Anxiety Disorders and Quality of Life among Patients with Hematological Cancer in a Malaysian Hospital

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ABSTRACT

Objective: The purpose of this study is to access the prevalence of anxiety disorders and quality of life factors among hematological cancer patients in a Malaysian hospital. **Methods:** This study used a cross-sectional research design. It was conducted at the Ampang Hospital in Kuala Lumpur, a tertiary referral center for hematological cancer. Anxiety disorders were diagnosed using the Mini International Neuropsychiatric Interview (MINI); quality of life was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) questionnaire. **Results:** A total of 105 hematological cancer patients participated in the study, which constituted a response rate of 83.3%. The prevalence of anxiety disorders in our sample ranged from 1% to 24.8%. Overall, compared to patients without anxiety disorders, hematological cancer patients with anxiety disorders reported impaired quality of life in regards to emotional functioning, cognitive functioning, insomnia, dyspnoea, nausea and vomiting, appetite loss and constipation ($p<0.05$). **Conclusion:** The findings of this study support the notion that, like other cancer patients, hematological cancer patients are vulnerable to developing anxiety disorders that could impact their overall quality of life. Therefore flexible cancer treatments should include a referral to a health professional or psychiatrist who is able to address a patient's mental health status and quality of life.

Keywords: Anxiety disorders, hematological cancer, quality of life

INTRODUCTION

Cancer diagnosis affects the lives of many patients, and the burden can be overwhelming for patients with psychiatric disorders. Cancer, particularly hematological cancer, can have a strong impact on a patient's mental health status.[1-2] Hematological cancer affects the blood cells or lymphatic system, which seriously impacts the lives of patients. Hematological cancer exists in various forms; leukemia, lymphoma and multiple myeloma are three different types of blood cancer.[3] In peninsular Malaysia, a total of 21,773 people were diagnosed with cancer. Lymphoma (4.2%) and leukemia (3.6%) in males and lymphoma (2.4%) in females were among the ten most frequently diagnosed cancers in peninsular Malaysia.[4]

Anxiety is a common psychiatric disorder diagnosed among cancer patients.[1-2, 5] The prevalence of anxiety disorders in hematological cancer patients has been found to be approximately 8.2%.[2] Many international western studies suggest that hematological and other cancer patients are at a higher risk of developing comorbid psychiatric disorders, especially anxiety.[2, 5-6] Anxiety covers a broad spectrum of disorders, which includes panic disorder without agoraphobia, panic disorder with agoraphobia, agoraphobia without history of panic disorder, specific phobia, social anxiety disorder (SAD), obsessive compulsive disorder (OCD), post traumatic stress disorder (PTSD), acute stress disorder and generalized anxiety disorder (GAD). Each anxiety disorder has a specific definition and symptoms, but all are related to anxiety.[7]

Hematological cancer is not only a life-threatening disease, but it also can adversely affect a patient's quality of life, particularly with regard to the level of functioning and clinical symptoms.[8-9] Thus, patients with hematological cancer appear to be at high risk for having both an anxiety disorder and poor quality of life.[1]

Given the important relationship between anxiety disorders and quality of life in patients with hematological

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cancer, it is important to know the prevalence of anxiety disorders (and the quality of life) of Malaysian hematological cancer patients. To our knowledge, no Malaysian data have been published on this topic, nor have there been any official attempts to fully understand the phenomena.

This study was conducted to fill this gap using a sample of hematological cancer patients from a Malaysian tertiary referral center. The data derived from this sample were used to determine the prevalence of various anxiety disorders and its effect on quality of life for these patients.

METHODOLOGY

This hospital-based study was conducted at the Ampang Hospital in Kuala Lumpur, Malaysia. Ampang Hospital is a tertiary referral center for hematological cancer in Malaysia. Data were collected for a period of 8 months, from May to December 2009; a cross-sectional study design was used. Sample size estimation calculated using the single proportion formula, $n = Z^2 P (1-P) / d2$.[10] The Z value is determined as 1.96 with $\alpha = 0.05$ level of significance. A previous study done by Prieto *et al.*, found the prevalence of anxiety among hematological cancer patients was 8.2%.[2] Hence, P equals to 0.082 was determined to be used in the formula. Symbol d in the formula is denoted for precision[10] and the d value was set at 5% or d=0.05 in the study. Hence from the formula a total of 116 patients were required in the study; 1.96^2 x 0.082 (1-0.082) / $(0.05)^2$ =116 patients. Additional 10 patients has been added making a total sample of 126 hematological cancer patients.

