Quality of Life among Patients with Brain Pathology in a Malaysian Hospital

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ABSTRACT

The objective of this study was to determine the prevalence of symptoms and problems in Malaysian brain pathology patients. A total of 100 respondents in Kuala Lumpur Hospital were included in this cross-sectional study. The study utilized European Organization for Research and Treatment of Cancer Quality Of Life questionnaire (EORTC QLQ-C30). Patient with a "symptom/problem" having the minimum response of "a little". A response of "quite a bit" was defined as having a "severe symptom/problem". The two most prevalent "symptoms/problems" among the neurological disorder patients were fatigue (65%; severe: 28%) and reduced cognitive functioning (64%; severe: 25%). The mean number of "symptoms/problems" ranged from 4.63 (meningioma) to 6.80 (cerebellar edema) while the mean number of "severe symptoms/problems" ranged from 1.39 (astrocytic glioma) to 2.8 (cerebellar edema). Therefore special attention should be given to these patients in order to improve the overall quality of life of the patients.

Keywords: Brain pathology, neurological disorder, quality of life, severity, symptomatology

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INTRODUCTION

The cancer incidence is 3.3 per 100,000 populations among brain and other nervous system disorders. This consists of male 3.6 and female 3.1 per 100,000 population in peninsular Malaysia (Omar et al., 2006). There are various forms of brain cancer which include malignant gliomas (34.6%), followed by medulloblastoma 11.3% and meningothelial tumours (3.1%) of all nervous system tumours in the year 2003 till 2005 in Peninsular Malaysia (Lim et al., 2008).

The main aim of brain tumour management was on tumour removal while the physician role was to develop state free of this disease. The quality of life of patients with brain disorder is often neglected and it leads to the deterioration of physical, emotional, and social functioning (Kim et al., 2016). The cancer patients appear to have poor quality of life even prior to their high dose chemotherapy treatment (Larsen et al., 2003). Study also reported that the cancer patients with various types of diagnoses showed variation in 'symptoms/problems' which impacted on their quality of life (Johnsen et al., 2009a; Johnsen et al., 2009b). Moreover the patients with metastasis stage found to have weak physical, psychosocial and poor quality of life (Yen et al., 2006). Therefore special attention should be given to the patient with poor quality of life to improve their overall curability of the disease.

A great deal of literature has been published from western data on other cancer patients (Brown et al., 2009; Costanzo et al., 2006; Distefano et al., 2008; Dodd et al., 2010; Mehnert et al., 2009; Mystakidou et al., 2005; Okamura et al., 2002; Oozeer et al., 2006; Reid-Arndt et al., 2009; Reimer et al., 2006; Sampogna et al., 2009; Zenger et al., 2009). According to what we know so far, there are limited published articles concerning the quality of life specifically for Malaysians brain pathology patients. Thus, the main aim of this study was to evaluate the quality of life in the patients with brain pathology in a referral centre in Malaysia.

MATERIALS AND METHODS

The study was done at Hospital Kuala Lumpur (HKL), a referral centre for neurological disorder cases. All the patients who visits neurosurgery clinic between (April 2016 to December 2016) with neurological disorder during the sampling period and fulfilled the inclusion criteria were included in the study.

The study respondents were selected following these criteria. First, the respondent must be with brain pathology. Second, the age of participant must be at least 18 years. Second, the participants should be able to well-versed in Malay, English, Mandarin or Tamil. Finally, the participant must be conscious and able to respond to our questionnaire.

The EORTC-QOL-30 questionnaire has been pre-tested and validated. This disease-specific questionnaire is used to evaluate the quality of life of cancer patients. The

questionnaire comprised of four languages including English, Malay, Mandarin and Tamil, was used in the study (Aaronson et al., 1993; Mustapa and Yian, 2007). The Malay version had been validated among Malaysian cancer patients and it has internal consistencies for Global Health Status (0.91), Functional domains (0.50-0.89) and Symptoms domains (0.75-0.99) and the sensitivity of the scale found in all the domains (Na et al., 2014).

The participants were excluded from the study if the patient wanted to withdraw from the study, mentally disabled, not able to be interviewed or required immediate treatment.

