



## LONGITUDINAL ASSESSMENT OF CHANGE IN THE SEVERITY OF STRESS, ANXIETY, AND DEPRESSION AND ITS CLINICOPATHOLOGICAL CORRELATION IN COVID-19 PATIENTS DURING THEIR INPATIENT STAY

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### ABSTRACT

**Background** – COVID-19 illness is associated with psychological distress. The contribution of isolated inpatient stay to this psychological distress is yet to be ascertained. The objective of the study was to assess the change in the severity of stress, anxiety, and depression in COVID-19 inpatients, as assessed on the day of hospital admission and on the day of discharge and its association with clinical variables. **Methods** – This was a longitudinal study with a sample of 104 patients admitted to the COVID-19 wards of a tertiary care hospital. Socio-demographic profile, COVID-19-related clinical variables, and laboratory parameters were recorded at baseline. The severity of stress (PSS scale), anxiety (HAM-A scale), and depression (HAM-D scale) were assessed on the day of hospital admission and on the day of discharge. The association between change in the severity of these and other variables was assessed. **Results** - Significant increase in the severity of stress (Z value = -4.93, p-value < 0.001), anxiety (Z value = -4.18, p-value < 0.001), and depression (Z value = -3.20, p-value < 0.001) were found from the day of admission to the day of discharge. There were no significant associations found between the clinical variables and the severity of stress, anxiety, and depression. **Conclusion** – There was significant increase in stress, anxiety, and depression during inpatient stay despite improvement in clinical variables.

**KEYWORDS** : COVID-19, stress, anxiety, depression, inpatient care, COVID-19 ward

### INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral illness that was declared a pandemic by the World Health Organization on March 11, 2020.<sup>[1]</sup> The disease itself, along with the perceived stigma and discrimination, may cause psychological issues in the patients suffering from the disease.<sup>[2]</sup> Since the beginning of the pandemic, issues related to mental health have been highlighted repeatedly. Various factors that may be responsible for this include the direct effects of the virus on the central nervous system, the neuropsychiatric effects of inflammatory markers, the psychological impact of contact isolation along with the stigma of getting infected, and disrupted social functions associated with serious illness.<sup>[3]</sup> Patients with COVID-19 hospitalization are especially at increased risk of developing psychiatric symptoms given the severity of their disease, the unique stress of hospitalization under contact isolation, and the possibility of iatrogenic psychiatric effects of medications and other interventions.<sup>[4]</sup>

Few previous cross-sectional studies found a higher prevalence of stress, anxiety, depression, and post-traumatic stress disorder in COVID-19 patients during their hospital stay.<sup>[4, 5, 6]</sup> There is minimal literature on assessment of change in the severity of the stress, anxiety and depression during the inpatient stay. Present study was done to fill this gap in the literature in COVID-19 patients. The other objective was to study any association between the change in the severity of stress, anxiety, and depression with socio-demographic and COVID-19-related clinical variables and lab parameters.

### MATERIALS AND METHODS

We used a longitudinal study design. All the patients admitted to COVID-19 wards in a tertiary care medical college and hospital over two months period between 25<sup>th</sup> May 2021 and 24<sup>th</sup> July 2021 (time-bound). Samples were screened for eligibility to participate in the study. The assessment was done at two points, 1<sup>st</sup> on the day of admission and 2<sup>nd</sup> on the day of discharge. All the patients above 18 years of age admitted to the COVID-19 ward in the tertiary care hospital with positive COVID RT-PCR test reports and patients with medical illness (diabetes, hypertension) were included in the study. Patients

with only Rapid antigen test (RAT) positive, RT-PCR negative and only HRCT positive suggestive of atypical pneumonia, pre-existing psychiatric illness (assessed by direct questioning "whether you have any psychiatric illness?") and substance abuse (except for nicotine), on ventilatory support (invasive or non-invasive) and persons with impaired capacity (altered sensorium or intellectual disability) were excluded from the study. During two-month period, total 189 patients admitted to COVID-19 wards were approached for participation in the study, out of which 52 were excluded as 38 were only RAT positive and 14 had previous psychiatric illness. So, 137 patients meeting inclusion and exclusion criteria were enrolled into the study.

