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Prevalence and associated factors of cancer-related fatigue among adult patients with cancer attending oncology units: an institution-based cross-sectional study design in the Amhara region, Ethiopia, 2022

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ABSTRACT

Introduction Cancer-related fatigue (CRF) continues to be a common problem among most patients with cancer. It is a subjective feeling of tiredness, weakness or lack of energy. CRF has a significant impact on social interactions, everyday activities and the general quality of life of patients with cancer worldwide. However, little is known about CRF in Ethiopia as well as in the current study area. Therefore, the aim of this study was to assess the prevalence and associated factors of CRF among adult patients attending oncology units at the comprehensive specialised hospitals in the Amhara regional state of Ethiopia.

Methods An institution-based cross-sectional study was conducted among adult patients with cancer undergoing treatment. A systematic random sampling technique was employed to select the study participants. An interviewer-administered questionnaire and participants' medical charts were used to collect the data. The questionnaire consisted of eight subsections, including sociodemographic characteristics, behavioural characteristics, Brief Fatigue Inventory, Performance Status Scale, Oslo Social Support Status, Hospital Anxiety and Depression Scale, Pittsburgh Sleep Quality Index, and clinical and medical factors. The data were entered into EpiData V.4.6 and exported into SPSS V.26 for analysis. The participants' characteristics were compiled using descriptive statics. Bivariable and multivariable logistic regressions were used to identify associations between dependent and independent variables. Variables with a value of $p<0.05$ were considered statistically significant.

Result A total of 326 randomly selected patients with cancer, undergoing treatment, participated in this study; the response rate was 94%. The prevalence of CRF was found to be 63.93% (95% CI 58.5% to 69.25%). Depression (adjusted OR (AOR) 1.975, 95% CI 1.009 to 3.865), poor sleep quality (AOR 3.309, 95% CI 1.057 to 10.345), poor performance status (AOR 1.983, 95% CI 1.176 to 4.70), cancer stage (AOR 3.242, 95% CI 1.016 to 10.342) and admitted patients with cancer (AOR 2.047, 95% CI 1.122 to 3.734) were associated with CRF.

Conclusion and recommendation The prevalence of CRF was found to be high. Stage of cancer, poor sleep quality, poor performance status, depression and hospital admission were significant factors. The results show that healthcare providers should focus on risk factors as well as CRF through early screening and management.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cancer-related fatigue (CRF) continues to be a public health problem among the cancer population.

WHAT THIS STUDY ADDS

⇒ Prevalence of CRF and its associated comorbidities were insufficiently investigated in Ethiopia, particularly in the study region.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study has big implications for the cancer population and healthcare providers.
⇒ Routine assessment of CRF by considering it as the 'sixth vital sign', ease of CRF screening and symptom management are very crucial.

BACKGROUND

Globally, cancer remains a major public health burden, ranking as the second leading cause of death in both the developed and developing countries.[1] The WHO's 2015 statistics report states that cancer is the primary cause of morbidity and mortality worldwide, accounting for 8.2 million reported deaths and 14.1 million new cases, with 5.3 million of those deaths occurring in low-income and middle-income countries.[2] According to the National Burden and Trend of Cancer in Ethiopia from 2010 to 2019, there were an estimated 53 560 new cases of cancer and 39 480 deaths in Ethiopia. The five most common

types of cancers in Ethiopia were leukaemia, cervical cancer, breast cancer, colon and rectum cancers, and stomach cancer. The most prevalent types of cancers in Ethiopia among the adult women population are breast cancer (%), cancer of the cervix (13.4%) and colorectal cancer (5.7%).[3]

