PREVALENCE OF SLEEP-WAKE CYCLE DISTURBANCE AMONG CANCER PATIENTS OF BHAKTAPUR CANCER HOSPITAL, NEPAL

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ABSTRACT

Objective: The aim of the study is to determine the prevalence of sleep-wake cycle disturbance in patient receiving chemotherapy.

Methods: A descriptive cross-sectional study was carried out in 2013. A total of 205 respondents, visiting Bhaktapur Cancer Hospital and who met eligible criteria were purposively sampled and interviewed face to face. Insomnia severity index (ISI) scale was used to grade insomnia. Descriptive statistics such as frequency and percentage was used to describe demographic data. Chi-square test was done to find out the association between prevalence of sleep-wake cycle disturbance and selected variables.

Results: Of 205 patients enrolled, 70.7% had sleep-wake cycle disturbances. The majority (71.21%) of respondents had some form of clinically significant insomnia. The ages of the patients ranged from 20 to 81 years with the mean age of 56.25 (standard deviation±13.87). More than half, i.e., 69.3% of the patients were female. Patients being treated with methotrexate were found to be more associated with the development of sleep-wake cycle disturbance. Tea/coffee drinking habit was found to be significantly associated with the prevalence sleep-wake cycle disturbance.

Conclusion: Sleep disorders are a common and often chronic problem for patients with cancer. Until recently, such symptoms have attracted little attention. This might be one of the reasons for increased prevalence of sleep-wake cycle disturbance. The consequences of insomnia are often minimized relative to those of cancer itself. Insomnia is prevalent, under recognized, undermanaged, and understudied among patients with cancer receiving chemotherapy. It is recommended to take early and adequate intervention for the reduction of increased prevalence rate of sleep-wake cycle disturbance.

Keywords: Chemotherapy, Prevalence, Sleep-wake cycle.

INTRODUCTION

Sleep is an area of functioning that is frequently impaired in cancer patients. Sleep disorders, such as difficulty falling asleep, problems maintaining sleep, poor sleep efficiency, early awakening, and excessive daytime sleepiness, are prevalent in patients with cancer [1].

It is estimated that nearly 45% of oncology patients experience sleep disturbances; this is nearly three times the estimate of its occurrence in the general population [2].

The sleep of cancer patients is often disturbed, yet sleeps disorders and their health consequences are often neglected in this population [3,4]. Sleep disturbances affect between 30% and 75% of newly diagnosed or recently treated cancer patients, a rate that has been reported as double that of the general population [5]. Surveys have suggested that sleep complaints in cancer patients consisted of difficulty falling asleep and difficulty staying asleep, with frequent and prolonged nighttime awakenings. Patients reported these complaints both before treatment and during treatment [6,7].

Sleep dysfunction has unfortunately become an increasingly problematic issue for many and is a significant issue for many patients with cancer and their caregivers. Patient themselves may fail to report their sleep difficulties to their physicians. The consequences of insomnia are often minimized relative to those of cancer itself [8].

Sleep is an essential component of a healthy life. Disrupted sleep can lead to a variety of physical and psychological dysfunctions including insomnia, chronic pain, respiratory dysfunction, obesity, stress, and anxiety. Patients with cancer often are affected by side effects such as pain or depression that can manifest as insomnia. They also can experience sleep deprivation from side effects of the treatment such as anemia, daytime fatigue, and the physiologic effects of medications [8].

Sleep disturbance is one of the most frequent side effects experienced by patients with cancer. Several studies have shown that many patients with cancer do not mention their sleep problems, with close to 80% assuming it is caused by the treatment, 60% wrongly assuming that the symptoms will not last, and almost half believing that their physicians cannot do anything to help them.

Furthermore, these sleep disorders lead to pronounced symptom distress: Sarna gathered symptom distress data on female lung cancer patients an average of 1.8 years after treatment and found that insomnia was a major concern; it ranked as the third highest cause of distress after fatigue and pain [9]. Despite these concerns, insomnia is often undetected and undertreated when detected, with only 16.6% of patients in one study having spoken to their physician about their sleep problems [7,10]. Evidence suggests that patients may be hesitant to voluntarily report symptoms associated with cancer-related insomnia.

According to the journal of clinical oncology, the rate of insomnia in patients with cancer is found to be nearly three times higher than the rates in the general population. Insomnia is prevalent, under recognized, undermanaged, and understudied among patients with cancer receiving chemotherapy.