As per the institution's policy, first approval from the Scientific Advisory Committee (SAC) and then from the Ethics Committee for Research on Human Subjects (ECRHS) of the institute was obtained. Written informed consent was obtained from all the participants and they were informed about their right to leave the study at any point of time without any impact on their ongoing treatment for COVID-19 illness. No additional financial burden was put on the subjects by participation in the study.

### ASSESSMENT TOOLS

The socio-demographic and clinical information was recorded anonymously in a pre-designed questionnaire. The information included age, sex, marital status, employment status, education, the income of the head of the family, and details of the primary caregiver. The socio-economic status was classified using a modified Kuppuswamy scale.<sup>[7]</sup> We also recorded clinical variables related to COVID-19 illness like Heart Rate, Temperature Blood pressure, respiratory rate, and Oxygen saturation (SPO2) on the day of admission and on the day of discharge to assess clinical improvement in COVID-19 illness. Laboratory investigations like haemoglobin (Hb), Lymphocyte, neutrophil count, serum urea, serum creatinine, serum bilirubin, d-dimer, ferritin, Lactate Dehydrogenase (LDH), Erythrocyte Sedimentation Rate (ESR), and C - reactive protein (CRP) were recorded only once during the inpatient stay.

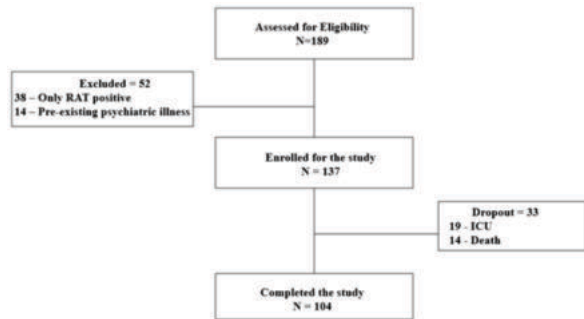
The severity of stress, anxiety, and depression was also assessed at the same two-time points. The level of stress was assessed using the perceived stress scale (PSS)<sup>[8]</sup> The severity of anxiety was assessed using the Hamilton Anxiety Rating Scale (HAM-A).<sup>[9]</sup> The severity of depression was assessed using the Hamilton Depression rating scale (HAM-D).<sup>[10]</sup> All these scales are already validated to estimate the change in the severity of stress, anxiety and depression over a period.<sup>[11,12,13]</sup>

**Statistical Analysis**

The collected data were analyzed using SPSS (Statistical Software for Social Sciences) software version 26. Initially, descriptive statistics were done using appropriate measures of central tendency. Association between the severity of stress, anxiety, and depression with socio-demographic and clinical variables was done using the Wilcoxon Signed Ranks Test and Spearman's Correlation. Significance was set with a 95% confidence level and a p-value <0.05 was taken as significant and highly significant when p<0.01.

**RESULTS**

During the study period, out of 137 subjects enrolled into the study and completed the 1<sup>st</sup> assessment. Of these 19 subjects were shifted to ICU and 14 died so the second assessment for these 33 patients was not done. So, the results presented below include only 104 subjects who completed both assessments.



**Figure 1:** Patient Eligibility, Enrolment And Study Completion

Out of 104 participants, 66 (63.4%) were male, 37 (35.5%) belonged to the age group of 31-40 years, 82 (79%) were from

rural areas and 99 (95.2%) were Hindu by religion. 36 (34.6%) subjects had education up to middle school, 43 (41.3%) worked as clerks, 89 (85.6%) were married and 82 (79%) had full-time jobs. As per the modified Kuppuswamy scale, 70 (67%) belonged to lower-middle class, 70 (67%) spouses were the most common caregivers as shown in Table-1. The average IPD stay in the COVID-19 ward was 8.23 (SD=2.9) days.

