

Covid-19 and Anxiety: An Analytical Study in Hospitalized Patients of a Tertiary Care Hospital in North India

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ABSTRACT

Background: The way the COVID-19 pandemic struck the world; it was bound to have stress-related repercussions among a lot of people, especially those who got infected with the virus. As per several community-based surveys, anxiety is one of the significant mental health issues that these patients are suffering from in addition to the primary illness. But, unfortunately, there is a scarcity of data on anxiety in hospitalized COVID-19 patients.

Aims: This study aimed to compare the prevalence and severity of anxiety between hospitalized COVID-19 patients with age and gender-matched controls admitted in medical wards.

Methods: This analytical study of hospitalized moderate to severe COVID-19 patients was conducted over two months (October to November 2020). A total of 103 patients were enrolled and were compared with age and gender-matched controls in a 1:1 ratio. Anxiety was assessed by the DASS-21 (Depression Anxiety Stress Scale) questionnaire.

Results: The majority of patients in the COVID-19 cohort, 55.4%, were > 60 years of age. The most common comorbidity in the COVID-19 cohort was hypertension in 51.5%, followed by Type 2 Diabetes Mellitus in 31.1%. DASS-21 score ≥ 20 , indicating a highly severe grade of anxiety was present in 39.8% of the COVID-19 cohort compared to 3.9 % in the control group with a p-value <0.001 . On multivariate linear regression analysis, age >60 and female gender significantly predicted anxiety in COVID-19 patients.

Conclusion: There is a high prevalence of severe anxiety among hospitalized patients in moderate to severe COVID-19 patients compared to non-COVID patients admitted to the same hospital. Anxiety is more prevalent in females and an elderly cohort of COVID-19, which highlights the importance of screening all hospitalized COVID-19 patients for psychiatric disorders, especially anxiety and the need to address it as early as possible and follow up for long term mental health sequel.

Keywords: anxiety, COVID-19, hospitalized, Mental health

JMS: 2021; 24(3):18-24 DOI: <https://doi.org/10.33883/jms.v24i3.1110>

INTRODUCTION

SARS-COV-2 started from Wuhan, China, by the end of 2019 and spread rapidly throughout China and the rest of the world. World Health Organization (WHO) officially labelled the disease caused by the virus as COVID-19 and designated it a global pandemic on March 11, 2020¹. Since its emergence, COVID-19 has infected more than 275 million people and killed more than 5.3 million globally since late January 2020². It has infected 34,695,110 and killed 4, 79,133 in India, and these figures continue to increase. In Jammu and Kashmir, it has infected 340,293

and killed 4518 till now³. Since the first reported case in Kashmir by a traveler in March 2020, there has been an exponential increase in the number of infected patients who need management in the community or the hospital, depending on disease severity.

Kashmir, which has been suffering from political turmoil

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Access this article online



Website:
www.jmsskims.org

DOI:
<https://doi.org/10.33883/jms.v24i3.1110>

How to cite this article: Shabir A, Mantoo S, Hafiz U, Mehfooz N, Siraj F, Hussain SA, Qadri SM, Bindroo M, Koul AN, Dangroo M, Ahmad Z, Sofi F, Shah S, Jan R, Hussain T. Covid-19 and anxiety: An Analytical Study in hospitalized patients of a Tertiary care hospital in North India. JMS 2021; 24 (3) 18-24

Received: 2021-08-04 Accepted: 2021-08-28



for the past three decades with a ratio of mental illness in 1 in 5 compared to 1 in 14 in a non-conflict zone, already has a high prevalence of anxiety, depression, stress and PTSD⁴. Similar data was seen in a survey done on participants of mhGAP in 2017⁵. Moreover, most mental health studies conducted in the Kashmir Valley over the past ten years consistently report a high prevalence of traumatogenic experiences and associated symptoms of mental distress⁶.

