Cancer Pain, Anxiety, and Depression in Admitted Patients at a Tertiary Care Hospital: A Prospective Observational Study

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Abstract

Context: Pain is the most common symptom in admitted cancer patients. The association between the severity of cancer pain and distress symptoms such as depression and anxiety is a subject of research. **Aims:** The aim is to study the prevalence of pain, anxiety, and depression in admitted cancer patients and determine the association between pain and anxiety and depression at a tertiary cancer care institute. **Settings and Design:** This was prospective observational study. **Subjects and Methods:** We enrolled 393 cancer inpatients prospectively after written informed consent. Their disease details, presence, severity, and character of pain were recorded. Numerical Pain Scale was used for pain scores, self-reporting Hospital Anxiety and Depression Scale for anxiety and depression. **Statistical Analysis Used:** Normal data were analyzed with parametric, nonnormal with nonparametric methods, and categorical with the Chi-square test. **Results:** The prevalence of moderate-to-severe pain was 41.5%, anxiety 20.3%, and depression 24.8%. Proportion of patients with anxiety and depression was 9.2% and 17.7% in patients with no pain; about 32.8% and 36.7% with severe pain, respectively ($P < 0.000$). In patients with no depression 6% had anxiety; with depression 44.9% had anxiety ($P < 0.000$). Odd's ratio to have anxiety and depression was 4.44 (95% confidence interval [CI] 2.0318–9.7024) and 2.92 (95% CI 1.5739–5.4186), respectively, in patients with pain as compared to no pain ($P < 0.00$). There was a positive correlation between pain, anxiety, and depression scores. **Conclusions:** There is strong association between the presence and severity of pain and distress symptoms such as anxiety and depression in admitted cancer patients.

Keywords: Association of cancer pain and distress, cancer pain, hospital anxiety and depression score, numerical pain scale, prevalence of anxiety, prevalence of depression

Introduction

Pain is one of the most common and studied symptoms in cancer patients. Cancer pain has a multimodal etiology-primary disease process, treatment effects, metastatic pathology, and sequelae in survivors. Cancer diagnosis resulting in high levels of emotional distress is a well-known human fact and is also established in studies.[1,2] Psychological symptoms of distress such as depression and anxiety are known to occur in a significant number of cancer patients and survivors.[3,4] These psychological symptoms may result in alteration of the patient's capability to tolerate the illness burden as well as various difficult treatment regimens that may have extended hospitalization. This may eventually result in worsening of quality of life and an appreciable increase in suicide risk.[5,6] Depression and pain are causally inter-related, where one may cause the other.[7,8] Spiegel *et al*., 1994[9] have, in fact, argued that pain may cause depression and that the same neurotransmitter pathways are shared by both depression and pain.

The total pain experienced by a cancer patient varies with a number of psychological factors, these factors may alter the pain perception not only in terms of intensity of pain but also the suffering experienced by the patient.[10] These psychological factors have not been well studied. Quantitative studies evaluating the association of cancer pain and distress symptoms such as depression and anxiety in a prospective manner are required in the Indian scenario. This study was designed to determine the anxiety and depression

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score in admitted cancer patients and correlate with their pain score.

Subjects and Methods

Type of study

This was prospective observational study.

Duration of study

This study was performed at Cancer Research Institute (CRI), Swami Rama Himalayan University, Dehradun, India between January 2018 and April 2018.

Aim

- To determine the pain, anxiety, and depression scores in admitted cancer patients
- To determine any association between the pain, anxiety, and depression scores in these patients.

Inclusion criteria

Patients with pathologically diagnosed cancer admitted at CRI giving written informed consent to participate in the study.

Exclusion criteria

Age <18 years or unconscious patient, unable to communicate or answer the questionnaire.

Sample size calculation

Using the following equation with alpha error as 5% the sample size was calculated to be 361 taking the prevalence of moderate-to-severe pain as 38%.[11]

$n = Z_{a/2}^2\ pq/d^2$

$d = 5\%$,

$P = 38\%$

Methods

The demographic and disease details were noted for the patients, the 11-point Numerical Pain Scale (NPS) was used to document the pain score of each patient, a body chart was used to note the sites of pain, the clinical assessment was made to characterize the pain as nociceptive, neuropathic, or mixed. The Hospital Anxiety and Depression Scale (HADS) was used in the native language of the patient as a self-reporting tool to measure the anxiety and depression scores. For pain NPS score of 1–3, 4–6 and 7–10 were classified as mild, moderate, and severe pain, respectively. For anxiety and depression, HADS score 0–7, 8–10 and 11–21 were taken as normal, borderline, and abnormal, respectively. Only patients with HADS score of 11–21 were classified to have anxiety or depression.

