Cross-sectional Study

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Prevalence and difference of COVID-19 symptoms, post-COVID conditions and duration of illness among the vaccinated and unvaccinated population: a cross-sectional study in Peshawar

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Background: Studies on coronavirus disease 2019 (COVID-19) symptoms, post-coronavirus disease (COVID) conditions, and vaccination outcomes in Pakistan are limited and inconsistent. The study investigated differences in symptoms and post-COVID conditions between vaccinated and unvaccinated individuals and the impact of vaccination on illness duration based on existing literature.

Methods: The study was a 3-month cross-sectional study conducted in Peshawar, Pakistan. It targeted individuals aged 16 and above who had contracted COVID-19 at least once during the recent pandemic, regardless of gender, and confirmed through reverse transcriptase polymerase chain reaction testing. The sample size was 250, determined using the WHO sample size calculator. Data were collected through questionnaires after obtaining verbal consent and analyzed using IBM SPSS version 26, taking into account their vaccination status along with other important variables.

Results: Among the 250 respondents, 143 (57.2%) were unvaccinated, while 107 (42.8%) were vaccinated at the time of contracting COVID-19. Unvaccinated subjects developed a greater variety of symptoms that lasted for longer durations ($P < 0.001$) with symptoms like dyspnea [55 (38.5%, $P = 0.011$)], anosmia [76 (53.1%, $P = 0.001$)], and chest pain [24 (16.8%, $P = 0.029$)] occurring at greater percentages. Sixty-one (42.7%) unvaccinated subjects reported post-COVID conditions as opposed to 29 (27.1%) among the vaccinated group [$P = 0.011$; odds ratio (OR) = 0.5; 95% CI = 0.29–0.86].

Conclusion: The study found that COVID-19 vaccination can reduce the duration and frequency of symptoms, as well as post-COVID conditions. This is the first research of its kind conducted in Peshawar, Pakistan, and may serve as a foundation for future research in this demographic.

Keywords: COVID-19, long COVID, outbreak and pandemic, post-COVID conditions, vaccination

Introduction

In December 2019, the first officially documented case of COVID-19 caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus was reported in the province of Wuhan, China, which quickly escalated into a pandemic[1]. COVID-19 primarily causes respiratory illness and presents symptoms that range from mild flu-like symptoms such as sore throat, cough, myalgia, fever, anosmia, diarrhea, and generalized body aches, to more moderate-to-severe respiratory symptoms of acute respiratory distress syndrome, which can lead to multiorgan failure and, eventually, death[1]. Although coronavirus is notorious for primarily targeting the respiratory

HIGHLIGHTS

- Our research sheds light on the effect of vaccination on the course of coronavirus disease 2019 (COVID-19) infection and concludes that there are downright visible benefits of coronavirus disease (COVID) vaccine in the different symptoms faced by COVID-19 patients.
- This is the first comprehensive research gathering data in the city of Peshawar, Pakistan, by correlating different aspects of the infection like duration of illness, kinds of symptoms developed, and post-COVID conditions.
- This research thus provides the basic data for further research and advancements on this topic.

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system, it can also affect other organs, resulting in a plethora of complications that impact major organ systems, such as the central nervous system, cardiovascular system, hematological system, gastrointestinal tract, hepatobiliary, and renal. Several mechanisms have been proposed to explain the virus-induced damage, including direct viral toxicity, dysregulation of the immune system, ischemic injury due to vasculitis or thrombosis, and dysregulation of the renin–angiotensin–aldosterone system (RAAS)[2].

Numerous neurological complications have been linked to COVID-19 infection[3,4]. Additionally, COVID-19 infection can cause acute heart failure. According to one study, acute heart failure may be present in 23% of patients in their initial course of COVID-19 infection, while cardiomyopathy can occur in 33% of patients[5].

The United States Food and Drug Administration approved two vaccines for the prevention of COVID-19 in December 2020. Multiple side effects have been reported during the clinical trials of these vaccines, including mild symptoms such as fever, myalgias, and injection site pain. Consequential side effects, such as anaphylactic shock, could also occur[6,7]. Other serious complications can occur postvaccination, such as Guillain–Barré syndrome, which was reported in an 82-year-old patient after receiving the first dose of the Pfizer-COVID-19 vaccine[8].

