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Psychological effects of COVID-19 on patients with cancer, their caregivers: A systematic review

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Abstract---There is limited study reporting the severity of anxiety and depression in cancer cohort and their caregivers. We aimed in this systematic review to determine the prevalence of stress, anxiety, depression among comprehensive cancer patient and their caregivers during COVID-19 pandemic. A systematic review search was performed on PubMed, PsycINFO, CINAHL, and Scopus till June 2021. PRISMA guidelines were used in this systematic review. Reviews were performed to collect all original research articles to describe prevalence of stress, anxiety, depression among the cancer patients and their caregivers. All analysis was done by using RStudio version 1.0.136. 4 studies from our search criteria were eligible for inclusion for anxiety symptoms. Meta-analyses revealed that no any significant difference in incidence of anxiety in cancer and their caregivers. The pooled odds ratio 1.00 [95% CI; 0.87- 1.15]. Pooled prevalence in patients and their caregivers 49% [25%; 74%] and 50% [26%; 73%] respectively. Anxiety was relatively higher in cancer patients and their care givers. Isolation, married caregivers showed most significant factor to increase anxiety in cancer patients and their care givers. This metaanalyses suggest that prevalence of anxiety in cancer patients and their caregivers were significantly increasing during COVID-19.

Keywords---stress, anxiety, depression, COVID-19, cancer caregivers, cancer patients, systematic review.

Introduction

The ongoing COVID-19 outbreak has emerged as a global pandemic which was declared as Public Health Emergency of International Concern (PHEIC) by the World Health Organization on January 30, 2020 (Harapan H et al., 2020). The rising number of cases has put tremendous stress on the government run health care systems in countries across the world (OECD 2020). The number of positive cases as well as death toll from COVID-19 has been on increase in worldwide (Chen N et al., 2020; Huang. C et al., 2020; Lescure.F.X.,2020; WHO COVID 19 situation report, 2020; Dai MY et al.,2020). The COVID-19 outbreak has affected cancer services provided by the hospital due to the national lockdown and other logistics arising from the same (Liang W et al.,2020). The timely implementation of various policies at administrative level has enabled continuation of cancer care as well as control the spread of COVID-19 (Van de Haar J.et al., 2020). However, despite this the immune-suppressive nature of cancer treatment and simultaneous risk of community transmission poses cancer patients at higher risk of contracting COVID-19 infection (Loeffen E et al., 2019; Carlisle PS et al., 1993; Kamboj M and Sepkowitz KA,2009; El-Sharif A et al., 2012). This leads to additional stress due to the fear of delay in cancer treatment as well as posing oneself at risk to the adverse sequelae of COVID-19 infection (Fujii Y et al., 1994; Markovic S et al., 1999; Faggioli P et al., 1997). An Italian cancer patient survey showed that a relatively large proportion of young patients felt personally at risk of severe complications from COVID-19 which led to life-style changes (Wang C et al., 2020). Chinese data reports that almost 50% of patients had symptoms of anxiety and depression even without the diagnosis of COVID-19 and 90%

expressed fear of cancer progression as well as fear of being infected with COVID-19 (Quteimat OM and Amer AM,2020). One of the major factors contributing to this is the reconfiguration of the oncology services as pandemic mitigation strategy. Such policies include delaying surgery, the introduction of regimens requiring less-frequent administration, employing less intense systemic therapies, deferring treatment in certain indications and hypofractionated radiotherapy (Wdowik MJ et al., 1997).

