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A Preliminary Survey of the Postacute Symptoms of COVID-19 among Hospital-Discharged Patients and a Proposed Quantitative Framework for Assessment

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Abstract

Background Following a massive outbreak of the coronavirus disease 2019 (COVID-19) pandemic, a significant number of survivors are still suffering from residual symptoms and complications. We designed a preliminary study to evaluate such symptom spectra in COVID-19 patients who had been discharged from the hospital.

Methods A telephone interview was conducted with 100-randomly chosen hospital-discharged COVID-19 survivors from the electronic patient record. The interview structure and method were developed by a panel of experts. A specially trained group conducted the interviews and data collection. The statistical analysis was performed in accordance with the data type (continuous and categorical). Group comparisons were also done between intensive care unit (ICU) versus general ward admission, and patients discharged between 3 and 12 weeks versus more than 12 weeks. Additionally, world clouds were used for better visualization of various prevalent symptoms.

Results Eighty-two participants were finally included for interview after preliminary screening. Fifty-three patients (64.6%) were male participants; 74.4% had at least one symptom. In general, fatigue, cough, insomnia, and shortness of breath were the most common persistent symptoms. Symptoms were more prevalent among the patients discharged from ICU compared with those discharged from the general ward. Cough, loss of appetite, depression, and incoherence were more common in patients after 12 weeks of hospital discharge.

Conclusion There is a wide range of persistent symptoms in the COVID-19 survivors who have been discharged from the hospital. Some symptoms arise or persisted even after 12 weeks. Based on the study results, available literature, and expert consensus, an assessment form has been developed that could be used for further research and clinical assessment of similar problems. Large-scale epidemiological study (longitudinal and cross-sectional) is needed to understand the nature and prevalence of the postacute phase of COVID-19 at the country level. The results of this study could inform the stakeholders and policymakers for taking necessary steps toward a further decision.

Keywords
- COVID-19
- long haulers
- postacute COVID-19
- persistent COVID-19 Symptoms
- post-COVID-19 manifestations
- post-COVID-19 syndrome

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Introduction

The coronavirus disease 2019 (COVID-19) or severe acute respiratory syndrome coronavirus 2 was detected dates back in December 2019 in Wuhan, China. Due to the high infectivity rate, it had a tremendous spread throughout the globe within a very short period of time.[1] It has caused millions of deaths worldwide with a variable clinical manifestation.[2] Apart from the usual clinical manifestation, COVID-19 has been recently known for its long term or persistent effect in many patients after recovery from the acute phase.[3] Till date there is no consistent term to describe this slow and progressing sequelae of COVID-19. Different authorities and literatures have explained this with terms such as, "Post-acute COVID-19," "Long-COVID-19," "Long Haulers," "Persistent COVID-19 Symptoms," "Post COVID-19 manifestations," "Long-term COVID-19 effects," and "Post COVID-19 syndrome."

Literatures are increasing with time, reporting various long-term symptoms and syndromes.[4,5] The pattern and characteristics are still not well understood on probable account of the geographical variability, clinical course, medication, and the presence of comorbidities. However, it has been accepted that COVID-19 is a multisystem disorder.[6] The probable natural history of the disease has been recently proposed based on the present understanding and available evidence.[3]

The National Institute for Health and Care Excellence (NICE)[7] has categorized the COVID-19 spectrum into three groups: (1) *Acute phase of COVID-19*, which includes sign and symptoms up to 4 weeks, (2) *Ongoing symptomatic COVID-19*, which includes sign and symptoms from 4 to 12 weeks beyond the acute phase, and (3) *Post-COVID-19 syndrome*, where any sequelae persisting or developed after an infection, consistent with COVID-19, continuing for more than 12 weeks and not attributable to alternative diagnoses. The last two categories, that is, "Ongoing symptomatic COVID-19" and "Post-COVID-19 syndrome" could be termed as "long COVID."