METHODS

A descriptive cross-sectional research design was used in In-patient and Out-patient Departments of Bhaktapur Cancer Hospital. It is one of the specialized cancer hospitals of Nepal. The study population consisted of all patients who have received at least one cycle of chemotherapy and

above 20 years of age attending this hospital and who were present at the time of data collection. A total of 205 respondents who met eligible criteria were purposively sampled and interviewed face to face.

A structured and semi-structured interview schedule consisting of questions-related demographic characteristics, type of cancer and insomnia severity index (ISI) for assessment of sleep-wake cycle disturbance developed by reviewing literature. The content validity of the instrument was established seeking the opinion of oncologist and related experts nurses and doctors. ISI is a standard scale whose validity and reliability is established. The instrument was then translated into the Nepali language, and opinion of language expert was obtained for comprehensibility and simplicity of language and for consistency of the content. The study was conducted after obtaining approval from the concerned authority. Anonymity, privacy, and confidentiality were maintained during as well as after data collection.

All patients who met the criteria and who gave informed consent were interviewed. Review of the patient's medical record file was done to confirm the diagnosis and number of cycle of chemotherapy. The collected data were reviewed daily for completeness and accuracy. Edited data were entered into the Statistical Package for Social Science Software version 16.0 for statistical analysis using descriptive and inferential statistics.

RESULTS

Among total respondents, 50.7% of the total respondents fall under age 60 and above, which is the largest age group. The ages of the patients ranged from 20 to 81 years with the mean age of 56.25 (standard deviation [SD]±13.87) at the time of the study. Regarding gender of the respondents, 69.3% were female and the remaining was male.

Among the total respondents, the majority (89.26%) of the patients in the study were non-smokers. Most (87.3%) of them were non-alcohol drinker, and majority (73.7%) of them were tea/coffee drinker (Table 1).

Out of total respondents, 25.4% had gynecological cancer, and minimal (2.4% each) had Non-Hodgkin's lymphoma, thyroid cancer, and leukemia (Table 2).

Among the total respondents, <½ (43.41%) were administered oxali/cis/carboplatin and minimal (1.95% each) were administered cytarabine, gemcitabine, and others (Table 3).

Among the total respondents, 36.6% were receiving the second cycle of chemotherapy (Table 4).

The prevalence of sleep-wake cycle disturbance in the study was found to be 70.7% in Bhaktapur Cancer Hospital (Table 5).

In this study, more than half (54.63%) of the respondents had difficulty staying asleep (Table 6).

The majority (71.21%) of respondents had some form of clinically significant insomnia. The mean ISI score was 2.46 (±1.17) in the study (Table 7).

The prevalence of sleep-wake cycle disturbance in 65 years and above age group was more than in 65 years and below age group. The differences seen in these two age group was statistically significant (p=0.021) (Table 8).

The prevalence among the respondents drinking tea/coffee was 76.2%, whereas among non-drinker was 55.6%. The differences seen in these two group was statistically significant (p=0.004) (Table 9).

The prevalence among the respondents using methotrexate was 74.5%. The differences seen in these two group was statistically significant (p=0.01) (Table 10).

Table 1: Socio-demographic information of respondents (n=205)

Variables	Frequency (%)
Age in years	
20-30	11 (5.4)
30-40	16 (7.8)
40-50	31 (15.1)
50-60	43 (21.0)
60 and above	104 (50.7)
Mean age is 56.25 years and SD±13.87	
Sex	
Male	63 (30.73)
Female	142 (69.26)
Smoking	
Smoker	22 (10.73)
Non-smoker	183 (89.26)
Alcohol	
Drinker	26 (12.7)
Non-drinker	179 (87.3)
Tea/coffee	
Drinker	151 (73.7)
Non-drinker	54 (26.3)

SD: Standard deviation

Table 2: Description about disease-related information of respondents (n=205)

Cancer diagnosis	Frequency (%)
Gynecological cancer	52 (25.4)
Breast cancer	35 (17.1)
Head and neck cancer	29 (14.1)
Stomach cancer	20 (9.8)
Lung cancer	19 (9.3)
Colorectal cancer	14 (6.8)
Bladder cancer	8 (3.9)
Others	7 (3.4)
Osteosarcoma	6 (2.9)
Non-Hodgkin's lymphoma	5 (2.4)
Thyroid cancer	5 (2.4)
Leukemia	5 (2.4)

