Depression and anxiety in patients with hematological malignancies, prevalence, and associated factors

Khadega A. Abuelgasim, MBBS, MD, *Gasmelseed Y. Ahmed,* MBBS, MPH, *Jamilah A. Alqahtani,* BSN, *Aseel M. Alayed,* BSN, *Ahmed S. Alaskar,* MD, FRCP, *Mansoor A. Malik,* MBBS, MD.

ABSTRACT

الأهداف: دراسة حدوث الاكتئاب والقلق والعوامل المؤثرة على المرضى المصابون بسرطانات الدم.

الطريقة: أجريت دراسة مستعرضة على جميع المرضى الذين يعانون من سرطانات الدم سواء كانوا منومين في جناح أمراض الدم أو حضروا لعيادة أمراض الدم في مدينة الملك عبدالعزيز الطبية الرياض خلال الفترة من مارس 2014 إلى يونيو2015م. تم استبعاد المرضى الذين يعانون من اضطراب عقلي. أجريت مقابلات فردية مع جميع المشاركين. وقد استخدم فيها استبيان مطور داخليا بعد التحقق من صحة الاستبيان، وكذلك استخدمنا استبيان صحة المريض –9 واستبيان اضطراب القلق العام–7.

النتائج: من بين 211 مشارك حدث ظهر الاكتئاب في 98 (46.5%) والقلق في 47 (22.3%). يعاني 38 (18.1%) من المشاركين من القلق والاكتئاب في وقت واحد. وجدنا ارتباط بين وجود حالات مرضية متعددة وتوتر الجو الأسري ووجود القلق والاكتئاب. في حين أنه لم تظهر علاقة بين التدخين، والدخل الشهري أو إذا كان المريض تحت العلاج وبين حدوث الاكتئاب أو القلق.

الخاتمة: ينتشر الاكتئاب والقلق بشكل كبير بين مرضى سرطانات الدم الذين يتلقون العلاج في مدينة الملك عبدالعزيز الطبية في الرياض. يجب على مقدمي الرعاية الصحية الذين يعتنون بهؤلاء المرضى أن يسارعوا باكتشاف وعلاج الاضرابات النفسية كالقلق والاكتئاب مما قد يودي إلى تحسن مرضهم و يعزز صحتهم النفسية.

Objectives: To study the prevalence and associated factors of depression and anxiety in hematological cancers (HC) patients.

Methods: We conducted a cross-sectional survey in all HC patients at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia between March 2014 and June 2015. We excluded patients with depression, or generalized anxiety disorder. We conducted a structured face to face interview using an internally developed and validated questionnaire (Patient Health Questionnaire-9 and Generalized Anxiety Disorder-7 patient's questionnaire with all participants).

Results: Among 211 participants, depression was detected in 98 (46.5%) and anxiety was detected in 47 (22.3%). Thirty-eight (18.1%) had concurrent anxiety and depression. Multiple co-morbidities and tense home atmosphere were predictive for anxiety and depression. We found no association between gender, smoking, income, or being on active therapy and depression or anxiety.

Conclusions: Depression and anxiety are highly prevalent in HC patients in KAMC. Health care providers should screen HC cancers for depression and anxiety; as early intervention possibly improve their disease outcome and will likely enhance their psychological wellbeing.

The emotional well-being of cancer patients is terribly affected by depression.[1] Adults cancer patients have very high prevalence of both anxiety and depression.[2] The prevalence of depression in cancer patients is more than in stroke patients, and patients with heart disease.[3] Depressed cancer patients suffer, they participate less in medical care, and they require longer hospitalization periods compared to those

