



Post-COVID Syndrome with relation to vaccination status in conformed COVID-19 infected patients in a tertiary care hospital

Allavarapu Ramya Sree^{1*}, Sethumadhavan², Purimitla Usharani³, BVVV Tejaswani⁴, C. Roopa⁵

^{1*} Tutor, Department of Microbiology, Dr.Patnam Mahender Reddy Institute of Medical Sciences, Chevella, Ranga Reddy district, Telangana, India

² Professor, Department of Microbiology, Aarupadai Veedu Medical College and Hospital, Puducherry, Tamil Nadu, India.

³ Associate Professor, Department of Microbiology, Dr.Patnam Mahender Reddy Institute of Medical Sciences, Chevella, Ranga Reddy district, Telangana, India

⁴ Assistant Professor, Department of Microbiology, Kamineni Institute of Medical Sciences, Narketpalli, Hyderabad, India.

⁵ Professor and Head, Department of Microbiology, SVS Medical College, Mahabubnagar, Telangana, India.

* Corresponding author

Allavarapu Ramya Sree

Tutor, Department of Microbiology,
Dr.Patnam Mahender Reddy Institute of Medical Sciences,
Chevella, Ranga Reddy district, Telangana, India
Contact number: +91-9491726905

Email:ramyams619@gmail.com

Abstract

Background: Post-covid syndrome is a long-term physical and mental health effect, which can linger for more than three months after the initial Covid-19 infection. **Objective:** The aim of the study was to investigate the severity and duration of post Covid-19 complications in vaccinated and unvaccinated people who got infected with SARS COV-2. **Materials and Methods:** It is a prospective study includes 1000 total number of cases. The study was conducted on 381 post-Covid syndrome patients. After enrollment, PCR confirmed COVID 19 infected were allowed to complete a questionnaire with questions regarding socio-demographic details, contact information, symptoms when diagnosed with SARS CoV2, medical co- morbidities and risk factors, current health status and present symptoms. To assess the post COVID syndrome in the general population, questions regarding their recovery after infection, the duration they required to become symptom free, any persistent symptoms and other or new ongoing symptoms will be recorded by personal interview. The patients complaints of breathlessness, fatigue and difficulty in concentrating and mood changes will be further evaluated by using modified dyspnea Medical Research Council scale. Depression, anxiety and stress scores were also measured from the study subjects. **Results:** Out of 1000 cases selected, a total of 381 patients completed the survey and satisfied the inclusion criteria. Among 381 cases, male were 234 and females were 147. The major post-Covid symptoms in first dose vaccinated individuals were fatigue (87%) followed by pains in legs and arms (86%). The major post-Covid symptoms in second dose vaccinated individuals were hair loss (68%) followed by depression, anxiety and stress scale (58%).

Conclusion: Double vaccinated participants as associated with reduced risk of reporting most of post acute COVID 19 symptoms. Our results suggest that vaccination may have a protective effect against long term Covid-19 symptoms.

Key words

SARS-COV-2, Post-covid syndrome, fatigue, DASS, Dyspnea

Introduction

“Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV-2) causes acute respiratory illness known as Corona Virus Disease (Covid-19)” [1] and it has resulted in the worst financial catastrophe ever documented since World War II and an explosive, devastating pandemic that has claimed many people. The disease spread explosively and quickly, and even after it was designated a global pandemic in March 2020, cases continued to be reported in some nations. The epidemiological data, especially the geographic distribution, is predicted to alter over time [1] because this explosive pandemic is still happening. According to the most recent WHO data release (Jan 2023), the cumulative number of reported cases was 761,402,282, and the cumulative total of deaths was 6,887,000. According to WHO statistics from 2023, there have been 44,707,525 cases with conformed COVID-19 and 530,841 reported deaths in India. Many mutant strains including Alpha, Beta, Gamma, Delta, and Omicron, have been reported till date [1]. Patients with COVID-19 may exhibit symptoms such as fever, coughing up expectorants, exhaustion, and shortness of breath, myalgia, rhinorrhea, sore throat, and diarrhoea. Sometimes the development of respiratory symptoms is preceded by a loss of taste or smell sensation. Atypical symptoms such as fatigue, diminished alertness, limited mobility, diarrhoea, loss of appetite, delirium, and absence of fever were found in immune-compromised hosts [1, 2]. The COVID-19 pandemic has been controlled mainly by testing for SARS-CoV-2 infections.

