

COVID-19 Related Mental Health Issues among Patients with Cancer: A Pilot Study

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ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) pandemic is associated with more psychological distress than its rampant spread, mortality, and morbidity. Cancer patients are at increased risk of mortality and morbidity than the general population. Due to this, there is a possibility that cancer patients may be suffering from a higher level of COVID-19 related anxiety, fear, and obsession.

Aim: To explore COVID-19 related mental health issues (anxiety, fear, and obsession) and its correlation in patients with cancer.

Materials and Methods: The present study was a cross-sectional pilot study which was conducted in a tertiary care teaching hospital located in Ratnagiri, Maharashtra, India. Patients receiving treatment for cancer (n=55) consequently at tertiary care teaching hospital of India were recruited. The Corona Anxiety Scale (CAS), Obsession with COVID-19 Scale (OCS), Fear of COVID-19 Scale (FCV-19S), Patient Health Questionnaire-9 (PHQ-9),

and Generalised Anxiety Disorder-7 Scale (GAD-7) were used to assess all eligible patients. Fisher's-exact test, Spearman's rank correlation, and logistic regression were used to analyse the data.

Results: Among the 55 patients (mean age was 49.64±13.08 years) with cancer, 11 (20%) had Coronavirus related anxiety and 2 (3.6%) had obsession related COVID-19, 22 (40%) had depression and 18 (32.7%) had GAD. CAS score positively correlated with FCV-19S score { $\rho=0.50$ ($p<0.001$)}, PHQ-9 score { $\rho=0.90$ ($p<0.001$)} and GAD-7 score { $\rho=0.74$ ($p<0.001$)}.

Conclusion: The COVID-19 related mental health issues (fear, anxiety), depression, and GAD were prevalent among patients with cancer. Further, COVID-19 specific issues may not be addressed in routine screening and evaluation in current practice. Therefore, there is an urgent need to develop systematic strategies to screen and develop specific mental health interventions for patients with cancer.

Keywords: Anxiety, Consultation liaison psychiatry depression, Coronavirus disease-19

INTRODUCTION

The COVID-19 pandemic has influenced every aspect of individual life and sabotaged diverse dimensions of health, economy, social life, etc. within a few months [1]. People with or without medical or mental illness is at the increased risk of developing mental health distress due to pandemic, public health measures, and the spread of virus [1]. The vulnerable population (i.e., people with medical co-morbidities like cancer, mental illness, personality traits) are at increased risk for developing the COVID-19 related distress along with the increased prevalence of the common mental disorder. Avoidance of these common mental health issues related to COVID-19 infection and public health measures can lead to serious consequences including suicides [2].

Besides, these issues can lead to non compliance to medical management of cancer including chemotherapy and radiotherapy, and increased risk of mortality and morbidity during this pandemic [3]. Published literature suggests that patients with cancer are more commonly associated with depression and GADs [3,4]. However, most of these studies have used traditional self-reported scales such as PHQ-9, GAD-7, and Beck Anxiety Inventory (BAI) [3,5].

These scales have limited utility to screen these populations for COVID-19 related mental health issues (e.g. anxiety, fear, or obsession) due to lack of face and construct validity [6]. Also, patients suffering from COVID-19 related anxiety should not be treated for GAD as measured on GAD-7 or BAI. Moreover, Position statement of the Indian association of palliative care recommends that patients receiving palliative care should be evaluated for mental health issues using validated measures and should be managed by appropriate interventions [7,8].

To address these critical limitations of previously published studies and estimate the COVID-19 specific mental health issues, authors attempted to evaluate the COVID-19 common mental health issues

(fear, anxiety, and obsession) and their relation with depression and anxiety using newly developed scales and traditional scales.

MATERIALS AND METHODS

In this cross-sectional pilot study, patients attending the oncology Out Patient Department (OPD) were invited to participate in the study during the period of May 2020 to June 2020. This was a pilot study conducted in a tertiary teaching hospital of Maharashtra, India in the initial stages of the pandemic and was approved by the Institutional Ethics Committee (IEC) (BKLW/RMC/LEC/42/2020).

Inclusion criteria: Patients with a diagnosis of cancer who were aged more than 18 years, treated for atleast six months and willing to give consent were included in the study.

Exclusion criteria: Patients with delirium, acute radiation syndrome and those diagnosed with COVID-19 were excluded from the study.