who are not depressed.[4] A significant percentage of patients with hematological cancers (HC) receives high dose chemotherapy and requires long periods of hospitalization. Hematological cancers patients who undergo hematopoietic stem cell transplant are even at a higher risk for depression and anxiety.[5] Non-medical factors such as personal traits, lower level of education, lower socioeconomic status, family conflicts and lack of family support are contributory factors to patient's emotional disturbance. Derogatis et al[6] first attempted to study the prevalence of psychiatric disorders in cancer patients using DSM-III in 1983. Among 215 cancer patients, 47% had evidence of at least one psychiatric disorder. Sixty- eight percent had adjustment disorder with depressed, or anxious mood. Thirteen percent were qualified for major depression.[6] Both improvement in survival and increased incidence of most cancer types increase the prevalence of depression and anxiety in such patients' population. It is important to identify psychiatric disorders in cancer patients; depression and anxiety are of particular importance as they generally lead to poor adherence to treatment, and therefore worse disease outcome.[7-9] Health care providers play a major role in screening, providing first line treatment, and referring patients for further evaluation and treatment for these conditions. Unfortunately, they are often over worked, busy and mostly not sufficiently trained to perform a proper psychological assessment. As a result, these mental disorders may go undetected and may lead to poor patients' outcome, longer recovery time and greater use of health care resources.[10] Data from the Middle East[2,11-13] pertinent was scanty, and studies were carried out mainly in patients with solid tumors. Given the different epidemiology of different types of cancers and the unique ethnic makeover and unique culture of the region, we elected to study the prevalence and associated factors of depression and anxiety in HC patients attending the King Abdulaziz Medical City (KAMC) Oncology Center, Riyadh, Saudi Arabia. We believe it is important to bring these important issues to the attention of health care providers caring for those patients.

Methods. We conducted our literature review by conducting multiple Pub Med search using the terms: depression, anxiety, hematological cancer, Middle East,

and Saudi Arabia. Our study was a cross-sectional survey and was conducted according to the principles of Helsinki.

The sample for categorical data formula was applied to calculate the optimal number of participants for this study. An effect size of depression in 17.8% and anxiety in 16.8% within cancer patients from a similar study was applied to obtain a sample capable of detecting statistical results with 95% levels of confidence and only 0.05 margin of error.[8]

After obtaining the approval from the King Abdullah International Medical Research Center Institutional Review Board, all patients ≥ 14 years with confirmed HC admitted to the hematology ward, or attended hematology clinic at KAMC, Riyadh were approached between March 2014 and June 2015, and were asked to participate in the study. Hematological cancers include acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM) were illegible. We included patients who are actively receiving therapy as well as those who have completed their therapy. Patients who are known to have depression, or generalized anxiety disorder were excluded. After obtaining the informed consent from the patient, or the patient's guardian in patients younger than age 18, a structured face to face clinical interview was conducted by one of our trained research assistants.

An internally developed and validated questionnaire was used to collect demographic, social, and financial data. Participants were also asked to self-report the type of HC they have and whether, or not they are actively receiving therapy for their cancer.

The Diagnostic and Statistical Manual of Mental Disorders-Third Edition (DSM-III), generally used to screen non-psychiatric patients for the presence of different psychiatric disorders, has many tools; among them are Generalized Anxiety Disorder-7 (GAD-7) and Patient Health Questionaire-9 (PHQ-9).[14] The GAD-7 standardized questionnaire, translated to Arabic language was used in our study to screen participants for anxiety.[15-18] It is a 7-item self-report scale with a score ranging from 0-3 for each question, providing 0-21 severity score. A score of 5-9 is a cut-off point to identify cases of mild generalized anxiety disorder, a score of 10 is a cut-off point for identifying cases with moderate GAD, while a score of 15 is indicative of severe GAD. We only reported moderate and severe GAD.

The PHQ-9 standardized questionnaire designed for use in non-psychiatric clinical settings and in research,

translated into Arabic language was used to screen participants for depression.[15-17] The PHQ-9 includes 9 items designed to screen for feeling worthless, or guilty, anhedonia, trouble focusing, low mood, sleep related troubles, fatigue, appetite disturbances, feeling slow or irritable and suicidal ideation. It has a 0-27 severity score. A cut-off point of 10 was used to identify depression in our study. After completion of data collection and accuracy check, data was transferred into an excel sheet and subsequently reviewed, and verified for consistency.