Despite Amhara being the second largest region in Ethiopia, it has only had five cancer treatment centres. This is because there is a lack of a surveillance system and limited accessibility to healthcare services for patients with cancer, resulting in a lack of local data on cancer epidemiology.[4] According to the National Burden and Trend of Cancer in Ethiopia from 2010 to 2019, morbidity and mortality among patients with cancer has rapidly increased in the Amhara region. A range of studies have revealed that fatigue is a common health issue among patients with cancer receiving chemotherapy and radiation therapy.[5–8] Patients with cancer are highly likely to encounter physical, psychological and socioeconomic burdens that diminish their overall and health-related quality of life during the treatment trajectory.[9] Cancer-related fatigue (CRF) is the most frequently reported clinical symptom among all the side effects of cancer and its treatment. It is a serious, distressing, devastating and complex clinical symptom that significantly lowers a patient's quality of life.[10–12] According to the Global Side-Effect Burden Score, CRF is the second most common side effect experienced by patients with cancer, next to pain.[13]

The National Comprehensive Cancer Network (NCCN) defines CRF as 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.[14] Evidence shows that the magnitude of CRF ranges from 25% to 99% during chemotherapy, and approximately a third of cancer survivors experience CRF.[13–15] Studies from the Netherlands, America and China have estimated the pooled prevalence of CRF to be 26.9%, 49% and 52%,[16–18] respectively. 90% of patients with cancer undergoing radiation therapy and 80% of those undergoing chemotherapy have reported feeling tired.[19 20] Fatigue may result from the cancer itself, due to the adverse effects of treatment or from a number of syndromes linked to concurrent malignancies while the exact source of the condition is unknown. In addition, sociodemographic, psychological and behavioural factors have a significant impact.[15] However, in Ethiopia, it is a problem that is poorly acknowledged, under-reported, under-treated, underinvestigated and given low priority.[21] Furthermore, because fatigue has been considered as an inevitable condition that should be endured rather than treated, healthcare providers often concentrate on other symptoms, like pain, nausea and vomiting.[22] This may be the reason why patients were disappointed with therapy, discontinued treatment and refused to go for their next appointment.[23] Previous studies attempted to emphasise on pharmacological and non-pharmacological methods for managing CRF.[24] Non-pharmacological management includes patient/family education and counselling, physical activities, behavioural intervention and providing nursing care. For contributing factors such as pain, emotional distress, sleep disturbance, nausea/vomiting and lack of appetite and unlike other symptoms, treatment of fatigue requires general supportive care developed by the NCCN and the oncology of nursing society.[14 25] Although knowledge about CRF is limited, there should be some data about the prevalence or trend of cancer, quality and development of treatment, or data on other cancer-related outcomes (such as death and survivorship). However, knowledge about CRF remains fragmentary and limited, and studies on CRF are scarce in Ethiopia.[21] This suggests that there is limited information about the magnitude, contributing factors and intervention modalities of CRF in our study area. Therefore, this study aimed to show the prevalence of CRF and associated factors in patients with cancer attending oncology units of comprehensive specialised hospitals in the regional state of Amhara, Ethiopia.

METHODS AND MATERIALS

Study design and setting

An institution-based cross-sectional study was conducted at comprehensive specialised hospitals that have oncology units in the Amhara regional state of Ethiopia in 2022. In this region, there are eight comprehensive specialised governmental hospitals of which four have oncology units; the Felege Hiwot Comprehensive Specialized Hospital (FHCSH), the Tibebe Gion Comprehensive Specialized Hospital (TGCSH), the Dessie Comprehensive Specialized Hospital (DCSH) and the University of Gondar Comprehensive Specialized Hospital (UoGCSH) have cancer treatment centres that provide oncology services. These specialised hospitals are located in Bahir Dar, Dessie and Gondar towns which are 552 km, 387 km and 727 km, respectively, from Addis Ababa, the capital city of Ethiopia. These comprehensive specialised hospitals treat about 1700 patients with cancer each year, providing chemotherapy and surgical treatment. There are 71 inpatient beds in the oncology unit of these four hospitals (FHCSH=20, TGCSH=12, DCSH=15 and UoGCSH=24).[26–29]

Source and study population

Source population

The source population included all adult patients with cancer attending the oncology units of comprehensive specialised hospitals in Amhara regional state.