Studies performed after the 2003 severe acute respiratory syndrome (SARS) and 2014 Ebola outbreaks indicated very high rates of psychological distress among those who had been quarantined. Suicide attempts were documented among some hospitalized patients. Long-term behavioral changes were also reported⁷. Like SARS, COVID-19 is an infectious disease and a biological disaster with severe mental health impacts in suspected cases under quarantine, confirmed cases in isolation and their families, health care workers and the general population¹⁰. Although most of the global attention has been focused on treating the respiratory and cardiovascular complications of the disease, a large proportion of COVID-19 patients are experiencing psychological problems, including anxiety, depression and stress¹¹. In addition, patients infected with a novel, a potentially fatal virus may experience fear of the disease itself, loneliness, anger, and anxiety for the welfare of friends and family. These emotions may be aggravated by fever, dyspnea and weakness, and the adverse effects of treatments such as a high dose of corticosteroid administration (11). Most of these patients are either hospitalized in COVID-19 wards or self-quarantined at home, depending on the severity of COVID-19 disease.

AIM

The primary aim of this study was to compare the prevalence and severity of anxiety between hospitalized COVID-19 patients with an equal number of age and gender-matched controls admitted in medical wards. The samples were assessed using the anxiety questionnaire of the DASS-21 (Depression Anxiety Stress Scale) anxiety screening tool. This is the first study in India of unique nature to the best of our knowledge. The assessment of anxiety was done in hospitalized COVID-19 patients by resident doctors posted in an Isolation ward and compared with non-COVID-19 patients as control. All other studies done worldwide in hospitalized COVID-19 patients have

been through telephone contact and not in-person. As verbal and non-verbal expressions are crucial in psychiatric assessment, this would not have been possible in telephonic assessment. Hence, we conducted an in-person assessment taking all the precautions as per recommended guidelines of WHO.

MATERIALS AND METHODS

Study overview

Eligible patients were enrolled at SKIMS, an urban tertiary care center, for two months, October to November 2020. The Institute Ethics Committee approved this study. A total of 103 COVID-19 patients were enrolled in the study, and an equal number of age and gender-matched controls were taken. After obtaining subject consent, investigators administered the DASS-21 questionnaire to the COVID-19 patients after a week of admission to the COVID-19 ward and hospitalized non-COVID 19 patients in medical wards that acted as a control. DASS-21 was translated in the local language Kashmiri by the investigators and forms filled by the investigator's bedside taking all precautions. More sophisticated questionnaires were not used to minimize the contact time of investigators with COVID-19 patients. As we explicitly focused on anxiety in COVID-19 and control patients, only the anxiety questionnaire of DASS-21 was used for screening. In addition, the investigators filled clinical Performa with patients' demographics and comorbidities.

Eligibility and recruitment

Patients were eligible for recruitment if >18 years of age and could provide verbal consent. All enrolled patients in COVID-19 wards had a positive test for COVID-19 by nasopharyngeal SARS-CoV-2 RT-PCR and WHO disease severity of moderate to severe and were able to answer questions. All critical patients requiring HFNC (high flow nasal cannula), NIV (non-invasive ventilation) and MV (mechanical ventilation) were excluded from the study. The control patients were taken from medical wards and were negative for COVID-19. Patients and controls were recruited by the faculty involved in taking care of both the areas (Isolation area for COVID patients and the non-COVID medical wards) after matching for the severity of illness and illness.

Study assessment

DASS-21 questionnaire was given to the patients. DASS-42

questionnaire was developed by Lovibond and Lovibond and is an instrument to assess the perceived severity of anxiety, depression and stress⁸. It was modified into a shorter 21-item version⁹. Several studies have been published on its reliability and validity worldwide. DASS-21 is a self-report instrument, and no special skills are required to administer it. Patients were asked to use a 4-point severity/ frequency scale to rate the extent of anxiety they have experienced over the past one week of hospital admission. The score for anxiety was calculated by summing the score. The recommended cut-off score for the severity scale was as follows. Normal 0-7, mild 8-9, moderate 10-14, severe 15-19 and extremely severe 20+.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean $\pm$ SD with 95% confidence intervals, and categorical variables were summarized as percentages. Student's independent t-test and ANOVA were employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was used to compare categorical variables. A p-value of less than 0.05 was considered statistically significant. All p-values were two-tailed.

