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Psychological Distress, Quality of Life and Coping in Cancer Patients: A Prospective Study

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SUMMARY

We present the results and conclusions of an observational prospective cohort design study using self-administered questionnaires to determine correlation between psychosocial factors and cancer outcome among 80 consecutive newly diagnosed treatment naïve cancer subjects who were being referred to the Oncology Clinic, Hospital Universiti Kebangsaan Malaysia. Subjects were recruited over a period of 43 weeks from October 2000 till July 2001. Follow-up assessments were carried out at 6-months and 12 to 26 months later. The prediction of survival time was performed by the Cox Regression Analysis method with adjustments for biological and psychosocial risk factors. It was noted that depression (p = 0.001), stage 4 cancer disease (p = 0.016), neurological (p = 0.032), gastrointestinal tract (p = 0.04), head and neck (p = 0.011), gynaecological (p = 0.005) and bone and soft tissue (p = 0.030) malignancies were independent and statistically significant prognostic factor of survival during the study period. It was further shown than depressed patients were found to have almost four fold greater risk of dying than non-depressed patients and patients with stage 4 cancer illness have a five fold greater risk of dying than patients with stage 1 disease. Furthermore, based on tumour types subjects with neurological, gynaecological, head and neck, bone and soft tissue and gastro intestinal tract malignancies were found to have approximately thirty-six, twenty-five, twenty-two, sixteen and seven fold greater risk of dying respectively when compared to subjects with genitourinary cancers. This study further affirms the need for health care providers to be aware of the psychological aspects of the cancer patient and provide appropriate therapy so as to ensure that this group of individuals would have enhanced survival rates.

KEY WORDS:
Depression, Survival, Cancer Patients, Cox Regression Analysi

INTRODUCTION

Although virtually all patients nearing the end of life are confronted with physical, psychological, social and spiritual challenges it can also offer prospect for personal growth and strengthening of relationships. When physical symptoms and agony are ameliorated and controlled, it becomes easier to attend to the patients' central concerns i.e. about their families, about their own psychological integrity and about finding meaning in their lives. Optimal end-of-life care necessitates a readiness to engage with patient in dealing with these areas[1]. Greater understanding of the common psychosocial concerns of cancer patients can improve both the clinical care as well as the medical personnel's sense of contentment and meaning in caring for the dying.

The role of psychosocial factors on disease progression and outcome of patients suffering from cancer have been a topic of considerable debate not only to the professionals but also lay people. The mass media in particular have played a vital role in the support and encouragement of the popular notion of overpowering cancer via "mind over body". In addition there also exist a number of self-help books as well as retreat centers where patients can learn imagery as well as relaxation techniques to get the better of this serious physical illness. Guided imagery (such as visualizing white cells attacking cancer cells), cognitive restructuring (such as thinking positive) and assertiveness training have been encouraged together with traditional health care for patient with cancer to fight the disease[2].

Over the last decade or so there has been a large body of literature investigating the influence of psychosocial factors on cancer progression and outcome which in turn could affect the survival of cancer patients. However, the results have time and again been conflicting. Some have reported correlations between different psychosocial variables[3,4,5,6]. Derogatis *et al*[3] affirmed that in women with metastatic breast cancer, the long-term survivors were more symptomatic overall, with particular increase measures of anxiety as well as alienation and considerably higher levels of dysphoric mood (e.g. depression, guilt) while short-term survivors demonstrated significantly reduced levels of hostility, with higher levels of positive mood. In addition, depressed patients have a three-fold greater risk of dying compared to non depressed patients after adjusting for prognostic factors among patients after Stem-Cell Transplantation for Malignant Diseases[6]. On the contrary others showed no such correlations[7,8]. To sum up these problems reviews by several authors[2,9] concluded that these conflicting outcomes could be explained by poor methodology such as failure to control adequately for a variety of disease-related factors, influence from treatment, psychological variables were assessed after the completion of treatment, difference in measurements of coping styles and multiple variables were tested retrospectively, varied definitions of outcome indicators, specific statistical analysis for survival analysis were seldom

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employed (i.e. Kaplan-Meier plots and Cox regression analysis), missing psychosocial data during follow-up, inadequate consideration of differences in tumor staging and subjective or non-standardized methods of evaluation. To further reinforce these controversies a caution that often comes to light in literature needs to be reiterated here i.e. "there is little firm evidence of a causal association between any psychosocial factor and cancer incidence, mortality or progression"[10]. As a result the question of impact of psychosocial variables on the course and outcome of cancer is still under discussion[11] and entails more research[12].