Study Procedure

Seventy five patients who consented for the study were recruited. A semi-structured form was used to collect socio-demographic data. COVID-19 related anxiety, obsession, and fear were assessed by using the Marathi version of the CAS, OCS, and fear of COVID-19 Scale [6,9,10]. In addition, Generalised anxiety and depression were measured by translated and validated GAD-7 and PHQ-9 scales.

Corona Anxiety scale (CAS): The CAS is a 5-item scale having robust reliability, validity, sensitivity, and specificity [9]. A self-report screen for identifying people who might suffer from an unhealthy degree of anxiety due to the COVID-19 pandemic, which mainly entails behavioural and physiological reactions of elevated fear and excessive worry about coronavirus and its related stimuli. It discriminates those with dysfunctional anxiety and non anxiety while using an optimised cut-off score of 9 [6,9]. The CAS captured information regarding how frequently respondents experienced COVID-19 anxiety in the past two weeks

regarding behavioural and physiological symptoms. They are scored using the 5-point Likert scale (0=not applicable to me, 1=hardly ever applicable to me, 2=sometimes applicable to me, and 3=Most of the times 4=very applicable to me daily). The level of anxiety is determined by taking the average of the scores (ranging from 0-4). A higher score indicates that an individual has more COVID-19 related anxiety. CAS is translated and available in several languages including Marathi [10].

The Obsession with COVID-19 Scale (OCS): The OCS is a self-reported, 5-item scale with robust reliability, validity, sensitivity, and specificity [6,11]. OCS was developed to detect maladaptive thinking about COVID-19 over the period of two-week time-frame. It is scored using a 5-point Likert scale, ranging from 0=not at all to 4=nearly every day. The scoring format is consistent with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) cross-cutting symptom measure. The OCS discriminates the non functional COVID-19 thinking patterns from those without such a pattern using an optimised cut-off score ≥ 7 and so that the higher the average, the greater the obsession of the individual regarding COVID-19. Elevated scores on a particular item or a high total score (≥ 7) may indicate problematic symptoms for the individual that might warrant further assessment and or treatment [12]. OCS is available in several languages including Marathi [10].

Fear of COVID-19 Scale (FCV-19S): The FCV-19S scale is a self-reported, Likert-scale, that consists of seven items and has possible scores range from 7-35 [13]. Responding to items on a five-point Likert scale (1=strongly disagree; 5=strongly agree), the FCV-19S has been found to be psychometrically sound in assessing fear of COVID-19 in different populations, including different ethnic groups [14]. An example item in the FCV-19S is "I cannot sleep because I'm worrying about getting coronavirus-19". A higher level of fear toward COVID-19 is indicated by the higher FCV-19S score. Moreover, different language versions of the FCV-19S used in the present study have been validated [15]. The higher scores are indicative of greater coronavirus fear. The scale has excellent validity, reliability, and availability in various languages [6].

Patient Health Questionnaire-9 (PHQ-9): PHQ-9 is a self-reported, Likert type scales used for screening the depression. The questionnaire has nine items which are scored as "0" (not at all) to "3" (nearly every day). The PHQ is part of Pfizer's larger suite of trademarked products, called the Primary Care Evaluation of Mental Disorders (PRIME-MD). The PHQ-9 takes less than three minutes to complete and simply scores each of the 9 DSM-IV criteria for depression based on the mood module from the original PRIME-MD [16]. Primary care providers frequently use the PHQ-9 to screen for depression in patients.

The PHQ-9 questions are based on DSM-IV diagnostic criteria for depression. The patient's experience over the previous two weeks in terms of level of interest, mood, sleep, energy, and eating habits is elicited. The questionnaires have excellent validity, reliability, sensitivity, and specificity to screen for depression. Cut-off points of 5, 10, 15, and 20 are interpreted as representing mild, moderate, moderately severe, and severe levels of depression on PHQ-9 [17,18].

Generalised Anxiety Disorder-7 Scale (GAD-7): GAD-7 scale has good reliability as well as validity. The GAD-7-is a useful tool with strong criterion validity for identifying probable cases of GAD. The scale is an excellent severity measuring tool and is strongly correlated with multiple domains of functional impairment and days with disability. The scores of 0,1,2, and 3 are assigned to response categories of 'not at all', 'several days', 'more than half the days', and 'nearly every day'. The total GAD-7 score is calculated by adding the scores of seven questions. Cut-off points for mild, moderate, and severe anxiety are 5, 10, and 15, respectively. Furthermore, the GAD-7 is a moderately good screening tool for other common anxiety disorders such as panic disorder (sensitivity 74%, specificity 81%), social anxiety disorder (sensitivity 72%, specificity 80%), and post-traumatic stress disorder (sensitivity 66%, specificity 81%) [19,20].

