possessed single comorbidity (Table 7).

Table 7. Comparison of deceased vaccinated and unvaccinated patients

Parameters		Deceased	
		Vaccinated (n=1)	Unvaccinated (n=4)
		n	n
Age (years)	Median	84	64.5 (46.8-72.5)
Gender	Male	-	3
	Female	1	1
Comorbidities	None	-	1
	Bronhial Asthma	1	1
	Diabetes	1	2
	Hypertension	1	2
Symptoms	Fever	1	3
	Cough	1	3
	Myalgia	1	4
	Arthralgia	1	1
	Anorexia	1	-
	Ageusia	-	2
	Anosmia	-	2
	Dyspnea	-	1
	Headache	-	1
Pneumonia	Yes	1	1
Vaccine	BBIBP-CorV	Double dose	-

DISCUSSION

An unprecedented surge in SARS-CoV-2 infections, driven by the newly emerged variants (alpha, kappa, and delta), was reported from Nepal recently (from May 2021 to July 2021).[14] An ever-growing number of studies concerning outcomes, efficacy, socio-economic parameters associated with vaccination in light of newly emerged SARS-CoV-2 variants have been performed in different parts of the world. However, a similar analysis concerning the significance of vaccines from low- and middle-income countries, including Nepal is severely lacking. To address this paucity, we conducted a cross-sectional study involving 299 patients to overview comorbidities, clinical signs and symptoms, and outcomes in COVID-19 patients, who were inoculated with different dose/s of SARS-CoV-2 vaccines.

This study showed that elevated risk of hospital admission in COVID-19 patients was independently associated

with adults (76.3%) and elderly (21.1%); male sex (61.2); professional degree holders (17.7%); professional workers (35.8%); hospitalization in a general ward (74.9%); multiple (≥3) symptoms at presentation (81.9%), including fever (79.3%), dry cough (61.2%), myalgia (52.5%), anosmia (46.8%), and dyspnea (42.1%) as chief clinical complaints; preexisting health conditions, including the history of hypertension (21.4%), diabetes (12.0%), and bronchial asthma (5.4%); and diagnosis of COVID-associated pneumonia (4.7%). The predisposition of the elderly to the SARS-CoV-2 infection has been previously noted in many studies and could be because of the declined immune function (e.g., T-cell and B-cell function) and an increase in type 2 cytokines production, which causes a deficiency in the ability to control viral replication and prolongs proinflammatory responses potentially leading to poor outcomes.[15] The increased disproportionate burden of SARS-CoV-2 infection for men in this study was also widely reported showing the increased vulnerability of males to COVID-19. This might have been attributed to the differences in the immune system, genetic polymorphism, lifestyle factors including smoking, and pre-existing comorbidities.[15] The observed signs and symptoms from this study were comparable to the findings of systematic review and meta-analysis which showed fever (88.7%), cough (57.6%), and dyspnea (45.6%) as the most prevalent symptoms in the COVID-19 patients.[16] Our findings of the underlying diseases associated with the COVID-19 patients are also in consensus with the same study which showed a correlation ship between cardiovascular diseases and diabetic mellitus with an increased incidence of SARS-CoV-2 infection.[16] In agreement with our findings, several other studies have revealed that COVID-19 patients are of moderate or severe disease.[17,18]

A total of 98.3% of the hospital admitted patients included in this study were symptomatic. Nearly three-fifths of patients (58.5%) had taken the vaccine. The vaccinated individuals who needed hospitalization due to infection with SARS-CoV-2 had an increased number of symptoms (≥3) (vaccinated: 86.8% vs. unvaccinated: 75.0%) (p>0.05) and comorbidities (≥2) (vaccinated: 15.5% vs. unvaccinated: 13.7%) (p>0.05) and were diagnosed with pneumonia (vaccinated: 6.3% vs. unvaccinated: 2.4%) (p>0.05). However, the Center for Disease Control and Prevention (CDC) has reported that the risk of infection, upon administration of the second dose of Pfizer-BioNTech and Moderna mRNA vaccines, was reduced by 90% at or after 2 weeks, and concluded that the vaccines were effective in preventing SARS-CoV-2 infections.[19] While our study showed a likelihood of vaccinated yet infected hospitalized patients to present with disease complications, our study is neither a survey nor an indicator of the population in general. A survey of a larger cohort from the general population would be needed to evaluate vaccine efficacy and any mitigation of symptoms or lack thereof. Instead, our findings showed that anyone who is still vulnerable to infection despite vaccination has a higher likelihood of developing complications. Hence, breakthrough infections are not to be taken lightly and such patients should be monitored from the early onset of the disease.