Variables	n (%)	
Age group (years)	21 – 30	13 (12.5)
	31 – 40	37 (35.5)
	41 – 50	25 (24.2)
	51 - 60	29 (27.8)
Sex	Male	66 (63.4)
	Female	38 (36.6)
Religion	Hindu	99 (95.2)
	Muslim	5 (4.8)
Locality	Rural	82 (79)
	Urban	22 (21)
Level of education	Primary school	20 (19.2)
	Middle school	36 (34.6)
	High school	14 (13.5)
	Bachelors/ diploma	15 (14.4)
	none	19 (18.3)
Occupational status	Technical	15 (14.4)
	Clerical	43 (41.3)
	Businessman	18 (17.3)
	Industry	24 (23.1)
	Skilled	4 (3.9)
Marital status	Married	89 (85.6)
	Single	15 (14.4)
Employment status	Student	2 (1.9)
	Part time	9 (8.5)
	Full time	82 (79)
	Housewife	11 (10.6)
Socioeconomic status	Upper middle	10 (9.6)
	Lower middle	70 (67.3)
	Upper lower	24 (23.1)
Caregiver relationship with participants	Parents	10 (9.6)
	Spouse	70 (67.3)
	Siblings	24 (23.1)

**Table 2: Change in stress level, anxiety, and depression and the Covid -19 related clinical variables from the day of admission and on the day of discharge**

Variables	PSS	HAM-A	HAM-D	Temperature	Pulse Rate	Respiratory rate	BP Systolic	BP Diastolic	Oxygen Saturation
Mean value (SD) on Admission	10.30 (9.10)	6.05 (6.54)	3.78 (4.57)	99.01 (1.54)	90 (9.79)	32 (32.8)	123.96 (9.75)	82.82 (6.14)	94.28 (10.2)
Mean value (SD) on Discharge	15.08 (9.88)	8.57 (8.65)	4.91 (5.83)	98.17 (0.60)	84 (6.28)	26 (9.73)	120.55 (5.56)	80.56 (5.56)	96.98 (9.88)
Difference	-4.78	-2.52	-1.13	0.84	6	6	3.41	2.26	-2.7
Z	-4.93 <sup>b</sup>	-4.18 <sup>b</sup>	-3.20 <sup>b</sup>	-5.94 <sup>a</sup>	-5.72 <sup>a</sup>	-3.11 <sup>a</sup>	-3.38 <sup>a</sup>	-3.74 <sup>a</sup>	-7.49 <sup>b</sup>
P value	0.000	0.000	0.001	0.000	0.000	0.002	0.001	0.000	0.000

Wilcoxon Signed Ranks Test. P<0.01 is highly significant, a=based on positive ranks, b=based on negative rank

**Table 3: Correlation In Clinical Variables With Stress, Anxiety, And Depression Scale From The Day Of Admission To The Day Of Discharge**

Spearman correlation	Diff. PSS	Diff. HAMA	Diff. HAMD
Temperature difference	r <sub>s</sub> (p)	.03(.75)	.05(.58)
Pulse Rate difference	r <sub>s</sub> (p)	-.02(.78)	-.08(.39)
Respiratory Rate difference	r <sub>s</sub> (p)	-.02(.77)	-.09(.92)
Oxygen saturation difference	r <sub>s</sub> (p)	-.31(.05)	.09(.31)
Systolic blood pressure difference	r <sub>s</sub> (p)	.08(.37)	.11(.25)
Diastolic blood pressure difference	r <sub>s</sub> (p)	.08(.38)	.09(.35)

