

THE HIGH BURDEN OF ANXIETY AND DEPRESSION AMONG CANCER PATIENTS UNDERGOING THE TRANSITION TO PALLIATIVE CARE

(A alta carga de ansiedade e depressão entre pacientes com câncer submetidos à transição para cuidados paliativos)

Ms. Daniela Batista Sorato

Em Psicologia

Ms. Fabiana Faria Rezende

Doutoranda em Psicologia

Fecha de recepción: 01-08- 2015

Fecha de aceptación: 22-09- 2015

Páginas 231 -242

Abstract.

The objective was to evaluate the indicators of pain, anxiety and depression through early screening in patients admitted to a palliative care oncology service. This was a cross-sectional with outpatients. We used the Hospital Anxiety Depression Scale; Visual Analog Scale of Pain and sociodemographic information from the medical record. 70 (32.6%) patients had some degree of pain. And moderate or excruciating 10 (5%), pain. It was found that 80 (37.2%) patients had anxiety and 84 (39.1%) depression. And 48 (22.4%) and 60 (27.9%) of them were within the moderate or severe levels for anxiety and depression respectively. Early tracking of pain, anxiety and depression is recommended to favor immediate patients admitted to hospice care practice.

Keywords: Early detection; anxiety; depression; palliative care.

Resumo.

O objetivo foi avaliar os indicadores de dor, ansiedade e depressão através de rastreamento precoce em pacientes admitidos em um serviço de cuidados paliativos oncológico. Este foi do tipo transversal com pacientes ambulatoriais. Utilizou-se a Hospital Anxiety Depression Scale; Escala Analógica Visual de Dor e informações sócio demográficas do prontuário. 70 (32,6%) dos pacientes apresentavam algum grau de dor. E 10 (5%) dor moderada ou insuportável. Detectou-se que 80 (37,2%) dos pacientes apresentaram ansiedade e 84 (39,1%) depressão. Sendo que 48 (22,4%) e 60 (27,9%) deles encontravam-se dentro dos níveis moderado ou severo para ansiedade e depressão respectivamente. O rastreamento precoce de dor, ansiedade e depressão é uma prática recomendável para favorecer atendimento imediato a pacientes admitidos em cuidados paliativos.

Palavras-chave: Detecção precoce; ansiedade; depressão; cuidados paliativos.

Background.

The transition from the prospect of achieving a cure to treatment at a palliative care service is often a traumatic period characterised by confusion, uncertainty and loss of control among patients and family members.¹⁻³ After patients have been told that their prognosis is poor, there is often an intense outpouring of emotions involving sadness, worry, grief, anger, blame and intermittent feelings of hope and fear.^{4, 5} The complexity of this process should not be underestimated, considering the various changes that may take place with regard to care patterns, role modifications, perspectives of loss and spiritual and psychosocial factors.⁶

Grief, despair and high levels of anxiety and depression are prevalent among patients with advanced cancer and need to be considered during treatment. Evidence indicates that although mental disorders are common during palliative care, they are underdiagnosed.^{5, 7} Often unrecognised and inadequately treated, mental disorders cause significant distress for patients and caregivers.⁸

Difficulty in accepting a poor prognosis is associated with greater rates of anxiety, depression and despair.^{9, 10} Lack of treatment for the psychological discomfort may be correlated with distress that is expressed as strongly as the distress that is induced by the underlying organic disease. In some cases, this distress may be associated with a greater chance of treatment failure.¹¹

Psychological disorders occur frequently and cause losses to the quality of life of cancer patients and family members. According to a report from the World Health Organization (WHO), approximately one-third of all individuals with cancer present some degree of anxiety and depression.¹² The WHO recommends that healthcare professionals remain alert with regard to identifying such abnormalities and that they are trained to institute optimal treatment. In day-to-day palliative care, psychological distress is as upsetting as physical distress and, for many individuals, less tolerable than physical distress. Thus, palliative care aims to treat the patient's physical symptoms and integrate this knowledge with the management of psychological aspects.^{13, 14}

The objective of this study was to evaluate the early indicators of anxiety and depression and their predictors among patients who were recently admitted to a palliative care facility.

Methods.

