

Anxiety and depression in patients with haematological neoplasms in Malaysia

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ABSTRACT

Background: It is not uncommon that anxiety and depression occur in patients with cancers, and past researches have shown that the quality of life of patients is negatively affected. This study aims to determine the prevalence of anxiety and depression of patients with haematological cancers in Malaysia and to investigate the possible association of these psychological symptoms with their quality of life.

Methods: This is a cross-sectional study where patients with haematological cancers attending two major hospitals were recruited. Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression scale (HADS). Quality of life (QoL) of these patients was measured using the European Organisation for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ C30). An overall summary QoL score in combination with financial difficulty score and global health score were used for analysis.

Results: A total of 319 patients were recruited. Thirty-three percent of patients had anxiety symptoms, 23.5% had depression symptoms. In summary the overall score of QoL is significantly lower in patients with higher scores for depression and anxiety, ($p < 0.05$). Patients who exhibit anxiety symptoms were more frequently female, still undergoing treatment whereas patients who had higher depression scores were older and had acute leukemias or myeloproliferative neoplasms. Patients who have depression are significantly associated with a higher financial difficulty score, $p < 0.05$.

Conclusion: The poor quality of life in patients who have anxiety and depression should raise awareness amongst the health professions treating them so that additional support can be provided.

KEY WORDS:

Anxiety, depression, quality of life, haematological cancers

INTRODUCTION

Haematological cancers account for approximately 6.5% of the total cancers diagnosed in the world.¹ In Malaysia,

haematological cancers accounts for 9.6% of the total cancers.² Patients with haematological cancers were reported as having the highest distress at the time of diagnosis as compared to other cancer patients.^{3,4} Haematological cancers are distinct diseases which in many ways different from solid tumours, not only in their presentation but also management.

It is well established that patients who had been diagnosed of cancers, whether solid cancer or haematological cancer exhibit anxiety and depression symptoms.^{4,7} According to a study by Linden et al., the prevalence rates of anxiety and depression are also different for various types of cancers. Patients with lung, gynaecological and haematological cancers were reported to have the highest level of emotion distress at time of diagnosis.⁴ A recent study by Clinton-McHarg et al., indicated that 27% of patients with haematological cancers reported anxiety and 17% reported significant depression.⁵ There are only few studies that has looked into the prevalence of anxiety and depression in patients with haematological cancers, especially in South East Asian countries. Most of the studies focused mainly on patients with solid tumours and yet, a recent paper noted that South Asian patients reported higher rates of depressive symptoms and experienced more physical symptoms compared to Caucasian patients.⁸⁻¹⁰

Presence of anxiety and depression symptoms has been proven to affect one's quality of life (QoL).¹¹⁻¹³ In patients with haematological cancers, QoL has also been consistently shown to be worse.¹³⁻¹⁵ Identifying and screening for this emotion distress is vital especially it had been demonstrated that cognitive-behavioural therapy will not only reduce symptoms of depression and anxiety, it can also result in improvement of QoL of patients.¹⁶

Since there is a dearth of information on the psychological stress and QoL amongst haematological cancer patients in the South East Asian region, this study aims to determine the prevalence of anxiety and depression symptoms in a larger population and to identify the possible relevant clinical factors and patients' demographics which may be associated with the risk of anxiety and/or depression. In addition, the effects of anxiety and depression symptoms on the QoL of these patients were also examined.

This article was accepted: 5 April 2019

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MATERIALS AND METHODS

This was a cross-sectional study where patients were recruited from two hospitals in Kuala Lumpur, the capital city of Malaysia. Patients who attended the haematology outpatient clinic, day-care and wards were approached for the study. The study was approved by both institutions' ethnic committee (UMMC 1010.34 and SJMC 201309.09). Written informed consents were obtained from all patients. Eligibility criteria included those who were 18 years and above, confirmed diagnosis of haematological cancers and able to communicate in English, Mandarin or Malay. Patients with previous psychological conditions were excluded. The recruitment period was from December 2013 to September 2014.

