Abstract

Introduction: Although erectile dysfunction (ED) is one of known long-term complications among male lymphoma survivors, it is not commonly reported, particularly in Southeast Asia. This study aimed to determine the prevalence of ED in lymphoma survivors in Malaysia and its association with anxiety and depression, and effects on quality of life.

Methods: This was a cross-sectional study conducted at a tertiary hospital in Malaysia. Patients were all male lymphoma survivors. The self-administered International Index of Erectile Function questionnaire was used to screen for ED. The Hospital Anxiety and Depression Score questionnaire was used to assess for anxiety and depression, and quality of life was assessed using the European Organization for Research and Treatment of Cancer quality of life questionnaire.

Results: Overall, 106 patients were recruited. Mean age was 55.7 years, with 61.3% of patients aged above 50 years. Only 67.0% of patients were sexually active and 81.7% of these reported the presence of ED, with only 4.2% having severe ED. Prevalence of ED among younger patients (age ≤50 years old) was 64.5%. The most common reason given by patients who were not sexually active was fatigue. Age was the only factor found to be associated with ED (p <0.005) and severity of ED increased with age. There was no association between ED and psychological stress or quality of life.

Conclusion: Prevalence of ED and absence of sexual activity in lymphoma survivors was high. This should serve as a reminder to the treating clinician to offer early treatment and counselling.

Keywords: Erectile dysfunction, lymphoma survivors, prevalence, Southeast Asian

INTRODUCTION

Sexual problems in patients are usually neglected by the treating physician and more so in the Southeast Asian region. This is not surprising given that discussion on sexuality is generally regarded a taboo subject in the region. Although there is paucity of data on sexual problems in this region, its prevalence has been reported to be one of the highest. The impact of sexual dysfunction should not be underestimated, especially when it has been shown to be associated with anxiety and depression in the normal population, and patients with chronic illnesses and cancers. In addition, the negative effect of sexual problems on quality of life (QOL) is increasingly being recognised.

For men, the most common sexual problem reported is erectile dysfunction (ED). The prevalence of ED was reported to be as high as 27.3% and 75% in survivors of testicular and colorectal cancers, respectively. The effects of surgery, chemotherapy and radiotherapy have been demonstrated as some of the causes for the impairment of erectile function in men. In addition, the indirect effect, such as concomitant psychological stress associated with diagnosis of cancers, can also lead to reduced libido. Depression has been
consistently found to be associated with worse sexual function in these patients.\cite{6,9,10}

Sexual dysfunction in patients with haematological disorders, especially lymphomas, has been studied and it was reported that sexual function in this group of patients is compromised, although less so when compared to patients with testicular tumours.\cite{33} A qualitative study in Australia found that patients with haematological malignancy maybe acutely distressed about their sexuality and recommended close follow-up.\cite{14} A more recent study in Korea reported more significant associations between sexual problems and health-related quality of life (HRQOL) in male lymphoma survivors when compared to women.\cite{9}

Although there is increasing data on the prevalence and impact of sexual dysfunction in lymphoma patients, there is paucity of such information in Southeast Asian countries. This study aimed to determine the prevalence of ED in male lymphoma survivors in Malaysia and establish its association with anxiety and depression, as well as effects of ED on patients’ QOL. It was the intention that results of the study would create awareness among treating physicians to address sexual problems in lymphoma survivors.

**METHODS**

This was a cross-sectional study, where all adult male lymphoma survivors under follow-up with the adult haematology unit at a tertiary hospital in Malaysia were invited to participate. Patients were eligible if they were aged over 18 years, and remained in remission and required no active treatment for more than one year. The study was approved by the local institute ethics committee. Informed consent was obtained from all participants.

Patients who consented were provided with the International Index of Erectile Function (IIEF-5) questionnaire, which has been validated both internationally and locally for assessment of male erectile function and is available in three different languages.\cite{15} The IIEF-5 consists of five questions relating to a person’s sexual performance, and focuses on erectile function and intercourse satisfaction. It has a sensitivity and specificity of 0.98 and 0.88, respectively.\cite{16} The respondents were categorised into mild (score 17–21), moderate (score 8–16) and severe (score ≤ 7) ED. In this study, patients were further categorised to three groups: no ED; mild-moderate ED; and severe ED, for analysis.

