Original Article

Comparison of severity of COVID-19 symptoms in Vaccinated versus Unvaccinated people; A Retrospective Cross-sectional study

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[1,2,3] *Analysis/Interpretation/Discussion*
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Abstract

Introduction: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. SARS-CoV-2, also known as severe acute respiratory syndrome coronavirus 2. Several vaccines against COVID-19 have been developed, yet people still hesitate to get vaccinated. There were concerns mainly regarding the safety, and partly the efficacy of vaccination against COVID-19. This research is intended to compare the severity of COVID-19 symptoms in vaccinated individuals against unvaccinated ones.

Methods: A retrospective cross-sectional study was conducted among total 720 individuals in 2 groups i.e., vaccinated and unvaccinated each comprising of 360 persons. the vaccinated and unvaccinated. The study was conducted in the Department of Medicine at Benazir Bhutto Hospital (BBH) Rawalpindi. Data was collected from the hospital records of BBH and NADRA (National Database & Registration Authority) Covid Helpline "1166". Chi-Square Test was applied to measure the relationship between vaccination status and severity of symptoms. $P<0.05$ was taken as significant.

Results: 63% of patients who experienced moderate symptoms and 57.1% of patients who experienced severe symptoms were vaccinated, whereas 56.5% of critical and 60% of patients who died were unvaccinated (P=0.002). The patients were divided into groups according to age as well. A total of 4 such groups were made. 52.1%. Individuals in Group 1 (18 to 37 years of age) experienced moderate symptoms whereas 51.3% of individuals in Group 4 (78 to 97 years of age) died.

Conclusion: A significant relationship between decreased severity of symptoms and vaccination status was observed thus reinforcing the efficacy of vaccination against COVID-19.

Introduction

The word Corona means "crown" in Latin. The virus looks like a sphere with spikes around it when seen with a very powerful microscope that uses electrons. Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) causes this contagious disease. Initial cases of this highly contagious virus were reported in the city of Wuhan, Hubei Province, China, in December 2019. After that, it rapidly spread across the world and caused 3.8 million deaths worldwide [2]. Coronaviruses are RNA viruses in nature. Corona Viruses (CoVs) induce infections in birds, mammals, and humans. This ailment is highly contagious and transmitted between people [3]. There are multiple causes of the spread of this contagious virus including direct contact with the infected individuals, contact with respiratory droplets, or contact with contaminated objects [4].

Several vaccines have been developed against Covid-19. These vaccines include Pfizer-BioNTech and Moderna which are mRNA vaccines. Some vaccines use human and primate adenovirus vectors such as AstraZeneca and CanSino. An inactivated whole virus vaccine is also available (by Sinopharm and Sinovac) [5]. Several evidences showed that double-dose vaccination offered greater immunity or protection compared to single or isolated vaccination [6]. Studies showed that two doses of Pfizer-BioNTech or Sinopharm vaccines decreased Coronavirus-associated hospitalizations [7]. Clinical trials showed that Sinopharm BBIBP-CorV provided a satisfactory efficacy of 78.89% in preventing new cases and mortality related to SARS-CoV-2 [8]. Sinopharm BBIBP-CorV has been shown to be highly protective against critical hospitalizations associated with COVID-19 and booster dose vaccination is associated with complete protection [9]. In many studies, vaccine efficacy against infections was 80-90% in fully vaccinated people. Fully vaccinated people were less prone to infections [10]. SARS-CoV-2 vaccines have ensured more protection with minimal deaths and severity of symptoms [11].

Several studies have been carried out to investigate the prevalence of Covid-19 that revealed that older age and the male sex were more prone to coronavirus infection. In means of co-morbidities, the strongest evidence of Covid-19 was recorded in hypertension, Type 2 diabetes mellitus, cardiac arrhythmias, depression, and obesity patients [12]. Its fatality rate varied in different ages and countries and could be over 15% [13]. Studies tell us that a median R_0 value (the average number of people who will contract a contagious disease from one person with that disease) for the Coronavirus is 5.7, assuming an interval of 6-9 days. Active supervision, isolation, contact tracing, and efforts like early social distancing are needed to stop Covid-19 spread [14].

The objective of this study was to compare the severity of symptoms in the vaccinated group of patients (with the Sinopharm BIBP COVID-19 Vaccine) versus the non-vaccinated group of patients.

