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Original Research Article

Long-COVID versus adverse event following COVID vaccination among students and staff of tertiary care teaching hospital

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ABSTRACT

Background: Long COVID is an important public health concern requiring proper defining, quantifying and describing following SARS-CoV infection with differentiation from adverse events due to COVID vaccination. So, this study was planned to analyze adverse effect of COVID19 vaccination or drug for COVID treatment versus consequences of COVID19 infection.
Methods: Self-reported data was collected through questionnaire-based survey by voluntary participation of healthcare staff. Percentage of participant developing various events was analyzed by enlisting sign, symptom, co-morbidity and medication history. Association between COVID-19 infection with number of doses of COVID-19 vaccine taken was analyzed by Chi Square Test with p value <0.05. Association between presence of specific sign, symptom after COVID infection or side effect after COVID vaccination was analyzed by Chi-Square Test with p value <0.05.
Results: Overall total 985 (59.58%) participants were analyzed and among them maximum number of participants (60.30%) reported as COVID-19 positive during the third wave with history of diagnosed COVID positive twice (57.87%). Participants with presence of co-morbidity were more likely to develop symptoms (p<0.001). On analysis, fever, body ache, headache, sore throat and fatigue were significantly more likely to develop after COVID infection as compared to after COVID vaccination (p<0.001).
Conclusions: This study by exploratory survey highlights heterogeneity of Long COVID sign or symptom that's seen predominantly in person with co-morbidity and a few of them were mimicking adverse events after COVID vaccinations.

Keywords: Adverse event following immunization, COVID19, Cross-sectional study, Healthcare staff, Long COVID

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first time notified in China in December 2019 but a systematic review concluded that there is currently insufficient evidence to provide precise definition of Long COVID Symptom and prevalence.[1,2] As per WHO "symptoms of post COVID-19 condition can persist from the initial illness or begin after recovery. The symptoms and effects of post COVID-19 condition can only be explained when other conditions with similar symptoms as post COVID-19 condition have been ruled out through a medical diagnosis and these symptoms may also change over time".[3] Although exceptional efforts from the scientific and medical community have been directed to sequence, diagnose, treat, and prevent COVID-19, individuals' long lasting effects after the acute phase of the disease are yet to be revealed.[4] COVID-19 can involve multiple systems and organs with persistence medical complications that last weeks to months after initial recovery.[5,6] The terminology to describe prolonged symptoms following COVID-19 illness has been described by different authors, such as "Long COVID-19", "post-acute COVID-19", "persistent COVID-19 symptoms", "chronic COVID-19", "post-COVID-19 manifestations", "long-term COVID-19 effects", "post COVID-19

syndrome", "ongoing COVID-19", "long-term sequelae", or "long-haulers" as synonyms. Most recently, terms like "post-acute sequelae of SARS-CoV-2 infection" (PASC), "long-COVID-19", and "post-acute COVID-19".[5,7-9] Symptoms, signs, or abnormal clinical parameters persisting two or more weeks after COVID-19 onset that do not return to a healthy baseline can potentially be considered long-term effects of the disease. Although such findings are mainly reported in severe and critical disease survivors, the lasting effects also occur in individuals with a mild infection who did not require hospitalization.[10-12] On the other hand, adverse events following immunization (AEFI) after receiving a COVID-19 vaccine is also important to distinguish the difference from the longstanding effects of COVID-19. Therefore, our study aimed to perform a qualitative questionnaire-based survey and analysis of self-reported case information by healthcare staff of the tertiary care teaching hospital, to enlist percentage of all the symptoms, signs, or abnormal laboratory parameters extending beyond the acute phase of COVID-19 and their association analysis with identification of predisposing and preventing factors.

METHODS

This is a questionnaire-based study was carried out after voluntary participation of MBBS students and faculties.

Aim and objectives

This study was carried out with an aim of identification of difference between long term complications of COVID19 virus infection, Long COVID (signs and symptoms) versus complication of COVID19 vaccination among faculties and medical students with identification of factors preventing (e.g., vaccination) or aggravating (e.g. co-morbidity) specific symptoms and sign.

Objectives of this study were to identify post COVID signs and symptoms after recovery from COVID-19 RTPCR or rapid antigen test (RAT) positive state, to identify adverse event following immunization (AEFI) - signs and symptoms after vaccination for prevention of COVID-19, to analyze association between COVID Infection during first, second or third wave were analyzed with number of dose of COVID-19 vaccine taken to analyze association between presence or absence of specific sign or symptom or AEFI after COVID infection as compared to after COVID vaccination.

