

Psychological Impact of Covid-19 on Immuno Compromised Patients

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ABSTRACT

Background: COVID-19 pandemic has had a global impact. Patients with HIV, cancer, on immunosuppressants, and renal transplants due to CKD need to balance the challenges associated with COVID-19 while ensuring that continued care cannot be compromised, stress beyond the coping mechanisms of patients may result in major depressive disorder and anxiety in chronic illness. The possible link between the chronic stress response, patients have an altered peripheral immune system, with impaired cellular immunity and increased levels of proinflammatory cytokines which may predispose patients to depression, and anxiety. Thus, Depression and anxiety is a common comorbidity in immunocompromised patients. This study aimed to evaluate the psychological effect of COVID-19 on these groups of patients. **Methods:** A Cross sectional Study on Patients with immune compromised states infected by COVID-19 was the main aim. The study includes 10200 covid infected patient admitted to Victoria hospital, a specialized covid hospital. Patients taken into study were aged above 18 years, of both sexes, with a history of immunocompromised state like HIV, cancer, on Immunosuppressants drugs and renal transplants due to CKD and infected by the COVID-19 (Confirmed by RT-PCR). Patients who were excluded were on life support, prisoners, patients were with pre-existing Psychiatric illness, neurodegenerative disorders, congenital or acquired brain damage, hepatic coma, drug dependence (Except ADS and NDS). Of 71 patients who fulfilled the above criteria found to have immunocompromised state were taken in study and 40 of them were found to have depression and anxiety. The tools used to assess were Patient Health Questionnaire, 9-item version (PHQ-9) and Generalized Anxiety Disorder Assessment 7-item version (GAD-7) was used to assess the anxiety and depression respectively. All the data obtained was entered into excel sheets (SPSS data sheets) and analysed using SPSS 24th version. **Results:** More than half (n =40; 50.4%) of the patients had psychiatric morbidity either in the form of depressive disorder or in the form of anxiety. Depression was slightly more prevalent (n=21; 29%) than anxiety (n=19; 26%). **Conclusion:** The results show that patients with immunocompromised states have the high prevalence of anxiety and depression.

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The world is witnessing a replacement public health threat since the start of this year. Coronavirus disease 2019 (COVID-19), caused by the novel Coronavirus SARS-CoV-2, originated in Wuhan, China towards the top of last year and was declared by (WHO) to be a 'Public Health Emergency of International Concern' (PHEIC) within a month of its emergence. The Covid illness 2019 (COVID-19) pandemic brought about by SARS Covid19 (SARS-CoV-2) has caused huge dreariness and mortality in patients and focused on medical care frameworks around the world. The clinical highlights and results of COVID-19 among immunosuppressed patients, who are at assumed danger for more serious illness yet who may likewise have diminished impeding provocative reactions, are not very much described. Presenting symptoms were similar to the non-immunocompromised population with fever, dry cough, dyspnoea, and diarrhoea being most frequent, though it is important to note some reports of asymptomatic infection in lung cancer patients^[2].

Patients with cancer are a unique group of patients because they need to access health care regularly for life sustaining cancer treatment. Delay in cancer treatment is detrimental to patients. Yet, patients with cancer are immunocompromised and may have poorer outcomes from COVID-19 should they get infected while seeking treatment.

Many patients with cancer fear dying alone, and the meaningful interpersonal relationships and physical presence of family members are essential to patients in their final hours. However, in this pandemic, a key policy to reduce the spread of COVID-19 is to encourage, and in many cases enforce, social distancing. The adverse effect of quarantine and social isolation on healthy individuals is well documented, little is known about how patients with cancer/ Immunocompromised patients with Covid 19 infection deals and cope during social isolation.

Evidence suggests that people living with HIV have a higher risk of becoming seriously ill from COVID-19 and people with HIV who are not on treatment or virally suppressed may be at an even greater risk.

This study aimed to better understand the psychological impact of COVID-19 on patients with cancer / Immunocompromised state who are admitted in tertiary covid center.