**Table 4: Descriptive analysis of Drop-out Patients**

Variables	Frequency (N)	Percent (%)
Gender	Male	19
	Female	14

Locality	Urban	6	18.2
	Rural	27	81.8
Education	None	10	30.3
	Primary School	7	21.2
	Middle School	4	12.1
	High School	6	18.2
	Bachelors/ Diploma	6	18.2
Religion	Hindu	32	97.0
	Jainism	1	3.0
Occupation	Professional	1	3.0
	Managerial	5	15.2
	Technical	2	6.1
	Clerical	7	21.2
	Businessman	1	3.0
	Industrial	1	3.0
	Skilled	12	36.4
	Unskilled	3	9.1
	Other	1	3.0
	Employment	Part time	5
Full time		12	36.4
Self employed		7	21.2
Housewife		8	24.2
Retired		1	3.0
Marital Status	Single	3	9.1
	Married	28	84.8
	Separated	1	3.0
	Widow	1	3.0
Caregiver	Spouse	28	84.8
	Parents	2	6.1
	Children	2	6.1
	Siblings	1	3.0
Cause of Drop-out	Death	14	42.4
	ICU	19	57.6
	Mean	SD	
PSS Scale	12.42	9.89	
HAM-A Scale	8.24	7.14	
HAM-D Scale	4.09	4.17	

Table-2 shows Change in stress level, anxiety, depression and the COVID -19 related clinical variables from the day of admission to the day of discharge. It is evident that there was a significant change in the level of stress (p-value<0.001), anxiety (p-value<0.001), and depression p-value<0.001) from the day of admission to the day of discharge.

Spearman's correlation was calculated between change in clinical variables (temperature, pulse rate, respiratory rate, oxygen saturation, systolic blood pressure) as measured on the day of admission and the day of discharge and HRCT score, Hb, Lymphocyte, neutrophil, urea, creatinine, bilirubin, d-dimer, CRP etc. There was very weak positive correlation between lymphocyte count and temperature change ( $r_s = 0.195$ ,  $p = 0.04$ ). A weak positive correlation was between pulse rate and d-dimer level ( $r_s = 0.242$ ,  $p = 0.01$ ). Change in oxygen saturation was weakly correlating with ESR values ( $r_s = 0.249$ ,  $p = 0.03$ ) of COVID-19 patients. Apart from this, there was no other significant correlation between clinical variables and lab parameters. There was no significant correlation between existing co-morbid illness (diabetes, hypertension) and the change in severity of stress, anxiety and depression.

Table-3 depicts Spearman's correlation between change in clinical variables and change in score of stress, Anxiety and Depression rating scales assessed on two time points. There was significant but weak inverse relationship between change in oxygen saturation and change in scores of

perceived stress scale ( $r = -0.318$ ,  $p$  value= 0.05). All other variables did not demonstrate any significant relationship.

Descriptive Analysis of subjects excluded after 1<sup>st</sup> assessment is shown in Table-4 which shows out of 33, 19 (57.6%) were male, 27 (81.8) belonged to rural area, 10 (30.3%) were uneducated and 32 (97%) were Hindu by religion. 12 (36.4%) subjects were skilled labour, 12 (36.4%) with full-time job, 28 (84.8%) married, and 28 (84.8%) spouses were the care givers.19 (57.6%) dropped out due to ICU admission and 14 (42.4%) died during the course of treatment.

## DISCUSSION

Majority of subjects in present study were in 4<sup>th</sup> and 6<sup>th</sup> decades of life and males, belonged to middle socioeconomic strata and were employed in clerical jobs and above category. This to some extent is due to socioeconomic strata receiving care from the center. These findings are similar to other studies from tertiary care hospitals.<sup>(4,5,6)</sup> Spouses and siblings were the most common care givers available for any support to these subjects. This is in line with Indian culture where spouses play major role of being primary care provider. Only 10% parents of the adult subjects were present due to obvious fear of suffering severe forms of COVID-19 illness in elderly. Most subjects in our study had a stable job at clerical level and above, however few other studies reported that a long history of freelancers and house workers represented their sample, and were more likely to be depressed.<sup>(5,6)</sup>