RESULT

Total 103 COVID-19 patients were enrolled in the study, and an equal number of controls were taken. The majority of patients in the COVID-19 cohort, 55.4%, were > 60 years of age, and 44.7% were 60-74 years. Mean $\pm$ SD age of cases was 56.5 ± 15.10 compared to the age in the control group, which was 54.5 ± 16.27 and were age and gender-matched. (Table 1).

Table 1: Age distribution of cases and controls					
Age (Years)	Cases		Controls		P-value
	No.	%	No.	%	
< 30	8	7.8	6	5.8	0.354
30-44	10	9.7	24	23.3	
45-59	28	27.2	23	22.3	
60-74	46	44.7	37	35.9	
≥ 75	11	10.7	13	12.6	
Total	103	100	103	100	
Mean ±SD (Range)	56.5±15.10 (18-87)		54.5±16.27 (22-97)		

Majority of the participants in both cohorts were married. 55% of COVID-19 cohort resided in rural area and it was similar in the control group. The most common comorbidity in the COVID-19 cohort was hypertension in 51.5% followed by Type 2 Diabetes Mellitus in 31.1% which was statistically significant p-value 0.001 and 0.005 respectively (Table 2).

Table 2: Underlying comorbidities in cases and controls

Comorbidity	Cases		Controls		P-value
	No.	%	No.	%	
Hypertension	53	51.5	30	29.1	0.001*
T2DM	32	31.1	15	14.6	0.005*
COPD	4	3.9	1	1.0	0.369
CHF	2	1.9	3	2.9	1.000
Renal failure	9	8.7	4	3.9	0.252
Hypothyroid	14	13.6	7	6.8	0.107
Malignancy	12	4.9	15	14.6	0.190
Depression	2	1.9	0	0.0	0.498
PVD	1	1.0	1	1.0	1.000

*Statistically Significant (P-value<0.05)

There was significant anxiety in the COVID-19 cohort group 82.5% with Mean $\pm$ SD score of anxiety was 19.1 ± 12.73 and 95% CI (16.63-21.62) compared to 56.3% with Mean $\pm$ SD score of anxiety 9.3 ± 6.31 and 95% CI (8.03-10.53) in the control group which is statistically significant with p-value < 0.001 (Table 3). DASS-21 score ≥ 20 indicating extremely severe grade of anxiety was present in 39.8% of COVID-19 cohort compared to 3.9 % in the control group with p-value < 0.001 .

Table 3: Comparison based on anxiety grading (DASS -21) in cases and controls

Anxiety Grading	Cases		Controls		P-value
	No.	%	No.	%	
Normal (0-7)	18	17.5	45	43.7	<0.001
Mild (8-9)	11	10.7	9	8.7	
Moderate (10-14)	20	19.4	35	34.0	
Severe (15-19)	13	12.6	10	9.7	
Extremely severe (≥ 20)	41	39.8	4	3.9	
Total	103	100	103	100	
Mean±SD (95% CI)	19.1±12.73 (16.63-21.62)		9.3±6.31 (8.03-10.53)		

After univariate linear regression analysis within the COVID-19 cohort, the DASS-21 anxiety score was higher in elderly (> 60 years), in females and in those with

comorbidities which was statistically significant. (Table 4)

Table 4: Correlation of anxiety score (DASS -21) with demographic variables within COVID cohort					
Variable		Mean	SD	95% CI	P-value
Age	< 60 Years	16.43	8.89	14.20-20.67	0.043*
	≥ 60 Years	20.32	10.11	15.84-22.79	
Gender	Male	16.89	10.31	13.87-19.92	0.026*
	Female	21.30	9.48	17.47-25.13	
Residence	Rural	18.38	11.45	15.29-21.48	0.934
	Urban	18.58	13.01	14.81-22.36	
Marital status	Married	18.81	12.48	16.27-21.35	0.337
	Unmarried	14.50	6.23	9.29-19.71	
Comorbidity	Nil	14.55	9.55	11.31-19.78	0.048*
	Single	39.46	8.53	15.39-23.41	

Then, we included these variables into multivariate linear regression analysis. Factors predicting anxiety in COVID-19 cohort is statistically significant for age and female gender (Table 5).