Study type, location and duration

Cross sectional questionnaire based qualitative study. Study was carried out by approaching to all medical (UG+ PG) students, interns and faculties of a tertiary care teaching hospital – Medical College and S.S. G. Hospital, Baroda, Vadodara.

Six Months duration (i.e., from 1st September 2022 to 28th February 2023)**.** Identity of participants and their data about filled questionnaires was kept confidential during data analysis and publication phase. Participants with specific sign or symptoms affecting daily life were referred to the concerned Specialist Doctor of the same tertiary care teaching hospital.

Inclusion criteria

Study was carried out by approaching all medical (UG+ PG) students and staff of Medical College and SSG Hospital Baroda (Tertiary Care Teaching Hospital of Baroda) who will voluntarily participate in the study. All Medical (UG+ PG) students and faculties of tertiary care teaching hospital, ready to participate in study voluntarily irrespective of their COVID positive status were included.

Exclusion criteria

Medical (UG+ PG) students and staff of tertiary care teaching hospitalwho were; Not ready to participate in study voluntarily and never vaccinated for COVID19 were excluded.

Sample size & sampling method

We had followed cluster sampling method and approached only medical (UG+ PG) students and faculties out of all population of college and hospital who got ready to participate in our study voluntarily. As the prevalence of Long COVID was not clearly defined, we had approached all medical (UG+ PG) students and faculties over a period of six months.

Study tool -questionnaire

Participants were analyzed for the following parameters by asking pre validated Questionnaire on "Post COVID-19 Syndrome versus Adverse Event After COVID vaccination" Demographic profile: Age, Gender, Designation, Academic Qualification.

Questions related to COVID19 Infection: Number of times diagnosed COVID positive by Rapid Antigen Test or RT-PCR COVID Positive by Rapid Antigen Test or RT-PCR report during First Wave (30 January 2020 to 15th Feb 2021), Second Wave (16th Feb 2021 to 15th December 2021), and Third Wave (After 16th December 2021), Pre-existing comorbidity before detection of COVID infection first time, Development of chronic disease like Asthma or COPD after recovery from COVID, Any history of injury or trauma after recovery from COVID Infection, Development of one or more symptoms/sign or diagnosis mentioned below after recovery from COVID, History of medicines taken during and or after recovery from COVID19.

Questions related to COVID19 vaccination

Number of dose/s of COVID Vaccine taken, Type of COVID vaccine taken and Development of one or more

symptoms/sign or diagnosis after any dose of COVID vaccination

Data collection methods

Questionnaire based study was carried out by approaching medical students and staff (faculties) of medical college and SSG Hospital Baroda. The survey question was shared online - posted by the study authors by social media by WhatsApp groups of medical students, interns, and faculties. The social media post contained brief information about the study, eligibility criteria and a link to the questionnaire. Participants gave their consent by answering 'yes' to a consent question. Students was approached by giving hard-copy or online web-link to fill up questionnaires after their lecture or practical (Except exam period).

Medical Staff/Medical Teachers was approached after their departmental meeting like case presentation/seminar /journal club. If one is not approachable by single visit, we had approached maximum 3 times over a period of one week gap at various departments. Participants' consent to participate voluntarily was taken offline or online after due information of benefits of this study by giving them Participant's Information Sheet. Participants were given option to fill up questionnaire by offline or online mode. Offline filled questionnaire was entered in Google Form and analysis of filled information will be done from Excel Sheet and free version of GraphPad Software. Qualitative analysis of post Covid Sign and symptom was done and descriptive case series was presented as a percentage of symptoms and sign in participants due to history of Covid positive status. Analysis of data was done as per vaccinated status, type of Covid infection (e.g. Covid positive during wave 1 or wave 2 or wave 3 in India), co-morbidity or multiple vaccination status. Participants with specific sign or symptom of concern were informed to consider for further evaluation and treatment by liaison with Medicine Department.

Analysis of data was done as per age, gender, COVID Infection as per wave in India e.g. COVID Positive during First Wave (30 January 2020 to 15th Feb 2021), Second Wave (16th Feb 2021 to 15th December 2021), and Third Wave (After 16th December 2021), co-morbidity, multiple infection status and vaccinated status. Participants with specific sign or symptom of concern were informed to consider for further evaluation and treatment with SpecialistDoctor/s.

Statistical analysis

Analysis of Qualitative data was done by percentage of participant developing various symptoms 14 days after COVID positive state. Analysis of Qualitative data was done by percentage of participant developing various symptoms after COVID vaccination.