Findings of the present study reveal that as compared to the day of admission, there was significant increase in the level of stress, anxiety, and depression in COVID-19 hospitalized patients at the time of discharge despite improvement in their clinical status. Available literature from longitudinal studies showing variable findings. A study from Rome, Italy reported significant anxiety, depression and suicide ideas persisted after 3 months of discharge from COVID-19 ward. Female sex, pulmonary chronic condition and previous mental disorder were significant predictors of persistence of anxiety and depression at 3 month follow up.<sup>[14]</sup> Another study from Rotterdam, Netherlands reported persistent health problems beyond pulmonary recovery even up to 6 months after hospitalization for COVID-19 illness. Authors reported a decreasing trend but a significant persistence of anxiety, depression and post-traumatic stress symptoms along with fatigue and non-pulmonary symptoms on assessment at 6 months follow up.<sup>[15]</sup> A study from New York, USA has reported significant reduction of stress, anxiety, depression on follow-up after 15 days. However, this study had a small sample of 58 subjects with a high drop-out rate of 28% for second assessment which was done via telephone interviews.<sup>[4]</sup>

Similarly, another Italian cohort study reported significant improvement in anxiety and depression in admitted COVID-19 subjects at 4 month and 1 year follow ups. Female sex, obesity and hypertension were risk factors for persistence of anxiety and depression in this cohort study.<sup>[16]</sup> Our study did not reveal significant correlation between demographic variables and stress, anxiety, depression. Another study from Switzerland reported persistence of psychological distress (depression and anxiety) after 30 days of discharge from hospital for treatment of COVID-19 illness.<sup>[17]</sup> Overall most of the literature supports the importance of identification and management of emerging psychiatric symptoms along with COVID-19 illness, Persistence of these symptoms beyond a year further emphasizes identification and management at earlier stages.

We did not find any correlation between frequency of interaction with the caregiver and severity of stress, anxiety, and depression in subjects. However, a study reported lack of support from caregivers and relatives as the key factor for anxiety and depression.<sup>[18]</sup> In our study severity of stress, anxiety and depression was not associated with demographic and social variables, maybe due to strong social support and intact family bonding in Indian settings. This differs from the findings of studies from other countries which reported that lack of social support for patients with COVID-19 is associated with depression and socioeconomic status bearing a major impact on the severity of depression.<sup>[19,20]</sup> There was weak correlation between clinical variables and laboratory parameters in our study. A meta-analysis of 42 subjects reported d-dimer levels as significant predictor of clinical deterioration. This was only laboratory variable found to have predictive importance to other 22 independent variables analysed in this meta-analysis.<sup>[21]</sup> Another study had reported mild anaemia as a single independent predictor of deterioration in patients with COVID-19 patients.<sup>[22]</sup> Haematological and biochemical laboratory parameters for differential diagnosis and prospective grading of COVID-19 is proposed as a simple, efficient model of triage to assist for hierarchical management of COVID-19 patients.<sup>[23]</sup>

The findings of our study highlight the need for the inclusion of psychological screening and appropriate management of all patients admitted to the COVID-19 ward which aligns with recommendations by other authors that cognitive behavioural therapy and progressive muscle relaxation training were found to be effective in reducing psychological distress in

COVID-19 patients.<sup>[24,25,26]</sup> During our study those patients with significant levels of anxiety and depression were provided treatment at the time of discharge itself. They were instructed to be on regular follow-up in psychiatry OPD after discharge from the ward. After completion of the study and preliminary analysis of data, to reduce the stress of admitted patients, we conducted stress management and relaxation sessions in COVID-19 wards itself. The strengths of this study are its longitudinal design that assessed change in levels of stress, anxiety, and depression during the inpatient stay of COVID-19 patients and that enables us to initiate appropriate management for the same at the time of discharge itself. The results of the study should be interpreted with the limitations of it being a single-centre study with an assessment of only inpatients. In few cases 2<sup>nd</sup> assessment was within 8 days. Sudden worsening of clinical status and deaths led to exclusion of 33 subjects from final analysis are few other limitations.

## CONCLUSIONS

There was a significant increase in the level of stress, anxiety, and depression during the inpatient stay of COVID-19 patients despite an improvement in fever and respiratory distress. This increase was not associated with socio-demographic, clinical profile, and lab related variables. Findings highlight the need for appropriate identification and intervention for psychological health as an essential part of care in COVID-19 wards.

## Conflicts Of Interest:

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**Key Message** - Psychological help and support should be an integral part of COVID-19 patients during their inpatient stay.

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