Questionnaires

Screening for anxiety and depression was based on the Hospital Anxiety and Depression Scale (HADS). The HADS had a total of 14 items divided into two subscales; anxiety subscale (7 items) and depression subscale (7 items).¹⁷ A score of ≥ 8 on either subscale was defined as substantial level of symptoms. The HADS had been validated in three languages; English, Malay and Mandarin to identify patients with cancers for significant anxiety and depressions.^{18,19,20}

The validated European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire was used to determine the overall QoL of these patients.^{21,22} Validated translated version of EORTC QLQ-C30 questionnaire was available in two other languages, Malay and Mandarin.^{21,23} The questionnaire comprised of 30 questions with nine multi-item scales; five functioning scales, three symptoms scales, a global health status (GHS) scale and six other single item of symptoms scales.²¹ Higher scores mean higher functioning for functioning scales and higher scores in symptoms scales would mean higher symptom level. EORTC QLQ-C30 Summary Score is calculated based on 13 scales (27 items) which excluded GHS and financial difficulties score was also included to supplement the 15 outcome profiles. The EORTC QLQ-C30 Summary Score had been validated and shown to be robust in capturing the overall QOL better than the global health status/QOL scale.²⁴ In this study, the EORTC QLQ-C30 Summary Score, GHS score and financial difficulty score were used for further analysis. Approval was obtained from the European Organization for Research and Treatment of Cancer Quality of life for the use of their questionnaires.

The questionnaires were administered to patients according to their preferred language and returned on the same day. The questionnaires were all self-rated and took approximately 20 minutes to complete. Patients' socio-demographics and disease status and treatment information were also obtained from patients and medical records.

Statistical Analysis

Descriptive statistics were used for the analysis of patients' characteristics including demographic factors and the HADS scores accordingly. Categorical demographic data among patients with anxiety and depression were compared using Chi-square test. Point-biserial correlation was used to determine correlations between QoL domains with anxiety

and/or depression. To determine factors associated with anxiety or depression, univariate binary logistic regression was used. Univariates with p-value ≤ 0.20 or were reported significant in other studies were further analysed using multivariate stepwise binary logistic regression to determine the p-value and adjusted odds ratio. A p-value of ≤ 0.05 was considered as statistically significant. Data was analysed using the Statistical Package for Social Sciences (SPSS) version 22.0.

RESULTS

A total of 330 patients were approached. 319 patients agreed to participate in the HADS questionnaires but only 252 of them agreed to participate in the QoL questionnaires. The mean age of the 319 patients was 51.7 years (range from 18-92 years). Characteristics of patients are showed in Table I.

In all, 32.9% and 23.5% of patients had anxiety and depression symptoms respectively. (Table I). Clinical factors such as gender, type of disease and treatment status appeared to be significantly associated with anxiety, whereas age, their education level, type of disease and treatment status were associated with depression (Table II). There was no significant difference of both anxiety and depression amongst the three ethnic groups.

For the 252 patients who had QoL data available for further analysis, all domains of QoL were significantly affected by anxiety whereas all domains except for symptoms of nausea and diarrhoea were significantly affected by depression. The EORTC QLQ-C30 Summary Scores are showed in Table III. The EORTC QLQ-C30 Summary Scores for patients with anxiety symptoms was significantly lower than those without, 85.3 vs 71.9 and similarly the EORTC QLQ-C30 summary score was also significantly lower in patients with depression, 68 compared to 84.7 in patients without depression. After multivariate analysis, female patients and patients who were still undergoing treatment were significantly associated with the presence of symptoms of anxiety. The EORTC QLQ-C30 Summary Score was also significantly adversely affected by the presence of anxiety (Table III). Older patients, patients with the diagnosis of acute leukaemia and myeloproliferative neoplasm were significantly more likely to have depression. Financial difficulties and EORTC QLQ-C30 Summary Scores were significantly affected by the presence of depression in the multivariate logistic regression analysis (Table IV).

DISCUSSION

The prevalence rate of 32.9% for symptoms of anxiety and 23.5% for depression in this study concurs to what was reported elsewhere.⁵ Fifteen percent of patients reported to have both anxiety and depression symptoms, which is similar to what was reported from Australia.⁵ Our paper is probably the first that reported the presence of anxiety and depression symptoms using the HADS in a large haematological cancer population in the South East Asia regions. Although there is a similar study by Ng et al., which demonstrated a higher prevalence rate in his small cohort of haematological cancer patients, the cut-off scores for