The administration of these scales along with socio-demographic proforma was done online (for those patients who have appointments with oncologists and have internet access) and by administration of printed forms [for those who didn't have phone or internet access under all standard precaution led by Indian Council of Medical Research (ICMR)]. The presence of any COVID-19-related symptoms, high-risk contact, and travel history was asked to all patients and advice was offered as per Indian Government guidelines [21].

STATISTICAL ANALYSIS

Descriptive analysis of socio-demographic, clinical variables and scores on scales was carried out using Statistical Package for the Social Sciences (SPSS) 20.0. SPSS Inc., Chicago, Ill., USA). Fisher's-exact test was used to assess the association between two categorical variables. A Kolmogorov-Smirnov test was used to assess the normality of data. The Spearman's correlation coefficient was used to find the correlation between scores of different scales and other variables. Logistic regression was carried out to predict the presence/absence of Corona Anxiety (CAS) with Age, FCV-19S, PHQ-9 (total score), GAD-7 (total), and OCS. All the statistical analysis was carried out while keeping statistical significance at 0.05.

RESULTS

Out of 75 patients approached for the study, 55 (mean age=49.64±13.08 years) completed the survey. Most of the patients were female (n=30, 54.5%), married (n=48, 87.3%), Hindu (n=53, 96.4%), and hailing from rural region (n=52, 94.5%) [Table/Fig-1].

Among the studied patients, the mean score on studied clinical scales were FCV-19S=17.02±4.42; CAS=5.16±4.52; PHQ-9=4.10±3.74; GAD-7=3.54±3.72 and OCS=1.83±2.20.

About 11 (20%) of the respondent patients were positive on CAS while only 2 (3.6%) were positive for OCS [Table/Fig-1]. About 22 (40%) of the respondent reported presence of depressive symptoms on PHQ-9, where 18 (32.7%) had mild symptoms, 3 (5.5%) moderate symptoms and 1 (1.8%) had severe symptoms. Also on GAD-7, 18 (32.7%) of the patient were screened positive, amongst them 12 (21.8%) has mild symptoms, 6 (11%) moderate symptoms of GAD.

Variables		Mean±SD/n (%)
Age (yrs)		49.64±13.08
Gender	Female	30 (54.5)
	Male	25 (45.5)
Religion	Muslim	2 (3.6)
	Hindu	53 (96.4)
Location	Urban	3 (5.5)
	Rural	52 (94.5)
Marital status	Single	5 (9.1)
	Married	48 (87.3)
	Widow	2 (3.6)
Duration of illness (yrs)	<1	14 (25.5)
	1	26 (47.2)
	2	6 (10.09)
	3	3 (5.5)
	4	3 (5.5)
	≥5	3 (5.5)
Type of cancer	Head and Neck	15 (27.27)
	Breast	15 (27.27)
	Digestive/Gastrointestinal	9 (16.36)
	Haematological	4 (7.27)
	Genitourinary	6 (10.09)
	Gynaecological	5 (9.09)
	Respiratory	1 (1.81)

Treatment modalities (current)	Chemotherapy (CT) only	29 (52.7)
	Radiotherapy (RT) only	5 (9.1)
	Combination (CT,RT or Surgery)	21 (38.18)
Compliance to treatment	Regular	52 (94.5)
	Irregular	3 (5.5)
PHQ-9	Positive	22 (40)
	Negative	33 (60)
GAD-7	Positive	18 (32.7)
	Negative	37 (67.3)
CAS	Positive	11 (20)
	Negative	44 (80)
OCS	Positive	2 (3.6)
	Negative	53 (96.4)

[Table/Fig-1]: Socio-demographic and clinical characteristics of patients with cancer (n=55).

The difference among patients screened positive for OCS and those of PHQ-9 or GAD-7 was insignificant ($p=0.28$, $p=0.48$) respectively. Further, there was a significant difference between patients screened CAS positive and PHQ-9 or GAD-7 screened positive ($p=0.004$, $p=0.0003$). Among the patients with cancer, 14 (25.45%) of them resulted positive on both PHQ-9 and GAD-7, and 32.72% (n=18) population were screened positive for either depressive symptoms or anxiety ($p=0.0001$) [Table/Fig-2].

