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Post COVID-19 Manifestations: An Observational Study in a Tertiary Care Hospital in Eastern India

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ABSTRACT

Background: Post-COVID-19 problems now exist worldwide with a significant number of mortalities, morbidity and incapacity. In this study, we evaluate the pervasiveness of post-COVID-19 syndrome given the different age groups and gender. Complications if present were documented and grouped.

Materials and Methods: Five hundred hospitalized patients during the mid episode of COVID-19 infection were observed for 15 months after being recovered and discharged from the hospital to find out any health problems related to COVID-19. We could collect health-related information of 500 such patients after our effort to communicate with 1670 patients

Result: Out of those 500 post-COVID-19 individuals 279 (55.8%) were normal, 48 (9.6%) persons expired and 173 (34.6%) had complications. Post-COVID-19 persons above 60 years of age were found to have more post-COVID-19 complications and a higher mortality rate. Among those males were predominant than females. Amongst different complications extreme weakness, lung problems, psychological difficulties and increased suffering from preexisting systemic diseases were found more common.

Conclusion: Death and complications in post-COVID-19 cases were found in a significant number of cases. However, most of them did not complete the full course of the COVID-19 vaccine indicating a positive role of COVID-19 vaccination in preventing post-COVID-19 syndrome conditions. Future research is needed for a better understanding of the mechanism of post-COVID-19 complications and death.

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Introduction

COVID-19 was declared a pandemic by The World Health Organisation on March 11, 2020. The first case of COVID-19 infection was reported in Wuhan, China in December 2019. In India, the first case was identified in Kerala on January 27, 2020, and in West Bengal state the first case was found on 17 March 2020 in Kolkata. COVID-19 disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a heterogeneous virus that has a wide range of symptoms, from asymptomatic to life-threatening and fatal disease, had devastating consequences on the global inhabitants. The clinical manifestations and mortality of COVID-19-positive patients have been well characterized, while there are concerns regarding post-acute sequelae of COVID-19 [1, 2].

Studies have shown that a large number of infected patients recovered from the initial phases of COVID-19 disease. However, current evidence suggests, that a considerable proportion of patients who have been infected with the virus continue to

have persistent symptoms and/or delayed complications with a duration beyond the initial episode of infection or develop after their recovery, referred to as "Long-term COVID-19" [3, 4]. According to WHO, research suggests that approximately 10-20% of COVID-19 patients are likely to develop prolonged symptoms that are associated with post-COVID-19 conditions. Though still it is impossible to predict how long post-COVID-19 conditions will last, according to several studies, it can be hypothesized lingering symptoms can last from weeks to months to years. The public is concerned only about the fatal outcome of COVID-19, and they are least interested in post-Covid conditions [Long COVID, Long Haulers, post-acute sequelae of SARS-CoV-2 infection (PASC)] [5]. According to a meta-analysis, there are several factors likely to influence the prevalence of long-term COVID-19 such as acute phase severity, geographic region, and selected socio-demographic characteristics like age and sex [6]. The worldwide prevalence of post-COVID-19 consequences in Asia, Europe, and the USA are more prominent which is approximately 49%, 43%, and 30% respectively. Reports have shown that prolonged symptoms are not distinct for older and younger age groups but the bulk of long COVID-19-exhibiting individuals across the included studies were older while compared to that, young age groups were in

a negligible number of those with persistent symptoms. There are emerging reports suggesting the study compares post-acute COVID-19 mortality with a reference population with mild, moderate, severe, and no history of COVID-19 as most of the evidence on post-COVID-19 sequelae is limited to hospitalized cases. It is often found that even mild COVID-19 may lead to many post-Covid conditions [7, 8]. Only a few studies are there on Post-Covid and still, there is no universal definition of it, thus we may consider this condition as different health problems continuing more than 4 weeks after a confirmed SARS-CoV-2 test which may even lead to death following definition given by CDC [9-12]. The complex pathogenesis of post-COVID syndrome and whether severe COVID-19-infected patients have a significant downstream mortality risk of 15 months is still unclear.