Studies suggest that COVID-19 vaccination can reduce the risk of mortality and hospitalization due to this disease [3]. As of November 2021, India had three vaccines approved against COVID-19 -(Covishield [ChAdOx1 nCoV-19; OxfordeAstraZeneca; manufactured by Serum Institute of India], Covaxin [BBV152; Bharat Biotech], and Sputnik V [Gam- COVID-Vac; Gamaleya Research Institute of Epidemiology and Microbiology] approved for emergency utilization. India’s vaccination drive picked up well from early 2021, mainly after the “second wave” of the pandemic in the country. Therefore, mass vaccination, in combination with the existing control measures, is one of the main elements of epidemic control.

NICE's definition of long Covid-19, also known as post-covid syndrome, is "signs and symptoms that develop during or after an infection consistent with Covid-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis." The post-acute COVID-19 syndrome, also known as extended COVID, is a term for the widely observed lingering symptoms, which also include fatigue, dyspnea, and chest pain. Data on the impact of SARS COV2 vaccination on Covid-19 infection symptoms are available. Post-covid syndrome is a term for these long-term physical and mental health effects, which can linger for more than three months after the initial infection. Data on virological traits and potential ongoing transmission risks, particularly of mildly symptomatic or asymptomatic SARS-CoV-2 post-vaccination infections, are still scarce because observational studies have mainly concentrated on end points like critical illness, the need for hospitalization, and death, the majority of them ignoring variation by particular vaccines [4]. Patients who continue to experience symptoms even after getting better from COVID-19 are increasingly

acknowledged as a rising population in need of treatment as we have fought various pandemic waves. Globally, survivors of COVID-19 have reportedly experienced effects on a variety of systems, including the cardiovascular, pulmonary, neurological, and neuropsychiatric systems. We must address and raise our understanding of the post-COVID-19 condition, which has been given its own section in the International Classification of Diseases (ICD). Recent studies have emphasized how the epidemic has affected people's mental health, as well as their physical health and other aspects of their quality of life [5-7]. The aim of the study was to investigate the severity and duration of post Covid-19 complications in vaccinated and unvaccinated people who got infected with SARS COV-2.

Materials and Methods

Materials and Methods

Study design and participants: It is a prospective study includes 1000 total number of cases. The study was conducted on 381 post-Covid syndrome patients. Among the 381 individuals, 101 were unvaccinated, 142 were taken first dose of vaccine and 138 were taken two doses of Vaccines. Among the 280 vaccinated individuals, 126 individuals had received Covaxin vaccine and 154 had received Covishield vaccine. Both IP and OP patients, who presented with Covid-19 symptoms to the Department of General Medicine, Tertiary Care Teaching Hospital, Hyderabad were included. The study was performed in the Molecular Virology Laboratory, Department of Microbiology, PMRIMS, Chevella. Informed consent was taken from each individual before the collection of swabs. The study was undertaken after obtaining approval from the Institutional Ethics Committee. All the patient demographic data like age, sex, and history of any illness have been collected. The details of the patient symptoms Fever, Cough, Tiredness, Loss of Taste and smell, Sore throat, Headache, Muscle pain, Rashes, Diarrhea and Shortness of breath were also included. The co-morbidities of the patients like Asthma, Diabetes, Clinical depression, Hypertension, Cancer and other conditions etc. were also studied.

Inclusion and Exclusion criteria: The study included all Post-Covid-19 syndrome individuals (both vaccinated and non-vaccinated). Children under ten years old and patients unwilling to consent were also excluded from the study. Individuals with mental or psychiatric severe issues and those with active tuberculosis were not allowed to participate in the study.