Scales	CAS (+)	CAS (-)	Total (n=55)	Fisher exact test
PHQ-9 (+)	9 (16.36%)	13 (23.63%)	22 (40%)	$p=0.004$
PHQ-9 (-)	2 (3.63%)	31 (56.36%)	33 (60%)	
Total	11 (20%)	44 (80%)		
Scales	CAS (+)	CAS (-)	Total (n=55)	Fisher exact test
GAD-7 (+)	9 (16.36%)	9 (16.36%)	18 (32.72%)	$p=0.0003$
GAD-7 (-)	2 (3.63%)	35 (63.64%)	37 (67.27%)	
Total	11 (20%)	44 (80%)		
Scales	PHQ-9 (+)	PHQ-9 (-)	Total (n=55)	Fisher exact test
GAD-7 (+)	14 (25.45%)	4 (7.27%)	18 (32.72%)	$p=0.0001$
GAD-7 (-)	8 (14.54%)	29 (52.27%)	37 (67.27%)	
Total (n=55)	22 (40%)	33 (80%)		
Total (n=55)	11 (20%)	44 (80%)		

[Table/Fig-2]: Cross-tabulations and Fischers-exact test analysis.

The relationship of scores on COVID-19 related scales (CAS, OCS, FCV-19S) and traditional scales (PHQ-9, GAD-7) with age, duration of illness and treatment, education (except PHQ-9, $p=0.27$, $p=0.04$), was statistically insignificant ($p>0.05$) [Table/Fig-3]. Scores on COVID-19 related scales positively and significantly correlated with each other and with scores of traditional scales (PHQ and GAD-7) [Table/Fig-3]. Further, the logistic regression results showed that higher score on FCV-19S was a significant predictor of coronavirus anxiety (OR=1.41, $p=0.025$) than screened positive on PHQ-9, GAD-7, and OCS-7 [Table/Fig-4].

Variables	FCV-19S	OCS	CAS	PHQ-9	GAD-7
Age	$p=0.08$ ($p=0.55$)	$p=0.18$ ($p=0.18$)	$p=0.01$ ($p=0.94$)	$p=0.02$ ($p=0.85$)	$p=0.14$ ($p=0.30$)
Education	$p=0.09$ ($p=0.48$)	$p=0.11$ ($p=0.40$)	$p=0.19$ ($p=0.16$)	$p=0.27$ ($p=0.04$)	$p=0.12$ ($p=0.37$)
Duration of illness (Years)	$p=0.13$ ($p=0.34$)	$p=0.12$ ($p=0.37$)	$p=0.10$ (0.43)	$p=0.10$ ($p=0.46$)	$p=0.11$ ($p=0.41$)
Duration of treatment	$p=0.23$ ($p=0.09$)	$p=0.30$ ($p=0.02$)	$p=0.05$ ($p=0.68$)	$-p=0.06$ ($p=0.63$)	$p=0.09$ ($p=0.51$)
OCS	$p=0.84$ ($p<0.001$)	--	--	--	$p=0.42$ ($p=0.001$)
CAS	$p=0.50$ ($p<0.001$)	$p=0.46$ ($p<0.001$)	--	--	--

PHQ-9	$p=0.34$ ($p=0.010$)	$p=0.28$ ($p=0.03$)	$p=0.90$ ($p<0.001$)	--	--
GAD-7	$p=0.47$ ($p<0.001$)	$p=0.42$ ($p=0.001$)	$p=0.74$ ($p<0.001$)	$p=0.76$ ($p<0.001$)	--

[Table/Fig-3]: Spearman correlation (p) among COVID-19 related scales (CAS, FCV-19S, OCS) with PHQ-9, GAD-7, age, education, duration (illness and treatment).

Variables	Odd's ratio	95% Confidence interval	B	Level of significance (FET)
FCV-19S (cont.)	1.419	1.04 - 1.92	0.35	0.025
OCS (Cat)	4.674	0.004-5793.876	0.154	0.671
PHQ-9 (Cat)	0.169	0.019 - 0 1.471	-1.99	0.107
GAD-7 (Cat)	0.160	0.023-1.094	-1.83	0.062
Constant	0.001	--	-7.81	0.145

[Table/Fig-4]: Logistic regression modelling analysis of coronavirus anxiety with OCS, PHQ-9, GAD-7, and FCV-19S.