Materials and Methods

Study Population: The retrospective study was conducted at a tertiary health care hospital in Kolkata, India. The COVID-19 patients hospitalized between 01.4.2021 to 06.01.2022 within Peerless Hospital & B. K. Roy Research Centre and discharged after COVID-19 Treatment are considered in this study. This study was started after obtaining approval from the Institutional Ethical Committee. Permission to access medical records from the medical record department was taken. The information available included age, gender, date of admission, and the date of discharge for novel coronavirus infection, and their contact details. This list included 2000 patients who were approached for participation in the current study. Out of those 2000 patients, we were able to contact 1670 patients. Among 1670 patients, 500 patients with the proper required information were finalized for the study.

Inclusion Criteria: Patients of all age groups, who were confirmed positive for COVID-19, and diagnosed by Polymerase Chain Reaction (RT-PCR) test on nasal and pharyngeal swab specimens were included in the study.

Exclusion Criteria: Patients with incomplete data and who were not hospitalized are excluded from this study. Patients who died during the treatment were also excluded from this study. Data beyond the above-mentioned time was not procured.

Data Collection: Five hundred Covid-19 discharged cases were followed for 15 months. A gap of a minimum of 4 weeks was intended to keep between the date of data collection and the onset of symptoms. The potential participants were explained about the study. All the participants were contacted telephonically and were enquired about their health status after the infection following a prepared questionnaire. Their vaccination details were recorded simultaneously. Patients died during the 15-month follow-up period, we enquired about the reason of death to ensure that it is related to the aim of this study. One information sheet was filled up for each patient by telephone contact and finally, the collected information was analysed.

Data Analysis: Since the study population contained confirmed cases of COVID-19 infection previously, the participants were divided into two groups one group with post-COVID-19 symptoms and another group without any long COVID-19 symptoms for further analysis. Male and female patients of both groups were separately categorized into different age groups (0-19, 20-39, 40-59, ≥ 60 years). All the male and female patients who died during the follow-up period were also categorized separately into different age groups.

Result

A total of 500 patients were included in this study, of whom 279 (55.8%) were normal, 48 (9.6%) expired and 173 (34.6%) had complications. Out of 500 participants, 301 (60.2%) were male and 199 (39.8%) were female. For the analysis purpose, we made a table to address different post-COVID-19 problems (Table 1). Among those 279 (55.8%) normal cases, 170 (56.47%) of them were males and 109 (54.77%) were females (Fig.1). Eighty (28.7%) patients were more than 40 years of age but less than 59 years of age; 48 (17.2%) were males and 32 (11.4%) of them were females. 158 (56.6%) patients were in the age group of more than 59 years, among them 98 (57.64%) were males and 60 (55.04%) were females. The 20-39 age group consisted of a total of 37 (13.2%) patients of whom 21 (12.35%) were males. Out of 109 (54.77%) normal females 16 (14.67%) were normal. In the age groups of 20-39, 40-59, and above 59 years old, the number of post-COVID-19 normal males and females was almost similar. A total of 4 (1.4%) normal patients were less than 19 years old; 3 (1.76%) were males and 1 (0.91%) was female which was negligible compared to other age groups. Out of a total of 279 (55.8%) normal patients, most of them irrespective of age group and gender took 2 vaccine doses along with the booster dose except 56 (20.07%) patients were done only with the 2nd dose of vaccination.

The complications of post-COVID-19 mentioned in the table (Table 1) were prevalent among the participants. Out of 500 participants, a total of 173 (34.6%) patients were suffering from the complications of long COVID-19; 102 (33.88%) were males and 71 (35.67%) were females. The most common complications were extreme weakness and increased COPD, cough, and lung problems. 59 (11.8%) patients showed extreme weakness and 75% of patients with extreme weakness were ≥ 60 years of age. 55 (11%) patients showed respiratory problems and 78.5% of patients suffering from respiratory problems were males. In the age group of 60 and above, 114 (65.89%) patients were suffering from post-COVID-19 complications out of the total 173 (34.6%) patients with complications. Among those 114 (65.89%) patients, 72 (70.58%) were males and 42 (59.15%) were females. Out of 44 (25.43%) patients, 24 (23.52%) were males and 20 (28.16%) were females in the 40-59 age group. Out of 13 (7.51%) patients in the age group of 20-39, 6 (5.88%) were males and 7 (9.85%) were females. Only 2 (2.81%) female patients were there in the age group of 0-19 which was negligible. The number of male and female patients with complications were almost the same under 59 years of age groups but the number of male patients increased above the age of 60 (Fig.2). Most of the patients were done with 2 vaccination doses along with the booster dose or only with 2 doses and only 39 (22.54%) of them were done with 1 vaccination dose.