However, a published article about these psychological impacts on uninfected or infected COVID-19 cancer patient or caregivers populations is scarce. Cancer patient is a unique group of patients because they need to access health care regularly (Eakin EG and Strycker LA, 2001; Riegel B and Carlson B, 2002; Bayliss EA et al., 2003; Boberg EW et al., 2003; Skalla KA et al., 2004; Mallinger JB et al., 2005). Delay in cancer treatment increases risk to the patients (Biagi JJ et al., 2011; Raphael MJ et al., 2016; Chen Z et al., 2008; Institute of Medicine Committee on Quality of Health Care in America, Crossing the quality chasm: a new health system for the 21st century, National Academy Press, 2001; Bleicher RJ et al., 2016). No such study reports that explains the severity of anxiety and depression in cancer cohort those are infected with COVID-19. This study aimed to better understand the psychological impact of COVID-19 on cancer patients and caregivers. We aimed in this meta-analysis to determine the prevalence of stress, anxiety, depression among the comprehensive cancer patient and their caregivers during the COVID-19 pandemic.

Methods

Electronic searches of on PubMed, PsycINFO, CINAHL, and Scopus performed till June 2021. The literature search was done by medical librarian assisted and first author.

Data searches

The target population was patients diagnosed with any diseases categorized under the term cancer (diagnosed with or without COVID-19). A hand search was carried out in Google Scholar to identify further relevant studies were used: (COVID-19 OR SARS-CoV-2 OR Severe Acute Respiratory Syndrome Coronavirus 2 OR 2019nCoV ORHCoV-19) AND (psychological Health OR psychological Health OR Depression OR Anxiety OR Stress OR Fear) AND (Cancer OR oncology OR caregivers). A detailed search strategy is reported in supporting information.

Study selection

Two authors separately performed the scrutiny of appropriate publications. First step involved assessing the titles and abstracts of all the available articles in serial order. Then, the full text of selected articles was studied. Repeated articles were removed using REFWORK. A PRISMA has been designed for presenting identification to selection of all articles/literature employed for this systematic review (Brandenburg D et al., 2019). Cross-sectional survey studies were included. The articles included were restricted to those in the English language only. The population who were not diagnosed with cancer got excluded. Articles

were also excluded if there were duplicates. General information was extracted from each report included: the first author, country, and year of publication, prevalence of anxiety, depression, fear and stress in cancer survivor and caregivers.

Data extraction and management

Data extraction was independently done by two review authors from included studies. All conflicts were managed by including a reviewing writer. The data was entered into an Excel spreadsheet. The entered info was verified by the expert.

Quality of evidence

The Newcastle-Ottawa Scale was employed for assessing the quality.

Data synthesis and analysis

The I² statistics were used to determine heterogeneity. Because of the possibility for variability, we utilised a random-effects model. Individual study results and aggregated obtained values were presented using forest plots. Funnel plots were used to measure publication bias. Potential biases have been examined using Eggers and Beggs test. All analyses was performed using R version 4.1.0, from the Comprehensive R Archive Network (R Core team, 2020) with General Package for Meta-Analysis “meta” package version 4.18-2.

Results

The first analyses were performed and provided with 485 unique articles. Studies were enrolled after screening titles and abstracts, 140 articles remained for detailed review. 345 articles were excluded due to those articles have not met inclusion criteria. As per inclusion criteria 102 studies were identified, remaining 106 of which were not found relevant. These all studies excluded due to no relevant outcome reported, meta-analysis and review, editorial, commentary and case report were excluded from systematic review. Consequently, 30 publications were excluded as per inclusion criteria and those were qualitatively analyzed. Figure 1 PRISMA flow diagram depicts the PRISMA (Preferred Reporting Items for Meta-analysis and Meta-Analysis) which details the search and selection process applied during the overview; of these 4 articles met the inclusion criteria for the prevalence calculation of anxiety in cross-sectional studies.