In regard to the clinical spectrum, several studies have reported fatigue and dyspnea as the most frequent symptoms after acute COVID-19.[4,8,9] Other symptoms such as joint pain, chest pain, cough, anosmia, rhinitis, red eyes, dysgeusia, headache, sputum, lack of appetite, sore throat, vertigo, myalgia, and diarrhea were also reported.[3,9] In addition to these general symptoms, specific organs dysfunctions have also been observed, particularly in the heart, lungs, and brain. The other spectrum of the disease could manifest as a hyperimmune response in the postacute phase or 2 to 5 weeks after the onset of COVID-19 infection. The manifestation includes prominent cardiovascular, gastrointestinal as well as mucocutaneous affection.[10] The pathogenesis is termed as *multisystem inflammatory syndrome (MIS)* in adults (MIS-A) and in children (MIS-C).[11] The clinicopathological understanding of MIS-C is well characterized,[10] whereas the MIS-A is not clearly distinct[12] and awaiting further investigation. This might be due to more severe and complex clinical course in adults compared with the children where distinct separation of inflammatory response from the usual clinical spectrum is difficult.

Due to the paramount importance to understand and manage such aftermaths, National Institutes of Health (NIH) has included a separate emerging section in their COVID-19 guidebook (https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/). NICE has also created a workforce to provide evidence-based understanding and guidance on postacute consequences.[7] However, no proper study has been published till date describing the postacute phase of COVID-19 in Indian population.

Sanjiban Hospital is the referral tertiary care center treating COVID-19 patients since the beginning of the outbreak in India. A special taskforce was also deployed to follow up the patients after the discharge from hospital. However, on having fragmentary reports of various symptoms persisting weeks even months after recovery, a structured post-COVID assessment was necessitated. We conducted this preliminary study to characterize the symptomatic array and prevalence of persistent symptoms after COVID-19 in patients discharged from this hospital, and to look into the feasibility for further study. Also, based on the results, obtained from this study, and expert consensus, we intent to develop an assessment form for further large-scale study and clinical assessment of post-COVID patients.

Methods

Study Setting

The study was conducted at Sanjiban Hospital, Howrah, India, which was the tertiary referral center during COVID-19 since April 2020. This is one of the largest tertiary care hospitals in West Bengal, having 600 beds and multispecialty facilities. Up to January 2021, it has served more than 4,500 COVID-19 patients referred from other hospitals. Patients treated here were contacted regularly to evaluate their general health status after discharge. In December 2021, a team of specialists was deployed to interview the discharged patients for any post-COVID sequel. The study was performed in the "Office of Medical Research &Data Management (OMRDM)" at the Hospital.

Interview Structure Development

A team was formed to prepare the interview structure consisted experts from various specialities such as pulmonology, neurology, general medicine, anesthesiology, surgery, psychology, research methodology, and statistics. The list of probable symptoms was prepared by consensus between all the members of the team. The assessment included present symptoms and its corroboration with the acute phase, or any newly appeared symptoms. Additionally, open-ended questions were also asked to find out any complaints beyond the list. All the records were maintained in a standardized proforma and imputed in a specially designed excel sheet.

Study Participants

A telephonic interview was conducted among the hospitalized patients discharged between June 2020 and August 2020. Upon agreeing to participate in the study, a

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structured interview was performed for each participant at different time points after discharge. The surveyed population was divided into two groups according to the duration, that is, 3 to 12 weeks and >12 weeks post-discharge. The symptoms comparison between intensive care unit (ICU) and non-ICU patients were also done.

Analysis Plan

We analyzed all the data using SPSS. The baseline information was analyzed and reported either as *n* (%) for categorical data or mean (μ) ± standard deviation (SD) for continuous data. Number (%) for symptoms prevalence were calculated in respect to the belonging group. All the detailed descriptions and symptoms not contained in the list were interpreted and modified into simpler version. Word cloud analysis was also done at different intervals to visualize the frequency of presenting symptoms.

