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Post-vaccination Severity and Outcome of COVID-19

Nimra Kanwal[a], Nauman Ismat Butt[b*], Samrina Sadaf[c*], Syed Asif Hussain[d], Anum Rasheed[e], Sadia Babu[f]

[a]*Medical Specialist, Department of Medicine, Agha Khan Medical Services Gilgit.*
[b]*Assistant Professor, Department of Medicine & Allied, Azra Naheed Medical College, Lahore.*
[c]*Consultant Pulmonologist, COVID ICU, Aga Khan Medical Centre Gilgit.*
[d]*Medical Officer, Department of Medicine, Aga Khan Medical Center Gilgit.*
[e]*Senior Registrar, Department of Medicine, POF Hospital, Wah Cantt.*
[f]*Senior Registrar, POF Hospital, Wah Medical College Wah Cantt.*
Correspondence:*nauman_ib@yahoo.com

ABSTRACT

BACKGROUND & OBJECTIVE: COVID-19 infection can occur even after vaccination but vaccination aids to reduce risk of severe COVID-19, hospitalization and mortality. Objective of present study was to determine severity and outcome of COVID-19 infection developed post-vaccination.

METHODOLOGY: This observational cross-sectional study was conducted at Agha Khan Medical Center Gilgit Pakistan from July 2021 to July 2022. COVID-19 infection was diagnosed by a positive COVID-19 PCR. After taking informed consent, 80 fully vaccinated patients of new onset COVID-19 aged 20-100 years of both genders were enrolled. Demographic information was noted and severity of COVID-19 infection assessed. All patients were followed up to 4 weeks of symptom onset, recovery or death whichever occurred earlier.

RESULTS: Mean age was 49.5±19.5 years with 47 (58.7%) males. Seven (8.8%) patients were smokers, 14(17.5%) hypertensive, 07(8.8%) diabetic, 05(6.3%) had ischemic heart disease and 04(5.0%) had asthma. Forty-eight (60.0%) patients had received Sinopharm vaccine, 21 (26.3%) Sinovac, 08 (10.0%) Cansino, 02(2.5%) Astrazeneca and 01 (1.3%) Moderna. Fifty-six (70.0%) had mild COVID-19 disease, 07 (8.8%) had moderate disease, 10(12.5%) had severe disease while 07(8.8%) had critical disease. Twenty-four (30.0%) patients were admitted with mean hospital stay 4.7±7.4 days. Sadly, 08(10.0%) patients passed away. Disease severity showed significant association with age p-value=0.014 and co-morbid conditions with p-value=0.013.

CONCLUSION: Post-vaccination COVID-19 illness was mild in more than two-thirds patients. Male sex, advanced age and presence of co-morbid diseases were associated with severe disease and mortality.

KEYWORDS: COVID-19, Vaccination, Disease Severity, Mortality.

INTRODUCTION

COVID-19 emerged as a potentially life-threatening, serious respiratory infection from Wuhan city of China in December 2019 and spread through aerosol transmission to become a global pandemic [1,2]. The first case of COVID-19 was diagnosed in Pakistan in February 2020 and has caused significant morbidity and mortality since then [3]. Clinical manifestations of COVID-19 vary from asymptomatic and mild illness to critical life-threatening illness. The most commonly reported symptoms of COVID-19 are fever, cough and dyspnea [4]. Patients who develop cytokine storm have severe disease and their condition can deteriorate rapidly thereby requiring assisted ventilation [5]. Increase in morbidity and mortality due to COVID-19 heralded the development of vaccines worldwide which help to reduce not only the risk of transmission but also the severity of illness and death. Various vaccinations approved throughout the world include Pfizer, AstraZeneca, Moderna, Sputnik, Cansino, Sinovac and Sinophram [6,7]. The first vaccination approved for use in Pakistan was the Chinese Sinophram followed by other vaccines later on [8].