Study population

The study population included all adult patients with cancer attending the oncology units of the four

comprehensive specialised hospitals during the study period in Amhara regional state, Ethiopia.

Eligibility criteria

Inclusion criteria

All patients with cancer age 18 years and above.

Pathologically proven patients with cancer.

Patients under treatment follow-up.

Exclusion criteria

Critically ill patients who were unable to comprehend and respond to questions.

Patients referred from other specialised cancer treatment hospitals in the Amhara region.

Sample size determination

The sample size was calculated using a single population proportion formula,

$$n = (X\alpha/2)^2 p\ (1-p)\, d^2,$$

where,

n=minimum sample size required for the study,

Z=standard normal distribution (Z=1.96),

CI=95% and α=0.05,

p=prevalence/population proportion (p=74%),

d=is a tolerable margin of error (d=0.05).

Considering 74% CRF among patients with cancer in Addis Ababa, Ethiopia,[21] 95% level of confidence, 5% margin of error and 10% non-response rate, the final sample size was 326.

Sampling technique

A systematic random sampling technique was employed to select the study participants from each of the comprehensive specialised hospitals after a proportional allocation for each hospital was properly calculated and assigned. Individual participants were chosen using the sampling interval. The sampling interval (k) was calculated as k=1070/326=3. The first participant was selected randomly using a lottery method from 1 to 3 and the subsequent respondents were chosen at regular intervals of 3. To prevent redundant data collection, the patients' medical record numbers and their follow-up log books were crosschecked and used carefully (figure 1).

Measures of the study

The dependent variable is CRF. The Brief Fatigue Inventory (BFI) instrument has a nine-item questionnaire about CRF and is validated in the Amharic language with a Cronbach's α of 0.97 in the past 7 days. Fatigue severity is evaluated by using an integer scale of 0 (no fatigue) to 10 (fatigue as bad as you can imagine). This scale is further classified into mild (1–3), moderate (4–6) and severe (7–10), as recommended by NCCN guidelines for screening and re-evaluation of CRF, with the cut-off score of clinically significant fatigue being ≥4 in the BFI Scale; whereas, scores of 0 (no fatigue) and 1–3 (mild) in the BFI Scale are not clinically significant for fatigue. This

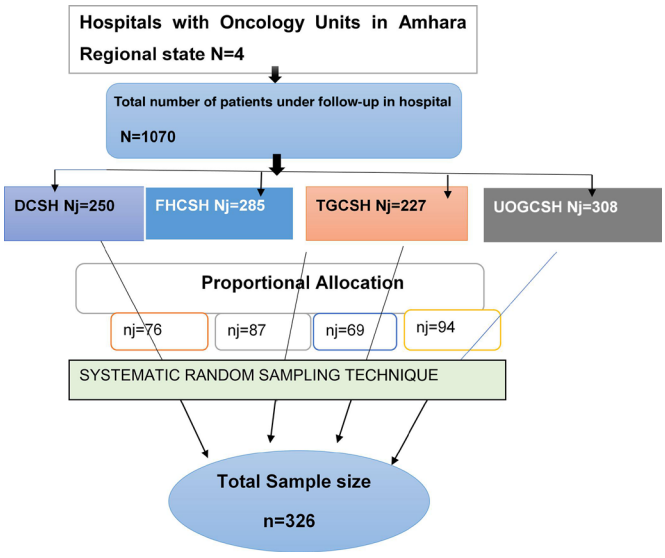

Figure 1 Schematic presentation of the sampling procedure on cancer-related fatigue and associated factors among adult patients at the oncology units of comprehensive specialised hospitals, Amhara regional state, Ethiopia, 2022. DCSH, Dessie Comprehensive Specialized Hospital; FHCSH, Felege Hiwot Comprehensive Specialized Hospital; TGCSH, Tibebe Gion Comprehensive Specialized Hospital; UoGCSH, University of Gondar Comprehensive Specialized Hospital.

recommendation has been made by the expert panel members of the NCCN.[30 31]

The independent variables include sociodemographic variables (ie, age, sex, marital status, educational status, employment status, religious status and occupational status), clinical factors (ie, type of cancer, stage of cancer, type of treatment (chemotherapy, radiotherapy, surgery or combination therapy), antipain medicine used and antiemetic used), medical condition (ie, anaemia and comorbidity, admission status), physical and behavioural factors (ie, performance status, sleep quality status, alcohol consumption status, cigarette smoking status, anxiety and depression status, and social support status).

