



Characteristics of psychiatric manifestations among hospitalized COVID-19 patients and their correlation with disease severity – a cross sectional study

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Abstract

Purpose: COVID-19 severity, characteristics of psychiatric symptoms using a brief psychiatric rating scale, and sociodemographic variables were explored and evaluated.

Methods: An exploratory study was conducted during the COVID-19 pandemic, from July 13th to July 26th 2020, in an isolation facility at the COVID-designated Sola hospital in Ahmedabad, India. A total of 201 inpatients diagnosed with COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) were included in this study. We assessed the presence and severity of psychiatric symptoms using the Brief Psychiatric Rating Scale (BPRS).

Results: Of the 201 COVID-19 patients, 63 (31.3%), 36 (18%), 16 (8%) and 14 (7%) experienced anxiety, tension, somatic concern and depressed mood respectively. The effect of the severity of COVID-19 on the mean of the total BPRS score was statistically significant ($F = 17.2, p = 0.000$). In the severe COVID-19 group, the mean of the total BPRS score (22.6 ± 4.8) was significantly higher than in the moderate (20.3 ± 4.0) and mild (19.1 ± 2.2) COVID-19 groups. High levels of serum ferritin, IL-6 and D-dimer were associated with the presence of neuropsychiatric symptoms like hallucinatory behavior and disorientation.

Conclusions: The majority of COVID-19 patients experienced anxiety, tension and somatic concern. The presence of serious psychiatric symptoms like hallucinatory behavior and disorientation were predominantly seen in severe COVID-19 patients with significantly high serum inflammation and coagulation markers.

Key words: inflammatory markers, neuropsychiatric manifestations, coronavirus disease (COVID-19).

INTRODUCTION

In January 2020, the first case of novel coronavirus (SARS-CoV-2) infection was reported in India. The World Health Organization (WHO) officially declared a pandemic on March 11, 2020. Since then huge numbers of cases have been reported globally. As of January 30th 2021, 101,561,219 COVID-19 cases have been confirmed and 2,196,944 deaths reported [1].

Several studies have indicated that the current pandemic has psychiatric consequences. For the prevention and reduction of the spread of coronavirus, most governments announced nationwide lockdowns, quarantine and physical distancing [2, 3]. Worries regarding the future, loneliness, frustration and fear of contracting the virus can be risk factors for the occurrence of mental disorders

[3, 4]. The mental status of hospitalized COVID-19 patients during the pandemic remains poorly understood. COVID-19-positive patients need to be treated in isolated hospitals [5]. After confirmation of a diagnosis of COVID-19 infection, psychological concerns such as fear of the progression of the illness, disability, premature death, and fear of viral transmission to others were likely to arise [6].

Although it is primarily a respiratory infection, SARS-CoV-2 affects multiple systems [7]. The severity of the symptoms among people infected are of a wide range which includes upper respiratory tract infection, lower respiratory tract infection, acute respiratory distress syndrome, and severe acute respiratory syndrome (SARS), neurological symptoms like headache, dizziness, altered senses of smell and taste, cough, asthenia and myalgia [8, 9]. Cere-

brovascular diseases like cerebrovascular stroke, encephalitis, and an altered sensorium are either due to the direct effect of the virus or indirect effects of immune response [8-10]. The virus has been detected upon examination of brain tissue and cerebrospinal fluid (CSF); from individuals with seizure, encephalitis, encephalomyelitis [11]. Systemic and tissue immune responses contribute to the pathophysiology of various neuropsychiatric illnesses [10, 12]. Inflammatory injury to the brain, an abnormal balance between pro-inflammatory (IL-6, TNF- α) and anti-inflammatory cytokines in the central nervous system CNS, immune system deregulations as well as infections, together with genetic vulnerability, abnormalities in neurotransmission, and stress, have been linked to the pathogenesis of depression, bipolar disorder and psychosis [10].

Studies conducted during the previous SARS epidemic also reported psychiatric symptoms like post-traumatic stress symptoms/post-traumatic stress disorder, anxiety and depression among patients infected with SARS-CoV-1 [13-15].