A total of 48 (9.6%) patients died during the follow-up session among whom 29 (9.63%) were males and 19 (9.54%) were females (Fig.3). 45 (93.7%) of the dead patients were from the age group of above 59; 27(93.10%) were males, out of a total of 29 (9.63%) males and 18 (37.5%) were females among those 19 (9.54%) dead female patients. Among those 18 dead female patients, most of them 9 (50%) were not vaccinated while among the 27 dead male patients most of them 16 (59.2%) were done with 2nd dose of vaccination. A single male and a single female patient died from the 40-59 age group of whom both were done with 2 doses of vaccination. A single male patient with complete vaccination died from the age group of 60 and above.

Table 1: This Shows Normal and Dead Post-Covid Patients Along with Different Post-Covid Problems

Post-COVID problem	Number (%)
Normal	238 (47.6%)
Expired	53 (10.6%)
Extreme weakness, bed ridden	59 (11.8%)
Increased COPD and lung problems, cough	55 (11%)
Others (Mainly age related, anemia, fever etc.)	24 (4.8%)
Increased diabetes	15 (3%)
Psychiatric problem	
Brain fog/Cognitive dysfunction and memory impairment	14 (2.8%)
Increased blood pressure	11 (2.2%)
Liver/Kidney/UTI problem	7 (1.4%)
Insomnia	7 (1.4%)
Stroke	6 (1.2%)
Imbalance gait	4 (0.8%)
Chest pain	3 (0.6%)
Increased uric acid	3 (0.6%)
Hair fall	2 (0.4%)

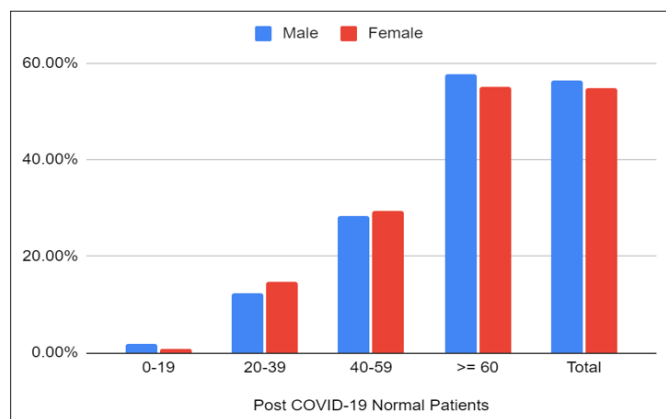


Figure 1: Percentage of Normal Patients in Male and Female Post-Covid Patients. The Number of Cases Between 0-39 Years Was Much Less Only 4 Cases Between 0-19 Years And 37 Cases Between 20-39 Years, thus The Differences Were Ignored. The Y-Axis Indicates Percentages and x-axis Indicates the Age Group in Years.

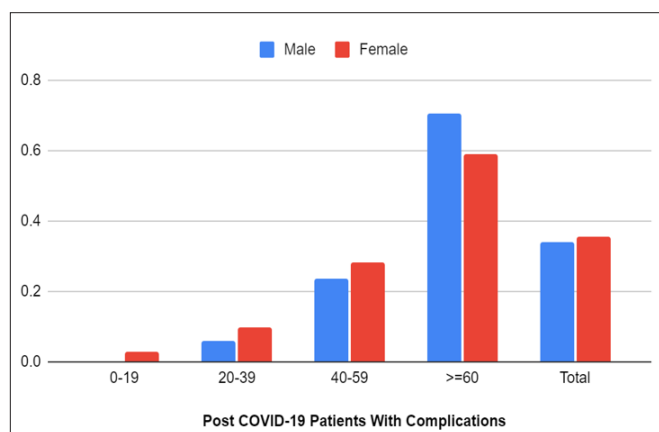


Figure 2: Percentage of Patients with Post Covid-19 Complications in Male and Female. The number of cases between 0-19 years were

much less. Only 2 cases between 0-19 years, thus the differences were ignored. The y-axis indicates percentages (x100) and x-axis indicates the age group in years