Table I: Demographic and clinical characteristics of patients

Demographic and clinical characteristics		Total (N=319) (%)
Age, in years	Mean±SD	51.7±16.5
	Median	53.0
	Range	18-92
Gender	Male	140 (43.9)
	Female	179 (56.1)
Ethnicity	Malay	108 (33.9)
	Chinese	170 (53.3)
	Indian	41 (12.9)
Education background	Primary school	73 (22.9)
	Secondary school	135 (42.3)
	College/ university	111(34.8)
Partner	No partner	103 (32.3)
	With partner	216 (67.7)
Underlying diagnosis	Lymphoma	197(61.8)
	Myeloma	25 (7.8)
	Chronic leukaemia	23 (7.2)
	Acute leukaemia	49 (15.4)
Years since diagnosis (N = 313)	MPN	25 (7.8)
	<1year	54 (17.3)
	1-5 years	115 (36.7)
Treatment status (N=318)	> 5 years	144 (46.0)
	Completed treatment	218 (68.6)
	Ongoing treatment	100 (31.4)
Hospital Anxiety and Depression Scale (HADS)	Anxiety scale <8	214 (67.1)
	≥8	105 (32.9)
	Depression scale <8	244 (76.5)
	≥8	75 (23.5)
	Both Anxiety and Depression scales ≥8	49(15.4)

Table II: Association of anxiety and depression access using the Hospital Anxiety and Depression Scale (HADS) with socio-demographics of patients

Patients Characteristics		Anxiety		P value	Depression		P value
		No	Yes		No	Yes	
Age	≤50	99 (69.7)	43 (30.3)	0.370	120 (84.5)	22 (15.5)	0.002*
	>50	115 (65)	62 (35)		124 (70.1)	53 (29.9)	
Gender	Male	104 (74.3)	36 (25.7)	0.015*	107 (76.4)	33 (23.6)	0.982
	Female	110 (61.5)	69 (38.5)		137 (76.5)	42 (23.5)	
Ethnicity	Malay	75 (69.4)	33 (30.6)	0.270	89 (82.4)	19 (17.6)	0.140
	Chinese	116 (68.2)	54 (31.8)		127 (77)	43 (23)	
	Indian	23 (56.1)	18 (43.9)		28 (68.3)	13 (31.7)	
Education level	Primary	44 (60.3)	29 (39.7)	0.304	47 (64.4)	26 (35.6)	0.010*
	Secondary	91 (67.4)	44 (32.6)		104 (77.0)	31 (23)	
	Tertiary	79 (71.2)	32 (28.8)		93 (83.8)	18 (16.2)	
Partner status	No	72 (69.9)	31 (30.1)	0.459	81 (78.6)	22 (21.4)	0.531
	Yes	142 (65.7)	74 (34.3)		163 (75.5)	53 (24.5)	
Duration since diagnosis	<1 year	31 (57.4)	23 (42.6)	0.185	36 (66.7)	18 (33.3)	0.058
	1-5 year	82 (71.3)	33 (28.7)		85 (73.9)	30 (26.1)	
	>5 years	99 (68.8)	45 (31.2)		118 (81.9)	26 (18.1)	
Type of disease	Lymphoma	146 (74.1)	51 (25.9)	0.009*	164 (83.2)	33 (16.8)	0.001*
	Myeloma	11 (44)	14 (56)		16 (64)	9 (36)	
	Chronic leukaemia	14 (60.9)	9 (39.1)		19 (82.6)	4 (17.4)	
	Acute leukaemia	28 (57.1)	21 (42.9)		32 (65.3)	17 (34.7)	
	Others	15 (60)	10 (40)		13 (52)	12 (48)	
Treatment status	Completed	168 (77.1)	50 (22.9)	<0.001*	181 (83)	37 (17)	<0.001*
	Ongoing	45 (45)	55 (55)		62 (62)	38 (38)	

*significant p value

Table III: Multivariate analysis of anxiety with demographics and Quality of Life (QoL)

Variables		Univariate logistic regression			Multivariate regression analysis		
		OR	95%CI	p	OR	95%CI	p
Gender	Male#						
	Female	2.85	1.30-6.28	0.009*	2.32	1.15-4.66	0.018*
Education	Primary#						
	Secondary	0.40	0.16-1.04	0.060	0.52	0.23-1.19	0.122
	Tertiary	0.53	0.20-1.42	0.203	0.65	0.28-1.51	0.314
Duration	<1year#						
	1-5 years	1.50	0.45-5.06	0.510	1.36	0.43-4.30	0.605
	>5 years	3.84	1.01-14.66	0.049	2.97	0.86-10.24	0.085
Underlying diagnosis	Lymphoma#						
	Myeloma	2.54	0.57-11.42	0.223	2.44	0.56-10.77	0.238
	Chronic leukaemia	0.96	0.23-4.05	0.955	1.02	0.24-4.22	0.984
	Acute leukaemia	2.13	0.82-5.532	0.121	2.24	0.91-0.54	0.079
	MPN	3.02	0.42-21.65	0.270	3.09	0.46-20.65	0.244
Treatment status	Completed#						
	Ongoing	2.17	0.65-7.27	0.208	2.30	1.22-7.37	0.017*
Global health status score		0.99	0.97-1.01	0.454	-	-	-
Financial difficulty score		1.00	0.99-1.02	0.465	-	-	-
EORTC QLQ-C30 Summary score		0.95	0.93-0.98	0.001*	0.95	0.92-0.97	<0.001*