It is possible that systemic infection with SARS-CoV-2, environmental stress, and immune reaction to the virus might be responsible for inducing or accelerating the development of psychiatric symptoms.

The aim of the present study was to assess the characteristics of psychiatric symptoms in hospitalized patients with COVID-19. This study addresses the psychiatric symptoms of such patients, and will be helpful to health care professionals in their formulation of better treatment and psychological interventions for the improvement of the mental and physical health of patients.

METHODS

Study design

An exploratory quantitative study was carried out to assess the presence of psychiatric symptoms among RT-PCR positive COVID-19 inpatients, and its correlation with disease severity, at a COVID-19-designated hospital Sola, Ahmedabad, India. Approval from the institutional ethics committee was sought. Data was collected from 201 patients who were admitted to Sola civil hospital from July 13th to July 26th 2020.

Participants

All patients who gave written informed consent were included in the study. For patients not in a position to give their consent, written or oral consent via telephone was sought from relatives. Sociodemographic data was collected, as reported by participants themselves or their relatives.

Study instruments

The severity of COVID-19 in all the patients was categorized as mild, moderate and severe according to the guidelines provided by the Indian Ministry of Health and Family Welfare Directorate General of Health Services (EMR Division) [16].

The Brief Psychiatric Rating Scale (BPRS-18) item includes symptoms of the majority of psychiatric presentations. The scale consists of 18 items, to be rated by a trained clinician. Each symptom is rated on a 7 point of severity scale ranging from 'not present' to 'extremely severe' (0 = not assessed, 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe). A score greater than one is considered to indicate the presence of a symptom. Total scores ranged from 0 to 126 [17].

Traditionally, the BPRS has been used to rate the severity of symptoms and to make prognoses through serial administration; therefore comparing scores across serial administrations is more important than an absolute score. For this reason, no absolute reference range is available by default.

Statistical analysis

SPSS software version 21 was used for the statistical analysis. Mean and Standard deviation for all BPRS scale variables were calculated. Categorical variables were analyzed using the Pearson's χ^2 test. In order to test the hypothesis that severity of COVID-19 had an effect on BPRS items and total score between groups, ANOVA was performed. To evaluate the nature of the difference between the means of the three groups, the one-way ANOVA was followed-up with Tukey HSD post hoc tests. Statistical differences between groups were considered to be significant when *p*-value was < 0.05.

RESULTS

Among the total of 201 participants 147 were male and mean age was 48.9 (\pm 15.8) years. Sociodemographic variables, BPRS score, history of psychiatric illness, co-morbidity and biomarkers did not show any significant correlation.

Correlation between COVID-19 severity and BPRS total score is shown in Table 1. Statistical analysis (one-way ANOVA) showed a significant positive correlation among them. Post hoc testing revealed a significant difference between the severe versus moderate and mild COVID-19 severity groups.

For each psychiatric symptom severity, total numbers (%) of participants are shown in Table 2. Anxiety and tension were most commonly present, at 63 (31.3%) and 36 (18%) respectively. While somatic concern and depressed mood were found in 16 (8%) and 14 (7%) respectively. Seven patients were found to have disorientation and halluci-

Table 1. COVID-19 severity and BPRS outcome

| COVID-19 severity | Number of participants (n = 201) | BPRS total score (mean ± SD) | F | One-way ANOVA (p-value) | Post hoc analysis |
|-------------------|----------------------------------|------------------------------|------|-------------------------|---------------------------|
| Mild (I) | 133 | 19.1 (± 2.2) | 17.2 | | |
| Moderate (II) | 36 | 20.3 (± 4.0) | | 0.000* | III > II = 1 ^a |
| Severe (III) | 32 | 22.6 (± 4.8) | | | |

*Correlation is significant at the 0.01 level. ^aThe mean difference is significant at the 0.05 level.