Without negating the fact that COVID-19 vaccination has been instrumental in bringing down the mortality rate and transmission of the virus, numerous moderate-severity to high-severity complications keep emerging around the globe, which is notorious for eventually causing multiorgan damage. This set of circumstances urges prompt attention and in-depth research studies to evaluate short-term and long-term complications of COVID-19 in people from various age groups based on different settings and also to explore the ever-rising opportunities for improvement of the existing vaccines[9].

The modes of transmission of the SARS-CoV-2 virus have been a dilemma. Although three primary modes have been suggested – contact, droplet, and airborne – the main modes of transmission are still being debated. Airborne transmission has been recognized as an important mode of transmission due to emerging evidence of viable SARS-CoV-2 presence, even in the absence of aerosol-generating procedures. Further research is needed to better understand the paradox of SARS-CoV-2 transmission and infectivity[10].

An important term linked to COVID-19 is 'post-COVID condition.' Post-COVID conditions, also known as long COVID or post-acute sequelae of SARS-CoV-2 infection, can cause a range of long-term symptoms in some people who have recovered from COVID-19. These symptoms can be diverse and may include fatigue, shortness of breath, brain fog, joint pain, chest pain, headaches, and loss of taste or smell. These symptoms can be persistent and may last for weeks or even months after the initial recovery from COVID-19. It is still unclear what causes these long-term effects, and they can affect people of all ages and health conditions, even those who have mild or asymptomatic COVID-19[11].

This scholarly article aims to comprehensively compare the symptoms, post-COVID condition, and duration of illness among vaccinated and unvaccinated COVID-19 patients of different age groups.

Methods

Study design and population

This cross-sectional study aimed to investigate the potential role of vaccination in reducing the overall impact and morbidity of COVID-19 among the general population. The study was conducted over a period of 3 months, from 1 June 2022 to 31 August 2022, in the city of Peshawar, Pakistan. The target population consisted of individuals who had contracted COVID-19 and were diagnosed through PCR testing, taking into account their vaccination status. The study adhered to the STROCSS (strengthening the reporting of cohort, cross-sectional and case–control studies in surgery) criteria[12].

The questionnaire was designed by thoroughly reviewing previous literature on the topic and streamlining it to make it applicable to the locality where the study would be conducted. However, a pilot study could not be carried out due to time and resource limitations.

Inclusion criteria were: individuals of any gender, aged 16 years and above, who had contracted COVID-19 infection one or more times and were confirmed through RT-PCR (reverse transcriptase polymerase chain reaction) testing.

The exclusion criteria for this study were as follows: patients who were unable to provide consent or who were not mentally capable of doing so, respondents who were diagnosed through methods other than PCR, such as rapid antigen or serological tests, and individuals who had never contracted COVID-19. In addition, individuals with chronic illnesses such as fatigue, myalgia, tremors, and other similar conditions were also excluded as these conditions could interfere with the assessment of post-COVID conditions.

Study sample

Taking into account the time and resource limitations, a sample size of 250 individuals was calculated for this study. The sample size was determined based on a 95% confidence interval and a margin of error of 6.2%, with a population target of 225 000 as reported locally. The calculations were carried out using the WHO sample size calculator. A convenient nonprobability sampling technique was used to select cases from various population settings such as schools, colleges, and workplaces. Data were collected by directly interacting with study subjects and transferring relevant information onto the questionnaire after obtaining informed consent from the participants.

Variables and operational definition

Data were collected from study participants on several variables, including age, gender, vaccination status, whether they were diagnosed before or after vaccination, symptoms developed, duration of illness, and post-COVID conditions.

Individuals were considered to have a positive vaccination status only if they had received a minimum of two doses of licensed COVID-19 vaccines, including Pfizer, Sinopharm, Sinovac, and/or Moderna, before contracting COVID-19 and had a government-assigned vaccination card. Those who were unvaccinated or had incomplete vaccination status at the time of contracting COVID-19, even if they were vaccinated afterward, were classified as having a negative vaccination status.

'Post-COVID conditions' were defined as any new, recurring, or continuing symptom/s lasting for 4 weeks or more that

appeared after a negative PCR test result. The term 'post-COVID conditions' is known by various names such as long COVID, post-COVID syndrome, long-term COVID, and so on. However, in this article, we have only used the first two terms to refer to this state.