Table 3: Treatment-related information of respondents* (n=205)

Type of cytotoxic drugs	Frequency (%)
Oxali/cis/carboplatin	89 (43.41)
Methotrexate	40 (19.51)
Fluorouracil	37 (18.04)
Adriamycin/Doxorubicin	36 (17.56)
Paclitaxel	32 (15.60)
Cyclophosphamide	27 (13.17)
Vincristine	13 (6.34)
Ifosphamide	10 (4.87)
Decarbazine	10 (4.87)
Others (anthracycline, bleomycin, docetaxel, epirubicin)	4 (1.95)
Cytarabine	4 (1.95)
Gemcitabine	4 (1.95)

*Multiple response

DISCUSSION

In this study, the ages of the patients involved ranged from 20 to 81 years with the mean age of 56.81 (SD±13.87) at the time of the study. The study group was categorized into six age groups. The majority (50.7%) of the patients were of age 60 years and above. More than half, i.e., 69.26% of the patients were female. This was quite similar to the study done in Canada, in which the ages ranged from 22 to 93 years, with mean age of 58 years and the majority (72%) of the patients were female [11].

Table 4: Chemotherapy cycle-related information (n=205)

Chemotherapy cycle	Frequency (%)
Second	75 (36.6)
Third	35 (17.1)
Fourth	29 (14.1)
Fifth	28 (13.7)
Sixth	38 (18.5)

Table 5: Prevalence of sleep-wake cycle disturbance (n=205)

Sleep-wake cycle disturbances	Frequency (%)
Absent	60 (29.3)
Present	145 (70.7)

Table 6: Insomnia problem-related information of the respondents (n=205)

Variables	Frequency (%)
Difficulty falling asleep	101 (49.26)
Difficulty staying asleep	112 (54.63)
Problem waking up too early	87 (42.43)
Dissatisfied with current sleep pattern	87 (42.43)
Sleeping problems noticeable to others	68 (33.17)
Worried/distressed about current sleep problem	69 (33.65)
Sleep problem interference with daily functioning	86 (41.95)

Table 7: Grading of insomnia (n=205)

Grade of insomnia	Frequency (%)
No clinically significant insomnia	59 (28.8)
Subthreshold insomnia	50 (24.4)
Moderate insomnia	39 (19.0)
Severe insomnia	57 (27.8)
(Mean ISI score is 2.46 and SD±1.17)	

SD: Standard deviation

This study shows the prevalence of sleep-wake cycle disturbance to be 70.7% in Bhaktapur Cancer Hospital. This is consistent with the prospective study done, in 2010, in which the prevalence was 87% [12]. Similarly, in the study done by Davidson *et al.*, in 2002, found a prevalence of 32% in a diverse group of more than 1000 cancer patients, while the figure rose to 63% in a sample of 97 patients with breast cancer [13]. Similarly, in the descriptive retrospective study done by Boonstra, in 2010, among 69 patients found a prevalence of 74% as measured by the ISI [14]. In contrary, the findings of different studies have shown great variability in the prevalence rate of this disorder in cancer patients, ranging between 30% and 50%, though some studies have found much higher figures [15]. Other studies say the rate may be much higher 75% of all cancer patients reporting long and short term insomnia. Similarly, in the study done by Portenoy *et al*. found the prevalence rates of insomnia varying from 48.6% to 60% [16].

These discrepancies are considered to be due to the different methodologies used in the evaluation and the characteristics of the population studied or even due to the sample size used.

This study shows 71.21% of the participants have some degree of clinically significant insomnia. Similarly, in the descriptive retrospective study done by Boonstra *et al.* [14], among 69 found that 74% of patients had some form of clinically significant insomnia. This is consistent with the prospective study done in Florida, in which 75% of the participants had some degree of clinically significant insomnia [17].