Table 2. The total numbers (%) of participants for each psychiatric symptom

| BPRS items | Range | Median | Mean ± SD | Skewness | BPRS items severity | | | | | | Total presence of each symptom, n (%) |
|----------------------------|-------|--------|-------------|----------|---------------------|-------------|-----------------|--------------------------|---------------|-------------------------|---------------------------------------|
| | | | | | Very mild, n (%) | Mild, n (%) | Moderate, n (%) | Moderately severe, n (%) | Severe, n (%) | Extremely severe, n (%) | |
| Somatic concern | 0-6 | 1 | 1.2 (± 0.9) | 3.5 | 3 (1.5) | 3 (1.5) | 6 (3.0) | 3 (1.5) | 1 (0.5) | 0 | 16 (8.0) |
| Anxiety | 0-7 | 1 | 1.7 (± 1.3) | 1.6 | 17 (8.5) | 22 (10.9) | 13 (6.5) | 8 (4.0) | 2 (1.0) | 1 (0.5) | 63 (31.3) |
| Emotional withdrawal | 0-3 | 1 | 1.0 (± 0.2) | 1.2 | 0 | 1 (0.5) | 0 | 0 | 0 | 0 | 1 (0.5) |
| Conceptual disorganization | 1-4 | 1 | 1.0 (± 0.3) | 8.0 | 1 (0.5) | 1 (0.5) | 2 (1.0) | 0 | 0 | 0 | 4 (2.0) |
| Guilty feeling | 0-3 | 1 | 1.0 (± 0.2) | 0.7 | 0 | 1 (0.5) | 0 | 0 | 0 | 0 | 1 (0.5) |
| Tension | 0-6 | 1 | 1.3 (± 0.9) | 2.5 | 15 (7.5) | 12 (6.0) | 6 (3.0) | 2 (1.0) | 1 (0.5) | 0 | 36 (17.9) |
| Mannerisms and posturing | 0-1 | 1 | 1.0 (± 0.0) | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Grandiosity | 1-6 | 1 | 1.0 (± 0.3) | 14.2 | 0 | 0 | 0 | 0 | 1 (0.5) | 0 | 1 (0.5) |
| Depressive mood | 0-6 | 1 | 1.1 (± 0.7) | 4.9 | 5 (2.5) | 4 (2.0) | 2 (1.0) | 1 (0.5) | 2 (1.0) | 0 | 14 (7.0) |
| Hostility | 1-6 | 1 | 1.1 (± 0.6) | 6.1 | 0 | 3 (1.5) | 2 (1.0) | 1 (0.5) | 1 (0.5) | 0 | 7 (3.5) |
| Suspiciousness | 1-4 | 1 | 1.0 (± 0.2) | 14.2 | 0 | 0 | 1 (0.5) | 0 | 0 | 0 | 1 (0.5) |
| Hallucinatory behaviour | 1-6 | 1 | 1.1 (± 0.7) | 5.3 | 0 | 0 | 2 (1.0) | 4 (2.0) | 1 (0.5) | 0 | 7 (3.5) |
| Motor retardation | 1-3 | 1 | 1.0 (± 0.1) | 14.2 | 0 | 1 (0.5) | 0 | 0 | 0 | 0 | 1 (0.5) |
| Uncooperativeness | 1-7 | 1 | 1.1 (± 0.7) | 6.3 | 0 | 3 (1.5) | 0 | 3 (1.5) | 0 | 1 (0.5) | 7 (3.5) |
| Unusual thought content | 0-1 | 1 | 1.0 (± 0.1) | -14.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Blunted affect | 1-4 | 1 | 1.0 (± 0.2) | 14.2 | 0 | 0 | 1 (0.5) | 0 | 0 | 0 | 1 (0.5) |
| Excitement | 1-4 | 1 | 1.0 (± 0.2) | 14.2 | 0 | 0 | 1 (0.5) | 0 | 0 | 0 | 1 (0.5) |
| Disorientation | 1-7 | 1 | 1.1 (± 0.8) | 5.5 | 0 | 0 | 1 (0.5) | 4 (2.0) | 1 (0.5) | 1 (0.5) | 7 (3.5) |

Score > 1 considered as presence of each symptom. Severity score: 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe.

natory behavior, so among them unusual thought content was not assessed.