It has been observed that COVID-19 infections can still occur even after adequate vaccination [9]. However, there is abundant evidence which highlights that vaccination leads to reduction in risk of severe COVID-19 disease, reduced hospitalization and decrease in mortality [10,11,12]. Antonelli et al. reported that compared to unvaccinated patients, vaccinated patients had a lower risk of symptoms after 28 days [13]. The mechanism by which COVID-19 vaccinations affect the sequelae of COVID-19 infection is still not completely understood. It is still unknown whether vaccinated patients have similar risk as compared to unvaccinated patients of developing COVID-19 complications such as stroke, thromboembolism and neuro-psychiatric complications. Furthermore, studies regarding differences in response to various COVID-19 vaccinations and ethnic variations are still scarce. The present study aimed to record the severity and outcome in vaccinated people who develop COVID-19 disease along with other measures such as duration of hospital stay, oxygen requirement and mortality.

METHODOLOGY

The present observational cross-sectional study was conducted to find out severity and outcome of COVID-19 infection developed post-vaccination at Agha Khan Medical Center Gilgit Pakistan from July 2021 to July 2022. COVID-19 infection was diagnosed as having a positive COVID-19 PCR and its severity was graded as shown in Table-I. Patients with respiratory infections due to other causes such as bacterial pneumonia, tuberculosis, interstitial lung fibrosis and bronchiectasis as assessed by detailed history and examination were excluded from the study. After taking approval from Institutional Review Board (IRB Number AKMCG/2022/1002) and obtaining written informed consent, all patients of new onset COVID-19 disease who had completed their COVID-19 vaccination, aged 20-100 years of both genders were included in the study using non-probability consecutive sampling technique.

Demographic information including age, gender, co-morbid diseases, addiction history, type of vaccination and duration since vaccination were noted. Severity of COVID-19 infection was assessed according to Table-I. Usual treatment as per hospital protocol was prescribed to all patients depending on disease severity. All patients were followed up to 4 weeks of symptom onset, recovery or death whichever occurred earlier. Data was entered and analyzed by SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables. Frequency and percentage were calculated for qualitative variables. Data was stratified to address confounders and effect modifiers by using Chi-square test and fisher's exact test with p-value<0.05 as significant.

RESULTS

Out of the 80 patients enrolled in our study, 47(58.7%) were male and 33 (41.3%) were female. Mean age of the patients was 49.5±19.5 years. 35(43.7%) patients were aged 40 or less while 45(56.3%) were older than 40 years of age. Out of the 80 patients, 07 (8.8%) patients were smokers, 03 (3.8%) reported naswar addiction while 01(1.3%) patient was alcoholic. Out of the 80 patients, 14(17.5%) patients had hypertension, 07(8.8%) patients had diabetes mellitus, 05 (6.3%) patients had ischemic heart disease, 04(5.0%) had asthma and 01(1.3%) had thalassemia while 49 (61.3%) patients had no co-morbid diseases. 58(72.5%) patients developed infection more than 4 weeks after completion of vaccination, 12 (15.0%) patients developed infection 2-4 weeks after completion of vaccination while 10(12.5%) patients developed infection within 2 weeks of vaccination completion. According to the vaccination type, 48(60.0%) patients had been vaccinated with Sinopharm, 21(26.3%) patients received Sinovac, 08 (10.0%) Cansino, 02(2.5%) Astrazeneca and 01 (1.3%) Moderna.

In our study, 56 (70.0%) had mild COVID-19 disease, 07 (8.8%) had moderate disease, 10 (12.5%) had severe disease while 07 (8.8%) had critical disease as shown in Table-II. 56(70.0%) patients did not require hospital admission. Fifty (62.5%) patients received outpatient care only while 06(7.5%) patients consulted through tele-consult online mediums as shown in Table-III. Twenty-Four (30.0%) patients were admitted to the hospital and mean hospital stay duration was 4.7±7.4 days. Sixteen (20.0%) patients required admission to the ICU while 08 (10.0%) patients were managed in COVID-19 isolation ward as shown in Table-III. Oxygen was given through nasal prongs in 18 (22.5%) patients while 07 (8.8%) patients required non-invasive ventilation (BIPAP/CPAP). Sadly, 08(10.0%) patients passed away.