Materials and Methods

This retrospective cross-sectional study was approved by the Ethical Review Board of Rawalpindi Medical University (M-27-47-21) on 4 Nov 2021. Since the data was collected from hospital records, informed consent was waived.

We took data from 720 (360 vaccinated and 360 unvaccinated) patients who got COVID-19 infection and were admitted to the in-patient COVID unit of Benazir Bhutto Hospital. The sample size of 720 was calculated using a confidence interval of 95%, the expected proportion of Covid infection in group 1 (vaccinated) was 4.6%, and the expected proportion of Covid disease in group 2 (unvaccinated) was 9% as reported by Moghadas SM et al [15]. The sampling technique was consecutive non-probability sampling. Only patients who had a positive Covid PCR test and had been vaccinated by the Sinopharm BIBP Covid-19 vaccine and received their second dose at least 4 weeks before the admission date were included. This is due to the reason that the Sinopharm BIBP Covid-19 vaccine is effective 2 weeks after the second dose [16] and because it takes 2 weeks for the symptoms of Covid-19 to appear in the patients and that's when they are likely to come to the hospital for admission [17]. All patients below 18 were excluded as the vaccination for individuals below 18 was not approved at the time of the study and data collection. Patients who had gotten a single dose of vaccine were excluded as well. The "Vaccination Status" was recorded from the hospital records, as they had data regarding the number of doses, dates of the shots administered, and the type of vaccine administered to the patient written there.

From the patient records, we recorded "Age, Gender, and Severity of Symptoms. Based on gender, they were recorded as either Male or Female. Symptom Severity was recorded as either "moderate, severe, critical, or death" based on the classification given in the COVID-19 treatment guidelines on the NIH (National Institute of Health) website. The "moderate" symptoms included individuals who had signs of lower respiratory disease during the clinical assessment or imaging, and who had oxygen saturation (SpO2) ≥94%. The "severe" symptoms included individuals who had SpO2 <94%, respiratory rate > 30 breaths/min, or lung infiltrates >50%. The "critical" symptoms included individuals who had respiratory failure, septic shock, or multiple organ dysfunction [18]. Vaccination status was either taken as vaccinated (where both doses had been administered) or non-Vaccinated (no vaccination). We took into account 7 co-morbidities which included Hypertension (HTN), Diabetes Mellitus (DM), Cardiovascular Disease (CVD), Asthma, Chronic Obstructive Pulmonary Disorder (COPD), Cerebrovascular Accident (CVA), and Chronic Kidney Disease (CKD). We made 3 groups of co-morbidities i.e., a single co-morbidity, 2 co-morbidities, and more than 2 co-morbidities as done in a study conducted by Akhtar H et al [19].

Statistical analysis was performed using IBM SPSS version 25.0.0.0. MS Excel was used for graphs while MS Word was used for tables. The chi-square test was applied to determine the relationship between vaccination status and the severity of symptoms. A 95% Confidence Interval was used. A P-value of<0.05 was considered significant.

Results

Out of 720 individuals, 350 (48.6%) were females and 370 (51.4%) were males. The included patients were divided into four subgroups according to age: Group 1 (18-37 years), Group 2 (38-57 years), Group 3 (58-77 years), and Group 4 (78-97 years). This was based on the age classification given by Dyussenbayev A [20]. The minimum age recorded in the data was 18 years

and the maximum age was 95 years. The range was calculated to be 77 years and the Standard Deviation was 17.093. Out of 720, 360 were completely vaccinated against COVID-19 whereas 360 were not. All of the vaccinated patients had received the Sinopharm BIBP Covid-19 Vaccine with doses between the months of May and October. COVID Symptoms were graded according to severity into 4 classes: Moderate, Severe, Critical, and Death. 200 (27.8%) presented with moderate symptoms, 126 (17.5%) with severe, 124 (17.2%) with critical and there were 270 (37.5%) death cases. The details are summarized in Table 1**.**