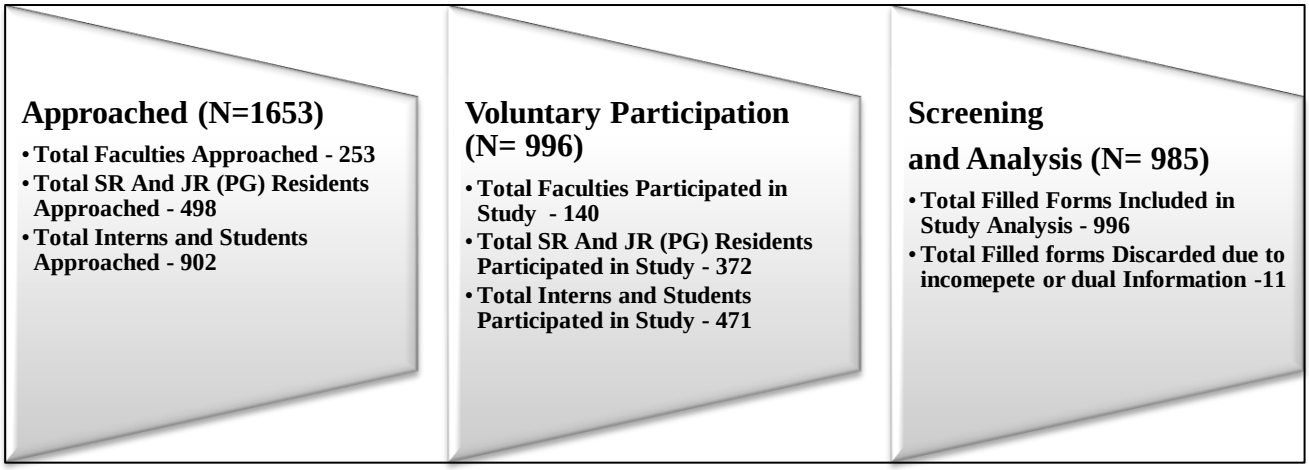

Figure 1: Enrolment of participant faculties and medical students with screening of filled forms.

Preventive factor analysis

Association between COVID Infection during first, second or third wave were analyzed with number of doses of COVID19 vaccine taken by Chi square test with association analysis at significance level of p value <0.05. Association between vaccinated status with presence or absence of specific AEFI (sign or symptom) was analyzed by Chi square test with association analysis at significance level of p value <0.05.

Aggravating factor analysis

Association between co-morbidity with presence or absence of specific Long COVID - sign or symptom was analyzed by Chi square test with association analysis at significance level of p value <0.05.

RESULTS

Overall, out of the total of 1653 healthcare staff members approached, 996 (60.25%) filled out the forms. After screening, a total of 985 participants (59.58%) were included in the final analysis, and 11 forms were removed from the analysis due to incompletely filled forms.

Looking at age-wise distribution of participants, majority of participants were between 18 to 36 years' age group. As per designation-wise distribution of participants, Medical Students (35.33%), Intern Doctors (12.49%) and Junior Residents (33.10%) comprised of predominant groups of participants followed by participation of faculties.

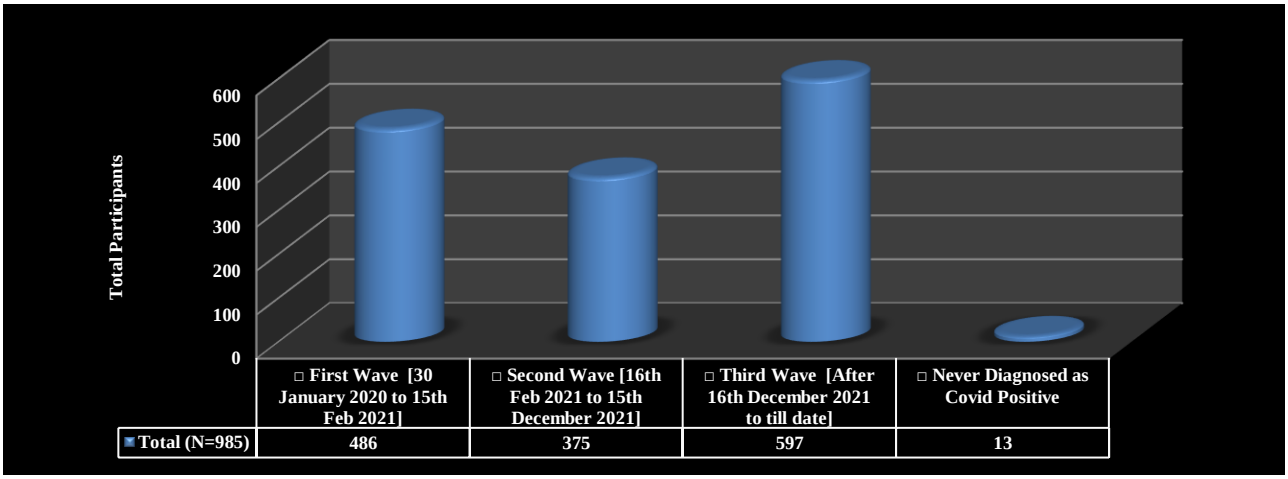

Figure 2: The time periods during which participants were diagnosed as COVID positive using either by Rapid Antigen Test (RAT) or RT-PCR lab test.