The Ethical Committees of the Ministry of Health and the Faculty of Medicine and Health Sciences, University Putra Malaysia, approved the study. All patients who were admitted to the hematology wards during this period were approached for participation. Informed consent was obtained from all who agreed to participate in the study. Eligible criteria for participation were: (1) hematological cancer patient; (2) able to communicate in English, Malay, Mandarin or Tamil; (3) at least 15 years of age; and (4) fit and conscious. Socio-demographic profiles of the subjects were obtained through a socio-demographic questionnaire. Clinical statuses of patients were confirmed through medical records.

Anxiety disorder diagnoses were confirmed using modules from the Mini International Neuropsychiatric Interview (MINI), version 6.00.[11] Modules used included: D - panic disorder; E - agoraphobia, F - social anxiety disorder or current social phobia [SAD]; G - obsessive compulsive disorder (OCD); H - post-traumatic stress disorder (PTSD) and N - generalized anxiety disorder (GAD). The MINI was developed based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria and the International Classification of Diseases (ICD-10). The disorders were determined based on "yes" or "no" answers to the questions on the MINI. Interviewers for this research were trained by senior psychiatrists who were certified to use the questionnaire. The questionnaire has been rated positively for sensitivity and specificity, with ratings of 96% and 88%, respectively.[11]

This study also utilized the European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) questionnaire, version 3.0, which has been pre-tested and validated.[12-13] This disease-specific questionnaire is used to evaluate the quality of life of cancer patients. The questionnaire consists of five functioning scales (physical, role, cognitive, emotional and social functioning), three symptoms scales (fatigue, pain and nausea/vomiting), a global health status scale and six single item scales (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties). The EORTC QLQ-C30 has 30 questions in total. Of these, 28 questions were rated using a 4-point scale (1= "Not at all", 2= "A little", 3= "Quite a bit" to 4= "Very much") and 2 questions were rated using a 7-point scale, ranging from "very poor" (1) to "excellent" (7).[12] Final scale scores are computed based on a scoring manual, and they range from 0 to 100. Higher scores on the functional and the global health status scales represent a high or healthy level of functioning and high global health status; higher scores on the symptoms and single item scales represent a high level of symptoms or problems.[12, 14]

The Statistical Package for Social Sciences (SPSS) program, version 17.0, was used to conduct Mann-Whitney U-tests to make comparisons between the quality of life for patients with and without anxiety disorders. One-tailed tests with a significance level of $p<0.05$ were used for the analyses.

RESULTS

One-hundred and twenty-six patients were approached for participation in our study between May and December 2009. The final sample included 105 patients, which made for a total response rate of 83.3%. Reasons for declining study participation among the patients approached included: (1) refusal to participate (n=6); (2) non-hematological cancer diagnosis (n=13) and (3) difficulties understanding the questionnaire (n=2).

The mean age of the study participants was 40.43 years (95% CI, 37.36-43.49), with a range of 15.00 to 77.82 years. Male patients had a higher mean age (43.61) than female patients (37.53). This difference was statistically significant (t = 1.991, df = 103, p=0.049).

The majority of the patients who participated in the study were female (52.4%). In terms of ethnicity, the majority of the patients who participated in the study were of Malay ethnic descent (60%), followed by Chinese descent

(24.8%). Those with Indian descent (13.3%) and the other ethnic groups (1.9%) represented a small proportion of the study population. In terms of diagnosis, 23.8% of the patients had non-Hodgkin lymphoma, 22.9% had acute myelogenous leukemia, 14.3% had acute lymphoblastic leukemia, 10.5% had Hodgkin lymphoma and 28.5% had other hematological cancer diseases.