This study used European Organization for Research and Treatment of Cancer Quality Of Life (EORTC QLQ-C30) likert scale format questionnaire, version 3.0. The consent was obtained from the patient before the questionnaires were distributed. Information such as socio-demographic profiles and clinical status were assessed from the patients and medical records.

All the scales ranged from 1 to 4 except for the global health status scale points with the scale from 1 to 7 (Aaronson et al., 1993). The questionnaire was divided into functioning scales, symptoms scales and global health status scale. The functioning scale comprised physical, role, cognitive, emotional and social domains. The symptoms scale consisted of fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties. The linear transformation was done referring to the EORTC scoring manual and all scores ranged from 0 to 100. A higher score indicates better functioning and good global health statuses. Conversely higher score for the symptom scale indicates more symptoms among the patients (Fayers et al., 2001).

The questionnaire did not have any cut-off points or defined thresholds to interpret functioning and symptom score as a case. Thus the percentage of frequencies of "symptoms/problems" and the frequencies of "severe symptoms/problems" were computed by referring to previous study methodology. Patient with a symptom/problem having the minimum response of "a little" and had function scale scores ≤ 67 and symptoms scale scores ≥33. While a response of "quite a bit" was defined as having a "severe symptom/problem" had function scale scores ≤34 and symptoms scale scores ≥ 66. The explanation of this method is shown in Figure 1 (Johnsen et al., 2009b). The number of "symptom/problem" and "severe symptom/problem" answers were determined for each person ranging from 0 to 14. The global health status scale was removed from this method, thus leaving 14 scales in total.

Statistical Package for Social Sciences (SPSS) program version 22.0 was used to analyze the data in this study. Descriptive statistics including mean, percentages and ranges were used to describe the sample characteristics.

Ethical clearance approval was sought from Human Research Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/16050178) and Medical Research & Ethics Committee (MREC) at the Ministry of Health (MOH) (NMRR-16-1134-29874 (IIR).
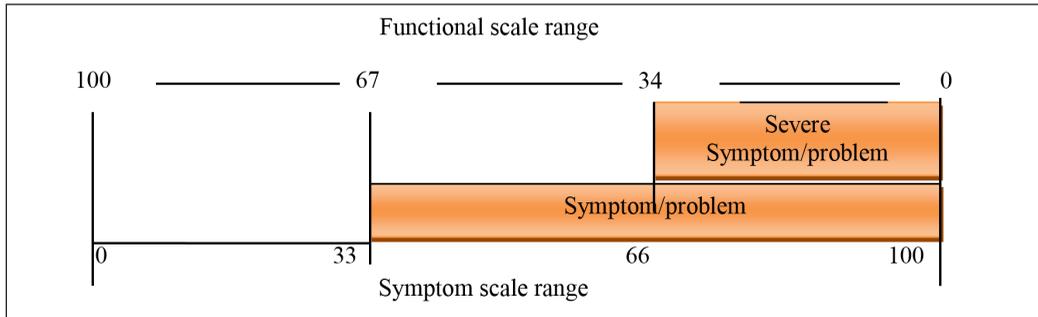
Figure 1. Illustration of the definition of 'symptom/problem' and 'severe symptom/problem'
Source: Johnsen et al., 2009b

RESULTS

The study had a response rate of 93.5%. The mean age of the respondents was 45.3 years (95% CI= 42.6, 47.9). Tables 1 and 2 shows the socio demographic profiles and clinical characteristics of the respondents respectively. Patients with brain pathology with majority of brain tumour patients were included in the study. The neurological disorders patients in the Table 2 defined as patients who was shown with brain tumour in the Magnetic resonance imaging (MRI) report but had not been confirmed in the biopsy results. The majority of the patients underwent surgery.