Table 1: Information related to the diagnosis of COVID-19 and the occurrence of COVID-19 or flu-like symptoms among the participants (n=985).

Question. How many times you were diagnosed COVID Positive by "Rapid Antigen Test" or "RT PCR"?	N	%
Once	329	33.40
Twice	570	57.87
Three times	71	7.21
>Three times	2	0.20
Never	13	1.32
Total	985	100.00
If your answer is "Never" then ... Have you ever suffered from "COVID or Flu Like Symptoms" during past 3 years (2020, 2021 or 2022) ? (Optional)		Total 13 Participants reported that they were never diagnosed COVID Positive by "Rapid Antigen Test" or "RT PCR"?
Yes		9
No		4

Table 2: Information related to the pre-existing co-morbidities among participants before the detection of their first COVID infection (n=985).

Question. Were you having any pre-existing co-morbidity before detection of COVID infection first time? (multiple options can be selected)	N	%
Diabetes mellitus	44	4.47
Hypertension	58	5.89
Tuberculosis	1	0.10
Obesity or overweight	5	0.51
Chronic heart disease	0	0.00
Chronic Kidney Disease (CKD)	0	0.00
Osteo-arthritis	3	0.30
Asthma	8	0.81
None of the above	866	87.92
Other	0	0.00

In response to a question about number of times detected positive for COVID-19 by "Rapid Antigen Test" or "RT PCR", the majority of participants (57.87%) reported being diagnosed as COVID positive twice during COVID pandemic. A significant proportion of participants (33.40%) reported being diagnosed as COVID positive once. A small number of participants reported being diagnosed as COVID positive three times (7.21%) or more than three times (0.20%). Overall, one person could be detected COVID positive once, twice or multiple times as per development of herd immunity. Here, majority of participants (60.30%) reported being diagnosed as COVID positive during the third wave, which occurred after 16th December 2021 and the remaining participants (49.34%) reported being diagnosed as COVID positive during the first wave (30th January 2020 to 15th February 2021). On the other hand 38.07% of participants reported being COVID positive diagnosis during second wave (16th February 2021 to 15th December 2021).

Table 3: Participants reported Post COVID signs and symptoms after recovery from COVID-19 RTPCR / Rapid Antigen positive state (n=985).

Question: Did you suffer from anyone or more symptoms / sign or diagnosis as mentioned below after recovery from COVID? (Multiple Options can be selected)	N	%
Sore throat	902	91.57
Fever (continuous/intermittent)	824	83.65
Cough	789	80.1
Headache (bilateral/unilateral/ tension type/ frontal/ occipital)	765	77.66
Bodyache/myalgia/muscle pain	548	55.63
Fatigue/weakness	269	27.31
Ageusia/loss of taste/ altered taste sensation	154	15.63
Insomnia	89	9.04
Dyspepsia/gastritis	76	7.72
Dyspnea/breathlessness	63	6.4
Weight gain	49	4.97
Anosmia/loss of smell /smell disorder	46	4.67
Exercise intolerance	46	4.67
Dizziness/Giddiness	36	3.65
Joint pain/arthralgia	26	2.64
Weight loss	16	1.62
Hypersomnia	14	1.42
Anxiety	5	0.51
Chest pain	4	0.41
Skin rash	4	0.41
Difficult to Swallow	3	0.3
Depression	0	0
Obsessive–compulsive disorders	0	0
Memory loss/memory complaints (short term/ long term/ both)/forgetfulness	0	0
Difficulty in concentration	0	0
Mucormycosis	0	0
Hearing loss/ tinnitus	0	0
Pedal edema	0	0
Avascular necrosis (AVN) of hip Joint	0	0
None of the above	0	0
Other	0	0