The observed clinical features of the disease were comparable between the vaccinated and the unvaccinated COVID-19 patients. This study showed substantial differences in presentation of fever (74.9% vs. 85.5%) (p>0.05), dry cough (61.7% vs. 60.5%) (p>0.05), myalgia (55.4% vs. 48.4%) (p>0.05), dyspnea (45.7% vs. 37.1%) (p>0.05), and anosmia (48.0% vs. 45.2%) (p>0.05) among vaccinated and unvaccinated patients, which was comparable to the findings of Rodriguez-Morales et al. (fever: 92.8% vs. 43.9%; cough: 63.4% vs. 22%, respectively).[20] The incidence of symptomatic infections in patients, who had been administered full dose (96.3%, 79/82) was lowered as compared to the single-dose vaccinated patients (100%, 175/175). Our findings were in line with the report reported by Surendra et al. which showed a lower incidence of symptomatic infections (double dosed patients: 12.0% vs. 14.2%; single dosed patients: 12.3% vs. 13.9%) and disease severity (double dosed patients: 1.2% vs. 3.4%; single dosed patients: 2.0% vs. 3.3%) as compared to the unvaccinated cohort.[21] Newly emerged SARS-CoV-2 strains such as P.1, B.1.351, B.1.1.7, and B.1.617 have undergone numerous mutations in the spike protein that are known to reduce the effectiveness of currently available first-generation vaccines.[22] Moreover, some of the patients from this study were infected within 10-14 days of administration of a vaccine, well before vaccines were effective, rendering such patients similar to the unvaccinated cohort. Such immediate viral infection could have restrained the production of antibodies against SARS-CoV-2 and hence, the vaccine could not have been effective in reducing disease manifestations.[23]

The higher incidence of in-hospital mortality in unvaccinated patients (n=4, 3.2%) (p>0.05) as compared to the vaccinated patients (n=1, 0.6%) was a significant finding of this study. The patient who was previously vaccinated yet succumbed to SARS-CoV-2 infection was found to be more likely to be associated with multiple complications, such as higher age (84 years) and with the presence of more than three comorbidities as compared to the unvaccinated patients, who were of lower median age (64.5 years) and had none or single comorbidity (Table 7). Although the mortality numbers are small, our observations indicate that the vaccines provide protection against deaths from the SARS-CoV-2 infection, and hence, the current vaccination must be continued further to prevent the COVID-associated in-hospital mortality.[22]

This study suffers from several limitations. Firstly, this study was conducted in only one tertiary care hospital in Nepal; thus, the finding may not be generalizable to a worldwide context. Secondly, the analyses were performed on a limited number of hospitalized patients, and the findings

may underestimate the actual incidence of disease, as many patients were under home isolation.

CONCLUSION

Patients with COVID-19 showed the presence of multiple symptoms (≥3) including, fever, dry cough, and anosmia and multiple comorbidities (≥2) including, hypertension and diabetes. Such clinical manifestations were ironically frequently observed for vaccinated COVID-19 patients rather than unvaccinated patients. However, the risks of in-hospital mortality due to COVID-19 in SARS-CoV-2 infected patients were more than three times higher for the unvaccinated patients as compared to the vaccinated patients. Hence, this study concludes that first-generation SARS-CoV-2 vaccines are effective in preventing in-hospital mortality among COVID-19 patients unless the patient is middle-old and possesses multiple comorbidities. Therefore, the current vaccination must proceed, in combination with non-pharmaceutical interventions to control the pandemic.

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