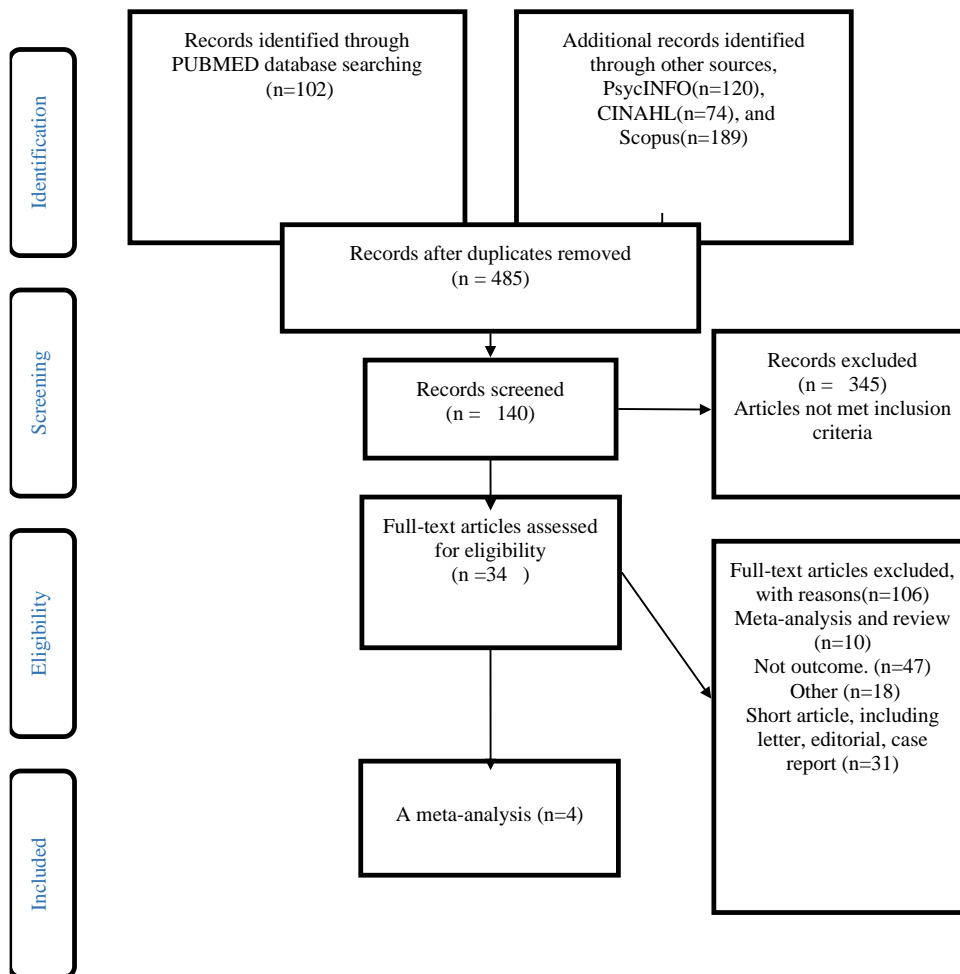


Figure 1. PRISMA flow diagram: PRISMA (Preferred Reporting Items for Meta-analysis and Meta-Analysis) chart demonstrates the systematic search method used in the overview

Study characteristics

Table 1 shows the characteristics of the included studies. The included studies were published till June 2021. Original articles or research articles provided data on prevalence of anxiety and published during the COVID-19 pandemic. These were included in systematic review.

Table 1
Characteristics of included studies

Lead Author	Year	Country	Study design	Sample size		Anxiety		Risk factors
				Patients	Caregivers	Patients	Caregivers	
Kennedy Yao Yi Ng	2021	Singapore	cross-sectional survey	624	408	19.10%	22.55%	worried about patients dying alone, caregivers who were married were more anxious
Isabella Amaniera	2021	USA	cross-sectional survey	281	281	70%	70%	isolation appeared, Food insecurity and financial hardship
Courtney E. Wimberly	2021	USA	cross-sectional survey	321	175	77%	77%	self-isolation , struggling to pay for basic needs, male sex
Shenmiao Yang,	2020	China	cross-sectional survey	1060	948	33%	31%	higher education level,increase of > 2 h/day of mobile phone use , no physical exercise

Quality assessment

Table 2 shows the results of the quality assessment. The studies were of excellent quality, with not a single study receiving a poor score on the Newcastle–Ottawa scale. The Newcastle-Ottawa Scale (NOS) used in studies for quality assessment observation. Following are the three dimensions of NOS scale: Selection, Outcome and Comparability. As a supplementary document, there is a list of all relevant questions. If the study passes specific requirements, it is given a total of 9 stars, encompassing 4 stars for selecting dimension, 2 stars for the comparable dimension, and 3 stars for the result dimension.