As the study was conducted on the general population, ethical approval was not required according to the policies of ethical review committees in Peshawar. These committees only review research that is specifically conducted and limited to educational institutions or hospitals, as outlined by the guidelines of our institutional research and ethical board (IREB).

Statistical analysis

The data were analyzed using IBM SPSS version 26 (Statistical Package for the Social Sciences). Frequencies of different symptoms were calculated, and the correlation between different variables was statistically tested using the χ^2 test. The Fisher exact test was used when the expected count was less than 5 in more than 20% of the cells in the 2×2 contingency table. The data were considered significant when the P value was less than 0.05.

Results

Among the total number of respondents, 143 had not received the COVID-19 vaccine at the time of contracting the virus, while 107 had been vaccinated.

Duration of illness

The vaccination status of the subjects had a significant statistical impact on the duration of illness. Among the respondents, 62 (57.9%) vaccinated subjects recovered within 3–5 days compared to only 31 (21.7%) unvaccinated subjects, indicating that unvaccinated subjects suffered symptomatic COVID for a longer duration (Fig. 1 and Table 1). Furthermore, the majority of participants who had COVID for more than 10 days were unvaccinated, with 30 (21%) unvaccinated compared to only 11 (10.3%) vaccinated individuals (Table 1). Additionally, 8 (5.6%) unvaccinated individuals and only 5 (4.7%) vaccinated individuals were sick for 16–20 days, while 9 (6.3%) unvaccinated individuals and only 1 person (0.9%) vaccinated were sick for more than 20 days ($P < 0.001$) (Table 1).

Symptoms

A significant decrease in symptoms was observed among the vaccinated individuals compared to the unvaccinated ones. Specifically, among the respondents, 55 (38.5%) unvaccinated individuals experienced dyspnea, while only 25 (23.4%) vaccinated individuals did ($P = 0.011$). Similarly, 76 (53.1%) unvaccinated individuals had anosmia/loss of taste, while only 34 (31.8%) vaccinated individuals did ($P < 0.001$). In addition, 24 (16.8%) unvaccinated individuals reported chest pain, while only 8 (7.5%) vaccinated individuals did ($P = 0.029$) (Table 2 and Fig. 2). There was also a decrease in the number of people experiencing fever, cough, fatigue, diarrhea, body aches, headache, and sore throat after vaccination, but the difference was not statistically significant (Table 2 and Fig. 2).

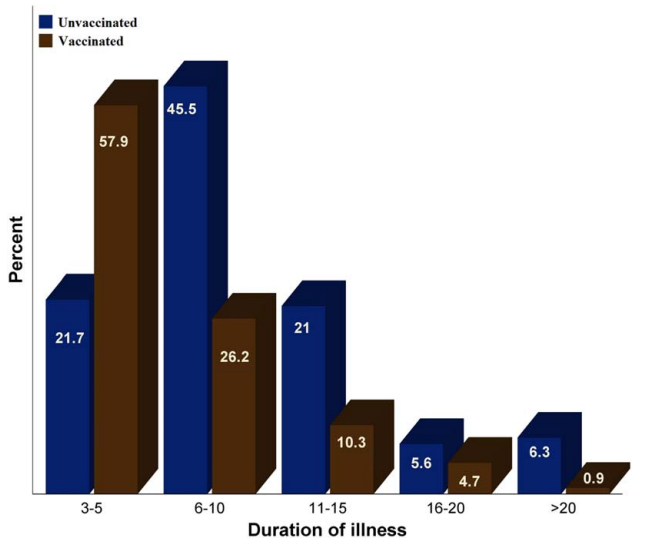

Figure 1. Comparison of the duration of illness in unvaccinated and vaccinated respondents with coronavirus disease 2019 (COVID-19). COVID, coronavirus disease.

Post-COVID conditions

After recovering from COVID-19, 61 (42.7%) unvaccinated individuals developed post-COVID conditions, while only 29 (27.1%) vaccinated individuals did, indicating a significant decrease in post-COVID conditions among vaccinated individuals ($P = 0.011$) (Table 3). Upon stratifying the data based on gender, it was found that females were slightly more prone to developing post-COVID conditions compared to males. Specifically, 46 (38.7%) females and 44 (33.6%) males developed these conditions. However, the finding was not statistically significant ($P = 0.404$).