Operational definition

CRF is a subjective feeling of tiredness, weakness or lack of energy. CRF is measured using the BFI Scale; patients with cancer who score ≥4 are classified as moderate to severe in the BFI Measurement Scale and are considered as having clinically significant fatigue which requires health education with a detailed fatigue assessment (including onset, pattern, duration, change over time, aggravating or alleviating factors, and interference in functioning) and a more focused history and physical exam that considers the patients' current disease, treatment status, and medication. Whereas, patients with cancer who score <4 in the BFI Measurement Scale are considered as not having clinically significant fatigue. If CRF is mild, the patient and the family should receive education about CRF and common strategies for its management such as the importance of reporting fatigue and not waiting for providers to bring up the subject.

Healthcare providers need to teach patients and families to treat fatigue as if it were the 'sixth vital sign'. In other words, not clinically significant fatigue means that no active treatment is mandatory. This cut-off point was based on recommendation by the NCCN expert panel members.[7 31–34]

Sleep quality is measured using the Pittsburgh Sleep Quality Index (PSQI). When the patient's sleep quality score =5, it is considered good sleep quality, whereas sleep quality is considered poor when the sleep quality score of the patients >5.[35]

Anxiety and depression are measured using the Hospital Anxiety and Depression Scale (HADS), and when a patient scores >10 points on HADS, the patient is considered to have anxiety and depression.[36]

The following questions are used to assess smoking status: 'Have you ever smoked cigarettes?' and 'Have you smoked cigarettes in the last 30 days?'. Based on the above questions, the responses can be categorised as never smokers, that is, individuals who have never tried cigarette smoking in their lifetime, and former smokers, that is, individuals who have ever smoked but had stopped smoking at the time of assessment. A current smoker is an individual who has smoked a cigarette one or more times in the past 30 days before the service.[37]

Alcohol consumption can be assessed with these questions: 'Have you ever consumed an alcoholic drink?' and 'Have you consumed an alcoholic drink within the past 30 days?'. Based on the above questions, the responses can be categorised as: former alcohol user, that is, an individual who has admitted to having ever used alcohol but stopped in the last 30 days; current alcohol user, that is, an individual who has consumed alcoholic drinks within 30 days preceding the study; and a never user is an individual who has never consumed alcohol in his/her lifetime.[38]

Performance status was assessed using the Eastern Cooperative Oncology Group-Performance Status (ECOG-PS) measuring tool, which ranges from 0 to 4. The performance status was considered good when the patient's score of ECOG-PS was 0–1, whereas the performance status was considered poor when the patients score of (ECOG-PS) was 2–4.[39]

Social support was assessed using the three-item Oslo Social Support Scale (OSSS-3). The patient's social support was classified into three categories. Patients who scored 3–8 points were considered to have poor support; patients who scored 9–11 points were considered to have moderate support; and patients who scored 12–14 points were considered to have strong support.[40]

Comorbidity is when a person has more than one disease related to an index disease.[41]

Data collection instruments and procedures

Data were collected using an interviewer-administered questionnaire, and participants' medical charts were reviewed as well. The questionnaire consisted of eight subsections, including sociodemographic characteristics, behavioural characteristics, the BFI, the performance status scale, the Oslo Social Support Status, the HADS, the PSQI, and clinical and medical factors.

The BFI contains nine items, which are rated using Likert Scales ranging from 0 to 10 with a global cut-off score of 4.