Table 2
Quality assessment of the included studies

Author	Year	Total score	Selection			Comparability		Outcome	
			Adequate samples	Total sample size	Non-respondents	Adequacy of exposure	Design and analysis	Reporting outcome	Statistical test
Kennedy Yao Yi Ng	2021	5		*	**	*	*		

Isabella Amaniera	2021	6	*			*	**	*	*
Courtney E. Wimberly	2021	4	*			*		*	*
Shenmiao Yang,	2020	6	*			*	**	*	*

Prevalence of anxiety in Cancer patients and their caregivers

4 studies were included in meta-analysis of anxiety in cancer patients and their caregivers. In total, 2286 patients and 1812 care givers reported from 4 studies. The percentages of anxiety were reported in Kennedy Yao Yi Ng et al.2021 was 19.10% in cancer patients and 22% in caregivers. Isabella Amaniera et al.2021 reported 70% in both patient and caregivers. Courtney E. Wimberly reported 77% percent in patient and caregivers. Shenmiao Yang reported 33% in patients and 31% in caregivers. Pooled prevalence in patients and their caregivers is 39% [38%; 41% fixed effect model]. Isolation, married caregivers has shown the most significant factor to increase anxiety in cancer patients and their care givers. The random-effects pooled estimated odds ratio of anxiety was 1.00 [95% CI; 0.87-1.15], with considerably less significant heterogeneity ($I^2=0\%$) throughout the studies ($p < 0.001$). Figure 2, Table 3 shows the degree of publication bias may also be assessed with the help of the Egger's (p -value= 0.496) and Begg's tests (p -value = 0.422), there were not found to be considerable publication bias detected by Egger's tests and Begg's correlation test. We used funnel plots for the assessment of publication bias by visual inspection as shown in Figure 3.

Table 3
Pooled odd ratio estimate for anxiety

Author	Odds ratio	Lower Bound	Upper Bound	%W (fixed)	Fixed effect model	p-value	I ²	Bias assessment			
									Odds ratio	Lower Bound	Upper Bound
Kennedy Yao Yi Ng et al.2021	0.81	0.60	1.10	20.60	1.00	0.87	1.15	0.935	0.0% [0.0%; 83.3%]	0.496	0.422
Isabella Amaniera et al.2021	1.00	0.70	1.44	14.80							
Courtney E. Wimberly et al.2021	0.99	0.64	1.53	10.00							
Shenmiao Yang et al.2020	1.10	0.91	1.32	54.60							

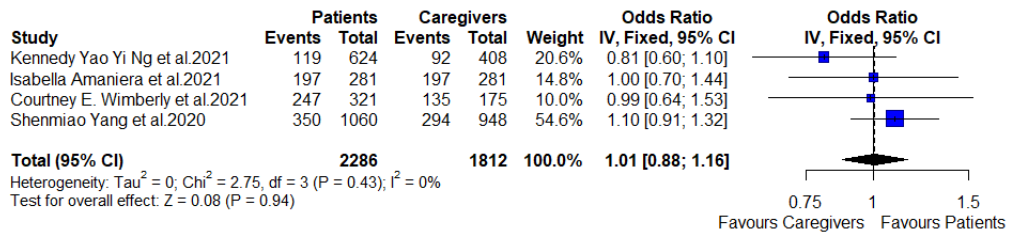


Figure 2. Forest plot using the random effect model. Horizontal bars indicate the amount of variation (95% confidence intervals of the parameter estimates). Sizes of squares indicate weight in the pooled effect size