We conducted this cross-sectional study of 215 oncological patients over the age of 18 years with a diagnosis of advanced cancer and without the possibility of a cure. The Ethics Committee of Barretos Cancer Hospital approved this study, and all of the patients signed the informed consent statement. These patients had been referred to the Palliative Care Outpatient Unit (PCOU) of Barretos Cancer Hospital (Barretos, São Paulo, Brazil) between April 2009 and December 2009. In the PCOU, the early identification of pain, anxiety and depression is a routine practice and is integrated with the admission process for all new patients.

A psychologist conducts the evaluation using a model for individual interviews targeted at assessing the patient's level of adjustment in transitioning to palliative care; investigating his history of mental disorders; evaluating the degree of social support; and determining the current indicators for pain, anxiety and depression.

The Barretos Cancer Hospital is composed of two units. Diagnosis, surgery, chemotherapy, radiotherapy and other invasive procedures are performed in Unit I. The Palliative Care and Pain Centre functions in Unit II. Patients who start to receive outpatient care in Unit II for the first time come either from this unit's own ward after discharge or are sent from Unit I. When patients and their caregivers arrive, they go to the outpatient reception desk and are subsequently directed to a room where members of the nursing team receive them. At this point, the patients are screened for cancer symptoms and to identify which members of the multidisciplinary team are needed to optimally evaluate this patient.¹⁵ A psychological assessment is essential for all new patients at the outpatient clinic. After the initial assessments, the psychologist will define the appropriate type of follow-up for each patient: whether the patient should be admitted to the unit's ward; whether he should enter the home attendance program; or whether he should return to the PCOU for a consultation.

Measurements.

To screen for psychological abnormalities, the Hospital Anxiety and Depression Scale (HADS) was applied. This instrument contains 14 questions in a 4-point Likert scale: seven anxiety indicators (HADS-A) and seven depression indicators (HADS-D). The depression and anxiety scores are the sum of questions HADS-D1 to HADS-D7 and questions HADS-A1 to HADS-A7, respectively. In accordance with the criteria suggested by Botega *et al.*¹⁶, patients with scores between 0 and 7 are classified as normal, scores between 8 and 10 are classified as mild cases of anxiety or depression, scores between 11 and 14 are classified as moderate cases of anxiety or depression and scores between 15 and 21 classified as severe cases of anxiety or depression.

To evaluate anxiety and depression, HADS does not use the somatic criteria that are commonly used for chronic diseases, such as fatigue, loss of appetite and sleep abnormalities. HADS is an instrument for evaluating specific subjective symptoms and determining whether additional diagnostic methods are suggested for disease identification or patient treatment¹⁷. This scale can be used for early detection of psychological distress among cancer patients, who can be followed up with psychiatric interventions.¹⁸ To determine the anxiety and depression indicators, a cut-off point of ≥ 8 was adopted. Having scores greater than or equal to the cut-off point of 11 for both anxiety and depression suggests a need for psychiatric assessment.

We used a visual analogue scale (VAS) to measure pain.¹⁹ VAS, a self-assessment instrument, consists of a 10-cm ruler, without numbers, on which the only indications were "absence of pain" at the left end (corresponding to 0 cm) and "intolerable pain" at the right end (corresponding to 10 cm). The participants were instructed to make a mark on the straight line that corresponded to their own assessment of the intensity of

their pain. The higher the value was, the higher the intensity of the pain would be. Socio demographic data were retrieved from the patients' medical files.

Statistical Analysis.

The chi-square test (or Fisher exact test) was used to assess the associations between the study variables. Correlation analyses were calculated using Spearman's rank test. For the comparison between the HADS scores and the length of time from diagnosis until the first consultation within the palliative care service, the time (in months) was categorised into three groups delimited by the 25th and 75th percentiles, i.e., < 25th vs. between the 25th and 75th percentiles vs. > 75th percentile. We used the significance level of $p < 0.05$. For our statistical analyses, we used SPSS version 18.

Results.

Clinical and socio demographic characteristics.

There was a slight preponderance of women (53.5%) in the study sample. Among this sample, 128 patients (59.5%) were ≤ 60 years of age, and the mean age was 57 years (standard deviation [SD] = 13). With regard to educational level, 25 patients (11.6%) were illiterate, 74 (34.4%) had not completed elementary education, 113 (52.6%) had at least completed elementary education and three (1.4%) had an unspecified schooling level.