DISCUSSION

The COVID-19 outbreak is leading to an epidemic of mental health issues such as stress, anxiety, depressive symptoms, insomnia, denial, anger, and fear among patients with cancer [1]. In this study, authors found increased Coronavirus related anxiety (20%) and fear about COVID-19 (17.02 ± 4.42) among patients with cancer. These COVID-19 related mental health issues are known to affect the healthcare utilisations, decision making for treatment choice, quality of life, and compliance with treatment [3,22,23]. Though the previous studies attempted to highlight the significance of these issues, no study attempted to estimate or measure the COVID-19 related mental health issues using standardised scales [3,4,18,24,25].

As expected, a higher prevalence of depression (40%) and anxiety (32.7%) was found among the patients with cancer receiving the treatment in the form of chemotherapy or radiotherapy than the previous study findings among general population [26]. However, these findings of the survey ran contrary to previous studies. Jaunjuan L et al., have found that the prevalence of anxiety (56%) and depression (43%) was among the patients with breast cancer (n=658) in China [5], whereas Wang Y et al., reported the prevalence of depression (23.4%) and anxiety (17.7%) along with COVID-19 related distress among the cancer patients (n=6213) from the same country which was lower than Indian population [4]. This could be due to the psychological impact of different stages of the pandemic as mentioned in the emotional epidemic curve [1]. Juanjuan L et al., had conducted a study in February 2020 while Wang Y et al., in April 2020. An early phase of the epidemic is often characterised by increased prevalence of fear, anxiety, and depression due to uncertainty, and lack of information which often decreases after some time [27,28].

Also, the study conducted among the patients with lymphoma had a higher prevalence of GAD (36 %) and a lower prevalence of depression (36%) during this pandemic [29]. This could be due to the use of Hospital Anxiety and Depression Scale-A (HADS-A) which has higher specificity and screening accuracy than PHQ-9 [30]. The recently conducted online survey from India (n=1685) reports that about two-fifth (38.2%) had anxiety and 10.5% of the participants recruited from the general population had depression during a period lockdown and COVID-19 pandemic. Both (Present and Grover S et al., study) has used reliable and validated tools i.e., PHQ-9 and GAD-7 [26]. However, this study findings suggest that patients with cancer receiving treatment were more depressed and were less anxious than general population. This could be due to the chronic nature of the illness, adverse effects of radiotherapy and chemotherapy, effects of lockdown on services, uncertainty, fear, and coping among patients with cancer. Besides, study by Grover S et al., had several limitations of being an online survey such as snowball sampling, data collection, the unpredictable response rate from participants. Thus, may not representable as the general population [26].

Among the patients with cancer, 14 patients (25.45%) were screened positive on both PHQ-9 and GAD-7, and 12 patients (21.81%) population screened positive for either depressive symptoms or anxiety. However, it is important to note that an increased score on GAD-7 in patients with depressive symptoms is strongly associated with multiple domains of functional impairment. Though, symptoms of depression and GAD has often had co-occurrence these symptoms have differing but independent effects on functional impairment and disability [31,32].

During interviews with some screened positive patients, most of the patients reported that they are worried more about their stay in the hospital, delaying treatment or appointment due to lockdown and other public health measures, and infecting their relatives. Most of the patients denied COVID-19 related anxiety instead they reported they are more worried about the prognosis of cancer and the adverse effect of on-going treatment. This could be an underlying reason for a low score of CAS, OCS while a higher score of PHQ-9 and GAD-7 in present study patients.

Despite having significant correlations among all scales, only scores on FCV-19 was able to predict the coronavirus anxiety among the patients with cancer. It can be due to possible under-reporting of CAS due to the use of a high cut-off score of 9 instead of 5 considering the population at risk of developing coronavirus related anxiety [33]. However, lowering the cut-off score of 9 may be required to reduce the under-diagnosis of Coronavirus related anxiety. Therefore, future studies are needed to reconsider the cut-off score without compromising the robust sensitivity and specificity of CAS.

In most of the previous epidemiological studies, the online platform was used to collect data [4,5,22-24]. Further, COVID-19 related scales are also developed by using online platform [6]. The online survey has several limitations [34]. These limitations include the restriction on internet access leading digital divide of people, motivation to respond, and comfort with self-reporting emotional and behavioural symptoms which often influence the participation rates, and the responses. In this study, authors have surveyed OPD providing these questionnaires due to the non availability of internet, poor, or low internet connection in the rural part of India. However, this method might have provided us more robust data than previously reported studies.