Table 1
Socio-demographic characteristics of neurological disorder respondents in HKL (n=100)

Characteristics	n	Percentage %)
Age (year)		
18-20	2	2.0
21-30	15	15.0
31-40	21	21.0
41-50	25	25.0
51-60	21	21.0
61-70	15	15.0
71	1	1.0
Gender		
Female	66	66.0
Male	34	34.0
Ethnicity		
Malay	78	78.0
Chinese	12	12.0
Indian	9	9.0
Others	1	1.0

Table 1 *(continue)*

Characteristics	n	Percentage %)
Religion		
Muslim	78	78.0
Buddhist	11	11.0
Hindu	7	7.0
Christian	3	3.0
Others	1	1.0
Marital status		
Single	24	24.0
Married	74	74.0
Widowed	1	1.0
Divorced	1	1.0
Children		
Yes	68	68.0
No	32	32.0
Highest level of formal education		
Primary	13	13.0
Secondary	48	48.0
College/University	38	38.0
No education	1	1.0
Highest certificate		
Primary School Evaluation Test (UPSR/PSET)	12	12.0
Lower Certificate of Education (PMR/SRP/LCE)	14	14.0
Malaysian Certificate of Education (SPM/SPMV/MCE)	29	29.0
Malaysian Higher School Certificate (STPM/HSC)	3	3.0
Certificate/Diploma	20	20.0
Degree	18	18.0
Master	3	3.0
No education	1	1.0
Occupation status		
Working	55	55.0
Not working	45	45.0
Working sector		
Government	21	21.0
Non government	31	31.0
Self employment	1	1.0
Not working	45	45.0
Semi goverment	2	2.0
Total monthly income household (RM)		
0-3000	53	53.0
3001-6000	13	13.0
6001-9000	8	8.0
>9001	4	4.0
others	22	22.0

Table 2
Clinical characteristic of brain disorder respondents in HKL

Characteristics	n	Percentage (%)
Year of diagnosis (n=92)		
2015-2016	34	34.0
2013-2014	17	17.0
2011-2012	11	11.0
2009-2010	6	6.0
2007-2008	7	7.0
2005-2006	3	3.0
<2005	14	14.0
Neurological disorders (n=100)		
Astrocytic glioma	13	13.0
Meningioma	19	19.0
Pituitary adenoma	15	15.0
Carvenoma	7	7.0
Schwanoma	5	5.0
Craniopharyngioma	3	3.0
Ethmoid	1	1.0
Frontal lobe tumour	1	1.0
Fibrosarcoma	1	1.0
Cerebellar edema	4	4.0
Germinoma	1	1.0
Hemorragic brain	3	3.0
Metastatic carcinoma	1	1.0
Brain lession	2	2.0
Mucopyocele	1	1.0
Aneurysm	1	1.0
Hydrocephalus	3	3.0
Unclassified neurological disorders	19	19.0
Treatment(n=70)		
Pharmacological medication group	27	27.0
Surgery group	38	38.0
Radiotherapy group	6	6.0

Table 3 shows the mean score of five multi-item function scales. The most severe impairment in functioning was the cognitive functioning (mean score=61). The cut-off value, indicates that 63% of brain pathology patients had impairment in their cognitive functioning (severity= 25%). Another leading symptom and problem among the patients was fatigue (severity=28%) which affected 65% of the patients.

Thirty-six percent of the patients had impairment in their physical functioning (severity=5%), followed 44% of the patients with impaired role functioning (severity=2%). Social functioning was impaired in 26% of patients (severity= 9%). In the symptoms

Table 3
Mean score and prevalence for the total sample and by diagnosis of brain disorders