The patients had been diagnosed between 1989 and 2009, and the median length of time (with interquartile range, 25th - 75th percentiles) between the cancer diagnosis and the first consultation in the Palliative Care Unit was 16 months (6-30 months).

The primary tumour sites were as follows: head and neck ($n = 37$, 17.2%), urinary tract ($n = 33$, 15.3%), lower digestive system ($n = 31$, 14.4%), breast ($n = 31$, 14.4%), upper digestive system ($n = 27$, 12.6%), gynaecological tract ($n = 22$, 10.2%), unknown primary ($n = 16$, 7.4%), lung ($n = 7$, 3.3%), bone ($n = 6$, 2.8%) and neurological ($n = 5$, 2.3%).

Pain, anxiety and depression indicators.

The mean (SD) pain score was 0.89 (1.8). Among the participants, 70 (32.6%) presented some degree of pain, and 15 (7%) presented a pain level of ≥ 4 on the VAS.

The mean (SD) HADS-A and HADS-D were 7 (4.1) and 7.3 (4.6), respectively. Using a cut-off point of ≥ 8 , 80 patients (37.2%) had anxiety indicators, and 84 patients (39.1%) had depression indicators. We observed that 48 (22.4%) and 60 (27.9%) of the patients already had moderate or severe levels of anxiety and depression (HADS scores of ≥ 11), respectively, thus suggesting the need for psychiatric assessment.

A strong association was observed between the presence of anxiety and depression ($p < 0.0001$); 54 patients (64%) presented anxiety and depression indicators. Additionally, there was a highly significant correlation between anxiety and depression levels ($r = 0.6$, $p < 0.0001$).

There were no significant associations between the presence of pain and anxiety ($p = 0.639$), between the presence of pain and depression ($p = 0.278$) or between the length of treatment before palliative care and the presence of anxiety ($p = 0.760$) and depression ($p = 0.427$) (Table 1). Otherwise, a weakly significant correlation was observed between depression and pain ($r = 0.15$, $p = 0.02$) but not between anxiety and pain ($r = 0.11$, $p = 0.09$).

There was a greater prevalence of HADS-A scores of ≥ 8 among breast cancer patients than among the remaining patients (18 of 31 patients, 58% vs. 70 of 184 patients, 38%, respectively; $p = 0.036$). There were no differences in anxiety and depression rates regarding the other primary tumour sites (data not shown).

Patients aged < 60 years reported higher levels of anxiety than patients older than 60 years (58 of 121 patients, 48% vs. 30 of 94 patients, 32%, respectively; $p = 0.018$) (Table 1). There was no difference in depression rates regarding age. Women reported higher rates of anxiety than men (59 of 115 patients, 51% vs. 29 of 100 patients, 29%, respectively; $p = 0.001$). The women also presented higher depression scores (66 of 115 patients, 57% vs. 34 of 100 male patients, 34%; $p = 0.001$) (Table 1).

Interestingly, patients with low educational levels reported lower rates of anxiety than did patients with higher educational levels (32 of 99 patients, 32% vs. 55 of 113 patients, 49%, respectively; $p = 0.016$). Furthermore, patients with low educational levels also presented lower depression rates (38 of 99 patients, 38% vs. 59 of 113 patients with higher educational levels, 52%; $p = 0.04$) (Table 1)

Table 1. Anxiety and depression levels according to the Hospital Anxiety and Depression Scale and their associations with clinical variables

Variable	HADS-A n (%)		p^*	HADS-D n (%)		p^*
	< 8	≥ 8		< 8	≥ 8	
Pain score (VAS)			0.639			0.278
0 to 3	119 (59.5)	81 (40.)		109 (54.5)	91 (45.5)	
4 to 10	8 (53)	7 (47)		6 (40)	9 (60)	
Age (years)			0.018			0.453
< 60	63 (52)	58 (48)		62 (51)	59 (49)	