Table 5: Multivariate linear regression depicting predictors of anxiety			
Variable	Odds Ratio	95% CI	P-value
Age ≥ 60 Years	2.69	1.92-5.71	0.036*
Female gender	4.26	3.73-7.45	0.013*
Single Comorbidity	1.05	0.36-3.04	0.928
Multiple Comorbidity	0.69	0.25-1.92	0.476

DISCUSSION

Patients admitted to the hospital for COVID-19 may be a cohort at increased risk of developing psychiatric symptoms due to the severity of their disease, the unique stress of hospitalization under isolation and the possibility of iatrogenic psychiatric effects of medications and other interventions. However, there is an overall scarcity of data for anxiety in hospitalized COVID 19 patients worldwide, especially in India. Some studies conducted in China and other parts of the world have done a telephonic assessment of anxiety and depression in COVID-19 patients. But our study has been carried out directly by the staff treating these patients.

In our study, most patients in the COVID-19 cohort, 39.8% (DASS-21 score ≥ 20), are in the highly severe grade of anxiety compared to 3.9 % in the control group, similar to a study by Yanyu Hu et al., which had 38.8% (GAD-7 ≥ 5) anxiety in COVID-19 inpatients¹². In an Italian study of 402 patients with COVID-19 evaluated in the emergency department and then screened for psychopathology

approximately one month after initial emergency department evaluation, about 56% of patients screened positive in at least one psychiatric domain. Of these, approximately 31% screened positively for depression, 42% for anxiety, and 28% for obsessive-compulsive symptoms¹³. Parker et al. was the first study to assess mood disorders in COVID-19 hospitalized patients. HADS-A mean score was 5.4 points; 21 (36%) participants had anxiety symptom scores ≥ 8 points which denoted clinically significant symptoms¹⁴.

Our data is consistent with psychiatric presentations of other severe coronavirus infections, including Middle East respiratory syndrome and severe acute respiratory syndrome-1 (SARS). Rogers et al.¹⁵ conducted a systematic review and meta-analysis of such presentations and identified depression and anxiety rates of 32.6% and 35.7%, respectively.

Within the COVID-19 cohort, the DASS-21 anxiety score was higher in females with a Mean ± SD of 21.30 ± 9.48, a statistically significant p-value of 0.026 similar to the study by Yanyu et al.¹².

In our study, the DASS-21 anxiety score was higher in the elderly (>60 years). Mean ± SD 21.30 ± 9.48, which was statistically significant p-value 0.043. So, older adults and those with severe disease are more susceptible to SARS-CoV-2, which may be associated with a higher frequency of comorbidities¹⁶, including anxiety.

The most common comorbidity in the COVID-19 cohort was hypertension in 51.5%, followed by Type 2 Diabetes Mellitus in 31.1%, which was statistically significant (p-value 0.001 and 0.005 respectively). There was a higher prevalence of hypertension and diabetes in our cohort due to moderate to severe COVID-19 disease. In our study, the DASS-21 anxiety score was higher in those with comorbidities than those without comorbidities. A systematic review and meta-analysis by Yanga et al. showed that the most prevalent comorbidities in COVID 19 patients were hypertension (21.1%) and diabetes (9.7%)¹⁷.