TABLE-I Frequencies of different variables

Variables		Number of patients 'n' (%)
Gender	Male	370 (51.4%)
	Female	350 (48.6%)
Age	Group 1 (18-37 years)	252 (13.3%)
	Group 2 (38-57 years)	252 (35.0%)
	Group 3 (58-77 years)	298 (41.4%)
	Group 4 (78-97 years)	74 (10.3%)
Vaccination Status	Complete	360 (50.0%)
	None	360 (50.0%)
COVID Symptoms	Moderate	200 (27.8%)
	Severe	126 (17.5%)
	Critical	124 (17.2%)
	Death	270 (37.5%)

Upon statistical analysis of the data, it was seen that of the patients who experienced moderate symptoms, 126 (63%) were vaccinated while 74 (37%) were not. Of those who experienced severe symptoms, 72 (57.1%) were vaccinated. Of the critical patients, 54 (43.5%) were vaccinated, and only 108 (40%) of people who died were vaccinated whereas 162 (60%) were not (p=0.00 BORDERS2) as seen in Table 2. This indicates a significant relationship between the

increasing severity of COVID-19 symptoms and unvaccinated people, and a decreasing trend of symptom severity is seen in vaccinated ones ($p<0.05$).

Table-II Severity of COVID symptoms experienced by vaccinated and unvaccinated patients

Vaccination Status	COVID Symptoms			
	Moderate n(%)	**Severe n(%)**	**Critical n(%)**	**Death n(%)**
Completely Vaccinated n (%)	126 (63.0%)	72 (57.1%)	54 (43.5%)	108 (40.0%)
Unvaccinated n (%)	74 (37.0%)	54 (42.9%)	70 (56.5%)	162 (60.0%)
Total n (%)	200 (100.0%)	126 (100.0%)	124 (100.0%)	270 (100.0%)

Furthermore, when the analysis was done with age versus the severity of symptoms, the largest percentage of individuals in Group 1 experienced Moderate symptoms (52.1%). Group 2 had a fairly equal distribution of symptoms with 70 (27.7%) individuals suffering from moderate symptoms, 56 (22.2%) suffering from severe, and 84 (33.3%) individuals who died. The largest percentage of individuals in Group 3 died (41.6%) and more than half of the individuals in Group 4 (51.3%) also died. Hence, a greater percentage of individuals faced death and critical symptoms in Groups 3 and 4 than those in 1 or 2 as seen in Table 3 ($p=0.002$).

Table-III Severity of COVID symptoms present in 4 age groups: Group 1 (18-37 years), Group 2 (38-57 years), Group 3 (58-77 years), Group 4 (78-95 years)

Age	**COVID Symptoms**				
	Moderate	**Severe**	**Critical**	**Death**	**Total**
Group 1 n (%)	50 (52.1%)	14 (14.6%)	8 (8.3%)	24 (25.0%)	96 (100.0%)
Group 2 n (%)	70 (27.7%)	56 (22.2%)	42 (16.6%)	84 (33.3%)	252 (100.0%)
Group 3 n (%)	72 (24.2%)	44 (14.7%)	58 (19.5%)	124 (41.6%)	298 (100.0%)

Group 4 n (%)	8 (10.8%)	12 (16.2%)	16 (21.6%)	38 (51.3%)	74 (100.0%)

There was no significant statistical correlation reported between gender and vaccination status (P=0.598). Similarly, no correlation was found between increasing age and vaccination status (P=0.274). As far as co-morbidities are concerned, 346 patients had no co-morbidity. 102 (28.3%) vaccinated and 104 (28.8%) unvaccinated patients had one co-morbidity, 54 (15%) vaccinated, and 58 (16.1%) unvaccinated patients had 2 co-morbidities. 30 (8.3%) of vaccinated and 26 (7.2%) of unvaccinated patients had more than two co-morbidities. The distribution of co-morbidities is shown in Table 4. No significant statistical correlation was found between co-morbidities and the vaccination status of patients. (p=0.901)

Table IV Distribution of co-morbids in vaccinated and unvaccinated individuals

Co-morbidity	**Vaccinated individuals n (%)**	**Unvaccinated individuals n (%)**	**Total n (%)**
Hypertension	100 (27.7%)	103 (28.3%)	203 (28.2%)
Diabetes Mellitus	80 (22.2%)	70 (19.4%)	150 (20.8%)
Cardiovascular Disease	48 (13.3%)	42 (11.6%)	90 (12.5%)
Asthma	14 (3.8%)	26 (7.2%)	40 (5.5%)
Chronic Obstructive Pulmonary Disease	22 (6.1%)	28 (7.7%)	50 (6.9%)
Chronic Kidney Disease	34 (9.4%)	28 (7.7%)	62 (8.6%)
Cerebrovascular Accident	12 (3.3%)	8 (2.2%)	20 (2.7%)