≥ 60	64 (68)	30 (32)	53 (56)	41 (44)
<i>Gender</i>		0.001		0.001
Male	71 (71)	29 (29)	66 (66)	34 (34)
Female	56 (49)	59 (51)	49 (43)	66 (57)
<i>Educational level</i>		0.016		0.044
Lower ^a	67 (68)	32 (32)	61 (62)	38 (38)
Higher ^b	58 (51)	55 (49)	54 (48)	59 (52)
<i>Time since diagnosis (months)</i>		0.760		0.427
≤ 6	31 (58.5)	22 (41.5)	26 (49)	27 (51)
6 - 30	65 (61)	41 (39)	55 (52)	51 (48)
≥ 30	31 (55)	25 (45)	34 (61)	22 (39)

Legend: HADS-A: Hospital Anxiety and Depression Scale-anxiety, HADS-D: Hospital Anxiety and Depression Scale-depression; VAS: visual analogue scale. ^ailliterate or incomplete elementary education; ^bat least completed elementary education; *chi-square test. Significant results appear in bold.

Discussion.

In the present study, the patients who were recently admitted to the unit were profiled, so their immediate needs for psychosocial attention could be better understood. We perceived that the patients with psychological disorders did not necessarily present pain. These patients arrived at the PCOU already presenting anxiety and depression. This finding made us realise that there other factors besides the concept of palliative care are associated with these disorders.

Mental disorders should be considered as an important source of distress for patients undergoing palliative care and their family members.¹¹ Among cancer patients, anxiety and depression are frequent responses at the time of diagnosis and throughout the different treatment stages.²⁰⁻²³

Several short instruments have been developed to screen for emotional distress.²⁴ The HADS is one of the recommended screening tools and is probably the most studied in the palliative care cancer setting.^{25, 26} The prevalence of anxiety and depression among cancer patients is discrepant between different studies, depending primarily on the gold standard criteria used.^{25, 27, 28} Our findings are similar to a previous study²⁹ that used the HADS in palliative care, i.e., approximately 35% and 40

- 45% of patients had anxiety and depression, respectively. In the present study, all positive cases were referred for specific attention.

Comparing the anxiety and depression findings from HADS, we observed that among the patients who presented depression, 64.3% also presented anxiety. This observation shows the importance of identifying the various signs and symptoms of anxiety and depression because they can occur concomitantly in many patients.^{23, 30, 31}

Although the correlation analysis showed that there was a significant association between pain and the depression scores, this association was weak and probably not clinically important. In this sense, our findings do not corroborate the proposition that higher pain levels are associated with greater anxious responses and more intense depressed moods. According to several authors, psychological disorders such as mood disorders and anxiety, seem to occur predominantly among patients who suffer from chronic pain.³²

Chronic pain is directly related to depression, and anxiety is part of a complex reaction of fear and lack of knowledge of the diagnosis.^{33, 34} Chen *et al.*³⁵ observed a greater prevalence of anxiety and, particularly, depression among patients who presented pain compared with cancer patients who were pain-free. However, the results from the present study partially contradict the reports in the literature. We found that 80 patients (37.2%) presented anxiety disorders and the 84 patients (39.1%) had depression, independent of any associated pain factor. Similarly, a Chinese study of 70 patients with advanced cancer and complaints of pain found that depression did not correlate with the severity of the pain.³⁶

Women represent a significant majority among cancer patients who present anxiety and depression.^{22, 36-38} The findings from the present study are in accordance with the literature regarding the association between female gender and diagnoses of both anxiety and depression. Moreover, younger patients are more prone to be identified with anxiety and depression,^{38, 39} perhaps because with increasing age, people acquire experience and resilience skills.⁴⁰ Young patients experience greater difficulty in adjusting to and accepting the losses associated with cancer than do elderly patients.⁴¹ We observed that younger patients were more anxious than older patients, but there was no association between depression and age.

The early referral of advanced cancer patients for palliative care is the most recommended approach today.⁴² There is strong evidence that advanced cancer patients present lower rates of anxiety and depression when treated by a palliative care team early during the course of their disease.⁴³ However, early referral may also be indicative that these patients had not received any proposals for therapeutic treatment before their referral to the Palliative Care Unit and that they were at greater risk for developing anxiety disorders. Our data do not justify the hypothesis that the length of time from diagnosis until palliative care referral might be an important issue because no associations were identified regarding psychological disorders.