The Hospital Anxiety and Depression Score (HADS) questionnaire is a well-established screening instrument for depression and anxiety in patients with cancer.\cite{17} It consists of 14 (seven on depression and seven on anxiety) items. A cut-off score ≥8 per subscale has been recommended as having the best sensitivity and specificity for identifying anxiety and depression. It has been validated in many studies in patients with cancer and is available in three languages (Bahasa Malaysia, Mandarin and English).\cite{18,19} Patients were provided the questionnaire according to their preferred language. There was no assistance provided to complete the questionnaire.

The HRQOL questionnaire used in this study was the European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30) version 3.0, which is a cancer-specific questionnaire.\cite{20,21} A linear transformation to a 0–100 scale of the EORTC QLQ-C30 version 3.0 questionnaire was carried out according to the EORTC scoring manual.\cite{22} High scores on the global and functional scales indicated good QOL. Low scores on the symptoms scales represented a less intense symptom experience.

Demographic data, such as age, ethnicity, education levels and concomitant medical illness, was included. Data collected was analysed using IBM SPSS Statistics version 25.0 (IBM Corp, Armonk, NY, USA). Biodemographic data was analysed using descriptive analysis. The association of ED with the biodemographic data was assessed using Chi-square test. The correlation between ED and anxiety/depression scores and QOL scores were measured using Spearman’s correlation. A \( P \) value <0.05 was considered to be statistically significant.

**RESULTS**

A total of 110 of 136 male lymphoma patients agreed to be interviewed. Three patients were excluded due to incomplete data and one was found to still have active disease. Mean age of patients was 55.7 (range 18–85) years. More than half (61.3%) of the patients were aged >50 years. 84.9% of patients were in a committed relationship and the remaining had no permanent partner. Sociodemographic and clinical characteristics of patients are listed in Table 1.

Approximately one-third (33.0%) of patients were not sexually active for at least six months before the time of interview. Among those who were sexually active, 81.7% reported the presence of ED. However, only 4.2% had severe ED. The prevalence of ED among younger patients (age ≤50 # years) was 64.5% whereas 93.0% of patients aged over 50 years had ED.

Table 2 shows the mean score of all QOL domains. Fatigue and financial difficulties scored highest in the symptoms scales. Age was the only factor found to be associated with ED and the severity of ED increased with age (\( p = 0.002 \)). Ethnicity, education level, types of treatment and duration of remission were not associated with ED. There was no association between the presence of ED and symptoms of anxiety or depression. QOL was also not found to be significantly associated with ED. Among patients who were not sexually active, the most common reason provided was ‘feeling too tired’ (57.6%) followed by ‘partners being too tired’ (21.2%) and ‘lack of interest in sex’ (15.2%) [Table 3].
DISCUSSION

Sexual dysfunction is common in cancer survivors and to the best of our knowledge, this is the first study that has focused on sexual dysfunction in male lymphoma survivors in Southeast Asia. According to a meta-analysis by Cheng et al., the overall prevalence of ED in the normal population in Asian countries was in the range 2%–81.8%, and in Malaysia, it was reported to be 22.4%–59%. In this study, the much higher prevalence of ED among lymphoma survivors in the country when compared to the normal population was worthy of note. The finding was consistent with other studies that have again illustrated the importance of evaluating sexual function in lymphoma survivors. When compared with testicular and colon cancer survivors, it would appear that the prevalence of ED was higher in our lymphoma survivors. It has been consistently shown to be one of the most important predictors for ED and the prevalence of ED increases with age. However, 64.5% of patients age 50 years and below in our study had some degree of ED. This was considerably higher when compared to normal Asian populations as well as studies from elsewhere. For instance, a recent study in Korea, with a similar patient population, found only 49.1% of non-Hodgkin lymphoma survivors had sexual problems. This relatively high rate of sexual problems in our male survivors warrants urgent attention. Further investigations, such as testosterone level, may be useful to determine whether abnormal hormone levels due to the effects of chemotherapy was a causative factor, as it has been reported that reduced testosterone and luteinising hormone levels are associated with reduced sexual function in lymphoma survivors.