Nevertheless, an article drawing principally from systematic reviews and meta-analyses[13] to furnish the relative efficacy of a range of psychosocial-mind-body interventions such as relaxation, (cognitive) behavioral therapies, meditation, imagery, biofeedback, and hypnosis in the treatment of health-related problems other than mental illness or psychological difficulties, revealed strong evidence of efficacy of mind-body therapies (e.g. relaxation, hypnosis, supportive group therapy) in amelioration of cancer symptoms (disease and treatment related). The authors further elucidated that the cumulative clinical evidence points strongly to the idea that medicine should take on a biopsychosocial stance rather than totally and firmly affirm a biologic-genetic model of health.

Above all, to the author's knowledge this was the first prospective study involving a heterogeneous group of subjects in which psychosocial data (in the form of psychological distress, Quality of life and coping) were assessed on three occasions (i.e. baseline, 6 months and 12-26 months) and subsequently correlated with disease outcome which was aimed at addressing the aforesaid important and unresolved matter.

MATERIALS AND METHODS

After the project was approved by the Department of Psychiatry technical and ethics committee, permission was obtained from the Head of Department of Oncology & Radiotherapy, HUKM where the sample was eventually gathered. The principle investigator explained the rationale of the study to the patients and the patient's written informed consent was obtained.

Subjects were interviewed over a period of 43 weeks from October 2000 till July 2001. Follow-up assessments were carried out at 6-months and between 12 to 26 months later. All subjects above 18 years of age who were aware of the diagnosis of cancer within three months prior to the interview and who were treatment naive (not undergone any form of treatment whatsoever) were included in the sample. Subjects excluded were patients with cancer of the oral cavity and adrenal glands since their treatment regimes are not standardized (as suggested by the Oncologist), organic brain syndromes, debilitating illness, previous psychiatric diagnosis, mental retardation and benign conditions.

During the first assessment participants were interviewed face to face using structured questionnaires that included demographic (i.e. age, gender, race/ethnicity, religion, marital status, occupation, and education level) and cancer characteristics (i.e. type of cancer and staging).

In addition three self-report instruments namely The Hospital Anxiety and Depression Scale (HADS) developed by Zigmond and Snaith[14], Medical Outcomes Study Short-Form General Health Survey (MOS-SF) developed by Stewart *et al*[15] (1988) and Coping Inventory for Stressful Situations (CISS) developed by Endler & Parker[16] (1990) were used to assess the subjects' psychological distress, Quality of life (QOL) and coping styles respectively. These three instruments were re-administered during the follow-up assessments.

Psychological distress was measured using the HADS. This is a brief assessment of anxiety and depression, consisting of 14 items divided equally into two subscales for anxiety (7 items) and depression (7 items). Individual items are scored from 0-3 to 3-0, depending on the direction of the item wording. The higher scores indicate the presence of problems. Using psychiatric diagnoses as a gold standard, HADS depression ratings of 7 or less were considered to be non-cases; scores of 8-10 were considered doubtful or borderline cases and scores of 11+ implies definite cases. The cut of point for a 'case' may be either the upper or the lower end of the borderline range. In this study, the researcher included all possible cases and hence, the lower end of borderline (score of 8 for each subscale) was used.

Quality of Life (QOL) was measured by means of the Medical Outcomes Study Short-Form General Health Survey (MOS-SF) questionnaire. This short 20-item instrument assessed six aspects of health i.e. physical functioning (PF), role functioning (RF), social functioning (SF), mental health (MH), health perception (HP) and pain (P). Physical functioning refers to limitations in a variety of physical activities. Role and social functioning are defined as limitations pertaining to health problems. Mental health is assessed in terms of psychological distress and well-being. Health perception is assessed by the patients' perception of their own health in general. Pain refers to differences in physical comfort. PF is composed of six items (Items 3, 4, 5, 6, 7, 8). The RF is a two-item scale (Items 9, 10). MH is composed of five items (Items 12, 13, 14, 15, 16). HP also has five items (Items 1, 17, 18, 19, 20). The other subscales are single-item indices. Item scores for each response are coded and displayed in parentheses. The pain and social functioning subscales have a possible score range of 1-6. These single item measures were scored so that high score represent better social functioning and more pain. The role functioning subscale has a possible score range of 0-6 and physical functioning subscale has a possible score range of 1-18. A high value signifies better functioning. The mental health subscale has a possible score range of 1-30 while the health perception subscale has a possible score range of 1-25 and both scales were scored by adding the item responses so that a high scores indicated better health. The total health perception score was obtained by summing all subscale scores for a possible score range of 0-91.