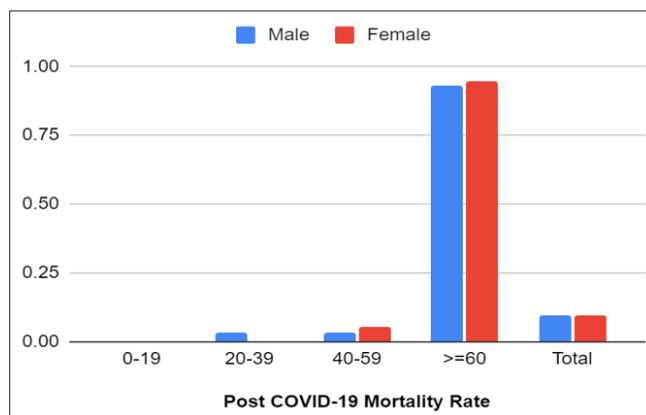


Figure 3: Percentages of Dead Post-Covid Patients Between Male and Female Patients. The y axis indicates percentages and X axis indicates the age group in years. The Highest Rate of Mortality Was Present in The Age Group Of 60 And Above

Discussion

Numerous research groups reported widespread persisting symptoms of post-COVID-19, to explore the general decrease in quality of life with long-term COVID-19, also trying to emphasize the putative pathophysiology, risk factors, and treatments. According to WHO, the major common reported long-term symptoms in COVID-19 patients are chronic fatigue, shortness of breath, chest pains, persistent cough, muscle and joint pain, trouble speaking followed by depression, anxiety, insomnia, heart palpitations, difficulties in concentration, dizziness, memory loss and brain fog. In this study, similar complications have been found among the participants. Among those complications, extreme weakness and increased COPD, lung problems, and cough were the most common symptoms. These extensive long-term symptoms were not only present in severe COVID-19 patients but also in patients who had mild to moderate disease though the patients who were initially more ill suffered more complications. Several reports disclose that these long-term COVID symptoms can appear after two weeks following the recovery of the initial phase of infection and can be continued for six months to one year. It can be hypothesized that people with pre-existing comorbidities have both greater chance and risk of complications of post-COVID-19, although further research is required to understand the relationship [13]. Most of the researchers and clinicians stated that coronavirus can trigger a massive inflammatory response during the post-COVID-19. Thus, it is necessary to scan cytokine networks in patients who have recovered from COVID-19 to assess whether the “cytokine storm” present during the disease continues and comes up with these long-term complications [14]. Again, some opined that antibodies, activated T cells, and vaccinations may lead to a hidden reservoir of the virus in the body [15]. In this study it was observed that most of the normal patients had taken 2 vaccines along with the booster dose and patients with no or incomplete vaccinations possess a higher risk of post-COVID-19 sequences. It is a fact that a booster dose of the COVID-19 vaccine is linked with a decreased risk of severe COVID-19 when compared to no vaccination [16,17]. Still, we are not sure how much and how long protection it can give to us.

Recent preliminary data highlighted a potential high-risk factor in the female gender aged between 40 and 50 but after the age

of 60 the risk level between male and female become similar for post-COVID-19 which is similar to the data that reflects that autoimmune diseases are more common in female but after age 60, it becomes similar between male and female through menopause. However, it is not yet clear whether due to a different immune system response during and after COVID-19, these gender differences, as well as other aspects of the disease may occur [18]. In this study, although the number of female patients with complications was a little higher than males in the age groups of 20-39 and 40-59, which can be considered almost similar the number of males with complications was much higher in the age group of 60 and above. On the other hand, studies have shown that sex hormones can affect the immune and inflammatory modulation during infection [19]. Sex hormones such as estrogen can promote both innate and adaptive immunity and testosterone has a suppressive effect on the immune system. Preliminary data disclose that there is a role of estrogen on vascular function and the endothelium and endothelium have a crucial role in COVID-19. Thus, there is a chance of lower severity of COVID-19 in the female population though further study is required.