The most commonly reported pre-existing co-morbidity was hypertension in 58 (5.89%) participants followed by Diabetes mellitus in 44(4.47%) participants. Other pre-existing co-morbidities, such as tuberculosis, obesity or overweight, osteoarthritis, and asthma, were reported by a relatively smaller number of participants. On statistical analysis by Chi Square test, significantly more number of participants with co-morbidity had developed cough ($\chi2=41.4$; df =1; p value <0.001), body-ache ($\chi2=177.33$; df =1; p value <0.001) and fever ($\chi2=38.9$; df =1 ; p value <0.001). Only two participants reported that they developed new onset asthma or COPD (chronic obstructive pulmonary disease) after recovery from COVID, regardless of the wave they were infected. On the

other hand, four (0.41%) participants had reported that they had experienced injury or trauma after recovering from the COVID infection. The majority of participants (99.59%) responded that they had not experienced any injury or trauma after recovering from COVID-19. In response to the question related to symptoms, signs, or diagnoses experienced by participants after recovering from COVID, the most commonly reported persistent symptoms/signs, or diagnosis was sore throat, followed by fever, cough, and headache.Other commonly reported symptoms were body ache, fatigue - weakness, ageusia/ loss of taste/altered taste sensation, insomnia, dyspepsia/gastritis,dyspnea/breathlessness, weight gain, exercise intolerance, anosmia/loss of smell/smell disorder, dizziness/ giddiness, joint pain/arthralgia, weight loss, followed by hypersomnia.

Table 4: Information on the medicines taken by the participants during COVID management or after recovery from COVID-19 (n=985).

Question. Please tick-mark all the Medicines those were taken during COVID Management or after Recovery from COVID19?	N	%
HydroxyChloroquine	43	4.37
Remdesivir	86	8.73
Azithromycin	189	19.19
Favipiravir	2	0.20
Ivermectin	31	3.15
Paracetamol	904	91.78
Cetrizine	846	85.89
Pheniramine Maleate	403	40.91
Steroid (Betamethasone/Dexamethasone)	28	2.84
Montelukast	164	16.65
Salbutamol	6	0.61
Ipratropium Bromide	5	0.51
Codeine	3	0.30
Dextromethorphan	821	83.35
Vitamin C	950	96.45
Vitamin D	187	18.98
Zinc	249	25.28
B -12	165	16.75
Calcium	124	12.59
Aspirin	356	36.14
Clopidogrel	16	1.62
Heparin / LMWH	4	0.41
None of Above/Never detected COVID Positive	13	1.32
Other	0	0.00

Participants were asked to select multiple options from the provided list of medicines that they took during COVID management or after recovery. The most commonly reported medicine taken by participants was paracetamol (91.78%) followed by cetrizine (85.89%), pheniramine maleate (40.91%), and dextromethorphan (83.35%). Some participants reported taking antibiotics such as azithromycin (19.19%) and ivermectin (3.15%). Vitamins and supplements such as vitamin C (96.45%), vitamin D (18.98%), zinc (25.28%), and B-12 (16.75%) were also reported by a significant number of participants. Medicines such as hydroxychloroquine, remdesivir, favipiravir, and salbutamol were taken by a smaller percentage of participants. Additionally, vitamins and supplements such as vitamin C, vitamin D, zinc, and B-12 were also taken by majority of participants.

The majority of participants being healthcare staff and students 85.48% (845 participants), have taken three doses i.e. first dose, booster dose and precaution dose of COVID19 vaccine and the remaining participants 14.52% (143) had taken two doses i.e. first dose and booster dose of COVID19 vaccine. On statistical analysis by Chi Square Test, significantly less number of participants developed COVID Infection who had taken extra dose/ precaution dose of COVID19 vaccine ($\chi 2=21.71$; df =2; p value <0.001). In answer to question regarding type of COVID vaccine taken by the participant healthcare staff, the majority of participant healthcare staff 974(98.88%), reported history of vaccination by Covishield vaccine.

A smaller percentage of participants 11 (1.12%), reported receiving Covaxin vaccine. (Table 6) presents the symptoms, signs, or diagnoses experienced by participants after receiving any dose of the COVID vaccination. In answer to question on adverse event after vaccination, the most commonly reported symptom after vaccination was pain or soreness at the injection site (76.75%) followed by fever (32.89%), body-ache, muscle pain, or myalgia (19.19%), and headache (12.79%). A smaller percentage of participants reported symptoms such as nausea (1.32%), vomiting (2.23%), sore throat (1.02%), and anosmia (0.30%). Participants have not reported adverse event like dyspnea or breathlessness, anxiety, anaphylaxis, diarrhoea, brain fog or clouding, a confused state, or swollen lymph nodes. A small percentage of participants reported joint pain (0.20%), skin rash (0.30%), and dizziness (1.22%). As per statistical analysis by Chi Square Test, in the same group of participants fever, bodyache, headache, sorethroat and fatigue were significantly more likely to develop after COVID infection as compared to after COVID vaccination ($\chi 2=307.88$; df=4; p value <0.001).