Consent

All potential participants were provided information details of the study at the very beginning. In accordance with ethical standards, telephonic consents were collected prior to the interview. We assured all the participants about the deidentification and anonymous handling of all the data.

Results

Total 100 patients discharged before 3 weeks or more were identified randomly from the electronic patient record. Of these, 94 could be contacted and approached, and 82 consented to participate in the study. Of nonconsenters, two patients died after few days of discharge and 10 patients refused to take part in the interview (4—unwilling to participate, 5—communication problem, and 1—unknown reason) (►**Fig. 1**).

The baseline age, age groups, and gender were comparable between groups in both the clusters, that is, general ward versus ICU and 3 to 12 weeks versus >12 weeks postdischarge. The age of the participants was between 21 and 81 years. Fifty-three (64.6%) patients were male participants, 26 (31.7%) were discharged from ICU, and 56 patients (68.3%) from general ward. Most common comorbidities were hypertension, diabetes mellitus, ischemic heart diseases, and chronic obstructive pulmonary diseases. Baseline data were statistically comparable (►**Table 1**).

Twenty-one (25.61%) patients could not identify any residual or newly appeared symptoms. Among 61 participants with persistent symptoms, fatigue was the most common (46.67% of total symptomatic patients). Other frequently appeared symptoms were cough, shortness of breath, loss of appetite, and constipation. In total, 47 different symptoms were reported in which, 32 were physical and 15 were mental symptoms (►**Table 2**). In addition to that, insomnia, depression, loss of memory, irritability, and traumatic stress were most commonly reported mental symptoms. Prevalence of symptoms in respect to the total included patients is visualized in ►**Fig. 2**. Cluster of symptoms in physical and mental domain were visualized as "word cloud" in ►**Figs. 3** and **4**, respectively.

General Ward versus ICU

Most of the commonly reported persistent complaints including fatigue, cough, insomnia, shortness of breath, loss of appetite, constipation, chest pain, exertional dyspnea, depression, irritability, and confusion were more prevalent among the patients discharged from the ICU, compared with the patients admitted and discharged from general ward. Few of the symptoms such as myalgia, weight loss, nausea, and incoherence were a bit more reported in patients of later group (►**Table 2**).

3–12 Weeks versus >12 Weeks Postdischarge

Symptoms such as fatigue, cough, insomnia, myalgia, and memory loss were more prominent in the patients discharged within 3 to 12 weeks. However, shortness of breath, loss of appetite, globus hystericus, chest tightness, trembling, depression, and incoherence were more prevalent in the group of more than 12 weeks postdischarge (►**Table 2**).

Discussion

Principal Finding

Our study found a vivid cluster of persistent symptoms after COVID-19 in patients once admitted in the hospital. Total 49

