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 underwent chemotherapy treatment between January and July 2013. A total of 205 patients were included in this study.

The aim of the study was to determine the prevalence of sleep-wake cycle disturbance in patients receiving chemotherapy. 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 were 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.
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 (89.6%) of the patients in
the study were non-smokers. Most (97.3%) 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 the 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**

| 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)     |

**Table 2: Description about disease-related information of respondents**

| 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**

| Type of cytotoxic drugs    | Frequency (%) |
|---------------------------|---------------|
| Oxali/cis/carboplatin      | 89 (43.1)     |
| 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)     |
| Hosphamide                 | 10 (4.87)     |
| Docetaxel, epirubicin      | 4 (1.95)      |
| Cytarabine                 | 4 (1.95)      |
| Gemcitabine                | 4 (1.95)      |

**Table 4: Treatment-related information of respondents**

| Type of cytotoxic drugs    | Frequency (%) |
|---------------------------|---------------|
| Oxali/cis/carboplatin      | 89 (43.1)     |
| 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)     |
| Hosphamide                 | 10 (4.87)     |
| Docetaxel, epirubicin      | 4 (1.95)      |
| Cytarabine                 | 4 (1.95)      |
| Gemcitabine                | 4 (1.95)      |

**Table 5: Description about disease-related information of respondents**

| 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)       |

**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].
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 that 74% of patients with breast cancer had insomnia, while the figure rose to 63% in a sample of 97 patients with breast cancer [13].

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 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, 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. This 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 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].

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, 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 the 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].

### 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)    |               |

### 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 | 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                           |       |         |           |

---

SD: Standard deviation
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 initial 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.

ACKNOWLEDGMENTS
The authors thank the participants who agreed to share their experiences with us. We also thank nurses of Bhaktapur Cancer Hospital, who helped us to include patients.

REFERENCES
1. Roscoe J, Kaufman M, Matteson-Rusby SE, Palesh OG, Ryan JL, Kohli S, et al. Cancer related fatigue & sleep disorders. J Clin Oncol 2010;28(2):26.
2. National Cancer Institute. Sleep Disorders. 2010. http://www.cancer.gov/about-cancer/treatment/side-effects/sleep-disorders-pdq. [Last retrieved on 2010 Mar 24].
3. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: A review. Eur J Cancer Care (Engl) 2001;10(4):245-55.
4. Savard J, Morin CM. Insomnia in the context of cancer: A review of a neglected problem. J Clin Oncol 2001;19(3):895-908.
5. Weissman MM, Greenwald S, Niño-Murcia G, Dement WC. The morbidity of insomnia unaccompanied by psychiatric disorders. Gen Hosp Psychiatry 1997;19(4):245-50.
6. Cimprich B. Pretreatment symptom distress in women newly diagnosed with breast cancer. Cancer Nurs 1999;22(2):185-94.
7. Engstrom CA, Strohl RA, Rose L, Lewandowski L, Stefanek ME. Sleep alterations in cancer patients. Cancer Nurs 1999;22(2):143-8.
8. Friese RS. Sleep and recovery from critical illness and injury: A review of theory, current practice, and future directions. Crit Care Med 2008;36(3):9.
9. Sarna L. Correlates of symptom distress in women with lung cancer. Cancer Pract 1993;1(2):21-8.
10. Haponik EF. Sleep disturbances of older persons: Physicians’ attitudes. Sleep 1992;15(2):168-72.
11. Palesh OG, Roscoe JA, Mustian KM, Roth T, Savard J, Ancoli-Israel S, et al. Prevalence, demographics, and psychological associations of sleep disturbances in cancer. University of Rochester cancer center–community clinical oncology program. J Clin Oncol 2009;28(2):292-8.
12. Beck SL, Berger AM, Barsevick AM, Wong B, Stewart KA, Dudley WN. Sleep quality after initial chemotherapy for breast cancer. Support Care Cancer 2010;18(6):679-89.
13. Davidson JR, MacLean AW, Brundage MD, Schulke K. Sleep disturbance in cancer patients. Soc Sci Med 2002;54(9):1309-21.
14. Boonstra L, Harden K, Jarvis S, Palmer S, Kavanagh-Carveth P, Barnett J, et al. Sleep disturbance in hospitalized recipients of stem cell transplantation. Clin J Oncol Nurs 2011;15(3):271-6.
15. Lee K, Cho M, Miaskowski C, Dodd M. Impaired sleep and rhythms in persons with cancer. Sleep Med Rev 2004;8(3):199-212.
16. Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Coyle N, et al. Symptom prevalence, characteristics and distress in a cancer population. Qual Life Res 1994;3(3):183-9.
17. Jonas J, Horgas A, Yoon S. Use of complementary and alternative therapies to manage cancer-related symptoms in hospitalized patients. J Undergrad Res 2011;12(3):7.
18. Degner LF, Sloan JA. Symptom distress in newly diagnosed ambulatory cancer patients and as a predictor of survival in lung cancer. J Pain Symptom Manage 1995;10(6):423-31.
19. Harrison LB, Zelefsky MJ, Pfister DG, Carper E, Raben A, Kraus DH, et al. Detailed quality of life assessment in patients treated with primary radiotherapy for squamous cell cancer of the base of the tongue. Head Neck 1997;19(3):169-75.
20. Savard J, Simard S, Hervouet S, Ivers H, Lacombe L, Fradet Y. Insomnia in men treated with radical prostatectomy for prostate cancer. Psychoncology 2005;14(2):147-56.
21. Usta Cidon E, Alonso P. Pilot study of insomnia prevalence in cancer survivors. Webmed Central Cancer 2013;4(3): WMC004161.
22. Palesh O, Roscoe J. Prevalence, demographics & psychological association of sleep disruption in patients with cancer. J Clin Oncol 2008;26(2):292-298.
23. O’Donnell JF. Insomnia in cancer patient. Clin Cornerstone 2004;6 Suppl 1:9.
24. Higdon JV, Frei B. Coffee and health: A review of recent human research. Crit Rev Food Sci Nutr 2006;46(2):101-23.
25. Kaye J, Kaye K, Madow L. Sleep patterns in patients with cancer and patients with cardiac disease. J Psychol 1983;114:107-13.
26. Vena C, Parker K, Cunningham M, Clark J, McMillan S. Sleep-wake disturbances in people with cancer part I: An overview of sleep, sleep regulation, and effects of disease and treatment. Oncol Nurs Forum 2004;31(4):735-46.
27. Liu L, Rissling M, Natarajan L, Fiorentino L, Mills PJ, Dimsdale JE, et al. The longitudinal relationship between fatigue and sleep in breast cancer patients undergoing chemotherapy. Sleep 2012;35(2):237-45.
28. Savard J, Liu L, Natarajan L, Rissling MB, Neukrug AB, He F, et al. Breast cancer patients have progressively impaired sleep-wake activity rhythms during chemotherapy. Sleep 2009;32(9):1155-60.