Diagnosis		PF	RF	EF	CF	SF	QOL	FA	NV	PA	DY	SL	AP	CO	DI	FI	Mean No symptom	Mean No severe symptom
Total N=100	Mean score	74.2	78.33	67.08	61.16	82.33	59.92	44.89	11.67	29.33	10.00	29.67	17.00	12.67	4.67	34.00	5.22	2.10
	(SD)	(23.45)	(22.41)	(27.56)	(30.71)	(27.61)	(22.02)	(31.10)	(23.98)	(30.16)	(21.97)	(39.04)	(32.31)	(25.85)	(14.23)	(39.92)		
	%symptoms	36.0	44.0	50.0	63.0	26.0		65.0	15.0	47.0	20.0	43.0	26.0	24.0	12.0	51.0		
	%severe	5.0	2.0	19.0	25.0	9.0		28.0	7.0	20.0	9.0	29.0	16.0	10.0	1.0	30.0		
Astrocytic glioma N=13	Mean score	75.38	80.77	64.74	53.13	88.46	63.46	45.30	5.13	24.36	10.26	12.82	17.95	5.13	0.00	20.51	4.85	1.39
	(SD)	(23.32)	(17.80)	(22.86)	(34.95)	(15.79)	(24.89)	(29.90)	(8.00)	(21.10)	(21.01)	(25.60)	(32.25)	(18.49)		(32.03)		
	%symptoms	38.5	46.2	61.5	76.9	15.4		76.9	0	46.2	23.1	23.1	30.8	7.7	0	38.5		
	%severe	0	0	15.4	30.8	0		30.8	0	0	7.7	15.4	15.4	7.7	0	15.4		
Meningioma N=19	Mean score	76.14	85.09	74.56	72.81	97.37	63.16	39.77	6.14	31.58	8.77	49.12	3.51	15.79	5.26	24.56	4.63	1.58
	(SD)	(20.40)	(17.48)	(25.23)	(28.44)	(8.36)	(17.64)	(29.93)	(11.40)	(25.39)	(18.73)	(43.56)	(10.51)	(34.01)	(12.49)	(36.59)		
	%symptoms	36.8	26.3	42.1	47.4	5.3		57.9	10.5	63.2	21.1	63.2	10.5	21.1	15.8	42.1		
	%severe	0	0	15.8	15.8	0		21.1	0	15.8	5.3	52.6	0	15.8	0	15.8		
Pituitary adenoma N=15	Mean score	69.78	74.44	61.11	48.89	78.89	67.22	46.67	13.33	30.00	8.89	26.67	33.33	15.56	2.22	35.56	5.67	2.73
	(SD)	(23.89)	(22.60)	(32.83)	(31.16)	(22.24)	(22.15)	(34.68)	(22.89)	(32.85)	(19.79)	(36.08)	(43.64)	(24.77)	(8.61)	(40.76)		
	%symptom	33.3	46.7	53.3	86.7	40.0		66.7	20.0	46.7	20.0	20.0	40.0	33.3	6.7	53.3		
	%severe	6.7	0.0	33.3	26.7	0.0		33.3	6.7	26.7	6.7	46.7	40.0	13.3	0.0	33.3		
Carvenoma N=7	Mean score	89.52	85.71	84.52	59.52	80.95	69.05	39.68	19.05	33.33	4.76	23.81	23.81	9.52	4.76	14.29	4.57	1.57
	(SD)	(16.71)	(15.00)	(20.65)	(25.20)	(24.40)	(21.90)	(33.25)	(37.80)	(28.87)	(12.60)	(25.20)	(41.79)	(16.27)	(12.60)	(26.23)		
	%symptom	14.3	28.6	28.6	71.4	28.6		42.9	28.6	42.9	14.3	57.1	28.6	28.6	14.3	28.6		
	%severity	0	0	0	28.6	14.3		28.6	14.3	14.3	0	14.3	28.6	0	0	14.3		
Schwanoma N=5	Mean score	81.33	76.67	55.00	53.33	80.00	50	44.44	6.67	30.00	6.67	20.00	20.00	13.33	0.00	60.00	5.00	2.40
	(SD)	(11.93)	(22.36)	(36.13)	(39.79)	(44.72)	(31.18)	(36.85)	(9.13)	(44.72)	(14.91)	(44.72)	(44.72)	(29.81)	(0.00)	(43.36)		
	%symptom	20.0	60.0	20.0	60.0	20.0		60.0	0.0	40.0	20.0	20.0	20.0	20.0	0	80.0		
	%severe	0	0	20.0	40.0	20.0		20.0	0.0	20.0	0.0	20.0	20.0	20.0	0.0	60.0		
Cerebellar edema N=4	Mean score	68.33	66.67	64.58	62.50	54.17	60.42	58.33	8.33	37.50	8.33	50.00	0	33.33	8.33	41.67	6.80	2.80
	(SD)	(26.32)	(23.57)	(29.17)	(47.87)	(41.67)	(27.53)	(33.18)	(16.67)	(43.83)	(16.67)	(57.74)	0	(47.14)	(16.67)	(41.94)		
	%symptom	50.0	75.0	50.0	50.0	75.0		75.0	25.0	50.0	25.0	50.0	0	50.0	25.0	75.0		
	%severe	0.0	0.0	25.0	25.0	25.0		50.0	0.0	50.0	0.0	50.0	0	25.0	0.0	25.0		
Other neurological disorder N=19	Mean score	68.07	66.67	60.96	57.89	76.32	54.39	49.12	14.91	30.70	15.79	28.07	14.04	10.53	7.02	43.86	5.63	2.69
	(SD)	(26.44)	(27.22)	(29.14)	(26.28)	(37.40)	(26.70)	(35.20)	(33.75)	(36.12)	(28.04)	(41.96)	(30.05)	(24.98)	(23.78)	(44.52)		
	%symptom	47.4	68.4	52.6	68.4	26.3		68.4	15.8	42.1	26.3	36.8	21.1	21.1	10.5	57.9		
	%severe	10.5	5.3	21.1	21.1	15.8		31.6	15.8	31.6	21.1	26.3	15.8	5.3	5.3	42.1		