Table 1 shows the prevalence of anxiety disorders (current episode) among hematological cancer patients. Approximately one-quarter (24.8%) of the sample had agoraphobia without history of panic disorder, 10.5% had GAD, 7.6% had SAD, 2.9% had panic disorder with agoraphobia, 2.9% had PTSD, 1.9% had OCD and 1% had panic disorder without agoraphobia.

Table 1:   Prevalence of anxiety disorders (n=105)

Anxiety Disorders	NO		YES	
	N	%	N	%
Panic disorder with Agoraphobia	102	97.1	3	2.9
Panic disorder without Agoraphobia	104	99.0	1	1.0
Agoraphobia without history of panic disorder	79	75.2	26	24.8
Social Phobia (Social Anxiety Disorder)	97	92.4	8	7.6
Obsessive Compulsive Disorder	103	98.1	2	1.9
Post Traumatic Stress Disorder	102	97.1	3	2.9
Generalized Anxiety Disorder	94	89.5	11	10.5

Mann-Whitney U tests were conducted to compare the quality of life of participants with or without anxiety disorders. Table 2 presents between-group differences in the quality of life mean rank score as a function of anxiety disorders. Patients with panic disorder with agoraphobia had a significantly lower cognitive functioning score ($p=0.014$), a significantly higher dyspnoea score ($p=0.017$) and reported significantly less pain ($p=0.045$). Patients with agoraphobia without a history of panic disorder were found to have lower emotional functioning ($p=0.043$) and cognitive functioning scores ($p=0.05$) compared to patients without the disorder. Hematological cancer patients with SAD had significantly lower scores in emotional functioning (p<0.001), cognitive functioning ($p=0.002$), and social functioning ($p=0.015$) and reported a significantly higher level of financial difficulties ($p=0.010$). Patients with OCD had significant impairment in role functioning ($p=0.050$), emotional functioning ($p=0.017$), cognitive functioning ($p=0.031$), and global health status ($p=0.048$) compared to patients without the disorder. Patients with OCD were also found to show more symptoms of nausea and vomiting ($p=0.023$) and appetite loss ($p=0.023$) compared to other patients.

Patients with PTSD were found to have significantly poorer social functioning ($p=0.043$) and more severe dyspnoea symptoms ($p=0.007$) than respondents without the diagnosis. Hematological cancer patients with GAD had significantly lower scores in physical functioning ($p=0.034$), role functioning ($p=0.007$), emotional functioning (p<0.001), and cognitive functioning ($p=0.017$) and had significantly higher scores in insomnia ($p=0.016$), constipation ($p=0.006$) and financial difficulties ($p=0.010$). Finally, patients with panic disorder without agoraphobia did not significantly differ from patients without the disorder in their quality of life scores.

Overall among the quality of life domains, the highly negative effect of anxiety disorders were significant for 6 domains for patients with OCD and GAD, 4 domains for patients with SAD, 2 domains for patients with panic disorder with agoraphobia and agoraphobia without panic disorder and 1 domain for patients with PTSD.

Table 2:   Between-group differences in the quality of life mean rank score as a function of anxiety disorders (n=105)