The Statistical Analysis Software SAS version 9.2. (SAS Institute Inc., Cary, NC, USA) was applied for data analysis and a p-value ≤0.05 was accepted as significant. Categorical variables were presented as counts and percentages, while continuous variables were reported as median with interquartile. Univariate analysis test was applied to study the association between mental health disorders and participants' characteristics.

Results. A total of 211 participants were enrolled in the study. **Table 1** shows the demographic and clinical characteristics. The median age of participants was 46 years (27-64). Using a cut-off score of 10, which represent moderate anxiety and depression in GAD-7 and PHQ-9 assessment scales, depression was detected in 98 (46.5%), and anxiety in 47 (22.3%) participants. Combined anxiety and depression were found in 38 (18.1%). Univariate analysis of associated factors anxiety and depression is presented in **Tables 2 & 3**.

Discussion. Hematological cancer patients are more likely to require intensive therapies, and at times prolonged hospitalization, compared with patients with solid tumors. This can have significant impact on their emotional wellbeing and can increase their susceptibility to physical and mental stress, and perhaps affect their disease outcome.[22] The prevalence of anxiety in HC patients were reported to be between 20% and 37%.[23] Our study showed that 22.3% of Saudi HC suffers from anxiety. Such highly significant percentage requires active and continuous screening in order to early diagnose, and refer patients to receive the appropriate therapy. Depression has been linked to altered immunity and lower survival rates in non-cancer patients.[24-26] Altered immunity can adversely affect cancer patients; this is of particular importance in HC patients receiving high dose chemotherapy. Effective treatment of depression in cancer patients has been linked to improvement in patients' adjustment to stress and decrement in the magnitude of their symptoms leading to better disease outcome at a lower cost.[27] The prevalence of depression in our cohort was 46.5%; a bit on the higher

side compared with the international reported rates of 17-51%. This is particularly concerning, as it has been shown that approximately 40% of patients with depression and cancer have suicidal thoughts on direct questioning; however, most people with depression are neither detected, nor treated.[28] It is not clear to us why depression is highly prevalent in our cohort. Coexisting anxiety and depression are found in 12-15% of HC patients and may result in more suffering and possibly worse outcome.[23,29,30] In our cohort, this prevalence was

Table 1 - Participants' characteristics of 211 enrolled in the study.

Characteristics	n (%)
Nationality	
Saudi	204 (96.7)
Others	7 (3.3)
Gender	
Male	121 (57.6)
Female	90 (42.7)
Education	
College and postgraduate	48 (22.8)
Elementary, middle and high school	110 (52.1)
Not educated	53 (25.1)
Employment	
Employed	70 (33.2)
Unemployed	141 (66.8)
Income	
Low income (≤10000 SR/month)	101 (47.9)
High income (>10000 SR/month)	110 (52.1)
Smoking	
Smoker	47 (22.3)
Non smoker	164 (77.7)
Marital status	
Married	134 (63.5)
Single	53 (25.1)
Widowed	21 (10.0)
Divorced	3 (1.4)
Family support	
Yes	96 (45.5)
No	115 (54.5)
Home atmosphere	
Relaxed	109 (51.7)
Tense	102 (48.3)
Comorbidities	
Comorbidity (both single and multiple)	115 (54.5)
No comorbidity	96 (45.5)
Type of cancer	
NHL	65 (30.8)
HL	41 (19.4)
ALL	41 (19.4)
AML	24 (11.4)
CLL	21 (10.0)
CML	7 (3.3)
MM	12 (5.7)
Actively receiving treatment	
Yes	161 (76.3)
No	50 (23.7)

NHL - non-hodgkin's lymphoma, HL - hodgkin's lymphoma, ALL - acute lymphatic leukemia, AML - acute myeloid leukemia, CLL - chronic lymphocytic leukemia, CML - chronic myeloid leukemia, MM - multiple myeloma, SR - Saudi Riyals

Table 2 - Univariate analysis of 211 participants with anxiety enrolled in the study.