METHODOLOGY

Source of Data

Immune-compromised Patients with COVID 19 positive status and admitted in COVID ward of Victoria Hospital, a specialized COVID treatment centre.

Methods of collection of Data

Study design: Cross sectional Study

Study period: September 2020 – June 2021

Place of Study: Victoria Hospital, BMCRI, Bangalore.

Inclusion Criteria:

Age: 18yrs. and above

Sex: Both male and female Patients with immuno-compromised state and infected by the COVID-19 (Confirmed by RT-PCR), Stable patients.

Exclusion criteria

- Minors under 18 years
- Patients under Custody
- Inability to consent (non-opposition) / People not willing to give informed consent
- Organic mental/ other disorders
- History of previous psychiatric illness

Methodology

Patients who are **immunocompromised** and infected by the **COVID-19**(Tested by RT-PCR), hospitalized in a Covid ward dedicated to the treatment of this co morbidity in Victoria Hospital, a specialized COVID 19 center were taken for the study. The participants were informed about the objectives and potential benefit of the study and oral informed consent was taken explained in local understandable language to patients.

All participants completed the questionnaire and Socio-demographic information, including the participants gender, age, marital status, and socio-economic background (e.g., education level), was collected.

Materials

Informed Consent form

Semi structured proforma for collection of socio-demographic profile and other clinical variables like chronicity of illness, medications used.

The **Patient Health Questionnaire, 9-item version (PHQ-9)** (Kroenke et al., 2001), For PHQ-9, the total scores of 5, 10, 15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively

Generalized Anxiety Disorder Assessment 7-item version (GAD-7)⁹ The cut off points used for the GAD-7 for mild, moderate, and severe anxiety were 5, 10, and 15, respectively.

Lab Investigations:

Blood samples were voluntarily obtained from hospitalized patients and the purpose of the study was explained to the patients.

The biomarkers included leukocyte count, platelet count, neutrophil count, lymphocyte count, monocyte count, C-reactive protein (CRP) level and Blood specimens were collected and analysed in a central laboratory within 2 hours.

All the data obtained was entered into the excel sheets (SPSS data sheets) and analyzed using SPSS 24th version. Results obtained were compared, with previous studies and then final conclusions were drawn.

Statistical analysis

The data collected is entered in SPSS software, will be analyzed statistically using descriptive statistics namely mean, median, standard deviation, percentage.

RESULTS

Table no 1: PHQ -10 questionnaire

CAT PHQ-10	Depression		Total	p value
	Yes	No		
mild depression	6(28.57%)	0(0%)	6(8.45%)	
moderate depression	14(66.67%)	0(0%)	14(19.72%)	
moderately severe depression	1(4.76%)	0(0%)	1(1.41%)	
Normal	0(0%)	50(100%)	50(70.42%)	
Total	21(100%)	50(100%)	71(100%)	

Table no 2: GAD -7 questionnaire

CAT GAD-7	ANXIETY		Total	p value
	Yes	No		
mild anxiety	10(52.63%)	0(0%)	10(14.08%)	
moderate anxiety	9(47.37%)	0(0%)	9(12.68%)	
Normal	0(0%)	52(100%)	52(73.24%)	
Total	19(100%)	52(100%)	71(100%)	

Table no 3: Indicates the results for Age and Depression

AGE CAT	Depression		Total	p value
	Yes	No		
20 to 40	4(19.05%)	6(12%)	10(14.08%)	
41 to 60	11(52.38%)	30(60%)	41(57.75%)	0.715
61 to 80	6(28.57%)	14(28%)	20(28.17%)	
Total	21(100%)	50(100%)	71(100%)	

Table no 4: Indicates the results for Age and Anxiety

AGE CAT	ANXIETY YN		Total	p value
	Yes	No		
20 to 40	1 (5.26%)	9(17.31%)	10(14.08%)	
41 to 60	11 (57.89%)	30(57.69%)	41(57.75%)	0.345
61 to 80	7 (36.84%)	13(25%)	20(28.17%)	
Total	19 (100%)	52(100%)	71(100%)	