This study shows that 46.82% of the patient had moderate to severe insomnia. This is consistent with the findings of the study done by

Table 8: Age and sleep-wake cycle disturbance of the respondents (n=205)

Age	Sleep-wake cycle disturbance (%)		Total	p value	Odd ratio
	Present	Absent			
65 years and below	104 (75.9)	33 (24.1)	137	0.021	
65 years and above	41 (60.3)	27 (39.7)	68		2.07
Total	145	60	205		

Table 9: Tea/coffee drinking and sleep-wake cycle disturbance (n=205)

Tea/coffee drinking	Sleep-wake cycle disturbance (%)		Total	p value	Odd ratio
	Present	Absent			
Drinker	115 (76.2)	36 (23.8)	151	0.004	2.55
Non-drinker	30 (55.6)	24 (44.4)	54		
Total	145	60	205		

Table 10: Use of methotrexate and sleep-wake cycle disturbance of the respondents (n=205)

Methotrexate	Sleep-wake cycle disturbance (%)		Total	p value	Odd ratio
	Present	Absent			
Yes	123 (74.5)	42 (25.5)	165	0.01	0.41
No	22 (55.0)	18 (45.0)	40		
Total	145	60	205		

Engstrom, in 1999, which showed that 50% of the patients rated their sleep problem as moderate, severe, or intolerable [7]. Similarly, in the study done by Degner, 1995 found the presence of moderate to severe insomnia among 30.9% of the patients [18]. In contrary is the findings of the study done by Harrison, in 1997, which showed that 41% of the patients had insomnia, out of which 78% reported moderate to severe insomnia [19].

This study shows that 49.26% had difficulty initiating sleep, 54.63% reported difficulty maintaining sleep, and 42.43% reported both initiating and maintaining sleep. This is consistent with the study conducted by Savard *et al.*, in 2005, which found that 4% had difficulty initiating sleep, 34% reported difficulties maintaining sleep, and 52% reported both initiating and maintaining sleep issues [20]. Similarly, in the study done in Oncology Department, UK, found that 54% had conciliation insomnia, 18% complained of maintenance insomnia, and 16% early morning awakening [21].

In this study, age is found to be an associated variable with sleep-wake cycle disturbance which is similar to the study done in Quebec, Canada (2008), in which there was a statistically significant association of overall insomnia complaints and prevalence of insomnia syndrome with age [22].

In this study, female had majority (71.8%) of insomnia prevalence which is consistent with some previous studies that have indicated that the female gender constitutes a significant risk factor for sleep-wake cycle disturbance [14]. Similarly, in a study done in New York found that male patients had a lower rate of insomnia complaints than female patients [22]. Furthermore, in the descriptive retrospective study done by Boonstra *et al.*, found that 87% of women reported insomnia compared to 67% of men [14].

This study has clearly revealed the absence of an association between sleep-wake cycle disturbance and patients who had a history of smoking and/or are currently smoking and alcohol consumption. These findings are inconsistent with the findings in a prospective study done in Philadelphia [23]. These differences are considered to be due to different characteristics of the population studied or even due to the different sample size used.

This study has clearly revealed the presence of an association between sleep-wake cycle disturbance and patients who had a history of tea/coffee consumption and/or currently drinking tea/coffee. These findings are consistent with the findings in a prospective study done in Philadelphia (2004) that predicts caffeine use as patient-related risk factors [23]. Similarly, in the study done by Higdon and Frei in 2006, showed that as with other caffeinated beverages, such as coffee and colas, the caffeine contained in many tea products could potentially cause adverse effects including insomnia and restlessness [24].

Methotrexate is found to be significantly associated with sleep-wake cycle disturbance in this study. It is consistent with a study done by Kaya et al. (1983) where it is well documented that chemotherapy agents, such as antimetabolites, can lead to insomnia [25]. It is also consistent with a study done by National Cancer Institute which states that side effects of chemotherapy can be a source of sleep disturbances due to disrupted sleep cycles [13]. Similarly, in the study done by Catherine showed that antimetabolites cause the risk of developing sleep disturbance in about 10-29% of the patients [26].

In this study, the cycle of chemotherapy was not significantly associated with the prevalence of sleep-wake cycle disturbance. This is consistent with a study done in California (2012) that states that there were also no significant associations between insomnia and chemotherapy cycles [27].

Similarly, this is inconsistent with the findings in the study done by Savard *et al.* (2009), in which it was determined that initially sleep-wake patterns were disrupted, and progressively sleep-wake patterns worsened as the number of treatments received increased [28].

CONCLUSION

Focus should be given on reduction of the prevalence rate of sleep-wake cycle disturbance. This can be done by: Making the health personnel and patients conscious toward preventing sleep disturbances and promoting good sleep habit and setting up insomnia-counseling clinic in every cancer hospital to be launched by the trained nurses.

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