Table 3 compares the mean score of all symptoms by BPRS with COVID-19 severity. The mean score of emotional withdrawal, feelings of guilt, and tension showed significant differences in the one-way ANOVA. The mild and moderate disease severity groups had significantly high emotional withdrawal, feelings of guilt, and tension compared to the severe disease severity group. While mean scores for hostility, hallucinatory behavior, uncooperativeness and disorientation also showed significant differences, the highest was in the severe disease severity group.

Seven patients who had hallucinatory behavior and disorientation also showed high serum ferritin and D-dimer value. Four among them had high levels of IL-6 too.

DISCUSSION

Neuropsychiatric consequences may result from direct neuronal invasion by virus, and indirectly through systemic inflammatory response by cytokines and imbalance of coagulation and fibrinolysis systems. Researchers also found blood-brain barrier dysfunction, neuronal damage and high levels of autoantibodies in the CSF of patients who had severe COVID-19 illness with neuro-

Table 3. Comparison of mean score of psychiatric symptoms among COVID-19 degree-of-severity groups

| BPRS items | Mean score of psychiatric symptoms among COVID-19 degree-of-severity groups | | | F | p-value One-way ANOVA | Post hoc analysis |
|----------------------------|---|----------------------------|---------------------------|------|--------------------------|---------------------------|
| | Mild (I) Mean ± SD | Moderate (II) Mean ± SD | Severe (III) Mean ± SD | | | |
| Somatic concern | 1.0 (± 0.5) | 1.3 (± 0.9) | 0.9 (± 1.0) | 1.8 | 0.165 | I = II = III |
| Anxiety | 1.3 (± 0.9) | 1.8 (± 1.5) | 1.5 (± 1.9) | 2.3 | 0.1 | I = II = III |
| Emotional withdrawal | 1.0 (± 0.0) | 1.0 (± 0.4) | 0.8 (± 0.4) | 7.9 | 0.001** | II = I > III ^a |
| Conceptual disorganization | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.0 (± 0.5) | 0.4 | 0.689 | I = II = III |
| Guilty feeling | 1.0 (± 0.0) | 1.1 (± 0.3) | 0.8 (± 0.4) | 16.1 | 0.000** | II = I > III ^a |
| Tension | 1.3 (± 0.8) | 1.2 (± 0.9) | 0.8 (± 0.4) | 6.6 | 0.002** | II = I > III ^a |
| Mannerisms and posturing | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.0 (± 0.0) | – | – | – |
| Grandiosity | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.2 (± 0.9) | 2.7 | 0.071 | I = II = III |
| Depressive mood | 1.0 (± 0.3) | 1.3 (± 1.1) | 1.2 (± 1.1) | 3.1 | 0.047* | I = II = III |
| Hostility | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.4 (± 1.3) | 8.8 | 0.000** | III > II = I ^a |
| Suspiciousness | 1.0 (± 0.0) | 1.0 (± 0.5) | 1.0 (± 0.0) | 2.3 | 0.101 | I = II = III |
| Hallucinatory behaviour | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.6 (± 1.6) | 11.8 | 0.000** | III > II = I ^a |
| Motor retardation | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.1 (± 0.4) | 2.7 | 0.071 | I = II = III |
| Uncooperativeness | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.8 (± 1.6) | 19.2 | 0.000** | III > II = I ^a |
| Unusual thought content | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.0 (± 0.2) | 2.7 | 0.071 | I = II = III |
| Blunted affect | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.0 (± 0.2) | 2.7 | 0.071 | I = II = III |
| Excitement | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.0 (± 0.2) | 2.7 | 0.071 | I = II = III |
| Disorientation | 1.0 (± 0.0) | 1.0 (± 0.0) | 1.9 (± 1.8) | 22.1 | 0.000** | III > II = I ^a |

*Correlation is significant at the 0.05 level. **Correlation is significant at the 0.01 level. ^aThe mean difference is significant at the 0.05 level.

logical manifestations like myoclonus, seizure, delirium, and encephalopathy [18]. Besides the above-mentioned factors, environments were also different for mild, moderate and severe COVID-19 patients during their hospitalization. In the ICU, patients had a longer hospital stay, restricted mobilization, lack of environmental stimulus and direct exposure to the deaths of neighboring patients. Therefore, different pathological processes and distinct environments may lead to different psychological presentations.