	QOL	PF	RF	EF	CF	SF	FA	NV	PA	DY	SL	AP	CO	DI	FI
No- Panic Disorder with Agrophobia	53.38	53.17	53.54	53.55	54.10	53.77	52.78	52.85	53.84	52.08	53.19	52.23	52.45	53.50	52.57
Yes- Panic Disorder with Agrophobia	40.17	47.33	34.50	34.33	15.67	26.67	60.33	58.00	24.50	84.33	46.67	79.33	71.83	36.00	67.50
z	-0.750	-0.328	-1.106	-1.083	-2.209	-1.546	-0.427	-0.312	-1.695	-2.132	-0.398	-1.586	-1.148	-1.191	-0.870
p-value	0.227	0.372	0.135	0.140	*0.014	0.061	0.335	0.378	*0.045	*0.017	0.346	0.057	0.126	0.117	0.193
No- Agoraphobia without history of Panic disorder	54.39	54.91	51.68	55.92	55.75	53.06	51.95	52.80	55.14	52.54	52.78	52.03	54.58	54.02	50.61
Yes- Agoraphobia without history of Panic disorder	48.77	47.19	57.02	44.12	44.65	52.83	56.19	53.60	46.50	54.38	53.65	55.94	48.21	49.90	60.27
z	-0.828	-1.126	-0.804	-1.724	-1.652	-0.034	-0.622	-0.124	-1.293	-0.315	-0.137	-0.593	-0.977	-0.725	-1.458
p-value	0.204	0.130	0.211	*0.043	*0.050	0.487	0.267	0.451	0.098	0.377	0.446	0.277	0.165	0.234	0.073
(No) SAD	53.84	53.54	53.56	56.36	55.49	54.82	51.98	52.74	53.70	52.53	52.45	51.81	52.63	53.42	51.08
(Yes) SAD	42.81	46.44	46.19	12.25	22.75	30.94	65.38	56.13	44.50	58.75	59.63	67.38	57.50	47.88	76.25
z	-0.997	-0.637	-0.682	-3.957	-2.998	-2.169	-1.206	-0.326	-0.847	-0.655	-0.697	-1.449	-0.459	-0.601	-2.335
p-value	0.160	0.262	0.248	***0.000	**0.002	*0.015	0.114	0.372	0.199	0.256	0.243	0.074	0.323	0.274	*0.010
(No) OCD	53.68	53.11	53.66	53.87	53.76	53.51	52.51	52.23	53.34	52.93	52.80	52.20	52.36	53.33	52.91
(Yes) OCD	18.00	47.50	19.00	8.00	14.00	26.75	78.00	92.50	35.50	56.75	63.25	94.00	86.00	36.00	57.50
z	-1.663	-0.259	-1.652	-2.120	-1.875	-1.252	-1.183	-2.000	-0.846	-0.207	-0.523	-2.006	-1.635	-0.967	-0.219
p-value	*0.048	0.398	*0.050	*0.017	*0.031	0.105	0.119	*0.023	0.199	0.418	0.301	*0.023	0.051	0.167	0.413
(No) PTSD	53.77	53.02	53.47	53.49	53.64	53.86	52.73	52.98	52.77	51.92	52.44	52.95	52.59	53.50	52.57
(Yes) PTSD	26.67	52.33	37.00	36.50	31.17	23.67	62.33	53.83	60.67	89.67	72.00	54.83	67.00	36.00	67.50
z	-1.540	-0.039	-0.957	-0.957	-1.292	-1.722	-0.543	-0.052	-0.456	-2.495	-1.194	-0.110	-0.854	-1.191	-0.870
p-value	0.062	0.485	0.170	0.170	0.098	*0.043	0.294	0.480	0.324	**0.007	0.116	0.456	0.197	0.117	0.193
(No) GAD	54.12	54.85	55.45	58.22	55.11	54.63	51.51	52.92	53.80	52.46	50.98	53.59	50.55	53.32	50.70
(Yes) GAD	43.45	37.18	32.09	8.41	34.95	39.09	65.77	53.68	46.18	57.64	70.23	48.00	73.91	50.27	50.70
z	-1.113	-1.828	-2.494	-5.158	-2.130	-1.629	-1.483	-0.085	-0.809	-0.629	-2.160	-0.601	-2.543	-0.381	-2.349
p-value	0.133	*0.034	**0.007	***0.000	*0.017	0.052	0.069	0.466	0.210	0.265	*0.016	0.274	**0.006	0.352	*0.010

*p < 0.05; **p < 0.01; ***p < 0.001

SAD, Social Anxiety Disorder; OCD, Obsessive Compulsive Disorder; PTSD, Post Traumatic Stress Disorder; GAD, Generalised Anxiety Disorder; QOL, Global quality of life; PF, Physical Functioning; RF, Role Functioning; EF, Emotional Functioning; CF, Cognitive Functioning; SF, Social Functioning; FA, Fatigue; NV, Nausea And Vomiting; PA, Pain; DY, Dyspnoea; SL, Insomnia; AP, Appetite loss; CO, Constipation; DI, Diarrhoea; FI, Financial difficulties

DISCUSSION

Data from the present study provide several important implications for understanding the impact of various anxiety disorders on patients' quality of life. The findings of this study support the notion that, like other cancer patients, hematological cancer patients are vulnerable to anxiety disorders, and these anxiety disorders subsequently impact a patient's quality of life.[2, 5-6, 8-9]