Several types of cancer may be associated with a high prevalence of depression, such as cancer of the oropharynx, pancreas, breast and lung.²² Among the populations studied, there were no significant associations between tumour site and depression. No primary tumour site was definitively associated with occurrences of depression. In contrast, breast cancer patients were more frequently anxious in our study. Considering the tendency among women to present anxiety, the association between anxiety and breast cancer is likely due to bias.

In the present study, we observed that patients with low educational levels reported lower anxiety and depression rates. We hypothesise that those patients had inadequate knowledge about their disease and prognosis and that this lack of information could diminish their distress. Barretos Cancer Hospital is a public institution that primarily receives underserved patients from all Brazilian states. Most of the patients are poor and have a low educational level. To the best of our knowledge, this study is the first report that an association between higher levels of psychological symptoms and low educational level has not been shown.

The present study has some limitations. The first limitation is that the low rates of pain found in our sample make it challenging to evaluate the interference of pain in psychological disorder scores. The second major limitation is the lack of outcome data. Because this was a cross-sectional study, we do not know how the depression and anxiety scores and their response to treatment (i.e., the outcome) evolved over time.

Assessing depression among patients with advanced cancer may be difficult for both healthcare professionals and the patients' caregivers. In addition to atypical symptomatic manifestations, depressed mood may be assessed as a normal reaction to the circumstances that patients undergoing palliative care experience.^{14, 44, 45}

In the present study, we found that cancer patients present a high prevalence of anxiety and depression during their first consultation in the PCOU. We are in agreement with others²⁶ that the early identification of psychological disorders using HADS seems to be a feasible strategy for use in clinical practice. Additionally, our findings suggest that there is a need for rigorous psychological evaluation of women, younger patients and patients with higher educational levels because these patients show a greater propensity to anxiety and depression during the transition to palliative care compared with the other patients.

Competing interests.

The authors declare that they have no competing interests.

Authors' contributions.

DBS assisted in the organisation and administration of the study, data gathering, data analysis and drafting of the text. AL-F provided final approval of the revised manuscript. NIV, CEP and BSRP were involved in drafting and revising the

manuscript for important intellectual content. RSJ and CEP collaborated in the statistical analysis and provided final approval of the revised manuscript. All of the authors received the final manuscript and reviewed it.

Acknowledgments.

We are grateful to Barretos Cancer Hospital, Pio XII Foundation. We thank the team members in the Department of Palliative Care, who always dedicate themselves to improving patients' and caregivers' quality of life. We thank Fabiana Faria Rezende of the Researchers' Support Group (NAP), the Quality Department and Dr. Maria Cristina O.S. Miyazaki and Dr. Neide A. Micelli Domingos at the Psychology and Health Laboratory (FAMERP).

References.

- 1.Davies B; Reimer JC; Martens N. (1990). *Families in supportive care--Part I: The transition of fading away: the nature of the transition.* J Palliat Care. 6(3): 12-20.
- 2.Larkin PJ; Dierckx de Casterle B, Schotsmans P. (2007). *Transition towards end of life in palliative care: an exploration of its meaning for advanced cancer patients in Europe.* J Palliat Care. 23(2): 69-79.
- 3.Duggleby W, Berry P. (2005). *Transitions and shifting goals of care for palliative patients and their families.* Clin J Oncol Nurs. 9(4): 425-8.
- 4.Bertero C; Vanhanen M; Appelin G. (2008). *Receiving a diagnosis of inoperable lung cancer: patients' perspectives of how it affects their life situation and quality of life.* Acta Oncol. 47(5): 862-9.
- 5.Mystakidou K; Tsilika E; Parpa E; Galanos A; Vlahos L. (2008). *Post-traumatic growth in advanced cancer patients receiving palliative care.* Br J Health Psychol. 13(Pt 4): 633-46.
- 6.Duggleby W; Wright K; Williams A; Degner L; Cammer A; Holtslander L. (2007). *Developing a living with hope program for caregivers of family members with advanced cancer.* J Palliat Care. 23(1): 24-31.
- 7.Radbruch L; Nauck f; Ostgathe C; Elsner F; Bausewein C; Fuchs M, et al. (2003). *What are the problems in palliative care? Results from a representative survey.* Support Care Cancer. 11(7): 442-51.
- 8.Morita T; Akechi T, Ikenaga M; Kizawa Y; Kohara H; Mukaiyama T, et al. (2005). *Late referrals to specialized palliative care service in Japan.* J Clin Oncol. 23(12): 2637-44.