Psychiatric symptoms as recorded on the BPRS-18 item scale were present in 80 (40%) out of the total of 201 patients, and except for two (mannerism and posturing, and unusual thought content) all other symptoms listed in the BPRS were present. The most common symptoms recorded were anxiety, tension, somatic concern and depressed mood, in 63 (31.3%), 36 (18%), 16 (8%) and 14 (7%) of patients respectively. Kong *et al.*, in their study in Wuhan, China, found the prevalence of anxiety and depression to be 34.7% and 28.5% respectively [6]. Liu *et al.*, also in China, found anxiety and depression to be 20.8 % and 29.2% respectively [19], albeit among recovered COVID-19 patients. Anxiety (31.3%), as assessed with the BPRS in our study, was higher, but depression (7.5%) was found to be lower. This might be due to differences in study population, settings and assessment tool used.

We found significant correlations between mean total BPRS scores across the mild, moderate and severe COVID-19 groups. Kong *et al.* found through the comparison of the mean scores of the Hamilton Rating Scale for Anxiety (HAMA) in COVID-19 patients with saturation > 93% and ≤ 93% were 6.05 and 8.75 respectively; patients with severe illness were more likely to be anxious [6]. Liu *et al.* found that higher disease severity predisposed patients to the development of moderate-to-severe anxiety, and severe depression [19].

In our study, we found that the characteristics of psychiatric symptoms were distinct in individuals with mild, moderate and severe COVID-19 illness. In multiple comparisons, results showed that mean scores for hostility, hallucinatory behavior, uncooperativeness and disorientation were found to be high in severe COVID-19 patients. In our study, of the 32 severely ill COVID-19 patients hallucinatory behavior and disorientation were present in 7 (21.9%). Similar findings by Huang *et al.*, in their retrospective study of 36 non survivors of COVID-19, suggest that 8 (22.2%) patients had symptoms of disturbance of consciousness [20]. Beach *et al.*, in their case series of delirium in COVID-19 patients, found that in all patients the levels of inflammatory markers were elevated, particularly C-reactive protein (CRP) [9]. In our study we also found that serum inflammatory and coagulation markers were raised in all patients with hallucina-

tory behavior and disorientation. Unfortunately, data on CRP level was not available in our study population. For psychosis, Masopust *et al.* in their research found that in drug-naive psychosis patients, coagulation activity was increased [21]. Whether hyper-coagulation predisposes patients to psychiatric symptoms needs further evaluation.

There was no significant correlation found between the characteristics of psychiatric symptoms in COVID-19 patients and various Sociodemographic variables like residence, type of family, socio-economic class, education, occupation, age, sex comorbidity and past history of psychiatric illness.

Very few studies of this kind have been conducted to date. The mental health of COVID-19 patients needs to be explored. In long course of COVID syndrome, scientists found various neuropsychiatric symptoms like anxiety, depression, apathy, anger, euphoria, and disinhibition [22]. The present study is warranted for the early detection of psychiatric disorders in their initial phase so that necessary measures can be taken to provide treatment. By understanding the psychological conditions of COVID-19 patients, clinicians should reinforce positive attitudes, familiar environment, and the improvement of their coping skills. This study will be helpful in the pro-

vision of a better quality of care and good clinical outcomes.

The strength of the study was that it was conducted offline and included patients with varying degrees of COVID-19 severity. The scale was employed by a trained clinician during the acute stage of infection.

The present study was carried out with some limitations, such as a cross-sectional study design, small sample size, single-center study and lack of comparison with the general population and other disease groups.

CONCLUSIONS

Our study points out the prevalence and severity of various psychiatric symptoms in hospitalized COVID-19 patients. The majority of patients experienced anxiety, tension, somatic concerns and depressive mood. Neuropsychiatric manifestations of COVID-19 were predominantly seen in patients with severe COVID-19, accompanied by evidence of high serum inflammation and coagulation markers. The results of the study indicate a need to pay attention to the psychological care of patients, especially those in the severe COVID-19 severity. Early recognition of symptoms and timely intervention will improve the mental health of patients.

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Conflict of interest

Absent.

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