Table no 5: Indicates the results for Gender and Depression

SEX	Depression		Total	p value
	Yes	No		
FEMALE	4(19.05%)	15(30%)	19(26.76%)	
MALE	17(80.95%)	35(70%)	52(73.24%)	0.341
Total	21(100%)	50(100%)	71(100%)	

Table no 6: Indicates the results for Gender and Anxiety

SEX	ANXIETY		Total	p value
	Yes	No		
FEMALE	4(21.05%)	15(28.85%)	19(26.76%)	
MALE	15(78.95%)	37(71.15%)	52(73.24%)	0.511
Total	19(100%)	52(100%)	71(100%)	

Table No 7: Indicates the results for marital status and Depression

marital status	Depression		Total	p value
	Yes	No		
Yes	17(80.95%)	45(90%)	62(87.32%)	0.435fe
No	4(19.05%)	5(10%)	9(12.68%)	
Total	21(100%)	50(100%)	71(100%)	

Table No 8: Indicates the results for marital status and Anxiety

marital status	ANXIETY		Total	p value
	Yes	No		
Yes	18(94.74%)	44(84.62%)	62(87.32%)	0.428fe
No	1(5.26%)	8(15.38%)	9(12.68%)	
Total	19(100%)	52(100%)	71(100%)	

Table No 9: Indicates the results for Education and Depression

Edu cat	Depression		Total	p value
	Yes	No		
Graduate	6(28.57%)	8(16%)	14(19.72%)	0.289
High school	4(19.05%)	12(24%)	16(22.54%)	
Illiterate	3(14.29%)	18(36%)	21(29.58%)	
Middle school	2(9.52%)	2(4%)	4(5.63%)	
Pre university	6(28.57%)	10(20%)	16(22.54%)	
Total	21(100%)	50(100%)	71(100%)	

Table No 10: Indicates the results for Education and Anxiety

Edu cat	ANXIETY		Total	p value
	Yes	No		
Graduate	4(21.05%)	10(19.23%)	14(19.72%)	0.753
High school	3(15.79%)	13(25%)	16(22.54%)	
Illiterate	5(26.32%)	16(30.77%)	21(29.58%)	
Middle school	2(10.53%)	2(3.85%)	4(5.63%)	
Pre university	5(26.32%)	11(21.15%)	16(22.54%)	
Total	19(100%)	52(100%)	71(100%)	

Table no 11: Indicates P value of significance for depression on the questionnaires and blood investigation.

Variables	Depression		p value
	Yes(n=21)	No(n=50)	
PHQ-9 score	10(9-12)	0(0-0)	<0.01
GAD-7 score	0(0-0)	0(0-6.5)	0.106
AGE	53(42-63.5)	55(47.75-62)	0.61
HB	10(8.15-11.35)	9.7(8.3-11.35)	0.89
TLC	7400(5200-9050)	6500(4850-8725)	0.438
N%	76(68-81.5)	70.5(62.75-76.25)	0.127
L%	14(8-18)	18(12-27.5)	-.026
N:L	5.4(3.9-7.78)	3.88(2.49-6.02)	0.034
1ST D-DIMER	1.06(0.61-2.02)	0.94(0.47-1.44)	0.420
CRP 1ST	35.37(3.43-57.31)	29.95(12.33-75.83)	0.270

Table no 12: Indicates P value of significance for anxiety on the questionnaires and blood investigation.