Variable	Anxiety n (%)	No anxiety n (%)	P-value
Gender			0.1861
Female	24 (51.1)	66 (40.2)	
Male	23 (49.0)	98 (59.8)	
Education			0.5539
College or postgraduate	12 (25.5)	36 (22.0)	
Elementary, middle and high school	26 (55.3)	84 (51.2)	
	9 (19.2)	44 (26.8)	
Not educated			
Employment			0.5758
Employed	14 (29.8)	56 (34.2)	
Unemployed	33 (70.2)	108 (65.9)	
Marital status			0.3276
Married	27 (57.5)	107 (65.2)	
Unmarried	20 (42.6)	57 (34.8)	
Support			0.8378
Yes	22 (46.8)	74 (45.1)	
No	25 (53.2)	90 (54.9)	
Home atmosphere			0.0159
Relaxed	17 (36.2)	92 (56.1)	
Tense	30 (63.8)	72 (43.9)	
Income			0.6188
High (≤10000 SR/month)	23 (49.0)	87 (53.1)	
Low(>10000 SR/month)	24 (51.1)	77 (47.0)	
Comorbidities			0.0001
Comorbidity (one or more)	39 (83.0)	76 (46.4)	
No comorbidity	8 (17.0)	88 (53.7)	
Actively receiving therapy			0.4056
Yes	38 (80.9)	123 (75.0)	
No	9 (19.2)	41 (25.0)	

Table 3 - Univariate analysis of 211 participants with depression enrolled in the study.

Variable	Depression n (%)	No depression n (%)	P-value
Gender			0.1468
Female	47 (48.0)	43 (38.1)	
Male	51 (52.0)	70 (62.0)	
Education			0.0145
College or postgraduate	25 (25.5)	23 (20.4)	
Elementary, middle and high school	41 (41.8)	69 (61.1)	
	32 (32.7)	21 (18.6)	
Not educated			
Employment			0.8862
Employed	33 (33.8)	37 (32.7)	
Unemployed	65 (66.3)	76 (67.3)	
Marital status			0.5213
Married	60 (61.2)	74 (65.5)	
Unmarried	38 (38.8)	39 (34.5)	
Family support			0.0678
Yes	38 (38.8)	58 (51.3)	
No	60 (61.2)	55 (48.7)	
Home atmosphere			0.0033
Relaxed	40 (40.8)	69 (61.1)	
Tense	58 (59.2)	44 (38.9)	
Income			0.7633
High(≤10000 SR/month)	50 (51.0)	60 (53.1)	
Low(>10000 SR/month)	48 (49.0)	53 (46.9)	
Comorbidities			0.0001
Comorbidity (one or more)	73 (74.5)	42 (37.2)	
No comorbidity	25 (25.5)	71 (62.8)	
Receiving treatment			0.2955
Yes	78 (79.6)	83 (73.5)	
No	20 (20.4)	30 (26.6)	

even higher at 18.1%. Al Zaben et al[13] recently reported association of low education, low socio-economic status and young age, and the presence of anxiety in Saudi breast cancer patients. Several other demographic, clinical and socioeconomic factors were linked to higher chance of developing anxiety, or depression in cancer patients. Among these factors are: gender, marital status, cancer type and stage, time since diagnosis, type of therapy received, being on active therapy, history of smoking, home atmosphere and family support.[1,11,13,23,30-32] While other studies showed no correlation between some of these factors with depression, or anxiety.[2,23]

In our study, tense home atmosphere and the presence of co-morbidities were significantly associated with higher prevalence of both anxiety and depression, regardless of other factors. Depression and anxiety are prevalent in cancer free patients with medical problems such as diabetes, stroke, and heart disease.[3,33] The effect of co-morbidities can be explained by the fact that cancer patients with co-morbidities perceive themselves as sick unlike those who previously healthy. In our study, lack of education was not found to be associated with anxiety contradicting what Al-Zaben et al[13] found in

Western Saudi Arabia breast cancer patients, but it was rather associated with depression. That can be explained by regional differences as our facility is located in the Central region. We found a trend of less anxiety among married participants; however the difference from unmarried was not statistically significant.