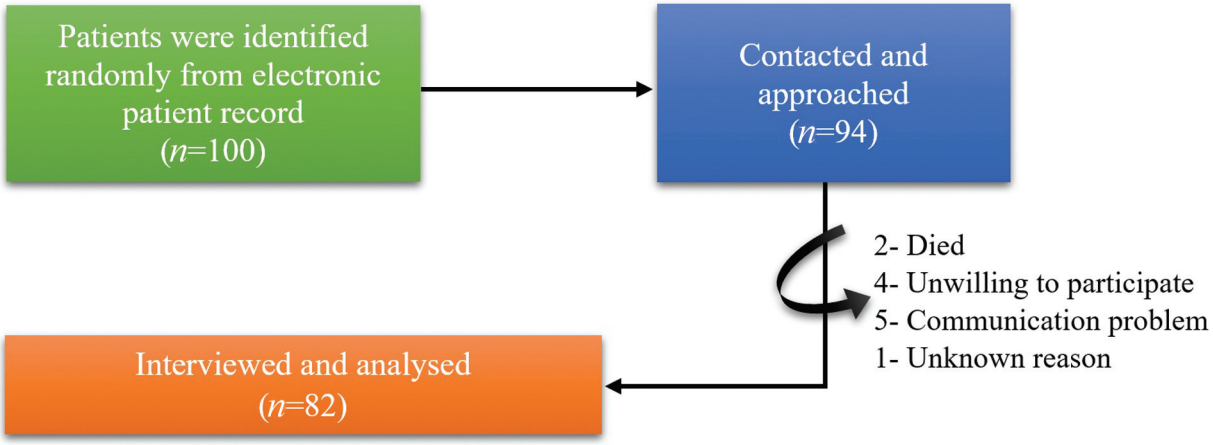

Fig. 1 Participant flow.

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Table 1 Baseline information

Variables	Total ($n = 82$)	Ward admitted			Duration after discharge		
		General ward ($n = 56$)	ICU ($n = 26$)	*p-Value*	3–12 weeks ($n = 40$)	>12 weeks ($n = 42$)	*p*-Value
Gender • Male • Female	53 (64.6) 29 (35.4)	35 (66.03) 21 (72.41)	18 (33.97) 8 (27.59)	0.352 (ns)	25 (47.17) 15 (51.72)	28 (52.83) 14 (48.28)	*0.156 (ns)*
Age, μ ± SD	56.48 ± 11.97	54.79 ± 13.1	60.14 ± 8.16	0.027 (ns)	54.73 ± 11.15	58.15 ± 12.61	*0.219 (ns)*
Age groups				0.182 (ns)			*0.112 (ns)*
• 21.0–40.0	11 (13.41)	10 (90.91)	1 (9.09)		6 (54.55)	5 (45.45)	
• 41.0–60.0	46 (56.10)	31 (67.39)	15 (32.61)		28 (60.87)	18 (39.13)	
• 61.0–81.0	25 (30.49)	15 (60.00)	10 (40.00)		6 (24.00)	19 (76.00)	
Comorbidities	71 (86.59)	45 (63.38)	26 (36.61)		34 (47.89)	37 (52.11)	
• Hypertension	42 (59.15)	21 (50)	21 (50)	0.292 (ns)	23 (53.49)	19 (44.18)	*0.157(ns)*
• Diabetes	31 (43.66)	14 (45.16)	17 (54.84)		21 (67.74)	10 (32.26)	
• COPD	18 (25.35)	6 (33.33)	12 (66.67)		14 (77.78)	4 (22.22)	
• IHD	23 (32.39)	4 (17.39)	19 (82.61)		9 (39.13)	14 (60.87)	
• Chronic kidney diseases	15 (21.13)	6 (40)	9 (60)		10 (66.67)	5 (33.33)	
• Cerebrovascular diseases	17 (23.94)	6 (35.29)	11 (64.71)		7 (41.18)	10 (58.82)	
• Hypothyroidism	19 (26.76)	7 (36.84)	12 (63.16)		11 (57.89)	8 (42.11)	
• Other	9 (12.68)	5 (55.56)	4 (44.44)		4 (44.44)	5 (55.56)	

Abbreviations: μ, mean; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IHD, ischemic heart diseases; ns, nonsignificant; SD, standard deviation.

types of symptoms were found in the participants included in this study. Among physical symptoms, fatigue was the most common, followed by cough, shortness of breath, constipation, loss of appetite, and myalgia, which were commonly reported. In mental sphere, insomnia, depression, memory loss, and irritability were most prevalent symptoms. We also observed some of the substantial differences in the prevalence of symptoms between the groups of two clusters (general ward vs. ICU and 3–12 weeks vs. >12 weeks postdischarge).

Comparison in Contrast to Other Studies

A qualitative study conducted on by Sudre et al[13] reported fatigue, headache, dyspnea, and anosmia as frequent persistent post-COVID symptoms. It also showed the prevalence was more likely with increasing age and body mass index and female sex. Another study by Logue et al[8] found fatigue and loss of smell or taste as the most prevalent symptoms at 6 months after COVID-19. Fatigue, anxiety, dyspnea, cough, and joint pain were also reported as the foremost symptoms in the other studies.[4,14,15] In contrast to these, our study revealed a little altered spectrum of symptoms particularly from Indian population.