The CISS is a self-report measure measuring the subjects coping strategies. It comprised 48 items which are divided into three main coping mechanisms i.e. 16 items assesses task-oriented coping, 16 items assesses emotion-oriented coping and 16 items assesses avoidance-oriented coping. The avoidance-oriented scale is further subdivided into 2 subscales: distraction (8 items) and social diversion (5 items). The respondents were asked to indicate how much they engage in the types of activities when they encounter a difficult, stressful or upsetting situation by circling a number from 1 (not at all) to 5 (very much). The raw scores of the CISS are obtained by summing up the scores for the three main coping scales (Task, Emotion and Avoidance) plus the 2 Avoidance subscales (Distraction and Social Diversion). The raw scores are then entered into the appropriate column in the profile form which will give the corresponding T-scores and percentiles. The higher the test scores for any one of the 5 subscales the greater the degree of coping activity for the person on the corresponding coping dimensions. The T-scores have a mean of 50 and standard deviation of 10 and scores between 40-60 are considered average while those below 40 as below average and those above 60 as above average.

The instruments were translated into Malay. Several revisions and back-translations were done to ensure that the translation was a fair one. The HADS has been validated and used previously in other studies[17]. However, to the authors' knowledge presently the translated version of MOS-SF and CISS has not been used in the local context.

The instruments were translated into Bahasa Malaysia. Several revisions and back-translations were done to ensure that the translation was a fair one. The HADS has been validated and used previously in other studies[17]. However, to the authors' current knowledge the translated versions of MOS-SF and CISS have not been used in the local context.

All data were analysed using the Statistical Package for Social Sciences (SPSS) version 10 computer program[18].

The length of survival was calculated from the distribution of the questionnaires to the patient's death or to 31st December 2002. Bivariate analyses of survival were based on the Kaplan-Meier product-limit estimates of the distribution[19] (using the non-parametric log-rank test[20]). Firstly the individual effects of the psychosocial and cancer characteristic variables were tested. Subsequently, the Cox proportional hazards regression model[21] was used to determine the association between the psychosocial variables, cancer characteristics and survival adjusted for multiple covariates. Psychosocial and cancer characteristics variables that proved significant in the bivariate tests (such as mental health, gender and stage of the disease) and other variables that deemed to affect predictors of survival based on literature (such as age, occupational status, education level, type of cancer, anxiety, depression total QOL and coping styles) were simultaneously entered into the Cox regression model. A p-value of less than 0.05 was taken as statistically significant.

RESULTS

A total of 221 new cases were referred to the Oncology unit during the study period i.e. October 2000 to July 2001 (i.e. 43 weeks). Follow-up assessments were carried out at 6-months and 12 to 26 months later. Twenty three (23) of these refused to participate in the study. Hence, the response rate was 89.6%. After the exclusion criteria a final cohort of 80 subjects were recruited. Three (3) subjects dropped out at the end of the study.

The overall survival period of the cohort was calculated as of 31st December 2002 which took into account all subjects since baseline. For this, the deceased group obviously comprised all who had expired during the study period due to cancer and its complications which numbered 31 while the censored patients consisted of 49 subjects. For the purpose of analysis, data obtained at 0 month was used.

There were no significant differences in psychological distress, QOL or coping scales seen in the cohort based on bivariate analysis at baseline and 6 months later.

Table I shows the socio-demography and cancer characteristics of the 80 subjects. The results showed that majority were in the age group of 40-49, female, Malay, married, employed, educated till SPM level, having female breast cancer and in stage 2 of the disease.

Table II represents the mean scores of the various scales and subscales used at baseline. The mean anxiety score (8.20) was higher than depression score (6.48). Subjects had the highest mean score of 20.20 for mental health while the lowest mean score of 3.29 for pain subscales. Moreover, the mean score was highest among subjects using avoidance subscales (56.73), followed by distraction (55.89), social diversion (54.44), emotion (50.74) and task subscales (48.11).

Table III illustrates the frequency distribution of the study variables by patient outcome status in type and stage of cancer showing significant difference between survivors and deceased. Pertaining to individual cancer group, it was noted that the percentage of deceased was highest with unclassified (100.0%), followed by lung and mediastinal (85.7%), genitourinary (75.0%), hematological (66.7%), bone and soft tissue (60.0%), head and neck (55.6%), skin (50.0%), gastrointestinal (47.1%), gynecological (28.6), female breast (5.3%), endocrine (0.0%) as well as neurological (0.0%) cancers respectively. In addition the proportion of deceased was also highest with stage 4 malignancies (84.2%), gradually declining with early stages of the disease.