The BFI is a validated assessment tool with adequate psychometric properties for use in symptom treatment, clinical management and research, globally. The BFI has been further validated in patients with cancer from Ethiopia using the Amharic version, yielding an overall Cronbach's α of 0.97.[42] Additionally, using the pretest results from this study, this tool has displayed a consistent Cronbach's α of 0.96. The BFI is divided into two sections: the first three questions describe the intensity of fatigue within a 24-hour period (present, usual and worst levels of fatigue), and the second six questions describe how cancer patients' fatigue interferes with their ability to function within a 24-hour period. The total fatigue score is calculated by combining the nine items.

The HADS was used to measure anxiety and depression and the reliability of HADS was good, with Cronbach's α coefficients of 0.86 (anxiety), 0.85 (depression) and 0.91 (total scale); validating the use of the Amharic language version for the cancer population in Ethiopia.[43 36] The ECOG was used to measure performance status.[44 45] The OSSS-3 was used to measure social support,[46 47] and sleep quality was measured using the PSQI.

The study participants were contacted following completion of their medical examination. After being informed about the study and providing informed consent, the participants were interviewed. The client's chart and register log book were also reviewed to retrieve some medical information that could not be captured through the interview.

Data quality assurance

To maintain the quality of the data, different measures were taken. The questionnaire was initially written in English, which was then translated into Amharic by an expert in the English language and a nurse, and translated back to English by additional experts to ensure consistency. Accordingly, adjustments were made based on their expertise. Second, a pretest was conducted to check the clarity and reliability of the tool. Third, training was provided to both the supervisors and the data collectors regarding the purpose and content of the questionnaire, appropriate interviewing techniques, how to approach patients and ethical considerations related to the study, including participant autonomy and information confidentiality. And lastly, to preserve the data quality, daily oversight was carried out during the data collection period.

Statistical analysis

Data were coded, cleaned and entered into EpiData V.4.6 and then exported to SPSS V.26 for analysis. Descriptive statistics such as frequencies and proportions were computed for categorical variables and presented using tables, diagrams and texts.

A binary logistic regression model was employed to determine the association between CRF and the independent variables. Bivariable and multivariable analyses were carried out to identify associations between the dependent and independent variables. Variables with a value of p<0.25 in bivariable analysis were included in the multivariable analysis and statistical significance and strength of association between dependent and independent variables were managed at p<0.05 with 95% CI. Model fitness was checked by the Hosmer-Lemeshow goodness-of-fit test. The value of p was 0.256 indicating that the model fitted to the data and multicollinearity assumption was checked by using a variance inflation factor and its values were 1–2, which indicate that no multicollinearity issue was found.

Patient and public involvement

All patients with cancer ≥18 years who voluntarily participated and provided written informed consent during the study period were involved in this study.

RESULT

Sociodemographic characteristics of the study participants

A total of 326 randomly selected patients with cancer undergoing treatment participated with a response rate of 94%. Of the total respondents, nearly two-thirds (62.3%) were female. The median age of the participants was 48 (IQR 23) years, with a range of 18–85 years. Around 66.6% of the participants were residing in rural areas. Regarding marital status, 74.8% of the participants were married. Nearly half of the participants (50.5%) were uneducated while 41.3% were farmers (table 1).

Behavioural characteristics of the study participants

Approximately half (51.5%) of the 305 study participants had ever taken alcohol. Of the people who had previously used alcohol, 28.9% were still drinking while

Table 1 Sociodemographic characteristics of the study participants attending oncology units in Amhara region, 2022 (n=305)

Variable	Category	Frequency	Percentage
Sex	Male	115	37.70
	Female	190	62.30
Age, years	18–28	34	11.10
	29–39	59	19.30
	40–50	94	30.80
	51–60	64	21
	>60	54	17.70
Residence	Urban	102	33.40
	Rural	203	66.60
Marital status	Married	228	74.80
	Divorced	25	8.20
	Single	24	7.90
	Widowed	28	9.20
Religious status	Orthodox	242	78.30
	Muslim	60	19.70
	Protestant	3	1
Educational status	Unable to read write	154	50.50
	Primary school	105	34.40
	Secondary and high school	28	9.20
	Collage and above	18	5.90
Occupational status	Unemployed	9	3
	Employed	27	8.90
	Student	14	4.60
	Farmer	126	41.30
	Merchant	49	16.10
	Retired	10	3.30
	Housewife	70	23

48.5% had given up on alcohol. Approximately 299 individuals (98%) had never smoked a cigarette, whereas 2% of participants had smoked in the past and 1.6% smoked presently.