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.
% symptoms, proportion of patients scoring 67 at the most for function scales or at least 33 for symptoms
% severe symptoms, proportion of patients scoring 34 at the most for function scales or at least 66 for symptoms.
No. of "symptoms", mean number of symptoms using the same cut-off point as in "% symptom" (quality of life excluded)
No. of "severe symptoms", mean number of symptoms using the same cut-off point as in "% severe symptom" (quality of life excluded)

counterparts, the most severe symptom was fatigue (mean score =44.89), followed by financial difficulties (mean score=34), insomnia (mean score=29.67), pain (mean score=29.33), appetite loss (mean score=17), constipation (mean score=12.67), nausea and vomiting (mean score=11.67), dyspnea (mean score=10) and diarrhea (mean score=4.67). Using the cut-off values, 65% of the patients had fatigue (severity 28%), 51% had financial difficulties (severity=30%), 47% had pain (severity=20%), 43% had insomnia (severity=29%), 26% had appetite loss (severity=16%), 24% had constipation (severity=10%), 15% had nausea and vomiting (severity=7%), 20% had dyspnea (severity=9%) and 12% had diarrhea (severity=1%).

In the study, the mean number of "symptoms/problems" was 5.22 while the mean number of "severe symptoms/problems" was 2.10. Overall, the cerebellar edema patients had the most symptoms and problems with a mean number of 6.80. The mean number of "symptoms/problems" ranged from 4.63 (meningioma) to 6.80 (cerebellar edema); the mean number of "severe symptoms/problems" ranged from 1.39 (astrocytic glioma) to 2.8 (cerebellar edema). Most shockingly, the study found 90% of the patients had at least one "symptom/problem".

DISCUSSION

The present study was aimed to determine the symptoms and problems affecting the quality of life of brain pathology patients. The study showed that the symptoms and problems were frequent among the patients. The cut-off value, indicates that 63% of the patients had impairment in cognitive functioning (severity = 25%). This finding is in agreement with previous case control studies, which found the patients with brain tumour had more cognitive impairment compared to healthy patients. The study not only demonstrated that the patients suffered more in cognitive impairment compared to healthy adults but the cognitive functioning worsened after the surgery (Zarghi, 2014). In the previous study among Malaysians with primary intracranial tumor, a small number of patients (n=38) was included in the analyses. The patients were identified with reduced cognitive functioning, emotional functioning and global health status before the surgery compared to after the surgery. The patients also tended to have more fatigue and pain symptoms before the surgery (Ooi & Mazlina, 2013).

In the current study also found the most severe symptom was fatigue which had the highest mean score followed by financial difficulties, insomnia and pain. This defined 65% of the patients had fatigue (severity=28%), financial difficulties (51%; severity: 30%), pain (47; severity=20) and insomnia (43%; severity=29%). The current study found 90% of all brain pathology patients having at least one "symptoms/ problems". Similarly in a

study done by Johnsen et al (2009a) also reported that the cancer patients had higher mean scores on the symptom scale and experienced fatigue followed by pain and insomnia. Comparing the cancer patients in each domain, fatigue (55%), reduced role functioning (49%), insomnia (46%), pain (37%) and dyspnoea (36%) were identified in the study. The study found 82% of all cancer patients fulfilled the criteria of at least one 'symptoms/problems' in their quality of life. The functional scale of role and physical functioning were found to be severely impaired in the patients (Johnsen et al., 2009b). The patients with reduced global quality of life found to have poor physical, cognitive, social and role functioning and more appetite loss and financial difficulties (Kim et al., 2016). In another study it was shown the patients had elevated symptoms of fatigue, pain, sleep disturbance and depression and reported poor functional status and low quality of life (Dodd et al., 2010). The patients who were appeared to be more fearful of their disease relapse had much more reduced quality of life, specifically in their fatigue, financial difficulties, emotional functioning, and appetite domains (Franssen et al., 2009).