DISCUSSION

As the COVID-19 pandemic continues to impact individuals worldwide, it is crucial to understand the long-term effects of the disease or the potential adverse reactions possibly associated due to medication or vaccination. We have tried to identify the difference between long-term sequelae of COVID-19 virus infection versus adverse event of medication or COVID vaccination. “Long COVID” term also presents with long-term residual symptoms defined as symptoms/sign ranging from 14 to 120 days post-viral infection.[13-15] In some studies, Long COVID sequelae were observed in 35-87% of participants

up to 6 months post-onset.[16,17] There are various international cohort studies to do follow-up after COVID-19 infection after recovery, but COVID vaccine-induced side effects requires identification and differentiation of further pathological consequences due to COVID virus infection versus antibody related immune cross reaction towards body tissue. In clinical trials, the vaccine was reported to be 93.2% effective in preventing COVID-19 illness and 98.2% effective in preventing severe disease.[18]

Table 5: Analysis of COVID positivity during first, second and third wave after COVID vaccination (n=985).

Number of dose/s of COVID vaccine taken by participant	Positive during first wave O (E), $[(O-E)^2/E]$	Positive during second wave O (E), $[(O-E)^2/E]$	Positive during third wave O (E), $[(O-E)^2/E]$	Row Totals
Only two doses	156 (187.85), [5.40]	189 (180.89), [0.36]	278, (254.26), [2.22]	623
Two doses+precaution dose	141 (109.15), [9.29]	97 (105.11), [0.63]	124, (147.74) [3.81]	362
Total	297	286	402	985

$\chi 2 = 21.71$; df =2; p value <0.001

Table 6: Participant reported adverse event following immunization signs and symptoms after vaccination for prevention of COVID-19 (n=985).

Did you suffer from anyone or more symptom /sign or diagnosis as mentioned below after any dose of COVID vaccination? (Multiple Options can be selected)	N	%
Fever	324	32.89
Headache	126	12.79
Nausea	13	1.32
Vomiting*	22	2.23
Bodyache / Muscle Pain / Myalgia	189	19.19
Fatigue / Weakness	43	4.37
Pain/soreness at injection site	756	76.75
Sore Throat	10	1.02
Anosmia	3	0.30
Dyspnea / Breathlessness	0	0.00
Anxiety	0	0.00
Joint Pain	2	0.20
Skin Rash	3	0.30
Anaphylaxis	0	0.00
Diarrhea	0	0.00
Dizziness	12	1.22
Brain fog /Clouding /Confusion State	0	0.00
Swollen Lymph Nodes	0	0.00
None of the above	59	5.99
Other	0	0.00

Table 7: Statistical analysis of commonly reported long COVID vs. AEFI.

Symptoms	After COVID Infection O (E), $[(O-E)^2/E]$	After COVID Vaccination O (E), $[(O-E)^2/E]$
Fever	824 (949.40), [16.56]	324 (198.60), [79.17]
Body-ache	548 (609.50), [6.21]	189 (127.50), [29.66]
Head-ache	765 (736.86), [1.07]	126 (154.14), [5.14]
Sore-throat	902 (754.22), [28.95]	10 (157.78), [138.41]
Fatigue (Weakness)	269 (258.02), [0.47]	43 (53.98), [2.23]

$\chi 2 = 307.88$; df =4 ; p value <0.001

Long COVID was poorly understood due to newer viral induced epidemic and as per online search database, only a few studies have conducted a large-scale investigation globally regarding COVID-19 sequelae, and we could not

found study has examined both the protective effect of vaccine or risk factors for each persisting symptom together.[19] In our study, out of the total of 1,653 healthcare staff members approached, 996 (60.25%) filled out the forms. After screening, a total of 985 participants (59.58%) were included in the final analysis. Overall maximum numbers of participation were from "Interns and MBBS Students" category. Majority of the participants were of age group around 20, while the age group of "18-24" comprises the largest number of participants, followed by age group of "25-30". In our study there was a maximum participation of M.B.B.S. students, followed by post M.B.B.S. junior residents, followed by "M.D." and "M.S." faculties and senior residents as participants. Analyses of answers reported by participants have shown that the majority of participants (57.87%) were diagnosed as COVID positive twice. In spite of being vaccinated, the majority of participants (60.30%) reported being diagnosed as COVID positive during the third wave when there was predominant Omicron variant of COVID19, which occurred after 16th December 2021 that supports immune escape theory, mutation theory of Omicron variant and protective effect of vaccine to prevent severe disease.[20,21]

Overall, significantly a smaller number of participants had developed COVID Infection during all three waves if they had taken extra dose / precaution dose of COVID19 vaccine.