Table IV reveals the final model of the multivariate analysis of survival. It shows that stage four cancer disease; gastro intestinal tract, head and neck, neurological, gynaecological, bone and soft tissue malignancies as well as depression were independent and statistically significant prognostic factor of survival during the study period.

Furthermore the model demonstrates (based on Relative Risk) that depressed patients were four times at risk of dying when compared to non-depressed subjects. It was also noted that stage 4 cancer patients were almost five times at risk of dying when compared to Stage I cancer patients.

The final model also shows that patients with neurological, gynaecological, head and neck, bone and soft tissue and gastro intestinal tract malignancies were almost 36, 26, 22,16 and seven times respectively at risk of dying during the study period when compared to patients with genitourinary cancers.

Table I: Frequency distribution of patient by socio-demography and cancer characteristics at baseline

Variable (n=80)		n	%
Age groups (years)	10-19	2	2.5
	20-29	8	10.0
	30-39	11	13.8
	40-49	26	32.5
	50-59	16	20.0
	60-69	14	17.5
	70-79	3	3.7
Gender	Male	43	46.2
	Female	37	53.8
Ethnicity	Malay	51	63.8
	Chinese	24	30.0
	Indian	5	6.2
Marital status	Married	58	72.5
	Unmarried/ Divorced/ Widowed	22	27.5
Occupational status	Employed	38	47.5
	Unemployed	25	31.3
	Pensioner	17	21.2
Educational level	No education	3	3.7
	Primary education	16	20.0
	Secondary education till SRP or Lower Certificate of Education	10	12.5
	Secondary education till SPM or GCE-O Level equivalent	29	36.3
	Tertiary education	22	27.5
Type of cancer	Female breast	20	25.0
	Unclassified	1	1.0
	Neurological	1	1.0
	Endocrine	2	3.0
	Haematological	3	4.0
	Skin	2	3.0
	Bone & soft tissue	5	6.0
	Gynaecological	8	10.0
	Gastro Intestinal Tract	17	21.0
	Lung & Mediastinal	8	10.0
	Head & Neck	9	11.0
	Genitourinary	4	5.0
Stage of cancer (n = 78)#	Stage 1	23	29.5
	Stage 2	25	32.1
	Stage 3	10	12.8
	Stage 4	20	25.6

Two subjects who had no proper staging system universally accepted were excluded i.e. acute lymphatic leukemia and multiple myeloma respectively

Table II: Mean HADS, MOS-SF and CISS score for the various scales and subscales among subjects at baseline

Scales	Sub-scales	Mean	SD
HADS	Anxiety	8.20	4.238
	Depression	6.48	4.483
MOS-SF	Physical functioning	14.03	3.166
	Role functioning	4.29	1.171
	Social functioning	3.93	1.613
	Mental health	20.20	2.757
	Health perception	14.30	2.735
	Pain	3.29	1.116
	Total QOL	60.15	5.966
CISS	Task	48.11	13.252
	Emotion	50.74	10.416
	Avoidance	56.73	10.988
	Distraction	55.89	10.009
	Social diversion	54.44	10.811

Table III: Frequency distribution of patient outcome status by type of cancer and stage of cancer at the end of the study

Variable (n=77)	Survivor group No. (%)*	Deceased group No. (%)*	Total No. (%)*	p-value
Type of cancer				
Female breast	18 (94.7)	1 (5.3)	19(100.0)	< 0.005
Others	27 (46.6)	31 (53.4)	58(100.0)	
Stage of cancer (n = 75)#				
Stage 1	19 (82.6)	4 (17.4)	23(100.0)	< 0.005
Stage 2	19 (79.2)	5 (20.8)	24(100.0)	
Stage 3	4 (44.4)	5 (55.6)	9(100.0)	
Stage 4	3 (15.8)	16 (84.2)	19(100.0)	

* Numbers in parenthesis are percentages in columns
# Two subjects who had no proper staging system universally accepted were excluded i.e. acute lymphatic leukemia and multiple myeloma respectively

Table IV: Multivariate Analysis of Survival by Cox Regression Analysis (n = 78*)