Post covid syndrome analysis:

This is a prospective study where data will be collected from individuals who are PCR confirmed covid19 infected patients diagnosed from December 2020 till november2021 patients from our tertiary care hospital will be included in this study contact information of patients will be available with us. After enrollment, PCR confirmed COVID 19 infected were allowed to complete a questionnaire with questions regarding socio-demographic details, contact information, symptoms when diagnosed with SARS CoV2, medical co- morbidities and risk factors, current health status and present symptoms. To assess the post COVID syndrome in the general population, questions regarding their recovery after infection, the duration they required to become symptom free, any persistent symptoms and other or new ongoing symptoms will be recorded by personal interview. Commonly reported symptoms in post-COVID syndrome include difficulty in breathing, fatigue, depression anxiety, stress, insomnia, weakness in arms and legs were also recorded. Depression scale assesses dysphoria, hopelessness, and devaluation of life, self-deprecation, and lack of interest/involvement. Anxiety scale assesses autonomic arousal, skeletal muscle effects, and

situational anxiety. Stress scale assesses difficulty relaxing, nervous arousal, easily upset, irritable, over reactive and impatient. Table 1 showed the score values for depression, anxiety and stress. The patients complaints of breathlessness, fatigue and difficulty in concentrating and mood changes will be further evaluated by using modified dyspnea Medical Research Council scale (Table 2). For FAS scale, score of 22 or more will be considered as threshold. For modified dyspnea Medical Research Council scale, Grade ≥ 1 dyspnea will be considered significant. For FAS scale, score of 22 or more will be considered as threshold. For DASS 21 scale, score for depression > 9 , score for anxiety > 7 and score for stress > 14 will be reported as significant (Table 3).

Table 1: Depression, anxiety and stress scores

	Depression	Anxiety	Stress
Normal	0-9	0-7	0-14
Mild	10-13	8-9	15-18
Moderate	14-20	10-14	19-25
Severe	21-27	15-19	26-33
Extremely severe	28	20	34

Table 2: Grade of dyspnea Symptoms

Grade 0	Not troubled by breathlessness expect on strenuous exercise
Grade 1	Shortness of breath when hurrying or walking up a slight hill
Grade 2	walks slower than contemporaries on the level because of breathlessness or has to stop for breath when walking at on place
Grade 3	Stop for breath after walking 100m or after a few minutes on the level
Grade 4	Too breathless to leave the house or breathless when dressing or undressing

Table 3: Fatigue scale

S.No	Fatigue scale questions	Never	Sometime	Regularly	Often	Always
1	I am bothered by fatigue (WHOQOL)	1	2	3	4	5
2	I get tired very quickly (CIS)	1	2	3	4	5
3	I don't do much during the day (CIS)	1	2	3	4	5
4	I have enough energy for everyday life (WHOQOL)	1	2	3	4	5
5	Physically I feel exhausted (CIS)	1	2	3	4	5
6	I have problems starting things (FS)	1	2	3	4	5

7	I have problems thinking clearly (FS)	1	2	3	4	5
8	I feel no desire to do anything (CIS)	1	2	3	4	5
9	Mentally, I feel exhausted	1	2	3	4	5
10	When I am doing something, I can concentrate quite well (CIS)	1	2	3	4	5

Results

Out of 1000 cases selected, a total of 381 patients completed the survey and satisfied the inclusion criteria. Among 381 cases, male were 234 and females were 147 (Figure 1). All were Covid-19 confirmed cases by antigen Test (Standard Q kit) and RT-PCR (PROMEA therapeutics). The test was performed by collecting the nasopharyngeal swab. Total 142 patients received at least one dose of SARS-COV 2 vaccine at the time of survey. 138 patients received 2 doses of vaccine and 101 were unvaccinated. The vaccinated and unvaccinated groups were comparable in terms of gender distribution and socioeconomic characteristics. The probability of developing post Covid-19 complications as positively associated with factors such as exposure to high viral load, severity of symptoms and duration of Covid-19. Unvaccinated is associated with a higher risk of developing post-Covid manifestations. Vaccination with at least 2 doses were asymptomatic at time of diagnosis compared to unvaccinated group and those who are symptomatic at baseline reported less symptoms compared with those unvaccinated individuals who received one dose were by large infected before being vaccinated. The major post-Covid symptoms in unvaccinated individuals were pains in legs and arms (97%) followed by fatigue (90.01%) (Figure 2). The major post-Covid symptoms in first dose vaccinated individuals were fatigue (87%) followed by pains in legs and arms (86%). The major post-Covid symptoms in second dose vaccinated individuals were hair loss (68%) followed by depression, anxiety and stress scale (58%) (Table4).