Clinical characteristics of the study participants

Of all the cancer cases reported, 81 (26.6%) were breast cancers and 20.7% were cervical cancers. More than a third of the participants were classified as stage 1 (37.7%) and stage 2 (36.7%), while the remaining participants had advanced cancer diagnoses (stages 3 and 4), of which 32.1% had a history of metastatic illness. Regarding the participants' cancer treatments, the majority of study participants (229 (75.1%)) were given chemotherapy only while 63 (20.3%) underwent both chemotherapy and surgery. On the other hand, around 22.6% of the study participants reported comorbid conditions. Considering the psychological conditions, around 45.6% and 56.7% of participants had symptoms of depression and anxiety, respectively. Based on the ECOG-PS Scale, around 58.4% of the study participants had poor performance status while 41.6% had good performance status. The majority (93%) of the study participants experienced poor sleep quality. Approximately, 60% of the study participants had poor social support (table 2).

CRF among the study participants

In this study, the magnitude of clinically significant CRF among the study participants was found to be 63.93% (95% CI 58.5% to 69.25%) (figure 2).

Factors associated with CRF

First, a bivariable binary logistic regression analysis was conducted. As a result, 12 independent variables were found to be statistically significant with a value of p<0.25. Subsequently, these variables were analysed using a multivariable binary logistic regression analysis. Consequently, five variables (ie, patients who had symptoms of depression, poor sleep quality, poor performance status, stage of cancer (stage 2 and stage 4) and admitted patients) were found to be statistically significant with CRF.

In this regard, the odds of having clinically significant fatigue among patients with cancer who had depressive symptoms were nearly two times higher as compared with that of patients who did not have depressive symptoms (adjusted OR (AOR) 1.975, 95% CI 1.009 to 3.865). The odds of having clinically significant fatigue among patients with cancer who had poor sleep quality were three times higher as compared with those who had good sleep quality (AOR 3.309, 95% CI 1.057 to 10.345). Likewise, the odds of having clinically significant fatigue among patients with cancer who had poor performance status was nearly two times higher as compared with that of patients who had good performance status (AOR 1.983, 95% CI 1.019 to 3.859). Regarding participants' clinical cancer stage, the odds of having clinically significant fatigue among patients with stage 2 cancer was 2.4 times higher as compared with that of patients who had stage 1 cancer (AOR 2.369, 95% CI 1.176 to 4.770). Likewise, the odds of having clinically significant fatigue among patients with stage 4 cancer was three times higher as compared with that of patients who had stage 1 cancer (AOR 3.242, 95% CI 1.016 to 10.342). The odds of having clinically significant fatigue among patients with cancer who were admitted to the hospital were two times higher as compared with patients with cancer who were served in the outpatient department (AOR 2.047, 95% CI 1.122 to 3.734) (table 3).