Although smoking was not very prevalent in our cohort, we found no association between smoking history and depression or anxiety. One would expect that patients receiving active therapy experience more psychological stress compared with those with completed their therapy; this was not proven in our cohort. One explanation could be that cancer patients always feel threatened and expect disease relapse at anytime, therefore, the stress continues throughout their lives regardless of their disease status.

Study limitations. First, this is a single institution's study; therefore, our results may not be representing all Saudi HC patients. Second: one quarter of our participants was illiterate, although not representative of the Saudi population, that could have affected the comprehension of the questionnaires presented to those participants.

The prevalence of anxiety in this patients' population seems to be in the same range compared with what is reported in the regional and international studies. Relatively higher prevalence of depression among this patients' population is of a particular concern. Health care providers ought to screen HC patients for depression and anxiety since early referral and intervention may not only improve their psychological wellbeing, but also their disease outcome.

References

1. Massie MJ. Prevalence of depression in patients with cancer. *J Nat Cancer Inst Monogr* 2004; 32: 57-71.
2. Jadoon NA, Munir W, Shahzad M, Choudhry ZS. Assessment of depression and anxiety in adult cancer outpatients: a cross-sectional study. *BMC Cancer* 2010; 10: 594.
3. Harter M, Baumeister H, Reuter K, Jacobi F, Hofer M, Bengel J et al. Increased 12-month prevalence rates of mental disorders in patients with chronic somatic diseases. *Psychother Psychosom* 2007; 76: 354-360.
4. Honda K, Goodwin RD. Cancer and mental disorders in a national community sample: findings from the national comorbidity survey. *Psychother Psychosom* 2004; 73: 235-242.
5. Mosher CE, Redd WH, Rini CM, Burkhalter JE, Du Hamel KN. Physical, psychological and social sequelae following hematopoietic stem cell transplantation: a review of the literature. *Psychooncology* 2009; 18: 113-127.
6. Derogatis LR, Morrow GR, Fetting J, Penman D, Piasetsky S, Schmale AM et al. The prevalence of psychiatric disorders among cancer patients. *JAMA* 1983; 249: 751-757.
7. Colon EA, Callies AL, Popkin MK, McGlave PB. Depressed mood and other variables related to bone marrow transplantation survival in acute leukemia. *Psychomatics* 1991; 32: 420-425.
8. Watson M, Haviland JS, Greer S, Davidson J, Bliss JM. Influence of psychological response on survival in breast cancer: a population-based cohort study. *Lancet* 1999; 354: 1331-1336.
9. Pamuk GE, Harmandar F, Ermantas N, Harmandar O, Turgut B, Demir M et al. EORTC QLQ-C30 assessment in Turkish patients with hematological malignancies Association with anxiety and depression. *Ann Hematol* 2008; 4: 305-310.
10. Powe BD, Finnie R. Cancer fatalism: the state of the science. *Cancer Nurs* 2003; 26: 454-465.
11. Alacacioglu A, Ulger E, Varol U, Yildiz I, Salman T, Bayoglu V. Depression, Anxiety and Sexual satisfaction in Breast Cancer Patients and their Partners- Izmir Oncology Group Study. *Asian Pac J Cancer Prev* 2014;15: 10631-10636.
12. Iqbal A. Common types of mental disorders in adult cancer patients seen at Shaukat Khanum Memorial Cancer Hospital and Research Centre. *J Ayub Med Coll Abbottabad* 2004; 16: 65-69.