Median(IQR) of scores	Anxiety		P value
	Yes(n=21)	No(n=50)	
PHQ-9 score	0(0-0)	0(0-9)	0.14
GAD-7 score	8(6-10)	0(0-0)	<0.01
AGE	57(50-67)	53(44.25-60.75)	0.292
HB	10(7.8-11.7)	9.7(8.53-11.3)	0.943
TLC	7200(5200-9200)	6600(4900-8450)	0.640
N%	73(66-81)	71.5(62-78.75)	0.359
L%	17(7-23)	17(12-24)	0.292
N:L	4.71(2.87-11.86)	4(2.64-6.06)	0.232
1ST D-DIMER	1.05(0.62-1.55)	1.01(0.49-1.59)	0.576
CRP 1ST	23.9(6.82-104.7)	35.16(9.58-59.81)	0.795

The following tables indicate the scores of immunocompromised patients on Depression and anxiety:

Table no 13: Indicates the number of patients with Cancer, HIV and CKD diagnosed with Depression and anxiety. Total sample N= 71

CANCER =5		HIV=5		CKD=61	
DEPRESSION	1	DEPRESSION	2	DEPRESSION	18
ANXIETY	2	ANXIETY	1	ANXIETY	16

Table no 14: indicates FISHER'S EXACT SIGNIFICANCE TEST on HIV patients and P values for Depression

HIV	Depression YN		Total	p value
	Yes	No		
Yes	2(9.52%)	3(6%)	5(7.04%)	0.629
No	19(90.48%)	47(94%)	66(92.96%)	
Total	21(100%)	50(100%)	71(100%)	

Table no 15: indicates FISHER'S EXACT SIGNIFICANCE TEST on HIV patients and P values for Anxiety

HIV	ANXIETY YN		Total	p value
	Yes	No		
Yes	1(5.26%)	4(7.69%)	5(7.04%)	0.595
No	18(94.74%)	48(92.31%)	66(92.96%)	
Total	19(100%)	52(100%)	71(100%)	

Table no 16: indicates FISHER'S EXACT SIGNIFICANCE TEST on Cancer patients and P values for Depression

cancer	Depression YN		Total	p value
	Yes	No		
Yes	1(4.76%)	4(8%)	5(7.04%)	0.534
No	20(95.24%)	46(92%)	66(92.96%)	
Total	21(100%)	50(100%)	71(100%)	

Table no 17: indicates FISHER'S EXACT SIGNIFICANCE TEST on Cancer patients and P values for Anxiety

cancer	ANXIETY YN		Total	p value
	Yes	No		
Yes	2(10.53%)	3(5.77%)	5(7.04%)	0.605
No	17(89.47%)	49(94.23%)	66(92.96%)	
Total	19(100%)	52(100%)	71(100%)	

Table no 18: indicates FISHER'S EXACT SIGNIFICANCE TEST on CKD patients and P values for Depression

CKD	Depression YN		Total	p value
	Yes	No		
Yes	18 (85.71%)	43(86%)	61(85.92%)	1.0
No	3 (14.29%)	7(14%)	10(14.08%)	
Total	21 (100%)	50(100%)	71(100%)	

Table no 19: indicates FISHER'S EXACT SIGNIFICANCE TEST on CKD patients and P values for Anxiety

CKD	ANXIETY YN		Total	p value
	Yes	No		
Yes	16 (84.21%)	45(86.54%)	61(85.92%)	1.00
No	3 (15.79%)	7(13.46%)	10(14.08%)	
Total	19 (100%)	52(100%)	71(100%)	

Features:

- Seventy-one (n = 71) patients were taken up for the study.
- The mean age of the patients was 52.5 years, majority of the patients were more than 40 years of age at the time of assessment.
- Males outnumbered the females.
- More than half (n =40; 50.4%) of the patients had psychiatric morbidity either in the form of depressive disorder or in the form of Anxiety.
- Depression was slightly more prevalent (n=21; 29%) than in anxiety (n=19; 26%).
- In most cases, depression was of moderate severity and very few patients had severe depression
- In terms of demographic and clinical correlates, there was no significant difference in the prevalence of depressive disorders & Anxiety
- There is no association between Bio markers.

DISCUSSION

The study aimed at finding out the psychological impact of Covid 19 on Immunocompromised patients and we could evaluate it on patients with Cancer, HIV and CKD however, the sub categories among these were not taken into consideration.