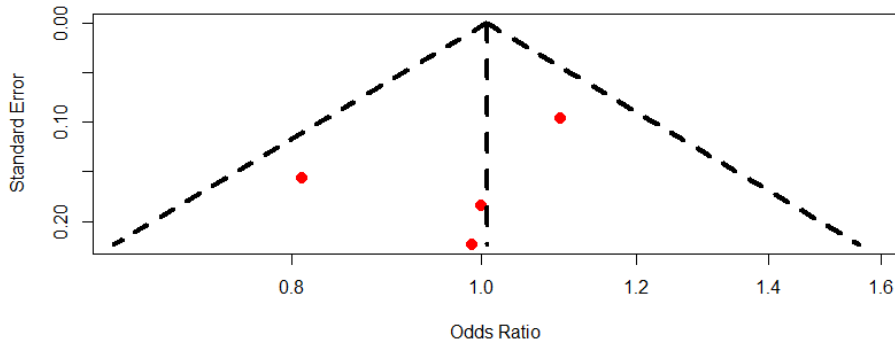


Figure 3. Funnel plot for potential publication bias of studies

Discussion

This is one of the best systematic reviews which were done on cancer and their caregivers to assess anxiety. The goal of this systematic review was to determine the level of anxiety in cancer patients and caregivers during the time of COVID-19 pandemic. COVID-19 and its impact on any cancer-related therapy, the occurrence of relapse, and the potential advancement of cancer illness could make cancer patients and their caregivers nervous. This might increase risk of level of anxiety and related symptoms. Our systematic review finding suggested that, cancer survivor and their care givers has experienced the increasing of anxiety during COVID-19. As compare to healthy control 30% more risk to chance of having anxiety in cancer survivor and their caregivers during COVID-19 pandemic.

The published meta-analyses and systematic review reported that, depression and anxiety in patients with cancers survivors and their caregivers due to cancer types, time and technique assessment anxiety, treatments (chemotherapy, radiotherapy, etc.) and time (pretreatment, on-treatment and post-treatment) of treatment, on follow-up, duration with cancer survivor, investing of your time for follow-up and standing of disease (inpatients, outpatient, palliative care) (Walker J et al., 2013; Watts S et al., 2014; Watts S et al., 2015; Yang YL et al., 2013;

Maunder R et al., 2003; Bai Ye et al., 2004). Moreover, cancer patients and their caregivers experienced higher levels of anxiety compared to healthy population. Published evidence of systematic reviews on cancer patients and their showed a better rate of each depression and anxiety throughout the COVID-19 crisis in some teams like the healthy communities, hospital workers and staff, COVID-19 diagnosed patient and pregnant women.

Study limitations

The present systematic review has many limitations. First, very limited evidence about cancer care givers anxiety related database. There have been restricted analysis done by various studies that not compared anxiety in cancer patients and their caregivers. Last, only 4 studies included, which may limit the generalizability of the finding.

Conclusions

Fears and anxiety related to COVID-19 are high in cancer patients and their caregivers. Half of cancer patients and their caregivers are more likely to show increased incidence of anxiety. There is a strong necessity to detect and treat anxiety in cancer patients and their caregivers to increase the quality of life and well-being. During this COVID 19 challenging time, the oncology community faces major issues related to mental health cancer patients and their caregivers.

Supporting Information

Provided with Supplemental Table 4: Search strategy and Table 5: NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (adapted for cross sectional studies)

Supplemental Table 4.

Search strategy.