9. Thompson GN; Chochinov HM; Wilson KG; Mcpherson CJ; Chary S; O'Shea FM, et al. (2009). *Prognostic acceptance and the well-being of patients receiving palliative care for cancer*. J Clin Oncol. 27(34): 5757-62.
10. Kolva E; Rosenfeld B, Pessin H; Breitbart W; Brescia R. (2011). *Anxiety in terminally ill cancer patients*. J Pain Symptom Manage. 42(5): 691-701.
11. Arrieta O; Ângulo LP; Nunez-Valência C; Dorantes-Gallareta Y; Macedo EO; Martinez-Lopez D; et al. (2013). *Association of Depression and Anxiety on Quality of Life, Treatment Adherence, and Prognosis in Patients with Advanced Non-small Cell Lung Cancer*. Ann Surg Oncol. 20(6): 1941-8.
12. Who. (2002). *National Cancer Control Programmes: Policies and Managerial Guidelines*. 2nd ed ed. Geneva, Switzerland: World Health Organization.
13. Meyer ha; Sinnott C; Seed PT. (2003). *Depressive symptoms in advanced cancer. Part 1. Assessing depression: the Mood Evaluation Questionnaire*. Palliat Med. 17(7): 596-603.
14. Lo C; Calzavara A; Kurdyak P; Barbera L; Shepherd F; Zimmermann, C. et al. (2013). *Depression and use of health care services in patients with advanced cancer*. Can Fam Physician. 59(3): e168-74.
15. Paiva CE; Faria CB; Nascimento MS; dos Santos R; Scapulatempo HH; Costa E, et al. (2012). *Effectiveness of a palliative care outpatient programme in improving cancer-related symptoms among ambulatory Brazilian patients*. Eur J Cancer Care (Engl). 21(1): 124-30.
6. Botega NJ; Pondé MP; Medeiros P; Lima MG; Guerreiro CAM. (1998). *Validação da escala hospitalar de ansiedade e depressão (HAD) em pacientes epiléticos ambulatoriais*. J Bras Psiquiatria. 47: 285-9.
17. Botega NJ; Bio Mr; Zomignani ma; Garcia C. Jr.; Pereira WA. (1995). *[Mood disorders among inpatients in ambulatory and validation of the anxiety and depression scale HAD]*. Rev Saude Pública. 29(5): 355-63.
18. Kugaya A; Akechi T; Okuyama T; Okamura H; Uchitomi y. (1998). *Screening for psychological distress in Japanese cancer patients*. Jpn J Clin Oncol. 28(5): 333-8.
19. Collins SL; Moore RA; Mcquay HJ. (1997). *The visual analogue pain intensity scale: what is moderate pain in millimetres?* Pain. 72(1-2): 95-7.
20. Apro M; Cull A. (1999). *Depression in breast cancer patients: the need for treatment*. Ann Oncol. 10(6): 627-36.