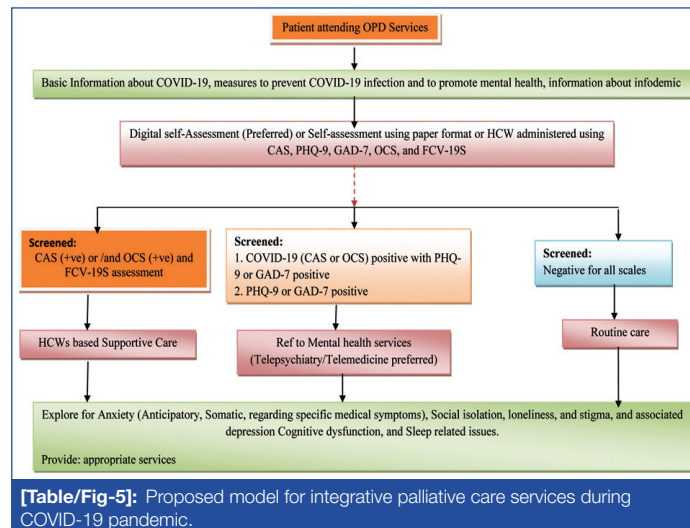
Only two patients (3.6%) were found to have positive scores from the OCS scale. Though the finding may not be significant in this study, it warrants the need to look out for the recent onset of obsessive-compulsive disorder, given the fact that safe hygienic practices like hand washing play a vital role in preventing infection; which has been fiercely propagated by World Health Organisation (WHO) and several medical organisations.

To the best of our knowledge, this is the first study that attempted to COVID-19 related mental health issues (anxiety, fear, and obsession) and its relationship with GAD and depression using standardised instruments. In addition, there was only one study that has attempted to evaluate the psychological impact of COVID-19 among patients with cancer [35]. Present study findings emphasise the need of assessing the common mental disorders along with COVID-19 related mental health issues in this pandemic which could otherwise be easily overlooked. Only those participants who attended OPD were included in this survey which adds on to methodological limitations of web-based or internet surveys (such as snowball sampling).

Future Direction

Both palliative care services and mental health services are poorly developed in India due to human resource deficits, stigma, and financial constraints [36]. In many instances, psychological need for patients suffering from cancer is often overlooked even during the prepandemic era. Based on present study findings with the

use of recently prepared scales, we would like to propose a patient care model for the mental health needs of patients with cancer during the COVID-19 pandemic. However, this stepped care model along with triage needs further evaluation in subsequent studies [Table/Fig-5]. Though this model was prepared based on cross-tabulation of results, before implementation in practice the clinician or researchers should consider the dynamic nature of COVID-19 pandemic, COVID-19 related stigmatising experiences, and screening or diagnostic properties these tools for underlying mental healthcare [37]. In this scenario, digital technology including artificial intelligence can help to predict and interpret the emerging and existing mental health issues [38].



Limitation(s)

First, this was a single-centre study, having a small sample size, and cross-sectional study design which has a recall bias especially for biological symptoms of chronic medical disorder and response bias. Second, authors used self-reported scales (PHQ-9, GAD-7, and CAS) which are proxy of underlying conditions and their diagnosis was not confirmed in a structured interview (e.g. Mini International Neuropsychiatric Interview-MINI) or clinician's interview. Third, the adverse effects of medications or medical conditions such as anaemia may have over-diagnosed depressive or anxiety symptoms. Fourth, present study have not used the scales related to other common mental disorders such as insomnia. Fifth, the various public mitigation efforts (e.g. restricted movement, lockdown) may have exaggerated the effects of depression or anxiety. Screening accuracy is dependent on prevalence and anxiety, as identified by the GAD-7, was relatively low in this population. Therefore, the CAS or OCS may require a lower threshold score to maximise sensitivity and specificity in this specific population. The scales CAS and OCS are yet to be validated in the local language (Marathi)

CONCLUSION(S)

The COVID-19 related anxiety and fear are highly prevalent among patients with cancer which may be an exaggeration of pre-existing, untreated common mental disorders or new ones due to public mitigations measures, infodemic, and fear. This study found co-existence of COVID-19 related anxiety and fear along with common mental disorders among the patients with cancer and these conditions may have a prognostic or predictive significance that needs immediate attention in terms of implementation of COVID-19 related mental health issues in routine clinical screening.

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