Note: # - Reference category; * - significant p value; OR – Odds Ratio; 95%CI – 95% Confidence Interval.

Table IV: Multivariate analysis of depression with demographics and Quality of Life (QoL)

Variables		Univariate logistic regression			Multivariate regression analysis		
		OR	95% CI	p	OR	95% CI	p
Age	≤50 years#						
	>50 years	4.46	1.43-13.84	0.010*	6.43	2.29-18.05	<0.001*
Education level	Primary#						
	Secondary	0.36	0.12-1.12	0.078	0.36	0.13-1.11	0.078
	Tertiary	0.38	0.11-1.31	0.125	0.38	0.12-1.21	0.101
Duration	<1 year#						
	1-5 year	1.71	0.40-7.24	0.468	0.34	0.1-1.16	0.085
	>5 years	1.71	0.35-8.28	0.507	0.46	0.22-0.96	0.038*
Underlying diagnosis	Lymphoma#						
	Myeloma	0.60	0.076-4.79	0.063	0.83	0.13-5.31	0.840
	Chronic leukemia	0.14	0.01-1.92	0.140	0.23	0.03-1.98	0.181
	Acute leukemia	7.33	2.18-24.64	0.001	6.41	2.20-18.72	0.001*
	MPN	44.83	4.70-428.01	0.001	33.69	3.95-287.55	0.001*
Treatment status	Completed#						
	Ongoing	1.83	0.37-8.97	0.456	1.49	0.49-4.94	0.516
Global health status score		1.00	0.97-1.029	0.803	--	--	--
Financial difficulty score		1.02	1.001-1.03	0.034*	1.01	1.00-1.03	0.028*
EORTC QLQ-C30 Summary score		0.94	0.91-0.97	<0.001*	0.94	0.92-0.97	<0.001*

Note: # - Reference category; * - significant p value; OR – Odds Ratio; 95%CI – 95% Confidence Interval.

diagnosis of anxiety and depression used are lower.⁸ One recently published study in Singapore reported prevalence rates of subsyndromal anxiety and depression to be as high as 69% and 38% respectively in cancer patients.²⁵ There are very few reports that specifically evaluated the psychological impact of the haematological cancer diagnosis in patients in this region.

Many other studies have shown consistently that female patients exhibit more anxiety symptoms.^{3,4,7,26,27} Similarly, this study demonstrated that female patients experienced more anxiety. It has been postulated that female patients are more likely to express their emotional concerns and report more of their symptoms whereas men in general tend to under-report their distress due to self-esteem.²⁸ There may be a need to identify male patients who are at risk by encouraging them to voice their concerns. Consistent with other studies, this study also reported a significantly higher frequency of depression symptoms in older patients.^{6,26} Possible reasons for this could be that older patients are more likely to have other medical illnesses and generally tolerate treatment poorly. However, we did not explore the co-morbidities in this study. As in other reports, we also found that the duration of cancer made no significant impact on patients' psychological health.^{5,8} We found no difference in the prevalence of anxiety and depression amongst the different ethnicities although Ng et al., revealed that Malay patients had lower levels of anxiety and depression.⁸ He postulated that the difference may have been due to the different coping mechanism. There are other surveys that also reported ethnic differences for coping with depression.^{10,29} Therefore, the lack of significant difference in anxiety and depression in three different ethnic groups of patients in this study will warrant further study to confirm.

It is not surprising that patients who were still undergoing active treatment were more anxious when compared with those patients who had completed their therapy.^{3,11} In this study, it is clearly demonstrated that patients who were still undergoing active treatment were significantly more likely to have anxiety. The postulation is that anxiety is more likely a reaction to an acute event and this is especially true in haematological cancer patients where the side effects of treatment can be severe and may require prolonged hospitalization.^{3,4,30} This should alert the treating physicians to be more cognisant of the psychological stress that patients have in order to institute early counselling and intervention.