Regarding the post-COVID conditions, a significant decrease was observed in the number of vaccinated individuals who experienced arthralgia ($P = 0.016$), myalgia ($P = 0.041$), anosmia/loss of taste ($P < 0.001$), and fatigue ($P = 0.007$) compared to the unvaccinated individuals (Table 4). However, the difference was not statistically significant for chest pain, palpitation, cognitive impairment, headache, mood changes, diarrhea, tremors, and vertigo (Table 4).

Discussion

This study aimed to compare the prevalence of SARS-CoV-2 infection-related symptoms and post-COVID conditions in the

Table 1

Comparison of illness duration between vaccinated and unvaccinated respondents.

	Unvaccinated ($n = 143$), *N* (%)	Vaccinated ($n = 107$), *N* (%)	*P*
Duration of illness (days)			< 0.001
3–5	31 (21.7)	62 (57.9)	
6–10	65 (45.5)	28 (26.2)	
11–15	30 (21.0)	11 (10.3)	
16–20	8 (5.6)	5 (4.7)	
> 20	9 (6.3)	1 (0.9)	

Table 2

Comparison of symptoms among vaccinated and unvaccinated respondents.

Symptoms	Unvaccinated ($n=143$), *N* (%)	Vaccinated ($n=107$), *N* (%)	*P*
Fever	128 (89.5)	89 (83.2)	0.143
Cough	99 (69.2)	69 (64.5)	0.429
Dyspnea	55 (38.5)	25 (23.4)	0.011
Anosmia/loss of taste	76 (53.1)	34 (31.8)	0.001
Fatigue	116 (81.1)	76 (71.0)	0.061
Chest pain	24 (16.8)	8 (7.5)	0.029
Diarrhea	30 (21.0)	22 (20.6)	0.936
Body aches	109 (76.2)	78 (72.9)	0.549
Headache	11 (7.7)	3 (2.8)	0.096
Sore throat	8 (5.6)	2 (1.9)	0.196

general population. Our results were consistent with predicted expectations, showing a statistically significant reduction in the severity of acute infections as well as postinfection conditions (Tables 1–4). These findings are similar to those observed in studies conducted globally during the COVID-19 pandemic.

A similar study was conducted by Fatima *et al.*[13] at Aga Khan Hospital, which compared the statistical difference in COVID-19 contraction between vaccinated and unvaccinated groups through a cohort study. The study concluded that both groups are susceptible to developing severe COVID-19 infections, but the proportion is significantly lower among vaccinated individuals (Table 2–4). This complements our findings.

A multicenter study conducted in LRH and DHQ, Batkhela, replicated our findings through a retrospective comparative study. The study reported hospitalization (10%) and intensive care unit (ICU) admission (14%) rates among nonvaccinated patients that were higher than those among vaccinated patients (Table 2–4)[14].

A study by Khan *et al.*[15] in Karachi during the delta variant wave further supports our results (Tables 2, 4). It states that vaccinated COVID-19 patients had a lower disease severity and showed improved outcomes compared to unvaccinated patients.

Our study found that receiving a complete course of COVID-19 vaccination affected the duration of the disease (Table 1 and Fig. 1). This finding is consistent with the study by Antonelli *et al.*[16], which demonstrated that patients with symptoms over 28 days are twice as many in unvaccinated versus vaccinated groups in their mobile phone-based community study. Similarly, Korishettar *et al.* reported that the duration of hospital stay was