The cancer patients treatment modalities also lead to increased level of fatigue, poor appetite and physical functioning and reduced quality of life (Johnsen et al., 2009b). At the pre and post operative stage, the patients are mostly effected in their emotional functioning and dyspnea symptoms. The patients also having more symptoms of fatigue before the surgery (Kim et al., 2016). Therefore it is becoming increasingly difficult to ignore the patient's poor quality of life and more attention needs to be given together with supportive care in order to improve the overall curability of the patients (Ernstmann et al., 2009).

CONCLUSION

The study proved that the patients with brain pathology in referral centre in Malaysia caused significant impairment in the quality of life. The fatigue and reduced cognitive functioning were two leading symptoms and problems among the patients. There is a significant improvement in cancer management, however the overall treatment will remain poor if medical personnel does not apply a balanced pharmacotherapy and psychotherapy management in order to improve the patients' quality of life.

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REFERENCES

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., ... & Kaasa, S. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *JNCI: Journal of the National Cancer Institute, 85*(5), 365-376.

Brown, L. F., Kroenke, K., Theobald, D. E., Wu, J. & Tu, W. (2009). The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. *Psycho-Oncology, 19*(7), 734-741.

Costanzo, E. S., Lutgendorf, S. K., Rothrock, N. E., & Anderson, B. (2006). Coping and quality of life among women extensively treated for gynecologic cancer. *Psycho-Oncology, 15*(2), 132-142.

Distefano, M., Riccardi, S., Capelli, G., Costantini, B., Petrillo, M., Ricci, C., … & Ferrandina, G. (2008). Quality of life and psychological distress in locally advanced cervical cancer patients administered pre-operative chemoradiotherapy. *Gynecologic Oncology, 111*(1), 144-150.

Dodd, M. J., Cho, M. H., Cooper, B. A., & Miaskowski, C. (2010). The effect of symptom clusters on functional status and quality of life in women with breast cancer. *European Journal of Oncology Nursing: The OfficialJournal of European Oncology Nursing Society, 14*(2), 101-110.

Ernstmann, N., Neumann, M., Ommen, O., Galushko, M., Wirtz, M., Voltz, R., … & Pfaff, H. (2009). Determinants and implications of cancer patients' psychosocial needs. *Supportive Care in Cancer, 17*(11), 1417-1423.

Fayers, P. M. A. N., Aaronson, N., Bjordal, K., Groenvold, M., Curran, D., & Bottomley, A. (2001). *EORTC QLQ-C30 Scoring Manual* (3rd Ed.). Brussels, Belgium: European Organisation for Research and Treatment of Cancer Brussels.

Franssen, S. J., Lagarde, S. M., Van Werven, J. R., Smets, E. M. A., Tran, K. T. C., Plukker, J. T. M., … & De Haes, H. C. J. M. (2009). Psychological factors and preferences for communicating prognosis in esophageal cancer patients. *Psycho-Oncology, 18*(11), 1199-1207.

Johnsen, A., Petersen, M., Pedersen, L., & Groenvold, M. (2009a). Symptoms and problems in a nationally representative sample of advanced cancer patients. *Palliative Medicine, 23*(6), 491-501. doi: 10.1177/0269216309105400

Johnsen, A. T., Tholstrup, D., Petersen, M. A., Pedersen, L., & Groenvold, M. (2009b). Health related quality of life in a nationally representative sample of haematological patients. *European Journal of Haematology, 83*(2), 139-148.