Strength of the Study

To our knowledge, this is the first study from India reporting on post-COVID-19 persistent symptoms. We showed a vivid spectrum of symptoms that can arise after the acute illness in this specified population. The study process was rigorous, an intrusive methodology and predefined protocol was adopted before the initiation of the study. Trained personnel and specialists handled every aspect of the study including, methodology, interview structure, data collection, and analysis. The symptoms in physical and mental sphere were also visualized through "word cluster" for better comprehension. Additionally, a "Post-COVID-19 Quantitative Framework for Assessment" (pC-QFA) (►**Supplementary file-1**, available online only) proforma is also developed for screening of post-COVID patients. The development of pC-QFA was based on the consensus between aforementioned team of experts, available literature on the topic, and the findings on the present study.

Limitation of the Study

One important caveat of this study is its generalizability. Being its preliminary nature, the study findings lack proper implementation on the population. The sample size could not be calculated beforehand due to the unavailability of similar study on the defined population. Severity of the symptoms could not be quantified on account of nonavailability of the quantitative assessment tool and uncertainty of their utility. Owing to the telephonic nature of the interview, there are possibilities of noncapturing any information, which might be relevant.

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Table 2 Persistent symptoms in the postacute phase of COVID-19 among the hospital-discharged patients

Symptom status	Total	ICU	General ward	3–12 Weeks	>12 weeks
Asymptomatic, *n (%)*	21 (25.9)	4 (19.1)	17 (80.9)	8 (38.1)	13 (61.9)
Symptomatic, *n (%)*	61 (74.4)	22 (36.1)	39 (63.9)	32 (52.5)	29 (47.5)
A. Physical symptoms, n (%)					
Fatigue	28 (45.9)	18 (81.8)	10 (25.6)	17 (53.1)	11 (37.9)
Myalgia	5 (8.1)	2 (9)	3 (7.6)	3 (9.3)	2 (6.8)
Loss of appetite	6 (9.8)	4 (18.1)	2 (5.1)	2 (6.2)	4 (13.7)
Loss of taste	1 (1.6)	–	1 (2.5)	1 (3.1)	–
Constipation	6 (9.8)	3 (13.6)	3 (7.6)	4 (12.5)	2 (6.8)
Aversion to fruits	1 (1.6)	–	1 (2.5)	1 (3.1)	–
Cough	19 (31.1)	14 (63.6)	5 (12.8)	9 (28.1)	10 (34.4)
Weight loss	2 (3.2)	–	2 (5.1)	1 (3.1)	1 (3.4)
Chest pain	4 (6.5)	3 (13.6)	1 (2.5)	2 (6.2)	2 (6.8)
Shortness of breath	11 (18)	9 (40.9)	2 (5.1)	3 (9.3)	8 (27.5)
Exertional dyspnea	5 (8.1)	4 (18.1)	1 (2.5)	3 (9.3)	2 (6.8)
Globus hystericus	4 (6.5)	3 (13.6)	1 (2.5)	1 (3.1)	3 (10.3)
Vomiting	1 (1.6)	–	1 (2.5)	–	1 (3.4)
Numbness	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Gingivitis	2 (3.2)	1 (4.5)	1 (2.5)	1 (3.1)	1 (3.4)
Diarrhea	2 (3.2)	1 (4.5)	1 (2.5)	1 (3.1)	1 (3.4)
Dysgeusia	2 (3.2)	2 (9)	–	2 (6.2)	–
Menorrhagia	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Chilliness	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Change of taste	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Chest tightness	2 (3.2)	1 (4.5)	1 (2.5)	–	2 (6.8)
Dyspepsia	3 (4.9)	3 (13.6)	–	1 (3.1)	2 (6.8)
Trembling	2 (3.2)	2 (9)	–	–	2 (6.8)
Fever	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Skin rash	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Vertigo	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Anemia	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Perspiration	3 (4.9)	2 (9)	1 (2.5)	2 (6.2)	1 (3.4)
Greying of hair	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Burning urine	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Cough with expectoration	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Nausea	2 (3.2)	–	2 (5.1)	1 (3.1)	1 (3.4)
B. Mental symptoms, n (%)					
Insomnia	13 (21.3)	9 (40.9)	4 (10.2)	7 (21.8)	6 (20.6)
Depression	9 (14.7)	5 (22.7)	4 (10.2)	4 (12.5)	5 (17.2)
Memory loss	8 (13.1)	4 (18.1)	4 (10.2)	5 (15.6)	3 (10.3)
Irritability	8 (13.1)	6 (27.2)	2 (5.1)	5 (15.6)	3 (10.3)
Confusion	4 (6.5)	3 (13.6)	1 (2.5)	2 (6.2)	2 (6.8)
Anxiety	3 (4.9)	3 (13.6)	–	2 (6.2)	1 (3.4)
Incoherence	4 (6.5)	1 (4.5)	3 (7.6)	1 (3.1)	3 (10.3)
Suicidal ideation	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Religious mania	1 (1.6)	1 (4.5)	–	1 (3.1)	–