Statistical tools

The data were entered in MS Excel 2010, and statistical analysis was performed using the SPSS software version 22 (HIHT University, Dehardun). The one-sample Kolmogorov–Smirnov test was used to determine the normality of the data. Normally distributed data were analyzed using parametric tests, nonnormally distributed data using nonparametric tests

and categorical data using the Chi-square test. The level of significance had the following criteria: the difference was said to be statistically significant if $P < 0.05$.

Results

A total of 393 patients were enrolled in the study and included in the analysis. There were 54.2% of female patients; the overall mean age was 52.1 years ± 13.84 standard deviation. Majority (83.7%) patients were in the age group 30–69 years. The most common primary sites of cancer in male were head and neck, hematological, and gastrointestinal; in female were genitourinary, breast, and gastrointestinal in that order. The most common pathology was carcinoma (78.6%). It was interesting to note that only 30% of patients were in the early stage of cancer, and 31.8% of patients had metastasis. Around half the patients had received chemotherapy (56.2%) or surgery (43%), but only 14.5% of patients had received radiotherapy [Table 1].

It was found that 41.5% of patients had moderate or severe pain at admission. The prevalence of anxiety was 20.3%, and depression was 24.8% [Table 2].

Association of the severity of pain and anxiety or depression

As detailed in Table 3, only 9.2% of patients with no pain had anxiety in contrast to 32.8% of patients with severe pain ($P = 0.000$). In patients with no pain 17.7% had depression, whereas in patients with severe pain as many as 36.7% had depression ($P = 0.000$). When scores of anxiety and depression were compared we found that in patients with no depression 6% had anxiety; in patients with depression 44.9% had anxiety ($P = 0.000$). The odds ratio (OR) of having anxiety was 4.44 (95% confidence interval [CI] 2.0318–9.7024) and depression 2.92 (95% CI 1.5739–5.4186) in patients with pain as compared to no pain at admission ($P = 0.000$) [Table 4]. The OR of having anxiety was 23.27 (95% CI 10.07–53.73, $P = 0.000$) if depression was present. A mild positive correlation was found between pain and anxiety scores; pain and depression scores 0.29 and 0.24 (Spearman's correlation coefficient), respectively. A moderate positive correlation was found between anxiety and depression scores (0.579). All P values were 0.000.

Multivariate analysis for factors affecting anxiety or depression

The variables (other than severity of pain) which could be confounding factors for presence of anxiety and depression were age, gender, stage of disease, number of metastasis, received radiotherapy, received chemotherapy, history of surgery for the cancer, number of pain sites, and type of cancer pain (nociceptive, neuropathic or mixed). All these demographic, disease, and outcome variables were assessed in relation to the presence of anxiety or depression using multivariate analysis. For numerical data ANNOVA and for categorical data mutinominal regression models were used. Patients who had received radiotherapy ($P = 0.009$), the severity of pain ($P = 0.000$), number of pain sites ($P = 0.006$),

Table 1: The baseline characteristics of the patients (*n*=393)