In our study, most commonly reported persistent symptoms/ signs/ diagnosis were sore throat (91.57%), followed by fever (83.65%), cough (80.10%), and headache (77.66%). Other commonly reported symptoms included body ache/myalgia/muscle pain (55.63%), fatigue and weakness (27.31%), anosmia/loss of smell/smell disorder (4.67%), and exercise intolerance (4.67%). On statistical analysis by Chi Square test,

significantly more number of participants with co-morbidity had developed cough, body-ache and fever. A smaller proportion of participants reported dyspnea or breathlessness (6.40%), insomnia (9.04%), weight gain (4.97%) and GIT complaints like dyspepsia, abdominal pain and gastritis for one month after recovery from COVID19. As per single UK centre case series for identification of residual gastrointestinal symptoms by COVID-19 infection, 6 months after the acute illness, 21 out of the 48 (43.8%) had developed with new GI symptoms, with abdominal pain affecting 14 (29.2%), diarrhoea nine (18.8%), constipation five (10.4%), nausea five (10.4%), and dyspepsia 14 (29.2%) since their COVID-19 illness.[22]

Another systematic review and meta-analysis for identification of gastrointestinal manifestations of long COVID has reported that "GI symptoms in patients were seen in 12% after COVID-19 and 22% as part of long COVID. Overall, loss of appetite, dyspepsia, irritable bowel syndrome, loss of taste, and abdominal pain were the five most common GI symptoms of long COVID.[23] In our study, none of the participants had reported any sign or symptom related to depression, obsessive-compulsive disorders, memory loss/memory complaints, difficulty in concentration, mucormycosis, hearing loss or tinnitus, pedal edema, avascular necrosis of the hip joint, or any other symptoms. As per other study, reported neuropsychiatric manifestations as a Long COVID among 200 hospitalized patients with severe-to-critical COVID-19 infection, it was found that at 4-7 months from disease-onset,significant proportion of patients experienced fatigue (53.5%), decreased mobility (37.5%) and pain (36.8%). Further neuropsychiatric symptoms included cognitive difficulties, mainly in concentration and short-term recall (12.5%), sleeping disturbances (14.6%), while 12.2% of patients became frail.[24] In another study, similar Long COVID symptoms were detected like fatigue, dyspnea, joint pain, cough, dysgeusia, anosmia, headache, sputum production, and diarrhea, but they were highly variable and different according to their occurrence and the time elapsed from their onset.[25,26]

In our study, analysis about the type of COVID vaccine taken by the participant healthcare staff has shown that the majority of participants (98.88%) had taken Covishield vaccine. Being healthcare staff, none of the participants reported being unvaccinated andany other vaccine types recipient wasnot identified. Adverse Event Following Immunization (AEFI) after COVID vaccine was analyzed and the most commonly reported symptom after vaccination was pain or soreness at the injection site (76.75%). Other frequently reported symptoms were fever (32.89%), bodyache, muscle pain, or myalgia (19.19%), and headache (12.79%). A smaller percentage of participants reported symptoms such as nausea (1.32%), vomiting (2.23%), sore throat (1.02%), and anosmia (0.30%).

As per statistical analysis by Chi Square Test, same group of participants were significantly more likely to develop fever, body ache, headache, sore throat or fatigue after COVID infection as compared to after COVID vaccination. There are doctors and students who reported a history of COVID positive status more than twice during all three waves. So those groups of participants require further study regarding decreasing severity of disease and advantage of vaccination as per participants reported feedback. Any new symptom sign after COVID19 Infection or COVID19 vaccination cannot be conclusively correlated due to COVID19 infection, immune reaction or adverse drug reaction with due consideration of pre-existing or newly developed acute or chronic disease, non-communicable or communicable disease, various physiological condition (e.g., osteoarthritis related to aging).[27] However, further study in the form of systematic review and meta-analysis of randomized clinical trial can help further to understand each symptom, sign or disease separately and in conjunction COVID-19, treatment

related to adverse drug reaction or adverse event following immunization after vaccination for COVID-19.

CONCLUSION

This study by exploratory survey highlights heterogeneity of long COVID sign or symptom that's seen significantly more in person with co-morbidity. We found a pattern of recurrence of COVID-19 infection and a few Long COVID sign or symptom were mimicking adverse events after taking booster and precaution dose of COVID vaccine.