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Table 2 (*Continued*)

Symptom status	Total	ICU	General ward	3–12 Weeks	>12 weeks
Impatient	2 (3.2)	2 (9)	–	1 (3.1)	1 (3.4)
Fear of serious ailment	1 (1.6)	1 (4.5)	–	1 (3.1)	–
Traumatic stress	7 (11.4)	5 (22.7)	2 (5.1)	3 (9.3)	4 (13.7)
Fear of falling	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Rage	1 (1.6)	1 (4.5)	–	–	1 (3.4)
Sleepiness	1 (1.6)	1 (4.5)	–	1 (3.1)	–

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit.

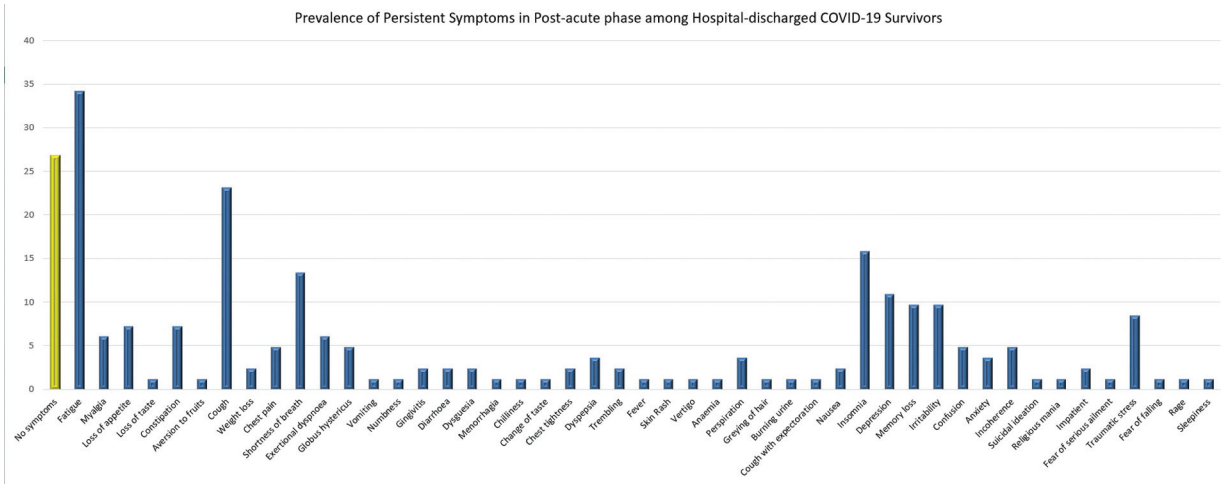

Fig. 2 Bar diagram showing the prevalence of symptoms.