In this study, the prevalence of anxiety disorders in Malaysian hematological cancer patients varies from 1% to 24.8%. The prevalence breakdown by type of anxiety disorder in our sample is: agoraphobia without history of panic disorder (24.8%); GAD (10.5%); SAD (7.6%); panic disorder with agoraphobia (2.9%); PTSD (2.9%); OCD (1.9%) and panic disorder without agoraphobia (1%). An earlier study by Prieto and colleagues found that the overall prevalence of anxiety disorders in hospitalized hematological cancer patients was approximately 8.2%.[2]

Previous studies have shown that cancer patients with anxiety disorders had a significantly poorer quality of life compared to patients without the disorder.[8-9] Similarly, Pamuk and colleagues (2008) showed that hematological malignancy patients with a diagnosed anxiety disorder had lower global quality of life, higher symptomatology scores and poorer cognitive, emotional and social functioning than those without a diagnosed anxiety disorder.[1] A study among advanced cancer patients found that the functional scales (role functioning, emotional functioning, and cognitive functioning) and the symptom scale (insomnia) were the most significant predictors of quality of life followed by dyspnoea, sleep disturbance and appetite loss. The study indicates the cancer patients have impaired social, emotional and global quality of life.[9] Quality of life impairment, especially in functioning score, also has been found to be associated with anxiety and depression in hematological cutaneous lymphoma cancer patients.[15]

In the present study, the impact of each type of anxiety disorders on quality of life domains was analyzed separately. First, we found that the prevalence of panic disorders in patients with hematological cancer ranged from 1% to 2.9%, depending on the panic disorder subtype. This includes panic disorder with agoraphobia (2.9%) and panic disorder without agoraphobia (1.0%). Panic disorder is defined as experiencing a state of intense apprehension with symptoms including shortness of breath, palpitations, discomfort, choking sensations and fear of losing control.[7] The prevalence rates found in our sample are consistent with a previous study of hospitalized hematological cancer patients for stem cell transplantation, which reported a prevalence rate of 1.4%.[2] However, other studies have found a prevalence rate for panic disorder of 20.75% in advanced inpatients, including both hematological and other types of cancer.[6] This difference may be accounted for by differences in methodological settings and compositions of the study populations.

Panic disorder with agoraphobia

Compared to hematological cancer patients who do not have panic disorder with agoraphobia, hematological cancer patients with panic disorder with agoraphobia had significantly lower scores on the EORTC-QLQ-30 cognitive functioning scale and pain symptoms scale and significantly higher scores on the dyspnoea symptom scale. This indicates the patients with panic disorder with agoraphobia have impaired cognitive functioning and more symptoms of dyspnoea. Previous studies have reported similar results related to impaired cognitive functioning of hematological cancer patients.[1] Patients with panic disorder with agoraphobia reported fewer pain symptoms; however, previous studies among hospitalized cancer patients found that patients without anxiety or depression have less pain interference than patients who have anxiety, depression or both diagnoses.[16] To our knowledge, no published studies have investigated the dyspnoea rates of cancer patients with or without anxiety; thus, comparisons with previous studies cannot be made.

Agoraphobia without panic disorder

Another type of anxiety disorder is agoraphobia. Patients with agoraphobia tend to avoid situations or places where escape or help might be impossible; the disorder is similar to having a panic attack or panic-like symptoms.[7] The prevalence in our study of agoraphobia without a history of panic disorder (24.8%) appears higher than other studies among other cancer patients, which have found a prevalence rate of 2.7% in patients aged 55 to 74 years old. In this previous study, the odds ratio of cancer patients developing agoraphobia was 0.40 among those aged 15 to 54 years and 5.94 among those aged 55 to 75 years old.[5]

Analyses showed that hematological cancer patients with agoraphobia without a history of panic disorder had significantly lower scores on the EORTC-QLQ-30 functional scales (cognitive function, emotion function) compared to respondents without this diagnosis. This finding is consistent with previous studies, which found that cancer patients were impaired in their emotional[9] and cognitive functioning.[1]

Social Anxiety Disorder (SAD)