Stratification of data with regards to COVID-19 disease severity (mild/moderate disease and severe/critical disease) revealed a significant association with age (p-value=0.014) and having co-morbid conditions (p-value 0.013) whereas there was no association of disease severity with sex (p-value=0.264), duration after completion of vaccination (p-value=0.417) and type of vaccination (0.220) as shown in Table-IV. Stratification of data with regards to Mortality revealed a significant association with sex (p-value=0.018) and having co-morbid conditions (p-value 0.049) whereas there was no association of disease severity with age

Table-I: Classification of Severity of COVID-19 Infection.

Severity of COVID-19	Clinical Features
Mild	Clinical features (fever, cough, sore throat, headache, body aches, loss of taste smell) with normal chest radiography and normal oxygen saturations
Moderate	Clinical features with <50% lung infiltrates on radiography and oxygen saturations >94% on room air
Severe	Clinical features with oxygen saturations <94% on room air, respiratory rate >30 breaths per minute or >50% lung infiltrates on radiography
Critical	Features of respiratory failure, hemodynamically unstable, septic shock or multi-organ failure

(p-value=0.073), duration after completion of vaccination (p-value=1.00) and type of vaccination (0.707) as shown in Table-V.

Table-II: Severity of COVID-19 (n=80).

Severity of COVID-19	n(%)
Mild	56 (70.0)
Moderate	07 (8.8)
Severe	10 (12.5)
Critical	07 (8.8)

Table-III: Doctor Consultation and Hospital Admission (n=80).

Doctor Consultation and Hospital Admission	n(%)
Outpatient Department	50 (62.5)
Online Tele-consult	06 (7.5)
Isolation Ward	08 (10.0)
COVID ICU	16 (20.0)

Table-IV: Stratification of data with regards to COVID-19 disease severity.

Clinical Parameters		COVID-19 disease severity		p-value
		Mild to moderate n(%)	Severe to critical n(%)	
Age	<40 years	32 (91.4)	03 (8.6)	0.014
	>40 years	31 (68.9)	14 (31.1)	
Sex	Male	35 (74.5)	12 (25.5)	0.264
	Female	28 (84.8)	05 (15.2)	
Co-morbid diseases	Present	20 (64.5)	11 (35.5)	0.013
	Absent	43 (87.8)	06 (12.2)	
Type of Vaccination	Sinopharm	40 (83.3)	08 (16.7)	0.220
	Other Vaccinations	23 (71.9)	09 (28.1)	
Duration After Completion of Vaccination	<4 weeks	16 (72.7)	06 (27.3)	0.417
	>4 weeks	47 (81.0)	11 (19.0)	

Table-V: Stratification of data with regards to Mortality.

Clinical Parameters		COVID-19 disease severity		p-value
		Present	Absent	
Age	<40 years	01 (2.9%)	34 (97.1%)	0.073
	>40 years	07 (15.6%)	38 (84.4%)	
Sex	Male	08 (17.0%)	39 (83.0%)	0.018
	Female	00 (0.0%)	33 (100.0%)	
Co-morbid diseases	Present	06 (19.4%)	25 (80.6%)	0.049
	Absent	02 (4.1%)	47 (95.9%)	
Type of Vaccination	Sinopharm	04 (8.3%)	44 (91.7%)	0.707
	Other Vaccinations	04 (12.5%)	28 (87.5%)	
Duration After Completion of Vaccination	<4 weeks	02 (9.1%)	20 (90.9%)	1.000
	>4 weeks	06 (10.3%)	52 (89.7%)	

*p≤0.05 is significant

DISCUSSION

The aims of successful vaccination are to stop or decrease the transmission of an infection and reduce risk of severe illness [14]. Despite vaccinations against COVID-19, the illness can still occur but there is often a decrease in disease severity and mortality risk [15]. Lopez-Bernal et al. demonstrated a significant lowering in symptomatic COVID-19 infection in older adults with a marked reduction in risk of severe disease [16]. Taquet et al. reported a marked lowering in risk of hospital admission, respiratory failure, assisted ventilation, thromboembolism, supplementary oxygen requirement and neuro-psychiatric disorders in patients who received just one dose of vaccine and the risk further reduced after successful completion of 2nd dose [17]. Another study demonstrated that severe COVID-19 illness after vaccination was associated with male gender, advanced age and presence of co-morbidities [18]. Post-vaccination COVID-19 infection was found to be more common in females while the disease remained mild, did not require hospital admission and caused no deaths [19].