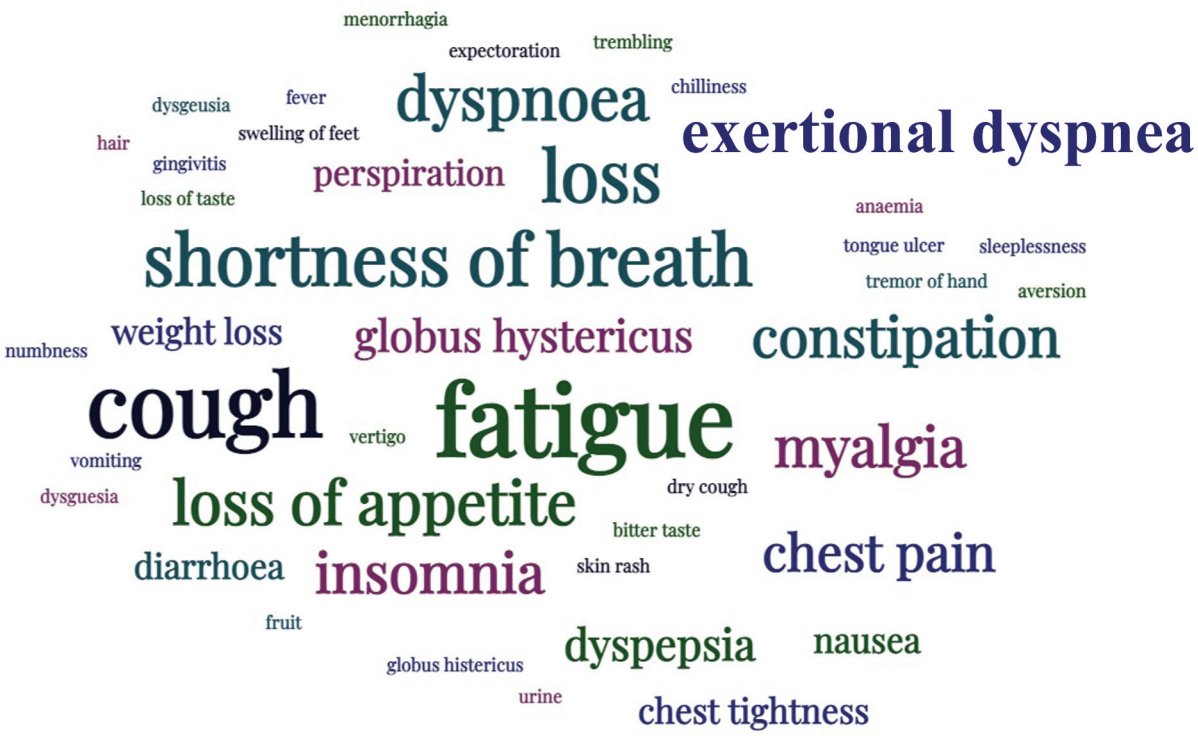

Fig. 3 Word cloud of physical symptoms.