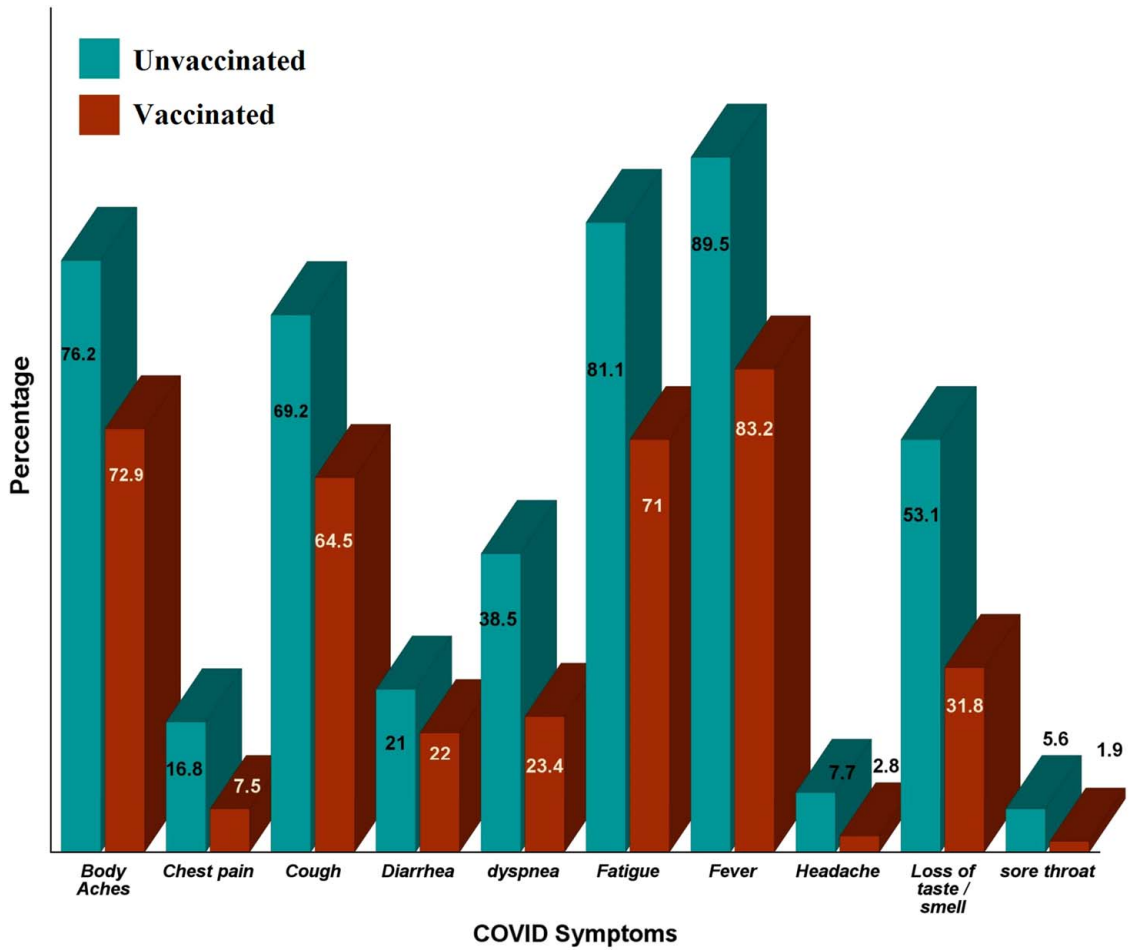

Figure 2. Comparison of the prevalence of coronavirus disease 2019 (COVID-19) symptoms among vaccinated and unvaccinated respondents.

Table 3

Comparison of post-COVID (coronavirus disease) conditions between vaccinated and unvaccinated respondents.

	Unvaccinated ($n=143$), *N* (%)	Vaccinated ($n=107$), *N* (%)	*P*	Odds ratio	95% CI
Post-COVID condition(s)			0.011	0.5	0.29–0.86
Yes	61 (42.7)	29 (27.1)			
No	82 (57.3)	78 (72.9)			

lower in vaccinated patients (average of 5.65 days) than in unvaccinated patients (average of 9.43 days)[17]. Our study focused specifically on the duration of illness (Fig. 1 and Table 1), which is not a common focus in many other studies that focus on determinants of severe COVID-19 and long COVID.

Post-COVID conditions, also known as 'long COVID,' are characterized by a collection of signs, symptoms, and conditions that emerge after an individual's initial COVID-19 or SARS-CoV-2 infection and endure for a minimum of 4 weeks. These may include multisystemic manifestations and exhibit a relapsing-remitting pattern, as well as a tendency to worsen or progress over time[18].

At the time of diagnosis, our study found significant variability in symptoms only for dyspnea (15.1% reduction), anosmia (21.3% reduction), and chest pain (9.3% reduction), with a *P* value less than 5% for all three (Table 2). Fever and fatigue were the most common symptoms in both vaccinated and unvaccinated groups, with no statistically significant difference (Table 2). While all symptoms were less common postvaccination, this difference was not statistically significant, and vaccination appears to be ineffective at preventing mild COVID-19 symptoms (Table 2). Other common symptoms, such as cough, fatigue, diarrhea, sore throat, and headaches, were also present in both groups (Table 2). This lack of protection is well observed, with Taquet *et al*.[19] reporting a similar lack of hazard reduction postvaccination using regression analysis and Kaplan–Meier curves.