In our study it was seen that male sex, increasing age and presence of co-morbid diseases were associated with severe disease. The findings of our study are similar to another study who reported that severe COVID-19 illness after vaccination was associated with both male gender and advanced age [18]. Similarly, studies reported that increased age was associated

with a higher risk of severe disease and post-covid sequelae [11,17]. The co-morbid conditions especially depression led to significantly longer recovery time [20]. However, these studies did not demonstrate any difference with regards to patient gender. Almadhi et al. demonstrated re-infection was significantly seen in male patients [21]. In our study with 80 patients developing COVID-19 post-vaccination, more than two-thirds of the patients (56, 70.0%) had mild disease while moderate disease was seen in 07 (8.8%).

Ten (12.5%) patients had severe disease while critical disease was seen in 07 (8.8%). Twenty-four (30.0%) patients were admitted to the hospital and 16 (20.0%) patients required ICU admission. All the 07 patients who developed critical disease were above the age of 40 years and of male sex. This is in contrast to findings of Vaishya et al. who demonstrated post-vaccination COVID-19 infection to be more common in females but the disease remained mild [19]. Further, studies demonstrated that age, sex, smoking and underlying diseases were not associated with post-vaccination COVID-19 [23]. Parameswaran et al. reported patients with pre-existing co-morbid conditions developed more severe COVID-19 illness after vaccination [18]. Another, study demonstrated that re-infection was highly associated with pre-existing co-morbid conditions such as HIV, obesity and pregnancy [22]. Seven patients developing critical disease in our study, 04 patients had ischemic heart disease and hypertension while 01 had diabetes mellitus.

In our study male sex, increasing age and presence of co-morbid diseases were associated with increased mortality risk. Butt et al. reported higher mortality to be associated with increasing age but not with the presence of co-morbid conditions [11]. Sadly, 08(10.0%) patients passed away in our study and all of them were male. Seven (15.6%) patients aged more than 40 years died compared to only 01 (2.9%) younger than 40 years. Furthermore, six (10.3%) patients who expired had developed illness more than 4 weeks after completion of vaccination. Smoking was seen in 01 patient, diabetes mellitus in 02 patients, ischemic heart disease in 03 patients and hypertension in 01 patient who passed away. Four (25.0%) patients who died had a hospital stay of longer than 10 days. According to the vaccination type, highest mortality was seen with Sinovac (14.3%) followed by Cansino (12.5%) and Sinopharm (8.3%). Similar study demonstrated that post-vaccination COVID-19 infection to be mild, not requiring hospital admission and causing no deaths [19]. Ozdemir et al. demonstrated post-vaccination COVID-19 to be a mild illness, not requiring hospitalization [23]. Therefore, it is recommended that proper awareness and knowledge [24] regarding the disease is crucial for prevention of mortality due to COVID.

CONCLUSION

We conclude that post-vaccination COVID-19 illness was of mild intensity in more than two-thirds of the patients. However male sex, increasing age and presence of co-morbid diseases were associated with severe disease and

increased mortality risk.

LIMITATIONS:
The present study has some limitations as well which need to be considered. Based in a single center, the present study had a relatively small sample size. Moreover, various types of vaccinations (Pfizer, Moderna, Asterazeneca) were not present in our study or were seen in low numbers making a detailed assessment difficult. Case control or cohort studies are a better option but require more resources and time. Using the results of our study as baseline data, researchers could plan more studies and generate further evidence regarding outcomes and severity of post-vaccination COVID-19 illness.

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Author's Contribution:

Nimra Kanwal: Conception and design, data collection, review and revisions.
Nauman Ismat Butt: Literature review, data analysis, interpretation, and manuscript Writing.
Samrina Sadaf: Conception and design, data collection, review and revisions.
Syed Asif Hussain: Conception and design, data collection, review and revisions.
Anum Rasheed: Literature Review, data analysis, and manuscript writing.
Sadia Babu: Literature review, data analysis, and manuscript writing.