Discussion

Research has shown that vaccination provides the best protection against COVID-19 infection [21]. Our study is based on clinical observation of the severity of COVID-19 symptoms in vaccinated (with Sinopharm BIBP COVID-19 Vaccine) and unvaccinated people and proves through a detailed statistical analysis of the data, the efficacy of vaccines against SARS-CoV-2 infection. As explained by Synowiec A et al, the assessment of disease severity focuses on common symptoms experienced by most patients ranging from little respiratory discomfort and flu

like symptoms to major diseases with accompanying injury of lungs, multiorgan failure, and death [22]. Keeping this in mind, our study's symptoms were graded into moderate, severe, critical, and death with moderate symptoms covering mild respiratory discomfort and influenza-like symptoms and critical symptoms covering multiorgan failure. Statistical analysis of the data showed that in the fully vaccinated individuals, disease symptoms were mostly moderate whereas in the unvaccinated individuals, critical and death cases were more prevalent, indicating that the relationship between vaccination status and severity of symptoms is significant. Previous studies have indicated that aging contributes to an increased vulnerability to COVID-19 and more severe symptoms due to the decline and dysfunction of immune response with age i.e., immunosenescence (a process of immune discomfort that occurs with age) [23,24]. Symptoms are generally milder in younger people while it can be inducing severe morbidity and mortality in older people [25]. Another study enlisted high-risk groups associated with severe COVID-19 infections, including individuals over 65 years of age [26]. Similarly, in the present study, patients were divided into age groups and it was proven that younger people mainly experienced moderate to severe symptoms whereas the oldest group of people mainly dealt with critical symptoms and death. This shows that older individuals have more chance of developing the detrimental effects of COVID-19 than younger people.

While there was a significant relationship between vaccination status and aging with the severity of COVID-19 symptoms ($P<0.05$), we observed no association of gender with the severity of COVID-19 symptoms ($P>0.05$). Conversely, another study conducted by Barek M et al. indicated that males were more likely to be infected by COVID-19 and developed more severe symptoms than women [27].

Yan Z et al. did a study to review the efficacy of vaccines and all COVID-19 vaccines. It showed promising immunogenicity, but the immunological outcome was better in younger people than the older ones [28]. Similarly, we also found the effectiveness of vaccines in reducing the severity of infection as was apparent by the lower number of critical patients and death in the individuals who got vaccination.

SARS-CoV-2 has been linked to low levels of Angiotensin Converting Enzyme-2 (ACE-2) which can lead to vascular aging, atherosclerosis, inflammation, and fibrosis. This can cause diseases like hypertension, renal failure, and cardiac fibrosis. Similarly, it has been reported that Hypertension, Diabetes Mellitus, and Chronic Kidney Disease were independent risk factors in patients with COVID-19 and indicators of poor prognosis as stated by Akhtar H et al [19]. Similarly, a study showed that patients with COVID-19 who required intensive care support were older and had several co-morbidities [29]. In our study, however, the prevalence of co-morbidities in both groups was essentially similar, and upon statistical analysis, it came out to be insignificant. So, the increased severity of symptoms and death in unvaccinated individuals is mainly attributed to their lack of vaccination instead of co-morbid or any other factor.

This study has potential limitations. It is a retrospective study with data gathered from patients who were admitted to wards from June to December 2021. The data is therefore bound to change if collected recently. Moreover, the study had a sample of 720 patients, and that too were

mostly residents of Rawalpindi and surrounding areas, hence it does not correctly represent the whole population of Pakistan. Also, our study deals with individuals vaccinated with just one type of vaccine (Sinopharm BIBP COVID-19 Vaccine). A study with a larger sample size and consisting of individuals from different parts of the country would deem way more accurate results.

Conclusion

Significant relationship between decreased severity of symptoms and vaccination status was observed thus reinforcing the efficacy of vaccination against COVID-19. Severity of COVID-19 symptoms was also found to be associated with aging.

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