Recent studies show that the increased risk of death from COVID-19 is not only limited to the initial period of COVID-19 disease but also there is a substantially increased risk of 12-month mortality during post-COVID-19 over those who are COVID-19 negative. Eventually increasing age, especially above 60 years has a higher post-COVID-19 mortality risk. According to the reports, patients who were hospitalized or suffered acute COVID-19 in the early episode of the disease possess a greater risk of downstream mortality than those who encounter mild to moderate symptoms in the initial phase [20]. Patients with mild or moderate infection in the early stage, who have been vaccinated against coronavirus, have no significant differences in mortality risk from COVID-19 negatives suggesting the value of vaccinations to substantially decrease and prevent death from the downstream complications of COVID-19. However, there are hospital-based studies that suggest the opposite. Here in this study, it was observed that most of the male patients who died were done with 2 doses of vaccination while most of the dead female patients were not vaccinated. Although the age group of 59 and above possesses a higher chance of mortality irrespective of gender, however, the mortality rate among males and females was almost the same irrespective of the age groups. So, the interplay between the COVID-19 vaccine and post-COVID-19 sequelae is yet to be determined.

Several reports revealed that there is a difference between the mortality rate of males and females. In some previous studies, it has been mentioned that severity of the COVID-19, females, and relatively younger age are important risk factors in POST-COVID condition development [21]. The spike protein of coronavirus contains the S1 subunit which is linked to receptor binding, contains the N-terminal domain and a receptor binding domain. The receptor binding site binds with enzymes (ACE2, TMPRSS2) which are critical for virus entry into the host cell. Both ACE2 and TMPRSS2 are highly expressed in the testis compared to the ovary, supporting the observation that the coronavirus may enter the human testis [22]. Similar results had been reported during SARS in 2003, where significantly higher mortality rates in males have been described though sex was not an independent predictor of mortality. As those reports are based on retrospective studies, better evolution of more specific sex and gender-related parameters are required to fully understand the mechanism.

Conclusion

There are some limitations of this study as it is based on only hospitalized cases, and reports and observations are subjective as it was based on electronic devices and questionnaires. There is a place for a detailed analysis and understanding of all the aspects associated with post-COVID-19 in the future. It was observed that the individuals who were hospitalized during the early phase of COVID-19 infection experienced a greater risk of death complications and readmission due to post-COVID-19. Patients with other comorbidities such as diabetes, cancer, chronic cardiovascular or kidney disease, or immunocompromised possess increased complications and mortality related to long-term COVID-19. The duration and expense of long-term symptoms the purpose of the disease and its severity are still unclear. The study of antiviral therapy for long-term complications is mandatory. Several reports reveal a clear difference between the number of male and female patients suffering from the symptoms of long-term COVID-19 as well as mortality showing that sex and gender-specific effects should be emphasized to develop approaches able to address the long-term effect of the disease. Future studies should evaluate the mechanism and the relation of this disease in the early stage of infection and the long-term COVID-19 symptoms with the mortality rate during post-COVID-19 needed to be studied thoroughly.

Summary Points

A significant number of COVID-19 patients, who have recovered from early infection are reporting signs and symptoms that emerge during or after the COVID-19 infection, persist for more than 12 weeks, and are not explained by any alternative diagnosis. This phenomenon is known as post-acute COVID-19 syndrome (PACS).

Some crucial factors can influence the post-COVID-19 syndrome like acute phase severity, time since infection, geographic region, age, and sex.

People of different age groups were found with persistent post-COVID-19 symptoms. However, people of more than 59 years were affected more and had a higher risk factor.

In the age groups of 0-59, the number of both male and female patients with complications was almost the same. Males with complications were affected more in the age group above 59. The mortality rate was higher in the age group of 60 and above irrespective of gender.

Most of the normal patients were done with complete vaccinations along with the booster dose while patients with 1 dose of vaccination or no vaccination were more vulnerable to post-COVID-19 sequences and had a greater chance of mortality.

Patients who suffered severe COVID-19 disease were likely to have a higher chance of post-COVID-19 sequelae.

Future research is needed to define post-acute COVID-19 syndrome correctly and properly.

Author contributions

SrijaniBasu: Performed the data collection, analysis, and manuscript preparation; **Satadal Das:** Designed and supervised the study; All authors read, corrected, and approved the final manuscript.

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Ethical conduct of research

This study was approved by the Institutional Ethical Committee. Informed consent was obtained from all participants included in the study.