Table 4

Post-COVID (coronavirus disease) conditions according to vaccination status.

Symptoms	Unvaccinated ($n=143$), *N* (%)	Vaccinated ($n=107$), *N* (%)	*P*
Arthralgia	38 (26.6)	15 (14.0)	0.016
Myalgia	35 (24.5)	15 (14.0%)	0.041
Dyspnea	7 (4.9)	4 (3.7)	0.762
Anosmia/loss of taste	39 (27.3)	6 (5.6)	<0.001
Fatigue	55 (38.5)	24 (22.4)	0.007
Chest pain	6 (4.2)	1 (0.9)	0.244
Palpitation	4 (2.8)	0 (0.0)	0.138
Cognitive impairment	5 (3.5)	3 (2.8)	1.000
Headache	16 (11.2)	11 (10.3)	0.819
Mood changes	16 (11.2)	10 (9.3)	0.637
Diarrhea	9 (6.3)	10 (9.3)	0.368
Tremors	2 (1.4)	2 (1.9)	1.000
Vertigo	2 (1.4)	2 (1.9)	1.000

However, this contrasts greatly with Simon *et al*.[20], who reported an odds ratio (OR) of – 85.13 for any COVID-19 symptoms, even after one dose of vaccination. Tran *et al*.[21] calculated a 7.5% reduction rate in symptom states between vaccinated and nonvaccinated groups. Antonelli *et al*.[16] reported an overall OR of less than 1 for almost all reported COVID-19 symptoms, such as anosmia, sore throat, hoarseness of voice, and tinnitus. Korishettar *et al*., who conducted a cohort study on trauma care center patients, documented various parameters and compared vaccinated to nonvaccinated groups, showing an improvement in oxygen saturation (95 vs. 89% averages), serum ferritin levels (282 vs. 708 ng/dl), and dyspnea (54 vs. 40.4%) in vaccinated patients, as well as a reduction in other symptoms such as fever, abdominal pain, and diarrhea, with an increase in vomiting occurring in the vaccinated group[17].

It is important to differentiate between vaccine efficacy in preventing recurrent COVID-19 and severe COVID-19 in patients who have been reinfected and our study's finding of minimal change in mild COVID-19 symptoms following vaccination. Vaccines play a crucial role in controlling the spread and infectivity, as well as the morbidity, of COVID-19.

Although various studies differ in their settings, population demographics, and follow-up duration, it is evident that vaccination can help in reducing certain symptoms, such as anosmia and dyspnea. The most significant benefit is seen in the prevention of severe COVID-19, which requires hospitalization and ICU admission. Previous studies have documented the ability of vaccination to reduce the likelihood of severe COVID-19[17,20,21]. Our study was community-based, and matched the results of other community-based studies but it did not focus on hospital settings. However, the significance of vaccination is reduced for other milder symptoms, such as cough, fever, and systemic malaise (Table 2).

Our study differentiated between acute symptoms and post-COVID conditions. We reported an OR of 0.5 ($P=0.011$) for the incidence of any post-COVID condition between the vaccinated and unvaccinated groups (Table 3). Other studies similar to ours have also shown a reduction in post-COVID conditions after vaccination[20]. Nahme *et al*. calculated an OR of 0.72 for post-COVID conditions postvaccination compared to the nonvaccinated group. They also reported a decrease in the prevalence of acute symptoms such as dyspnea (OR $=0.34$) and changes in taste (OR $=0.38$), as well as a decrease in the prevalence of any single symptom (OR $=0.60$)[22]. Ayoubkhani *et al*.[23] found an OR of 0.87 and 0.91 for one and two vaccine doses, respectively. They also reported that the largest numerical decreases after the first vaccine dose were observed for loss of smell (– 12.5%, $P=0.02$), loss of taste (– 9.2%, $P=0.13$), and trouble sleeping (– 8.8%, $P=0.15$). After the second vaccine dose, the largest numerical decreases were observed for fatigue (– 9.7%, $P=0.01$), headache (– 9.0%, $P=0.08$), and trouble sleeping (– 9.0%, $P=0.08$).