Compared with patients without cancer with COVID-19, those with cancer appeared to have an increased risk of severe outcomes including intubation and death after adjusting for other COVID-19 risk factors.

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In addition to immunosuppression, people living with HIV might be at risk of more severe COVID-19 due to overlapping medical characteristics that are known risk factors for severe COVID-19 disease—On the other hand, HIV might be protective against severe COVID-19 as immunosuppression could help temper the cytokine storm of COVID-19 and some antiretrovirals may have theoretical activity against SARS-CoV-2.

The association between COVID-19 and intense cytokine release raises the possibility that immunosuppression may actually temper the exuberant inflammatory response in this infection. Severe COVID-19 disease has features of cytokine release syndrome and secondary hemophagocytic lymph histiocytosis seen in patients with other viral infections.

Important aspect of COVID-19 as related to kidney disease is, given the highly infectious nature of Covid-19 patients with CKD, kidney transplantation recipients, and those with glomerular diseases may be at increased risk for infection and associated morbidity, especially in the light of the underlying immunocompromised state. The global COVID-19 pandemic has had a significant influence on clinical aspects and management of these patient populations.

Taking these immunocompromised conditions into consideration and diagnosed with Covid-19 there is a huge psychological impact on these patients predominantly being Depression and anxiety.

In our sample of the 71 cases, 5 patients had cancer, 5 has HIV and remaining 61 were diagnosed with CKD.

As indicated in Table no 13, of the 5 patients with cancer, 2 had anxiety and 1 had depression, while 2 had depression and 1 had anxiety among those with HIV and 18 were found to have depression and 16 had anxiety among CKD patients.

Depression and anxiety are common psychological ailments found among the immunocompromised patients suffering from cancer, HIV and CKD, to add to this when these patients were infected with Covid-19 these psychological ailments have been found to increase manifold. These patients who are threatened with death and death anxiety had their families together during their treatment phase but Covid-19 introduced a social anxiety factor which may have increased their depression and anxiety.

A 53-question survey by Yu Qian et al., on the patients' perception of the impact of COVID-19 and a total of 129 confirmed cancer patients hospitalized completed the surveys. The results of HADS showed 69 (53%) patients and 65 (50%) patients had anxiety and depression, majority of patients expressed fear of becoming infected themselves (85%) or their family (91%), and of cancer progression due to treatment delay (91%). In total 127 participants (98%) reported that their life was affected by COVID-19, and 91 participants (70%) reported that they needed mental support, which was similar in our study when we asked reasons for stress and our patients reported 29%, 26% depressive symptoms and anxiety symptoms

A Systematic Review and Meta-analysis by Erfan Ayubi et al., Thirty-four studies were included in the systematic review, of them 21 studies included in meta-analysis. The overall prevalence (95% CI) of depression among patients with cancer according to PHQ-9 ≥ 5 (mild, moderate and severe symptom) was 0.34 (0.19, 0.49); $I^2 = 98.65$, $P\text{-value} < 0.001$ while the overall prevalence of mild, moderate and severe anxiety (GAD-7 ≥ 5) was 0.31

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(0.17, 0.45); $I^2=99.08\%$, $P\text{-value}<0.001$. In our study more than half ($n=40$; 50.4%) of the patients had psychiatric morbidity either in the form of depressive disorder or in the form of GAD. Depression was slightly more prevalent ($n=21$; 29%) than in GAD ($n=19$; 26%). In most cases, depression was of moderate severity and very few patients had severe depression

Study done by A Shankar et al., aimed to screen the patients with various malignancies for the presence of depressive disorders and anxiety disorder using phq and gad, Slightly less than half ($n=248$; 46.4%) of the patients had psychiatric morbidity either in the form of depressive disorder or in the form of GAD. Depression was slightly more prevalent ($n=200$; 37.5%) than in GAD ($n=191$; 35.8%). most cases, depression was of moderate severity and very few patients had severe depression Majority of the patients ($n=293$; 54.9%) were more than 50 years of age at the time of assessment. Males ($n=293$; 54.9%) outnumbered the females ($n=241$; 45.1%). in our study we found nearly half that Of all the participants 29%, 26% depressive symptoms and anxiety symptoms respectively using same scales and Majority of the patients were more than 40 years and males outnumbered and most cases have moderare depression and anxiety.