Kim, C. W., Joo, J. D., Kim, Y. H., Han, J. H., & Kim, C. Y. (2016). Health-Related Quality of Life in Brain Tumor Patients Treated with Surgery: Preliminary Result of a Single Institution. *Brain Tumor Res Treat, 4*(2), 87-93. doi: 10.14791/btrt.2016.4.2.87 [doi]

Larsen, J., Nordström, G., Björkstrand, B., Ljungman, P., & Gardulf, A. (2003). Symptom distress, functional status and health-related quality of life before high-dose chemotherapy with stem-cell transplantation. *European Journal of Cancer Care, 12*(1), 71-80.

Lim, G., Rampal, S., & Halimah, Y. (2008). *Cancer incidence in Penisular Malaysia, 2003-2005*. Kuala Lumpur: National Cancer Registry.

Mehnert, A., Lehmann, C., Graefen, M., Huland, H., & Koch, U. (2009). Depression, anxiety, post-traumatic stress disorder and health-related quality of life and its association with social support in ambulatory prostate cancer patients. *European Journal of Cancer Care, 19*(6), 736-745.

Mustapa, N., & Yian, L. (2007). Pilot-testing the Malay version of the EORTC Questionnaire. *Singapore Nursing Journal, 34*(2), 16-20.

Mystakidou, K., Tsilika, E., Parpa, E., Katsouda, E., Galanos, A., & Vlahos, L. (2005). Assessment of Anxiety and Depression in Advanced Cancer Patients and their Relationship with Quality of Life. *Quality of Life Research, 14*(8), 1825-1833. doi: 10.1007/s11136-005-4324-3

Na, Y. W. L., & Chc, Y. (2014). The Malay Version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ C30): Reliability and Validity Study. *The International Medical Journal of Malaysia, 9*(2), 45-50.

Okamura, M., Yamawaki, S., Akechi, T., Taniguchi, K., & Uchitomi, Y. (2002). Psychiatric disorders following breast cancer recurrence: prevalence, associated factors and relationship to quality of life. *Japanese Journal of Clinical Oncology, 35*(6), 302-309.

Ooi, A. L., & Mazlina, M. (2013). Functional status and health-related quality of life in patients with primary intracranial tumour. *The Medical Journal of Malaysia, 68*(6), 448-452.

Omar, Z. A., Ali, Z. M., & Tamin, N. S. I. (2006). *Malaysian cancer statistics data and figure peninsular Malaysia 2006*. Retrieved July 01, 2016, from http://www.moh.gov.my/v/c_report?mode=public.

Oozeer, N. B., Paleri, V., Benbow, J., Downs, C., & Kelly, C. (2006). The effect of co-morbidity on quality of life in patients treated with radiotherapy for head and neck squamous cell cancer. *Clinical Otolaryngology, 31*(6), 583-583.

Reid-Arndt, S. A., Hsieh, C., & Perry, M. C. (2009). Neuropsychological functioning and quality of life during the first year after completing chemotherapy for breast cancer. *Psycho-Oncology, 19*(5), 535-544.

Reimer, J., Voigtlaender-Fleiss, A., Karow, A., Bornfeld, N., Esser, J., & Franke, G. H. (2006). The impact of diagnosis and plaque radiotherapy treatment of malignant choroidal melanoma on patients' quality of life. *Psycho-Oncology, 15*(12), 1077-1085.

Sampogna, F., Frontani, M., Baliva, G., Lombardo, G. A., Alvetreti, G., Di Pietro, C., … & Abeni, D. (2009). Quality of life and psychological distress in patients with cutaneous lymphoma. *The British Journal of Dermatology, 160*(4), 815-822.

Yen, J. Y., Ko, C. H., Yen, C. F., Yang, M. J., Wu, C. Y., Juan, C. H. & Hou, M. F. (2006). Quality of life, depression, and stress in breast cancer women outpatients receiving active therapy in Taiwan. *Psychiatry and Clinical Neurosciences, 60*(2), 147-153.

Zarghi, A. (2014). Assessment of Cognitive Impairments, Depression, Anxiety and Quality of Life among Brain Tumor Patients and Healthy Adults. *Neuroscience Journal, 1*(2), 55-60.

Zenger, M., Brix, C., Borowski, J., Stolzenburg, J. U., & Hinz, A. (2009). The impact of optimism on anxiety, depression and quality of life in urogenital cancer patients. *Psycho-Oncology, 19*(8), 879-886.