21. Sivesind D; Baile WF. (2001). *The psychologic distress in patients with cancer.* Nurs Clin North Am. 36(4): 809-25, viii.
22. Massie MJ. (2004). *Prevalence of depression in patients with cancer.* J Natl Cancer Inst Monogr. (32): 57-71.
23. Brenne E; Loge JH; Kaasa S; Heitzer E; Knudsen AK; Wasteson E. (2011). *Depressed patients with incurable cancer: Which depressive symptoms do they experience?* Palliat Support Care. 1-11.
24. Mitchell; AJ. (2010). *Short screening tools for cancer-related distress: a review and diagnostic validity meta-analysis.* J Natl Compr Canc Netw. 8(4): 487-94.
25. Wasteson E; Brenne E; HIGGINSON IJ; Hotopf m; Lloyd-Williams M; Kaasa S; et al. (2009). *Depression assessment and classification in palliative cancer patients: a systematic literature review.* Palliat Med 23(8): 739-53.
26. Mitchell AJ; Meader N; Symonds P. (2010). *Diagnostic validity of the Hospital Anxiety and Depression Scale (HADS) in cancer and palliative settings: a meta-analysis.* J Affect Disord. 126(3): 335-48.
27. Qiu J; Yang M; Chen W; Gao X; Liu S; SHI S; et al. (2012). *Prevalence and correlates of major depressive disorder in breast cancer survivors in Shanghai, China.* Psychooncology. 2012; 21(12): 1331-7.
28. Sartori SB; Landgraf R; SIngewald N.(2011). *The clinical implications of mouse models of enhanced anxiety.* Future Neurol.6(4): 531-71.
29. O' Connor M; White K; Kristjanson LJ; Cousins K; Wilkes L. (2010). *The prevalence of anxiety and depression in palliative care patients with cancer in Western Australia and New South Wales.* Med J Aust. 193(5 Suppl): S44-7.
30. Keogh E; Mccracken LM; Eccleston C. (2005). *Do men and women differ in their response to interdisciplinary chronic pain management?* Pain. 114(1-2): 37-46.
31. Rhondali W; Perceau E; Berthiller J; Saltel P; Trillet-Lenoir V; Tredan O; et al. (2012). *Frequency of depression among oncology outpatients and association with other symptoms.* Support Care Cancer. 20(11): 2795-802.
32. Tavoli A; Montazeri A; Roshan R; Tavoli Z; Melyani M. (2008). *Depression and quality of life in cancer patients with and without pain: the role of pain beliefs.* BMC Cancer. 8: 177.

33. Averill PM; Novy DM; Nelson DV; Berry LA. *Correlates of depression in chronic pain patients: a comprehensive examination*. Pain. (1996) 65(1): 93-100.
34. Gagliese L; Jovellanos M; Zimmermann C; Shobbrook C; WARR D; Rodin G. (2009). *Age-related patterns in adaptation to cancer pain: a mixed-method study*. Pain Med. 10(6): 1050-61.
35. Chen ML; Chang HK; Yeh CH. (2000). *Anxiety and depression in taiwanese cancer patients with and without pain*. J Adv Nurs. 32(4): 944-51.
36. Kai-hoi Sze F; Wong e. (2000). LO R, Woo J. *Do pain and disability differ in depressed cancer patients?* Palliat Med. 14(1): 11-7.
37. Stark D; Kiely M; Smith A; Velikova G; House A; Selby p. (2002). *Anxiety disorders in cancer patients: their nature, associations, and relation to quality of life*. J Clin Oncol. 20(14): 3137-48.
38. Strong V; Waters R; Hibberd C; RUSH R; Cargill A; Storey d; et al. (2007). *Emotional distress in cancer patients: the Edinburgh Cancer Centre symptom study*. Br J Cancer. 96(6): 868-74.
39. Brintzenhofe-Szoc KM; Levin TT; Li Y; Kissane DW; Zabora JR. (2009). *Mixed anxiety/depression symptoms in a large cancer cohort: prevalence by cancer type*. Psychosomatics. 50(4): 383-91.
40. Holland JC; Breitbart WS; Jacobsen PB; Lederberg MS; Loscalzo MJ; Mccorkle R. (2010). *Editors Psycho-oncology*. New York: Oxford University Press.
41. Pandey M; Sarita GP; Devi N; Thomas BC; Hussain BM; Krishnan R. (2006). *Distress, anxiety, and depression in cancer patients undergoing chemotherapy*. World J Surg Oncol. 4: 68.
42. Smith TJ; Temin S; Alesi ER; Abernethy AP; Balboni TA; Basch EM, et al. (2012). *American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care*. J Clin Oncol. 30(8): 880-7.
43. Temel JS; Greer JA; Muzikansky A; Gallagher ER; Admane S; Jackson VA, et al. (2010). *Early palliative care for patients with metastatic non-small-cell lung cancer*. N Engl J Med. 363(8): 733-42.
44. Mcpherson CJ; Addington-HALL JM. (2004). *Evaluating palliative care: bereaved family members' evaluations of patients' pain, anxiety and depression*. J Pain Symptom Manage. 28(2): 104-14.