Figure 1: Gender-wise distribution of cases

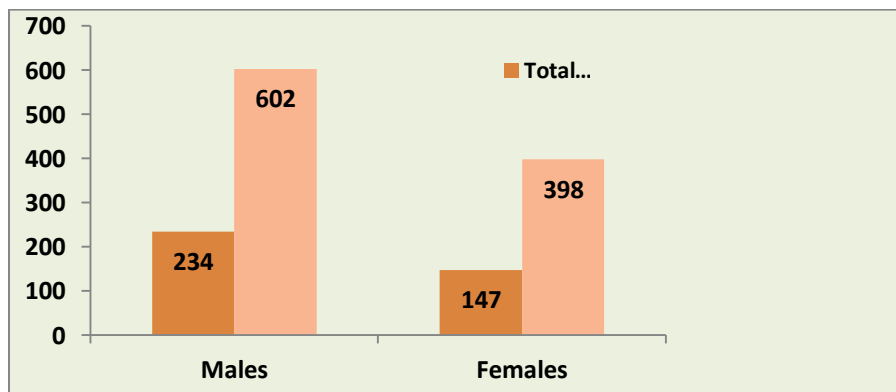
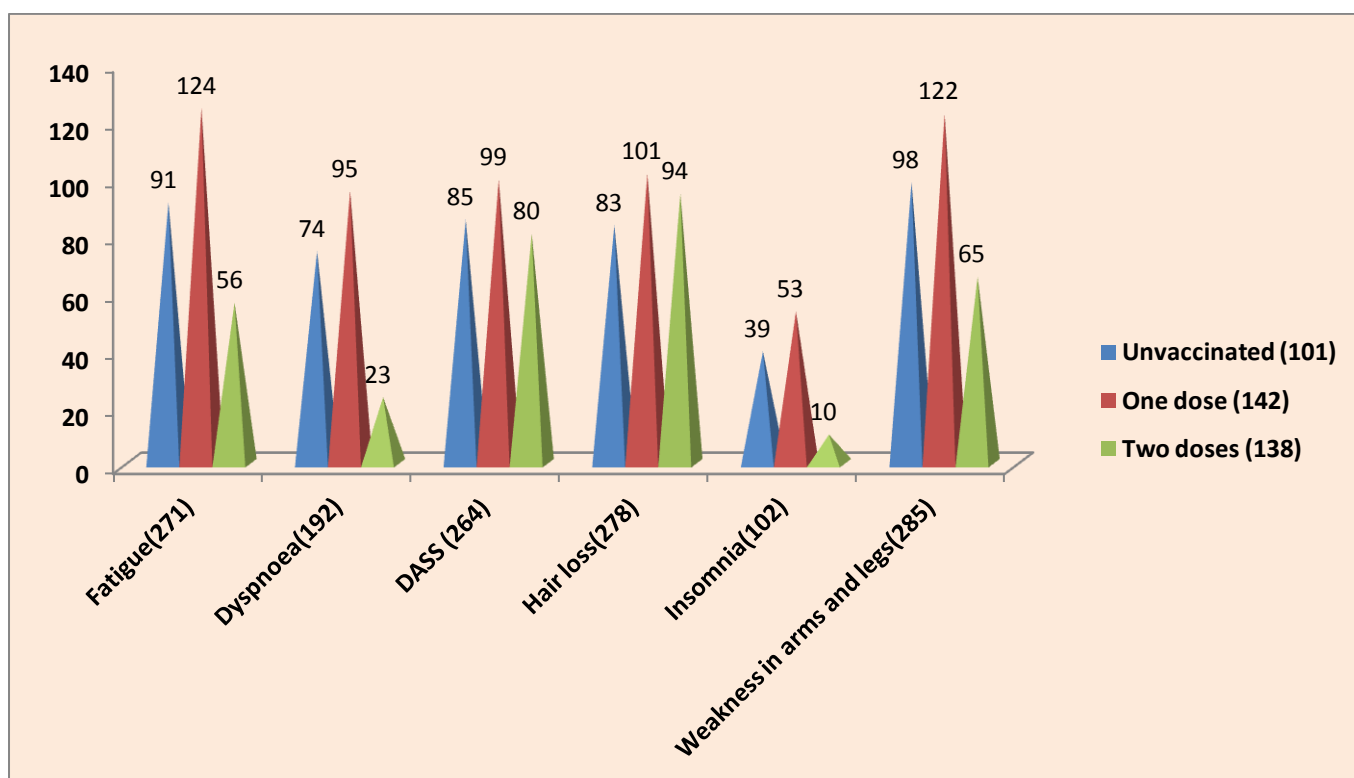