Variable	Number of patients (%)		
	Male	**Female**	**Overall**
Gender	180 (45.8)	213 (54.2)	393
Mean age years±SD	52.62±14.64	51.70±13.14	52.13±13.84
Age group (years)			
10-19	2 (1.1)	1 (0.5)	3 (0.8)
20-29	10 (5.6)	11 (5.2)	21 (5.3)
30-39	24 (13.4)	26 (12.2)	50 (12.7)
40-49	38 (21.2)	55 (25.8)	93 (23.5)
50-59	35 (19.6)	55 (25.8)	91 (23.0)
60-69	49 (27.4)	46 (21.6)	95 (24.1)
70-79	17 (9.5)	16 (7.5)	33 (8.4)
80-89	4 (2.2)	3 (1.4)	7 (1.8)
Primary site			
Limb	4 (2.2)	1 (0.5)	5 (1.3)
Skin	2 (1.1)	1 (0.5)	1 (0.3)
Retroperitoneum	2 (1.1)	0	2 (0.5)
Brain	4 (2.2)	1 (0.5)	5 (1.3)
Breast	0	47 (22.1)	47 (12)
Gastrointestinal	33 (18.3)	26 (12.2)	59 (15)
Genitourinary	17 (9.4)	88 (41.3)	105 (26.7)
Head and neck	47 (26.1)	5 (2.3)	52 (13.2)
Hematological	34 (18.9)	24 (11.3)	58 (14.8)
Hepatobiliary	7 (3.9)	9 (4.2)	16 (4.1)
Lung	23 (12.8)	9 (4.2)	32 (8.1)
Unknown	7 (3.9)	2 (0.9)	9 (2.3)
Pathology			
Carcinoma	131 (72.8)	178 (83.6)	309 (78.6)
Leukemia	14 (7.8)	11 (5.2)	25 (6.4)
Lymphoma	15 (8.3)	12 (5.6)	27 (6.9)
Sarcoma	8 (4.4)	6 (2.8)	14 (3.6)
Other	12 (6.7)	6 (2.8)	18 (4.6)
Stage			
Early	50 (27.8)	68 (31.9)	118 (30.0)
Advanced	72 (40.0)	78 (36.6)	150 (38.2)
Metastatic	58 (32.2)	67 (31.5)	125 (31.8)
Number of metastasis			
0	122 (68.2)	146 (68.5)	268 (67.8)
1	40 (22.3)	48 (22.5)	89 (22.5)
2	16 (8.9)	13 (6.1)	29 (7.3)
3	1 (0.6)	5 (2.3)	6 (1.5)
4	0	1 (0.5)	1 (0.3)
Treatment received			
Surgery	65 (36.1)	104 (48.8)	169 (43.0)
Radiotherapy	31 (17.2)	26 (12.2)	57 (14.5)
Mean fractions of radiotherapy±SD	18.37±12.45	22.87±9.69	22.56±11.48
Chemotherapy	91 (50.6)	130 (61.0)	221 (56.2)
Mean cycles of chemotherapy±SD	3.47±2.78	3.57±2.46	3.53±2.59

SD: Standard deviation

and HADS score demonstrating anxiety (*P* = 0.000) were found on multivariate analysis to be associated significantly with the presence of depression. Only the severity of

Table 2: The outcome variables pain, anxiety, and depression scores

Outcome variable	Number of patients (%)		
	Male	**Female**	**Overall**
Pain at admission			
No or mild pain	98 (54.7)	130 (61.0)	229 (58.0)
Moderate or severe	81 (45.3)	83 (39.0)	164 (41.5)
Anxiety scores			
Normal	108 (60.3)	115 (54.0)	224 (56.87)
Borderline	39 (21.8)	50 (23.5)	89 (33.5)
Abnormal	32 (17.9)	48 (22.5)	80 (20.3)
Depression scores			
Normal	60 (33.5)	89 (41.8)	150 (38.0)
Borderline	72 (40.2)	73 (34.3)	145 (36.7)
Abnormal	47 (26.3)	51 (23 9)	98 (24.8)

pain (*P* = 0.000), number of pain sites (*P* = 0.000), and HADS score demonstrating depression (*P* = 0.000) were found on multivariate analysis to be associated significantly with the presence of anxiety [Table 5].

DISCUSSION

A meta-analysis on the prevalence of any type of cancer pain was published by van den Beuken-van Everdingen *et al*.[11] They found the prevalence of cancer pain to be 39.3%, 55.0%, and 66.4% after curative treatment, during anticancer treatment and in advanced or terminal disease, respectively. Moderate-to-severe pain, using NPS score was reported in 38.0% (NPS > 4) of all patients in the meta-analysis. In the present study, the NPS score of 4–10 indicating moderate or severe pain was found in 41.5% of patients.