References

1. Salamanna F, Veronesi F, Martini L, Landini M P, Fini M (2021) Post-COVID-19 syndrome: the persistent symptoms at the post-viral stage of the disease. A systematic review of the current data. *Frontiers in medicine* 392.
2. World Health Organization (2021) A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021 (No. WHO/2019-nCoV/Post_COVID-19_condition/Clinical_case_definition/2021.1). World Health Organization.
3. Mainous III A G, Rooks B J, Wu V, Orlando F A (2021) COVID-19 post-acute sequelae among adults: 12-month mortality risk. *Frontiers in medicine* 8: 2351.
4. Alkodaymi M S, Omrani O A, Fawzy N A, AbouShaar B, Almamlouk R, et al. (2022) Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: a systematic review and meta-analysis. *Clinical Microbiology and Infection* 28: 657-666.
5. Alwan N A (2020) Surveillance is underestimating the burden of the COVID-19 pandemic. *The Lancet* 396: e24.
6. Chen C, Hauptert S R, Zimmermann L, Shi X, Fritsche L G, et al. (2022) Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review. *The Journal of infectious diseases* 226:1593-1607.
7. Gorna R, MacDermott N, Rayner C, O'Hara M, Evans S, et al. (2021) Long COVID guidelines need to reflect lived experience. *The Lancet* 397: 455-457.
8. Petersen M S, Kristiansen M F, Hanusson K D, Danielsen M E, A Steig B, et al. (2021) Long COVID in the Faroe Islands: a longitudinal study among nonhospitalized patients. *Clinical Infectious Diseases* 73: e4058-e4063.
9. Tenforde M W, Kim S S, Lindsell C J, Rose E B, Shapiro N I, et al. (2020) 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. *Morbidity and mortality weekly report* 69: 993.
10. Michelen M, Manoharan L, Elkheir N, Cheng V, Dagens D, et al. (2020) Characterising long-term covid-19: a rapid living systematic review. *medrxiv* 10: 08-20246025.
11. Davis H E, Assaf G S, McCorkell L, Wei H, Low R J, et al. (2021) Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine* 38.
12. Tabacof L, Tosto-Mancuso J, Wood J, Cortes M, Kontorovich A, et al. (2022) Post-acute COVID-19 syndrome negatively impacts physical function, cognitive function, health-related quality of life, and participation. *American journal of physical medicine & rehabilitation* 101: 48.
13. Nalbandian A, Sehgal K, Gupta A, Madhavan M V, McGroder C, et al. (2021) Post-acute COVID-19 syndrome. *Nature medicine* 27: 601-615.
14. Peluso M J, Lu S, Tang A F, Durstenfeld M S, Ho H E, et al. (2021) Markers of immune activation and inflammation in individuals with postacute sequelae of severe acute respiratory syndrome coronavirus 2 infection. *The Journal of infectious diseases* 224: 1839-1848.
15. Ledford H (2021) How vaccination affects the risk of Long Covid. *Nature* 599: 546-548.
16. Accorsi E K, Britton A, Shang N, Fleming-Dutra K E, Link-Gelles, et al. (2022) Effectiveness of homologous and heterologous Covid-19 boosters against Omicron. *New England Journal of Medicine* 386: 2433-2435.
17. Andrews N, Stowe J, Kirsebom F, Toffa S, Sachdeva R, et al. (2022) Effectiveness of COVID-19 booster vaccines against COVID-19-related symptoms, hospitalization and death in England. *Nature medicine* 28: 831-837.
18. Kharroubi S A, Diab-El-Harake M (2022) Sex-differences in COVID-19 diagnosis, risk factors and disease comorbidities: A large US-based cohort study. *Frontiers in public health* 10: 1029190.
19. Raimondi F, Novelli L, Ghirardi A, Russo F M, Pellegrini D, et al. (2021) Covid-19 and gender: lower rate but same mortality of severe disease in women—an observational study. *BMC pulmonary medicine* 21: 1-11.
20. Senjam S S, Balhara Y P S, Kumar P, Nichal N, Manna S, et al. (2021) Assessment of Post COVID-19 Health Problems and its Determinants in North India: A descriptive cross section study. *medRxiv* 10.
21. Munblit D, Nicholson T R, Needham D M, Seylanova N, Parr C, et al. (2022) Studying the post-COVID-19 condition: research challenges, strategies, and importance of Core Outcome Set development. *BMC medicine* 20: 1-13.
22. Pradhan A, Olsson P E (2020) Sex differences in severity and mortality from COVID-19: are males more vulnerable? *Biology of sex Differences* 11: 1-11.

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