However, some studies have reported no significant differences in outcomes, such as Taquet *et al*.[19], who found no significant difference in many neurological symptoms, attributing this finding to the possibility of nonimmunogenic mechanisms. Their findings of reductions in certain conditions, such as myalgia (HR $=0.78$, 95% CI $=0.67$–0.91), fatigue (HR $=0.89$, 95% CI $=0.81$–0.97), and pain (HR $=0.90$, 95% CI $=0.81$–0.99), mirror our findings, as arthralgias, myalgias, anosmia, and fatigue were the most significantly reduced postvaccination

(reductions of 12.6, 10.5, 21.7, and 16.1%, respectively) (Table 4). Wisnivesky *et al*.[24] similarly did not observe any significant differences in their 6-month follow-up study postvaccination.

The overall trend leans in favor of the idea that vaccination reduces the occurrence as well as the individual number of post-COVID conditions. Mahase[25] noted in her literature review that COVID vaccination doses reduce the probability of post-COVID conditions.

An important point to highlight about long COVID is that several studies have suggested a gender disparity in its incidence and severity. For instance, in a study conducted by Sudre *et al*.[26], it was found that women were more likely to report persistent symptoms after a COVID-19 infection, including a higher occurrence of fatigue, dyspnea, and anxiety. Another similar study was carried out by Townsend *et al*.[27] showed that females were more likely to report continuing fatigue, along with other symptoms attributed to long COVID. Similarly, our study found that females had a higher prevalence of developing these symptoms, with 46 (38.7%) females and 44 (33.6%) males developing them. However, this difference was not statistically significant ($P = 0.404$).

A good approximation can be made that vaccination dose indeed reduces the rate of post-COVID-19 conditions, but there is a more pronounced effect on certain outcomes than others, with anosmia, fatigue, abnormal taste, and pain being the most consistent. Interestingly, our study did find a weak positive association with vertigo postvaccination, similar to how some studies report more vomiting in vaccinated groups[17]. The exact pathophysiology and sequence of events in 'long COVID' have yet to be fully studied.

Strengths and limitations

- This is the first study to gather data related to COVID-19 in the Peshawar region.
- The forms were filled under the active surveillance of the authors to reduce errors during data collection.
- Concrete evidence linking complications such as post-COVID stroke and Guillain–Barré syndrome to COVID-19 infection could not be assessed in this research and therefore were not included in our findings.
- This study cannot be applied to the general population as we used convenient nonprobability sampling.
- Despite our efforts to actively monitor and collect data, educational barriers among participants may have increased the likelihood of response bias.

Relevance and implications

This research provides much-needed data on the effects of vaccination on the course of COVID-19 in the low-income regions of Peshawar, north-western Pakistan.

This data can serve as a foundation to better understand the impact of COVID-19 in these areas and inform future strategies to combat the pandemic.

Conclusion

Our research concluded that the COVID-19 vaccine provides visible benefits in alleviating different symptoms experienced by COVID-19 patients. The vaccinated respondents reported a reduction in symptoms such as dyspnea, anosmia, and chest pain. Additionally, vaccinated patients experienced shorter disease states, confirming the effectiveness of the vaccine in treating COVID-19.

While our research supports the use of vaccines to combat the pandemic, there were limitations in our study. These included small sample size, a lack of consideration for different vaccine types, and a lack of follow-up data for patients. Further research is needed to better understand COVID-19's pathophysiology and treatment modalities, and we hope that our findings will serve as a starting point for similar studies in this demographic.

Ethical approval

Not applicable as research was conducted on the general population. No patients were involved in this research.

Consent

Informed consent was obtained from the respondents before filling out the questionnaire. All sorts of identifying details were fully omitted.

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This research received no funding of any sort from any funding agency.

Author contribution

A.R.: data collection, data analysis, figures and tables, and results; M.T.I.: data collection, materials and methods, and data analysis; A.A.: data collection and introduction; BD.K.: abstract and proofreading; K.U.A.: discussion; M.S.F.: data collection and materials and methods; A.K.R.: literature review; M.S.K.: data collection and literature review; M.H.M., R.F., H.Y., and M.D. K.: data collection.

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

Research registration unique identifying number (UIN)

1. Name of the registry: Research Registry.
2. Unique identifying number or registration ID: research-registry8735.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

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