In our study, one-fourth patients were found to have depression and one-fifth anxiety. These distress symptoms cannot be neglected because various studies have conclusively shown an association between depressive disorders and reduction in quality-of-life indices, compliance to treatment modalities, the psychological perception of different physical symptoms and most importantly prognosis. In a meta-analysis, in cancer patients, the pooled mean prevalence of depression ranged from 8% to 24%.[12]

Cancer pain is now recognized as the fifth vital sign. Depression and anxiety in cancer patients is still not evaluated and recorded routinely. Bhatnagar *et al*.,[13] in their retrospective review of 686 pain assessment forms found that function psychological symptoms were recorded at a low rate-anxiety 1.2% and depression 4.4% in cancer patients. Many cancer patients imagine a prolonged, painful dying process and equate cancer with death and treatments which may be debilitating to say the least. Cancer is perceived as threat and a source of anxiety in many. Assimilating medical information relating to cancer and making informed medical decisions is often

overwhelming for patients – all while continuing to manage various responsibilities such as family, work, and other. Cancer care professionals must recognize anxiety early and mange it in cancer patient populations. The challenge lies in judging if the anxiety in a patient is disproportionate to the threat presented by cancer since it is to be realized that the disease is associated with some real threat in every case. It may be normal for the patient to experience anxiety for 7–10 days after receiving the bad news. The levels of this normal anxiety may vary as the degree of real threat varies with the history and progression of cancer. Not only cancer but also treatment can affect the psychosocial well-being, placing these patients at risk of depression,[14] sleep dysfunction and fatigue[15] during treatment and on follow-up. Kandasamy *et al.*, 2011[16] found in advanced cancer patients that spiritual well-being was a significant component of the quality of life, and that it was closely related to various physical and psychological symptoms of distress, especially in palliative care setting.

Worsening pain may increase psychological distress symptoms such as depression and anxiety, and the effect is evident across the cancer disease spectrum. Zaza and Baine,[17] in their systematic review, found a strong association between cancer pain and psychological distress (mood disturbance, anxiety, and depression). In this study, we found that as the severity of pain increased; the prevalence of anxiety increased by 23.6%, and depression by 19%. Melkam Alemayehu *et al.*,[18] found OR of major depressive illness to be four in patients with pain than in patients with no pain. In this study, the OR of depression was 2.29, and anxiety 4.44 in patients with pain as compared to patients with no pain. In a study on Indian patients, Lewis *et al.*,[19] found a positive correlation between distress and pain score in 30 patients receiving radiation therapy for the head-and-neck cancer. In the present study, the linear correlation between pain and anxiety or depression was mildly positive, but it was moderately positive between anxiety and depression.

CONCLUSIONS

The prevalence of moderate and severe pain is high in admitted cancer patients in this study. A fair proportion of cancer patients have anxiety and depression which needs to be recognized and addressed adequately. There is strong association between the presence and severity of pain and distress symptoms such as anxiety and depression in admitted cancer patients at all stages of disease. However, the results of this study are not enough to conclude the causality of depression and anxiety in cancer patients to the pain they experience, further cohort studies are required to better understand this important aspect.

Conflicts of interest

There are no conflicts of interest.

Table 3: Cross-tabulation of severity of pain with hospital anxiety and depression scale scores

Variable	Severity of pain, *n* (%)				P*
	No	Mild	Moderate	Severe	
Anxiety score					
Normal	89 (68.5)	53 (71.6)	27 (44.3)	55 (43)	0.000
Borderline	29 (22.3)	14 (18.9)	15 (24.6)	31 (24.2)	
Abnormal	12 (9.2)	7 (9.5)	19 (31.1)	42 (32.8)	
Depression score					
Normal	67 (51.5)	30 (40.5)	19 (31.1)	34 (26.6)	0.000
Borderline	40 (30.8)	30 (40.5)	28 (45.9)	47 (36.7)	
Abnormal	23 (17.7)	14 (18.9)	14 (23)	47 (36.7)	
Total	130	74	61	128	

*Chi-square test

Table 4: Cross-tabulation of hospital anxiety and depression scale scores

Depression score	Anxiety score			Total	P*
	Normal	Borderline	Abnormal		
Normal	119 (79.3)	22 (14.7)	9 (6)	150	0.000
Borderline	80 (55.2)	38 (26.2)	27 (18.6)	145	
Abnormal	25 (25.5)	29 (29.6)	44 (44.9)	98	

*Chi-square test

Table 5: Multivariate analysis of factors associated with anxiety or depression

Variables	Anxiety		P*	Depression		P*
	Absent	Present		Absent	Present	
Patients received radiotherapy (%)	14.38	21.25	0.075	12.2	26.53	0.009
Median pain score	3	7	0.000	3	5	0.000
Patients with >1 pain site (%)	23.32	48.75	0.000	26.44	34.7	0.006
Patients with anxiety				12.2	44.9	0.000
Patients with depression (%)	17.25	55.00	0.000			

*ANOVA and multinomial regression

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