13. Al-Zaben FN, Sehlo MG, Koenig HG. A cross-sectional study of anxiety and marital quality among women with breast cancer at a university clinic in western Saudi Arabia. *Saudi Med J* 2015; 36: 1168-1175.
14. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington (DC): American Psychiatric Association; 1980.
15. Lowe B, Decker O, Muller S, Brahler E, Schellberg D, Herzog W et al. Validation and Standardization of Generalized Anxiety Disorder Screener (GAD-7) in the General Population. *Med Care* 2008; 46: 266-274.
16. Patient Health Questionnaire Screeners. GAD-7/GAD7 Arabic for Tunisia. [Accessed 2013 April 10]. Available from URL: http://www.phqscreeners.com/pdf/03
17. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; 166: 1092-1097.
18. Self-reported illness and health status among Gulf War veterans, 1997. A population-based study. The Iowa Persian Gulf study Group. *JAMA* 1997; 277: 238-245.
19. Patient Health Questionnaire Screeners. PHQ-9/PHQ9 Arabic for Tunisia. [Accessed 2013 April 10]. Available from URL: http://www.phqscreeners.com/pdf/02
20. Löwe B, Kroenke K, Herzog W, Gräfe K. Measuring depression outcome with a brief self-report instrument: sensitivity to change of Patient Health Questionnaire (PHQ-9). *J Aff Disord* 2004; 81: 61-66.
21. Kroenke K, Spitzer RL, Williams JB. PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16: 606-613.
22. Mongomery C, Pocock M, Titley K, Lloyd K. Predicting psychological distress in patients with leukemia and lymphoma. *J Psychosom Res* 2003; 5: 289-292.
23. Clinton-McHarg T, Carey M, Sanson-Fisher R, Tzelepis F, Bryant J, Williamson et al. Anxiety and depression among haematological cancer patients attending treatment centers: Prevalence and predictors. *J Aff Disord* 2014; 165: 176-181.
24. Schleifer SJ, Keller SE, Bond RN, Cohen J, Stein M. Major depressive disorder and immunity. *Arch Gen Psychiatry* 1989; 46: 81-87.
25. Kiecolt-Glaser JK, Glaser R. Depression and immune function: central pathways to morbidity and mortality. *J Psychosom Res* 2002; 53: 873-876.
26. Kiecolt-Glaser JK, McGuire L, Robles TF. Psychoneuroimmunology: psychological influences on immune function and health. *J Consult Clin Psychol* 2002; 70: 537-547.
27. Spiegel D. Cancer and depression. *Br J Psychiatry Suppl* 1996; 30: 109-116.
28. Akechi T, Okamura H, Nkano T. Gender differences in factors associated with suicidal ideation in major depression among cancer patients. *Psycho Oncology* 2010; 19: 384-389.
29. Romito F, Montanaro R, Corvasce C, Di Bisceglie M, Mattioli V. Is cancer related fatigue more strongly related to haematological or to psychological factors in cancer patients. *Support Care Cancer* 2008; 16: 943-946.
30. Santos FR, Kozasa EH, Chauffaille Mde L, Colleoni GW, Leite JR. Psychosocial adaptation and quality of life among Brazilian patients with different haematological malignancies. *J Psychosom Res* 2006; 60: 505-511.
31. Pinder KL, Ramirez AJ, Black ME, Richards MA, Gregory WM, Rubens RD. Psychiatric disorder in patients with advanced breast cancer: prevalence and associated factors. *Eur J Cancer* 1993; 29: 524-527.
32. Linden W, Vodermaier A, Mac Kenzie R, Greig D. Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender and age. *J Affect Disord* 2012; 141: 343-351.
33. Gemeay EM, Moawed SA, Mansour EA, Ebrahim NE, Mousa IM, Nadrah WO. The association between diabetes and depression. *Saudi Med J* 2015; 36: 1210-1215.