Study by Qian Guo et al, cross-sectional study utilized a mixed-methods approach to investigate the mental status of hospitalized patients with COVID-19 and how it relates to the presence bio-markers of peripheral inflammation found a considerable proportion of patients reported depression (62 [60.2 percent], the total score of PHQ-9 above 4), and anxiety (59 [55.3 percent], the total score of GAD-7 above 4) symptoms. The correlation analysis revealed no significant relationship between psychological assessments and inflammatory indicators when looking at the entire patient group, our study found that Of all the participants 29%, 26% depressive symptoms and anxiety symptoms respectively and no correlation between psychological assessments and inflammatory markers.

This cross-sectional study examined Psychological Impact in immune compromised patients with COVID 19 in our study we found that of all the participants 29%, 26% depressive symptoms and anxiety symptoms respectively, study by Ling-Ling Dai et al., in Jiangnan Fangcang Shelter Hospital in Wuhan have found 18.57%, 13.36%, anxiety symptoms, depressive symptoms respectively which was low comparable to our study.

A cross-sectional survey of patients, caregivers, and HCWs at the National Cancer Centre Singapore was performed over 17days during the lockdown by Kennedy Yao Yi Ng et al., found prevalence of anxiety (ie, $GAD-7 \geq 10$) was 19.1%, for patients which is similar to our participants reported 26% anxiety symptoms respectively.

Studies of the prevalence of depression in cancer patients referred for psychiatric consultation report a prevalence of major depression ranging from 9% to 58% although Massie and Holland reported a low prevalence of depression (9%), our participants reported 29% depressive symptoms respectively.

Sri sai priya sudarisan et al., conducted an cross sectional study on 234 immunocompromised patients attending palliative care unit and found mean age was 50 years and females outnumbered and prevalence of depression was 70% no other socio demographic found significant, Our study showed 29%, depressive symptoms and males outnumbered.

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A review article by Adrian i et al., on peripheral markers on psychological impact on depression established that raised CRP levels were associated with an increased risk of subsequent depression Higher ESR was identified in depressed patients compared to healthy volunteers compared to our study we found no significant correlation of peripheral biomarkers on anxiety and depression.^[13]

Six large studies have investigated the relation between anxiety disorders and CRP (Pitsavos et al. 2006; Liukkonen et al. 2011; Copeland et al. 2012; Vogelzangs et al. 2013; Wagner et al. 2015; Tayefi et al. 2017); all found that anxiety disorders are significantly associated with increased CRP levels, indicative of a low-grade inflammation our study we found no significant correlation of peripheral biomarkers on anxiety.

Rakesh Kumar et al., in his study of a total of 120 patients as regard to gender 48.3 % were male and rest 51.7% were female Result shows that 56.7% and 64.2% patients were suffering from anxiety and depression respectively. 54(45.0%) & 14 (11.7%) patients had mild and severe anxiety respectively. 29 (24.2%), 39 (32.5%) and 2 (1.7%) patients had mild, moderate and severe depression respectively. Compared to our study 71 patients males outnumbered females and result showed, majority of the patients were more than 40 years and found 29%, 26% depressive symptoms and anxiety symptoms respectively.

Limitations Of the Study

1. The sample of the study was relatively small.
2. Study might have been influenced by somatic symptoms of immune compromised patients.

Future Directions

1. Sub categories of cancer can be considered.
2. The number of years into immunocompromised state can be considered and a comparative study of the number of years can be taken up.

CONCLUSION

In conclusion, the general estimates of depression and anxiety among patients were considerable. Evidence from this systematic review and meta-analysis may highlight the importance of preventing, treating and identifying the foremost important determinants of depression and anxiety among patients during the COVID-19 pandemic.

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Conflict of Interest

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