Multivariate logistic regression of factors predicting anxiety in the COVID-19 cohort is statistically significant for age and females. It is well known that women have a higher lifetime prevalence of mood and anxiety disorders¹⁸. Females reported higher scores in self-rated stress and GAD-2 than males during the COVID-19 outbreak in

China¹⁹. There is a potential role of the sex hormones oestradiol and progesterone. It is proposed that women might be more vulnerable to these disorders because of monthly and life-span fluctuations of these hormones, which modify neurotransmitters and neurosteroids and influence cognition and behavioral processes²⁰. In our study, elderly COVID-19 patients had higher anxiety scores Mean $\pm$ SD (20.32 $\pm$ 10.11) compared to younger patients Mean $\pm$ SD (16.43 $\pm$ 8.89), which was statistically significant. Multiple studies have shown a higher prevalence of anxiety in hospitalized elderly patients. In a UK study by Yohannes et al., the prevalence of anxiety in 173 hospitalized patients was 43%²¹. However, there is a lack of data comparing anxiety in elderly COVID-19 hospitalized patients with the younger age group, especially in low-income countries. The increased anxiety in the elderly age group might be due to comorbidities and fear of death.

COVID-19 is a biological disaster in which fear, uncertainty and stigmatization are common.

These act as barriers to appropriate medical and mental health interventions. Our results suggest the need for systematic psychiatric screening for individuals diagnosed with COVID-19 infection. Screening for common psychiatric manifestations of COVID-19 can be performed using standard psychiatric screening tools, including the Hospital Anxiety and Depression Scale (used in this study), the Patient Health Questionnaire (for depression), the Generalized Anxiety Disorder Scale (for anxiety), the Confusion Assessment Method (for delirium), and the Primary Care Posttraumatic Stress Disorder Screen for DSM-5 (for posttraumatic stress disorder). Clinicians can use these screening tools to identify patients needing specialist psychiatric consultation. As most health professionals working in COVID-19 isolation units do not receive any mental health training, we suggest that training health professionals in providing mental health care can reduce psychological distress in patients. A training mechanism can be devised for the same purpose, e.g., the training can be delivered using IASC (Inter-Agency Standing Committee) devised guide on basic psychosocial skills for COVID-19 responders. Patients in whom psychiatric symptoms are confounded by ongoing medical complications, evaluation and management by a consultation-liaison psychiatrist can be sought as it remains

the gold standard²². Electronic devices such as smartphones and We Chat or other social media-based services could be set up to provide psychological counselling for patients and safe communication between patients and their families to decrease the psychological effects of isolation¹¹. As per the MSF study, the main coping strategies adopted by Kashmiri adults were praying, talking to a family member, friends and keeping busy²³. According to the Global Burden of Disease study, treating mental health problems is vital as these are among the leading contributors to disability worldwide²⁴. In Kashmir, the Royal College of Psychiatry led the mhGAP programme in 2013, trained doctors and other allied professionals who are in first contact in inpatient settings in assessing mental illness, appropriate referral and management of mental illness²⁵. We need further research and timely mental health interventions in Kashmir because of decades of political turmoil and psychological, social and economic issues after the COVID-19 pandemic.

This study could establish a link between COVID-19 illness and anxiety in hospitalized patients. Moreover, we also found that anxiety is more prevalent in females and an elderly cohort of COVID-19. Therefore, research, psychiatric training and practice in this regard should consider sex and gender aspects much more strongly²⁶.

Our study has several limitations. Firstly, only some patients who could provide informed consent were eligible to enroll. So, patients with respiratory symptoms requiring invasive support rendered them nonverbal and were underrepresented, making it difficult to ascertain the relationship between severity of illness and psychiatric symptoms. Secondly, our sample size was small as non-COVID patients were managed mainly by the primary and secondary care hospitals (in the peripheries). Thus we did not have a large sample size of these non-COVID hospitalized patients in tertiary care during the pandemic.

CONCLUSION

There is a high prevalence of severe anxiety among hospitalized patients in moderate to severe COVID-19 patients compared to non-COVID control patients admitted in the same hospital. Anxiety is more prevalent in females and an elderly cohort of COVID-19. This highlights the importance of screening all hospitalized COVID-19 patients for psychiatric disorders, especially anxiety and the need to address it as early as possible and follow up for long

term mental health sequel. Early psychological crisis intervention can reduce the prevalence of adverse psychological outcomes caused by the COVID-19 outbreak.

Conflict of Interest: None

Funding: None

Written informed consent : Taken

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