PUBMED		
Search	Query	Results
#1	(((((Depression[MeSH Terms]) OR (Depression[Title/Abstract])) OR ((Major depressive disorder[MeSH Terms]) OR (Major depressive disorder[Title/Abstract]))) OR ((Depressive disorder[MeSH Terms]) OR (Depressive disorder[Title/Abstract]))) OR ((anxiety[MeSH Terms]) OR (anxiety[Title/Abstract]))) AND (((Neoplasms[MeSH Terms]) OR (cancer[Title/Abstract])) OR (cancer caregiver[Title/Abstract])) (tumor[Title/Abstract])) AND (((COVID-19[MeSH Terms]) OR (COVID-19[Title/Abstract])) OR (SARS-CoV-2[MeSH Terms])) OR (SARS-CoV-2[Title/Abstract]))	102
SCOPUS		
Search	Query	Results
#1	(TITLE-ABS-KEY ("Depression") OR TITLE-ABS-KEY ("Major depressive disorder") OR TITLE-ABS-KEY ("Depressive disorder") OR TITLE-ABS-KEY ("anxiety")) AND (TITLE-ABS-KEY ("Neoplasms") OR TITLE-ABS-KEY ("cancer") OR TITLE-ABS-KEY ("cancer caregiver") OR	189

	TITLE-ABS-KEY ("tumor")) AND (TITLE-ABS-KEY ("COVID-19") OR TITLE-ABS-KEY ("SARS-CoV-2"))	
PsycINFO,		
Search	Query	Results
#1	(TITLE-ABS-KEY ("Depression") OR TITLE-ABS-KEY ("Major depressive disorder") OR TITLE-ABS-KEY ("Depressive disorder") OR TITLE-ABS-KEY ("anxiety")) AND (TITLE-ABS-KEY ("Neoplasms") OR TITLE-ABS-KEY ("cancer") OR TITLE-ABS-KEY ("cancer caregiver") OR TITLE-ABS-KEY ("tumor")) AND (TITLE-ABS-KEY ("COVID-19") OR TITLE-ABS-KEY ("SARS-CoV-2"))	120
CINAHL		
Search	Query	Results
#1	(TITLE-ABS-KEY ("Depression") OR TITLE-ABS-KEY ("Major depressive disorder") OR TITLE-ABS-KEY ("Depressive disorder") OR TITLE-ABS-KEY ("anxiety")) AND (TITLE-ABS-KEY ("Neoplasms") OR TITLE-ABS-KEY ("cancer") OR TITLE-ABS-KEY ("cancer caregiver") OR TITLE-ABS-KEY ("tumor")) AND (TITLE-ABS-KEY ("COVID-19") OR TITLE-ABS-KEY ("SARS-CoV-2"))	74

Table 5: NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (adapted for cross sectional studies)

Selection: (Maximum 4 stars)

1) Representativeness of the sample:

- a) Truly representative of the average in the target population. * (all subjects or random sampling)
- b) Somewhat representative of the average in the target population. * (non-random sampling)
- c) Selected group of users.
- d) No description of the sampling strategy.

2) Sample size:

- a) Justified and satisfactory. *
- b) Adequately powered to detect a difference. *
- c) Not justified.

3) Non-respondents:

- a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory (>60%). *
- b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
- c) No description of the response rate or the characteristics of the responders and non-responders.

4) Ascertainment of the exposure (coronavirus outbreak):

- a) Reported COVID-19 cases in the country by the time of investigation. *
- b) No reported cases of COVID-19 in the country by the time of investigation.

Comparability: (Maximum 2 stars)

- 1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled:
 - a) The study controls for the most important factor (select one). *
 - b) The study control for any additional factor. *

Outcome: (Maximum 3 stars)

- 1) Assessment of the outcome:
 - a) Structured interview with a trained psychiatrist/interviewer. **
 - b) Training before the self-reported survey. **
 - c) Self report without training. *
 - d) No description.
- 2) Statistical test:
 - a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
 - b) The statistical test is not appropriate, not described or incomplete.

Declarations

Author contribution

All contributors participated in the research, data gathering, creating or updating the article, granted official approval of the published version, and agreed to be liable for all components of the project.

Declaration of competing interest

The authors report no conflicts of interest in the present work.

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