There were no significant associations between ED and other variables, such as ethnicity, education level and comorbidities. Although educational levels and the presence of other medical illnesses, especially diabetes mellitus and cardiovascular diseases, have been shown to affect sexual function, we did not find any such significant association and this was likely due to the small sample size of our cohort. Ethnicity has not been shown to be a significant factor for sexual problems, as has been demonstrated in another study. Many studies have demonstrated that emotional stress, especially depression, affect sexual function in cancer survivors. However, we did not find any association of worse depression with ED in our group of patients. Similarly, we did not find any significant association of worse QOL in patients with ED, although other studies have reported otherwise. Physical health, and emotional and social functioning were some of the areas that were demonstrated to affect the sexual function of male lymphoma survivors. The lack of significant results in our study may be on account of our small patient population. Therefore, more elaborate studies, with larger sample sizes, are warranted to establish these associations.

It should be noted that approximately one-third of all male survivors in our study were not sexually active when compared to only 10% of healthy Malaysian men. 'Feeling tired' was the most commonly used reason for not engaging in sexual activities, and fatigue was also one of the most common symptoms reported. Sexual problems have been consistently shown to be more pronounced in patients with fatigue. In our study, there was no association found between other

**Table 1. Demographics and clinical characteristics of male lymphoma survivors (n=106)**

| Demographic                      | No. (%) |
|----------------------------------|---------|
| **Age group (yr)**               |         |
| 18-50                            | 41 (38.7) |
| >50                              | 65 (61.3) |
| **Partner status**               |         |
| No                               | 16 (15.1) |
| Yes                              | 90 (84.9) |
| **Ethnicity**                    |         |
| Malay                            | 34 (32.1) |
| Chinese                          | 53 (50.0) |
| Other                            | 19 (17.9) |
| **Education level**              |         |
| Primary                          | 15 (14.2) |
| Secondary                        | 47 (44.3) |
| Tertiary                         | 44 (41.5) |
| **Prior treatment**              |         |
| Chemotherapy                      | 68 (64.2) |
| Radiotherapy                      | 2 (1.9)  |
| Combination                       | 21 (19.8) |
| HSCT                             | 13 (12.3) |
| **Other medical illness**        |         |
| Yes                              | 56 (52.8) |
| No                               | 50 (47.2) |
| **ED category**                  |         |
| No ED                            | 13 (12.3) |
| Mild-moderate                    | 55 (51.9) |
| Severe                           | 3 (2.8)  |
| Not sexually active              | 35 (33.0) |
| **Anxiety**                      |         |
| No                               | 95 (89.6) |
| Yes                              | 11 (10.4) |
| **Depression**                   |         |
| No                               | 93 (87.7) |
| Yes                              | 13 (12.3) |

ED: erectile dysfunction; HSCT: haemopoietic stem cell transplantation
medical illness and fatigue. Fatigue was a common problem among patients with various types of cancers, including lymphoma, and could persist for years among cancer survivors, with interference in daily life.[32] According to National Comprehensive Cancer Network, cancer-related fatigue is a “distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.”[33] Cancer-related fatigue is often under-recognised and undertreated. A majority of treating physicians may not view this as an important aspect that needs to be addressed. It is recommended that all patients with cancer be evaluated for cancer-related fatigue, not only at baseline but also with every major change in the patient’s care management protocols or health. Therefore, it is pertinent that healthcare providers be cognisant of this unmet need and begin counselling and implementing forms of interventions, such as exercise, that have been shown to be effective.[34]

The present study had several limitations. Firstly, the relatively small number of lymphoma survivors included did not allow us to arrive at any strong conclusions. The fact that nearly one-third of patients were not sexually active during the interview may have contributed to the lack of significance between psychological stress and QOL and ED. However, despite these limitations, the present study has called attention to sexuality being an important aspect of cancer patient care, especially for countries where it is often neglected.

In conclusion, the high prevalence rate of sexual problems among male lymphoma survivors, especially younger survivors, confirms the importance of addressing this unaddressed and under-recognised problem. Screening patients for sexual problems and fatigue should be included in the routine care of patients with cancer, so that appropriate and early interventions can be provided to improve their overall QOL.

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**Conflicts of interest**

There are no conflicts of interest.

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