Table 4: Post-Covid symptoms in vaccinated and un-vaccinated individuals

Post-COVID symptoms (N=381)	Unvaccinated (101) 26.5%	1 st dose vaccine (142) 37.3%	2 nd dose (138) 36.2%
Fatigue (271)	91(90.01%)	124(87%)	56(41%)
Dyspnoea (192)	74(73.26%)	95(67%)	23(16%)
DASS scale (264)	85(84.15%)	99(70%)	80(58%)
Hair loss (278)	83(82%)	101(71%)	94(68%)
Insomnia (102)	39(38.61%)	53(37%)	10(7%)
Weakness in arms and legs (285)	98(97%)	122(86%)	65(47%)

Figure 2: Post-Covid symptoms in vaccinated and un-vaccinated individuals



Discussion

The conclusion that immunization might be utilized as a preventive strategy for lowering post-Covid symptoms was supported by numerous studies that showed vaccination decreased the chance of acquiring post-Covid-19 symptoms in patients affected with mild to moderate COVID-19. Two doses may be more beneficial than one, according to preliminary evidence. There have been incidences of post-vaccination breakthrough COVID-19 infections recorded,

despite the COVID-19 vaccines' accelerated approvals across the globe. The increase in SARS-CoV-2 Delta infections is evidence that those who have received vaccinations are nonetheless at risk for contracting illnesses. In the present study, there were 381 Covid-19 confirmed cases by antigen Test (Standard Q kit) and RT-PCR (PROMEA therapeutics). All the 381 subjects were suffered with post-Covid syndrome. Total 142 patients received at least one dose of SARS-COV 2 vaccine at the time of survey. 138 patients received 2 doses of vaccine and 101 were unvaccinated. The incidence of post-vaccination infection was largely consistent with earlier data [8-10]. Regarding the gender-based distribution of cases, we interpret the current investigation's findings that men experience a higher proportion of post-vaccination infections than women do, and the findings corroborate those of a prior study [11]. Despite the fact that the syndrome of post-acute sequelae of COVID is still poorly understood, the National Institutes of Health held a meeting in December 2020 to examine the most recent research on this syndrome and to identify any knowledge gaps. These syndrome symptoms, such as anosmia, respiratory problems like cough or dyspnea, sadness, anxiety, cognitive dysfunction, and/or exhaustion, may last for several weeks to months after acute COVID-19 has passed, in both vaccinated people and those who have not received the vaccine. This was demonstrated by Wisnivesky et al. 2022, who carried out a bigger prospective analysis of post-COVID patients and did not discover a significant difference in change in PASC symptoms or other objective measures between vaccinated and unvaccinated individuals. In the present study, the post-covid syndrome was seen more in fully vaccinated individuals (36.2%) than unvaccinated individuals (26.5%) [12]. The findings were in line with Tsuchida et al.'s conclusion that those who have a worsening of long-COVID symptoms after immunization are also those who exhibit an excessive immune response to vaccination, as evidenced by an elevated incidence of antibody titers [13]. In this short prospective trial, we found no evidence that COVID vaccination seemed to improve or alter the symptoms of Post-covid syndrome. The COVID vaccine is still crucial for extra immunological defence against reinfection, but it doesn't seem to help COVID-19 patients' post-COVID symptoms or other related symptoms. Additional research is needed to understand the mechanisms underlying Post-Covid symptoms and to identify effective treatments for these patients.