Social phobia, or social anxiety disorder (SAD), is characterized by avoidance behaviors related to exposure to social

or performance situations.[7] The present study found a higher prevalance rate for social anxiety disorder (7.6%) than was reported in a study of hematological cancer patients receiving stem cell transplantation treatment (1.8%).[2] This study also revealed that hematological cancer patients with SAD had significantly lower scores in emotional functioning, cognitive functioning and social functioning and had significantly higher financial difficulties. This finding is consistent with previous findings that have found impaired emotional functioning,[9] cognitive functioning[1] and social functioning[1, 9] in cancer patients. The finding of higher levels of financial difficulties in the present study also is consistent with other Malaysian studies. Studies have found that finances are one of the main problems faced by cancer patients, especially those in the transplantation treatment, because only two government hospitals subsidize the cost of treatments. Other organizations (such as universities, welfare and non-governmental organizations) help patients by fundraising to cover the cost of treatments, but patients often still face financial difficulties.[17]

Obsessive-Compulsive Disorder (OCD)

OCD is characterized by obsessions that cause anxiety and/or compulsions that serve to neutralize anxiety. In the present study, the prevalence rate of OCD was 1.9%. In terms of quality of life, hematological cancer patients with OCD had significantly lower role functioning, emotional functioning, cognitive functioning and global health status scores than patients without OCD. They also had significantly higher scores on the physical symptoms scale (nausea and vomiting, as well as appetite loss). This finding is consistent with previous studies which found impaired emotional functioning,[1, 9] cognitive functioning and poor global health status.[1]

Post traumatic stress disorder (PTSD)

PTSD is characterized by patients re-experiencing traumatic situations with increased arousal and avoidance. The prevalence of PTSD in the present study was 2.9%. However, this prevalence rate was far lower than the prevalence rate of 17% of PTSD found in a previous study of hematological cancer patients.[18]

Hematological cancer patients with PTSD had significantly higher dyspnoea scale scores and lower social functioning scale scores compared to patients without the disorder. The finding of impaired social functioning is consistent with previous studies.[1]

Generalized anxiety disorder (GAD)

GAD is defined as persistent and excessive anxiety and worry for a period of at least 6 months. The prevalence of GAD in this study (10.5%) was higher than the prevalence rate of 1.8% reported by Prieto and colleagues.[2] Analyses showed hematological cancer patients with GAD were more likely to have lower functional scale scores (physical functioning, role functioning, emotional functioning, cognitive functioning) and lower symptoms scale scores (insomnia, constipation and financial difficulties) compared to patients without the disorder. The present study is consistent with earlier studies investigating emotional functioning[1, 9] and cognitive functioning.[1] Insomnia has been found to be a significant predictor of quality of life.[9] Another study among Hodgkin lymphoma patients found that impaired physical health was also a predictor of quality of life; patients who rated poor physical health rated their overall quality of life as worse compared to the general population. Hodgkin lymphoma patients who have financial difficulties also rated their mental health status poorly compared to the general population. Inability to work may account for the complications in physical and mental health in patients with Hodgkin lymphoma.[19]

LIMITATIONS

This study has a number of important limitations that need to be considered. First, the method of assessing anxiety and quality of life used in this study limited the symptoms reported to the patient's recall at the time of the interview. The numbers of patients eligible for participation in this study were also limited by the patient's physical status and their ability to respond. Finally, some self-rated questionnaires were answered by the respondents themselves or were read to them to clarify their responses. These three limitations should be noted and considered when interpreting results.

CONCLUSION

This research has provided us with some insight into the prevalence of various types of anxiety disorders (as well as the quality of life) among Malaysian hematological cancer patients. The findings demonstrate that the rates of comorbid anxiety disorders for Malaysian hematological cancer patients are similar to those for hematological cancer patients in other countries.[1, 9] This study also found that different types of anxiety disorders impacted a patient's quality of life domains differently. Among anxiety disorders, only patients diagnosed with OCD reported poorer global health status. If anxiety disorders are left untreated, it may impair the patient's cancer management systems; therefore, patients with anxiety should be referred to their health professional or psychiatrist in order to improve their mental health status and quality of life.

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