VARIABLES		B	SE	Wald	df	p-value	Exp (B)
Gender		-0.624	0.666	0.876	1	0.349	0.536
Age		-0.304	0.443	0.471	1	0.493	0.738
Occupational status		0.728	0.426	2.925	1	0.087	2.072
Educational level		-0.112	0.401	0.078	1	0.780	0.894
Stage of cancer (overall)				8.765	3	0.033	
Stage of cancer (comparing with stage 1)	Stage 2	-0.080	0.461	0.030	1	0.863	0.923
	Stage 3	-0.367	0.545	0.454	1	0.501	0.693
	Stage 4	1.582	0.658	5.777	1	0.016**	4.867**
Type of cancer (overall)				15.469	11	0.162	
Type of cancer (comparing with genitourinary)	Lung & Mediastinal	2.085	1.073	3.772	1	0.052	8.044
	Gastro Intestinal Tract	1.995	0.973	4.202	1	0.040**	7.354**
	Female Breast	1.839	1.064	2.985	1	0.084	6.289
	Head & Neck	3.106	1.215	6.535	1	0.011**	22.332**
	Gynaecological	3.241	1.160	7.806	1	0.005**	25.563**
	Bone & soft tissue	2.782	1.280	4.723	1	0.030**	16.152**
	Skin	2.819	1.479	3.632	1	0.057	16.762
	Others	2.825	1.453	3.781	1	0.052	16.857
	Neurological	3.594	1.674	4.611	1	0.032	36.375**
	Hematological	3.197	1.677	3.634	1	0.057	24.467
	Endocrine	0.995	1.400	0.505	1	0.477	2.704
Psychological distress	Anxiety	-0.757	0.404	3.508	1	0.061	0.469
	Depression	1.462	0.450	10.576	1	0.001**	4.314**
Quality of life subscales	Physical functioning	0.612	0.422	2.102	1	0.147	1.845
	Role functioning	-1.017	0.431	5.564	1	0.085	0.362
	Social functioning	-0.121	0.384	0.099	1	0.753	0.886
	Mental health	-0.071	0.370	0.037	1	0.848	0.932
	Health perception	-0.073	0.379	0.037	1	0.847	0.929
	Pain	-0.662	0.402	2.702	1	0.100	0.516
Total quality of life		-0.097	0.367	0.071	1	0.791	0.907
Coping styles	Task	0.284	0.465	0.372	1	0.542	1.328
	Emotion	-0.405	0.463	0.767	1	0.381	0.667
	Avoidance	0.409	0.925	0.195	1	0.658	1.505
	Distraction	-0.470	0.775	0.367	1	0.545	0.625
	Social diversion	0.230	0.636	0.130	1	0.718	1.258

*Analysis excluded two subjects (acute lymphatic leukemia and multiple myeloma) who had no proper staging system universally accepted
Exp (B) denotes RR (relative risk). **RR significant at 0.05 level

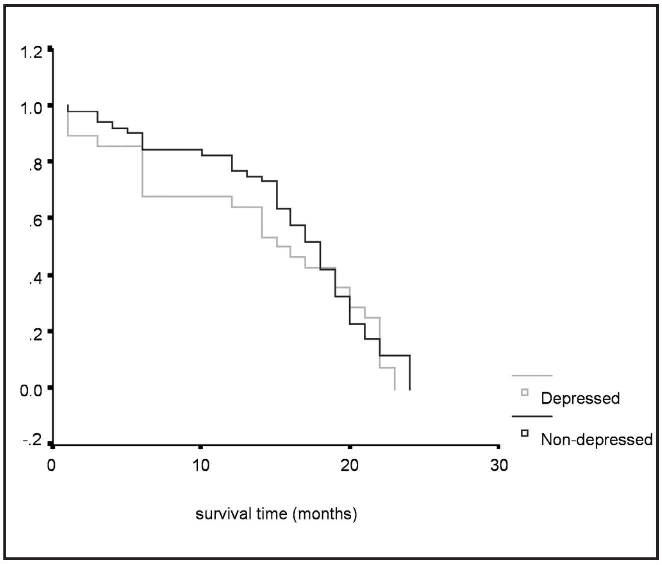

Fig. 1: Kaplan-Meier cumulative curves between depressed and non-depressed patients at baseline evaluated during 3rd assessment. There was no significant association in the plot of survival probability (p = 0.4468), although there was a tendency for better survival among non-depressed subjects when compared to depressed subjects

DISCUSSION

The main strength of this study was its prospective nature. It started prior to the onset of treatment and as a consequence assured that the psychological events evaluated were not affected by previous treatment.