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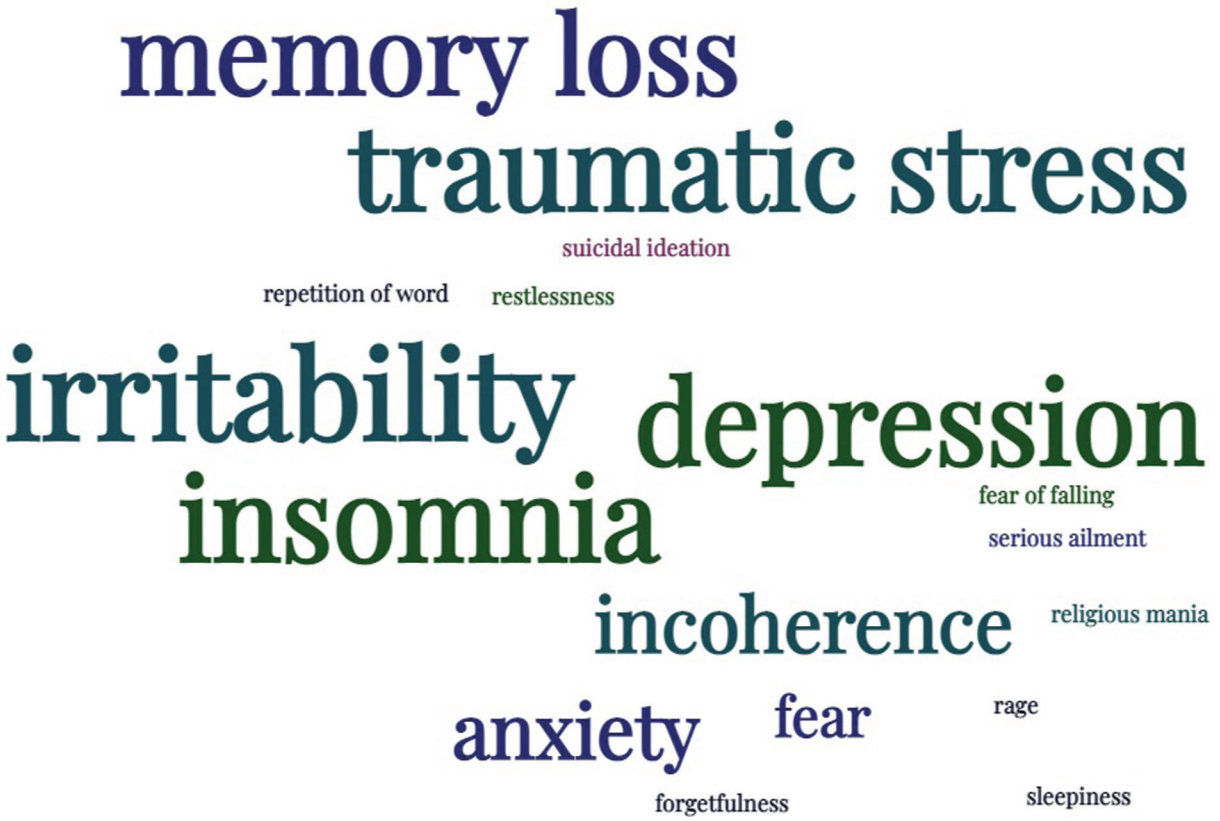

Fig. 4 Word cloud of mental symptoms.

Further Recommendation

This preliminary pilot study can assist in many of the aspects of conducting a large-scale similar survey in future. Future studies could be designed with proper sample size based on these findings. Further studies can also look for specific symptoms' prevalence and predictors for such persistence and development.

Implications

This study provides a boon to design the further large-scale studies in varied permutations of methodology. The present findings point out the prevalence of varied symptoms in the postacute phase of COVID-19 among hospital-discharged patients at different time-points. Clinicians also can be used to screen and grade the postacute symptoms based on the pC-QFA (►**Supplementary file-1**, available online only) according to their convenience. This proforma can also be validated and altered in future in accordance with the need and nature of the utilization.

Conclusion

There are varied cluster of physical and mental symptoms that could be found after COVID-19 in patients discharged from the hospital. Fatigue, cough, shortness of breath, insomnia, depression, memory loss, irritability, and traumatic stress were the most commonly reported symptoms. Some differences in the symptomatic prevalence could be observed between different cohorts of patients. However, we recommend a large-scale study to obtain a generalizable conclusion regarding prevalence and predictors of postacute symptoms after COVID-19 infection. A framework for assessment was developed using various sources that may be used for clinical assessment and in future studies of similar nature.

Conflict of Interest
None declared.

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