Conclusion

This study will aid in analyzing the effectiveness of COVID vaccination in the participants and guide us for further booster doses of vaccine administration and requirement. Double vaccinated participants as associated with reduced risk of reporting most of post acute COVID 19 symptoms. Our results suggest that vaccination may have a protective effect against long term Covid-19 symptoms.

References

1. Hu, B., Guo, H., Zhou, P. et al. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol* 2021;19:141–154. <https://doi.org/10.1038/s41579-020-00459-7>.
2. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020. <https://www.nice.org.uk/guidance/ng188>.
3. Mehdinezhad H, Karim B, Ahmadi N, Ahangar RM, Asadolahzadeh A, Haddad-Zavareh MS, Khoshkhou F, Qolami Z, Gorji NM, Delavar MA. Vaccination status and outcomes of COVID-19 patients admitted to a tertiary hospital in Iran during the dominant Delta variant period. *Immun Inflamm Dis*. 2023 Feb;11(2):e790. doi: 10.1002/iid3.790. PMID: 36840484; PMCID: PMC9950873.

4. Brunner-Ziegler S, Spath T, Kornek G, König F, Parschalk B, Schnetzinger M, Strauß RP, Savic R, Foit A, Resch H, Thalhammer F. Postvaccination infections among staff of a tertiary care hospital after vaccination with severe acute respiratory syndrome coronavirus 2 vector and mRNA-based vaccines. *Clin Microbiol Infect.* 2022 Apr;28(4):596-601. doi: 10.1016/j.cmi.2021.11.023. Epub 2021 Dec 13. PMID: 34915073; PMCID: PMC8667425.
5. Samlani Z, Lemfadli Y, Errami AA, Oubaha S, Krati K. The Impact of the COVID-19 Pandemic on Quality of Life and Well-Being in Morocco. 2020 Jun 24 [cited 2020 Sep 8]; Available from: <https://www.preprints.org/manuscript/202006.0287/v1>.
6. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun.* 2020 Oct;89:531-42.
7. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol.* 1989;46(10):1121-3.
8. Swift M.D., Breeher L.E., Tande A.J., Tommaso C.P., Hainy C.M., Chu H., et al. Effectiveness of messenger RNA coronavirus disease 2019 (COVID-19) vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a cohort of healthcare personnel. *Clin Infect Dis.* 2021;73 e1376–e9.
9. Haas E.J., Angulo F.J., McLaughlin J.M., Anis E., Singer S.R., Khan F., et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet.* 2021;397:1819–1829.
10. Tande A.J., Pollock B.D., Shah N.D., Farrugia G., Virk A., Swift M., et al. Impact of the COVID-19 vaccine on asymptomatic infection among patients undergoing pre-procedural COVID-19 molecular screening. *Clin Infect Dis.* 2021:ciab229. doi: 10.1093/cid/ciab229.
11. Pollett S.D., Richard S.A., Fries A.C., Simons M.P., Mende K., Lalani T., et al. The SARS-CoV-2 mRNA vaccine breakthrough infection phenotype includes significant symptoms, live virus shedding, and viral genetic diversity. *Clin Infect Dis.* 2021:ciab543. doi: 10.1093/cid/ciab543. Online ahead of print.
12. Wisnivesky JP, Govindarajulu U, Bagiella E, Goswami R, Kale M, Campbell KN, Meliambro K, Chen Z, Aberg JA, Lin JJ. Association of Vaccination with the Persistence of Post-COVID Symptoms. *J Gen Intern Med.* 2022 May;37(7):1748-1753. doi: 10.1007/s11606-022-07465-w. Epub 2022 Mar 9. PMID: 35266128; PMCID: PMC8906626.
13. Taquet M, Dercon Q, Harrison PJ. Six-month sequelae of post-vaccination SARS-CoV-2 infection: a retrospective cohort study of 10,024 breakthrough infections. *Brain, Behav, Immun.* 2022; 103: 154-162.