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REFERENCES

1. Xiong Q, Xu M, Li J. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clin Microbiol Infect. 2021;27(1): 89-95.
2. Michelen M, Manoharan L, Elkheir N. Characterising long-term covid-19: a rapid living systematic review. MedRxiv. 2020.
3. Coronavirus disease (COVID-19): Post COVID-19 condition. Available at: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-post-covid-19-condition?gclid=EAIaIQobChMIrYWb8cCpgAMVFBmDAx0Ueg7WEAAYASAAEgImaPD_BwE. Accessed on 20 February 2023.
4. Hannah REO-O, Diana B, Edouard M, Joe H, Bobbie M, Charlie G, et al. Coronavirus Pandemic (COVID-19). 2021. Clin Microbiol Infect. 2020;26(3):145-9.
5. Townsend L, Dowds J, O'Brien K. Persistent Poor Health Post-COVID-19 Is Not Associated with Respiratory Complications or Initial Disease Severity. Ann Am Thorac Soc. 2021.
6. Vink M, Vink-Niese A. Could Cognitive Behavioural Therapy Be an Effective Treatment for Long COVID and Post COVID-19 Fatigue Syndrome? Lessons from the Qure Study for Q-Fever Fatigue Syndrome. Healthcare. 2020;8(4):32-8.
7. Lamprecht B. Is there a post-COVID syndrome?. Pneumologe, 2020;3:1-4.
8. Kingstone T, Taylor AK, O'Donnell CA, Atherton H, Blane DN, Chew-Graham CA. Finding the 'right' GP: a qualitative study of the experiences of people with long-COVID. BJGP. 2020;4(5):32-9.
9. Ngai JC, Ko FW, Ng SS, To KW, Tong M, Hui DS. The long-term impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. Respirol. 2010;15(3):543-50.
10. Gemelli A. Post-COVID-19 global health strategies: the need for an interdisciplinary approach. Aging Clin Exp Res. 2020;32(8):1613-20.
11. Greenhalgh T, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute COVID-19 in primary care. BMJ. 2020;370:3026.
12. Goertz YMJ, Van Herck M, Delbressine JM. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ. 2020;6(4):32-8.
13. Shah W, Hillman T, Playford ED, Hishmeh L. Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. BMJ. 2021;372:136.
14. Mahase E. COVID-19: what do we know about "long covid"?. BMJ. 2020;370:2815.
15. Callard F, Perego E. How and why patients made long Covid. Soc Sci Med. 2021;268:113-26.
16. Halpin SJ. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. J Med Virol. 2021;93:1013-22.
17. Huang C. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397:220-32.
18. El Sahly HM, Baden LR, Essink B, Doblecki-Lewis S, Martin JM, Anderson EJ, et al. Efficacy of the mRNA-1273 SARS-CoV-2 vaccine at completion of blinded phase. N Engl J Med. 2021;385(19):1774-85.
19. Miyazato Y. Prolonged and late-onset symptoms of coronavirus disease 2019. Forum Infect Dis. 2020;7: 507.
20. Ao D, Lan T, He X, Liu J, Chen L, Baptista-Hon DT. SARS-CoV-2 Omicron variant: Immune escape and vaccine development. Med Comm. 2022;3(1):e126.
21. Keeton R, Tincho MB, Ngomti A. T cell responses to SARS-CoV-2 spike cross-recognize Omicron. Nature. 2022.
22. Cooney J, Appiahene P, Findlay R, Al-Hillawi L, Rafique K, Laband W, Shandro B, Poullis A. COVID-19 infection causing residual gastrointestinal symptoms - a single UK centre case series. Clin Med. 2022;22(2):181-3.
23. Choudhury A, Tariq R, Jena A, Vesely EK, Singh S, Khanna S, et al. Gastrointestinal manifestations of long COVID: A systematic review and meta-analysis. Therap Adv Gastroenterol. 2022;15:175.
24. Gautam N, Madathil S, Tahani N, Bolton S, Parekh D, Stockley J, et al. Medium-term outcome of severe to critically ill patients with Severe Acute Respiratory Syndrome Coronavirus 2 Infection. Clin Infect Dis. 2021;74:301-8.
25. Wang, X. et al. Clinical features and outcomes of discharged coronavirus disease 2019 patients: a prospective cohort study. Q J Med. 2020;113:657-65.
26. Tenforde MW, Kim SS, Lindsell CJ. Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a

Multistate Health Care Systems Network - United States, March-June 2020. Morb Mortal Wkly Rep. 2020;69(30):993-8.
27. O'Mahoney LL, Routen A, Gillies C. The prevalence and long-term health effects of Long Covid among hospitalised and non-hospitalised populations: A systematic review and meta-analysis. Clin Med. 2022; 55:101762.

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