An interesting observation this study provided in the multivariate model was the independent and significant statistical prognostic factor of survival for depression (p = 0.001), stage 4 cancer disease (p = 0.0016), gastro intestinal tract (p = 0.040), head & neck (p = 0.011), neurological (p = 0.032), gynaecological (p = 0.005), bone and soft tissue malignancies (p = 0.030). However, there were no significant differences seen in the cohort based on bivariate analysis at baseline and six months later. Since the Cox model took into account multiple covariates concurrently, it is quite evident that many confounders were operating which were masking associations that were real and thus produced a spurious relationship in the bivariate analysis.

Based on relative risk (RR), the model further illustrated that depressed subjects when compared to non-depressed subjects had an almost four fold (RR = 4.314) greater risk of dying during the study period. This was similar to the findings of Loberiza *et al*[6] who also examined prospectively the relationship of depression and survival after haematopoietic stem-cell transplantation in 193 patients between 6 and 12 months after similarly controlling for covariates by the Cox proportional hazards regression model and found that depressed as compared to non-depressed individuals had a three fold higher risk of dying. In this study there was no standardized measure of depression although it was defined as being present in any person who reported being bothered by depression and who had four or more of the following symptoms (anxiety, difficulty concentrating, feelings of isolation, fatigue or loss of memory). Furthermore, Watson *et al*[5] also looking at homogenous population of breast cancer subjects came to a similar deduction.

In contrast, Derogatis *et al*[3] assessed 35 women with metastatic breast cancer and showed that long-term survivors (subjects who lived for one year or more) reported more symptoms such as depression, guilt and anxiety while those who died less than one year (short-term survivors) were less symptomatic. The short-term survivors demonstrated significant lower levels of hostility and higher level of positive mood. It should be noted that their patients, suffered from predominantly more advanced disease in addition to having a much smaller sample size (n = 35) when compared to this study (n = 80). Furthermore, it is acknowledged widely that women have higher prevalence of depressive disorder[22]. Consequently, to start with their subject selection was already biased since it included only females and hence would spuriously report higher level of depression. Therefore, the study by Derogatis *et al*[3] should be interpreted with caution.

The findings from this study have important clinical implications. A multi-disciplinary team approach to the management of these individuals was vital in order to treat them adequately and effectively. Fort Lauderdale[23] quoted that "one of the challenges in implementing standards of care for psychosocial illness associated with cancer is removing the stigma linked with such a diagnosis". Hence with the aid of the National Comprehensive Cancer Network that is a coalition of 16 leading United States cancer center the term "distress" was preferred instead of "psychiatric" or "emotional" to avoid a negative connotation. As a consequence the patients are not embarrassed and thus, making it easier for the medical personnel to talk to them regarding their mental well-being in a comfortable and relaxed manner. She went on to recommend the multidisciplinary approach to manage cancer distress based on "distress thermometer" whereby two levels of categories were identified i.e. mild and moderate to severe. The primary team (e.g. oncologist, nurse, social worker or pastoral care-giver) could generally manage the former while the latter would be referred to the psychologist or psychiatrist. The current management of cancer at HUKM is generally in tandem with that of the United States. Regrettably, the term "distress" is not commonly used by medical personnel at HUKM. Certainly this could prevent more patients seeking further assistance due to the aforementioned stigma from the predominant use of the terms psychiatric or emotional. It is hoped that this would change in the future to ensure optimal and holistic management of cancer patients.

It should be emphasized that our study did not explain how depression worsens the outcome of the cancer but suffice to state that depression was a predictor. Neither could we confirm if depression was preceding the cancer.

This study was limited by the use of the HADS screening questionnaire which could not have revealed a true picture of the prevalence of depression in a given population. A diagnostic tool for depression would have certainly overcome this limitation. This was not carried out as the researchers felt that since they were following up the cases on three occasions, the cohort of predominantly out-patient subjects would have found it time-consuming and consequently would not have cooperated fully with the study. Thus, this could have influenced the study outcome.

CONCLUSION

Medical personnel need to be cognizant of the psychosocial aspects of the cancer patient (in addition to the biological factors) and make timely referral, if required, to ensure that the patient receives prompt, adequate and efficient treatment so as to improve their survival period. The current practice is that cancer patients are not routinely referred to a psychologist or a psychiatrist. This study indicates the need for future prospective studies to investigate the role of pharmacological and psychosocial interventions in improving survival of cancer patients.

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