Majority of other studies do not differentiate the types of haematological cancers when determining the prevalence of anxiety and depression.^{4,8,11,31} In this study, we identified that patients with acute leukaemia and myeloproliferative neoplasms had the highest prevalence of depressive symptoms, which is in contrast to what was reported.⁵ Instead, some studies identify patients with lymphoma as having the highest prevalence of psychological distress.^{3,32} This finding should be interpreted cautiously as most of the studies including this study have unequal sample sizes for each disease and the number of patients with leukaemias and myeloproliferative neoplasms are small. However, patients who had been diagnosed of acute leukaemias had been shown to demonstrate clinically significant traumatic stress which is associated with other psychological distress.³³⁻³⁵ There have been no studies which had specifically looked into

myeloproliferative neoplasms, and the number of patients in this study is too small to make any convincing conclusion although it can be hypothesized that patients with myeloproliferative neoplasms are generally older and this may be one of the possible confounding factors.

A systematic review by Allart-Vorelli et al., indicated that the different dimensions of QoL are worse in patients with haematological cancers when compared to the healthy population.¹⁵ In this study, we found that the mean score for GHS for patients is 71.9 and is better than what is reported elsewhere.³⁶ In this study, we found that cognitive functioning followed by emotional functioning were the most affected and similar to the report by Priscilla et al., fatigue and financial difficulties are consistently the most prevalent symptoms.¹² It is well established that QoL of patients are affected by the presence of symptoms of anxiety and depression.^{11,12,14} We have clearly demonstrated here that almost all domains of QoL are negatively affected with the presence of anxiety and depression symptoms. The summary score of QoL showed obvious differences amongst patients with depression or anxiety and demonstrated significant lower score when patients have both symptoms of anxiety and depression. Therefore, this finding emphasizes the importance of early identification of patients at risk of psychological stress for early and appropriate interventions such as cognitive behavioural therapy. This is especially relevant when this type of behavioural therapy has been shown to be effective in managing anxiety and depression and has also resulted in long term improvement of QoL.¹⁶

The often-high cost involved in the treatment of cancers have severely affects the financial situations of patients and their families. This is particularly pertinent in the South East Asian regions where up to 75% of patients experienced financial hardship within a year of diagnosis.³⁷ Financial burden has always been playing a significant role in the psychological health of cancer patients, not only limited to haematological cancers but also other cancers.^{18,32,35,37,38} In this study, we found that the presence of symptom of depression is significantly associated with high financial difficulty score and it is reasonable to assume that financial difficulties faced by patients contributed to their depressive symptoms. It is therefore important that physicians to take into account the financial status of patients and families, and to engage patients in the management plans which should include the cost implications of the treatment.

Study Limitation

One of the limitations of this study is that this is a cross-sectional study which does not allow us to evaluate the causality relationship of symptoms of psychological with QoL. The relatively large number of patients who refused to participate in the QoL questionnaire may also have affected our results. There may also be potential bias in the findings as patients were recruited from two different hospitals and the cohort may have different financial background which we did not capture. Another weakness of this study is the small sample size of other haematological cancers except for lymphoma. However, this study reports the largest number of haematological cancer patients in the South East Asian countries to date and in addition, the study included QoL information of these groups of patients where data is generally lacking in this part of the world.

Clinical Implications

In conclusion, this study is one of the few studies which specifically explored the psychological distress of haematological cancer patients in the South East Asian regions. The results revealed that there is a high prevalence of anxiety and depression symptoms amongst the haematological cancer patients and their QoL is adversely affected. Our results should encourage health care professionals to be more cognizant of the psychological symptoms that patients have, so that appropriate therapy and counselling can be provided in a timely manner. In addition, financial burden which contribute further to the psychological stress in patients should not be undermined and early interventions and support by relevant authorities and staff may help to alleviate some of these problems.

FUNDING

The study was funded by University Malaya High Impact Research Grant (UM HIR grant E-000008-20001)

CONFLICT OF INTEREST

The authors declared that they have no conflict of interests.

ACKNOWLEDGEMENT

We would like to thank SN Lee Hong Lean who assisted in recruiting some of the patients and Dr Haris Abdul Rahman and Dr Ng Soo Chin for agreeing for their patients to participate in this study.

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