DISCUSSION

In this study, the magnitude of clinically significant CRF was 63.9% (95% CI 58.5% to 69.25%). Compared with other studies from different parts of the world, the prevalence of clinically significant CRF in this study was relatively higher than that in three general hospitals in Norway (53%),[48] general hospitals in Shanghai, Suzhou, Wuxi and Nantong in eastern China (52.5%),[30] and systematic literature review studies in Germany (48%)[49] and Brazil (25%).[50] This observed difference could be due to differences in the measurement tools of CRF, the sampling techniques, the study populations, the socioeconomic and sociodemographic characteristics of the study participants, and the differences in sample sizes. For example, in Norway, the reason could be the difference in the populations studied, the data collection methods and the differences in the tools used. The study population in Norway comprised patients with gynaecological cancer, and telephone survey methods and Fatigue Questionnaire tools were used with cut-point[48] differences. While on the contrary, the current study includes all adult patients with cancer, the data collection method was interviewer-administered and the instruments used were different. This could be the reason for the variation in the previous study and the current study. In Brazil, EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire) instruments were used, the cancer population was served in the outpatient department and telephone survey methods were used,[50] which could have had an impact on the findings of the earlier study.[50] Furthermore, the variation in the magnitude of CRF among the studies might be due to differences in the country's quality of healthcare provision to the cancer population, such as quality of the diagnostic equipment, the recording and reporting systems, the healthcare delivery policy of the country and the healthcare-seeking behaviour of the study participants.

The results of this study were relatively comparable to those of studies in Iran, Italy, Germany and Japan, and the CRFs were reported to be 62.1%, 59.5%, 60% and 58.9%,[7 51–53] respectively. This similarity could be due to the study design, the tools used for the measurement of outcome variables and the pathological nature of the cancers.[51 52] In the current investigation, the patients who had symptoms of depression, poor sleep quality,

Table 2 Clinical characteristics of the study participants attending oncology units in comprehensive hospitals in the Amhara region, 2022 (n=305)

Variable	Category	Frequency	%
Types of admission	Inpatient	174	57
	Outpatient	131	43
Types of primary cancer	Breast cancer	81	26.60
	Colorectal cancer	40	13.10
	Cervical cancer	63	20.70
	Lung cancer	24	7.90
	Skin cancer	28	9.20
	Prostate cancer	10	3.30
	Other	59	19.30
Stage of cancer	Stage 1	115	37.70
	Stage 2	112	36.70
	Stage 3	37	12.10
	Stage 4	41	13.40
Duration of cancer since diagnosis	<2 years	159	52.10
	≥2 years	146	47.9
Types of cancer therapy	Chemotherapy	229	75.10
	Radiotherapy	3	1
	Surgery + chemotherapy	62	20.30
	Surgery + radiotherapy	10	3.30
	Surgery	3	0.30
Antipain medication used	No	62	20.30
	Yes	243	79.70
Antiemetic medication used	No	132	43.30
	Yes	173	56.70
Methods of cancer diagnosis	CT scan	189	62
	MRI	78	25.60
	Haematological investigation	38	12.50
Anaemia	No	182	59.70
	Yes	123	40.30
Comorbidity	Yes	69	22.60
	No	236	77.40
Types of comorbidity	DM	46	15.10
	Hypertension	11	3.50
	HIV/ADIS	9	3
	Hepatic disease	3	1
History of metastasis	No	207	67.90
	Yes	98	32.10
Patient performance	Good	127	41.60
	Poor	178	58.40
Depression	No	166	54.40
	Yes	139	45.60
Anxiety	No	132	43.30
	Yes	173	56.70

Continued

Table 2 Continued

Variable	Category	Frequency	%
Sleep quality	Good	21	6.90
	Poor	284	93.1
Social support	Poor	183	60
	Moderate	117	38.40
	Strong social support	5	1.60

DM, diabetes mellitus.

poor performance status, cancer stage 2 or stage 4, and were admitted to hospital, were significantly associated with CRF. The odds of having clinically significant fatigue among patients with cancer who had depressive symptoms were nearly two times higher as compared with those of patients who did not have depressive symptoms. The result of the current study was consistent with that of studies conducted in China,[17 44] Taiwan,[53] Italy,[54] Canada[55] and Norway.[56] Cancer and its treatment can raise proinflammatory cytokine levels, which directly affect neurotransmitter levels in the central nervous system. Serotonin (a mood stabiliser) and its precursor tryptophan increases dramatically, and depression and fatigue follow.[57 58] Moreover, depression results in a lack of energy, mood changes and appetite, which could increase the level of fatigue.[5 57] A history of depression and stressful experiences in pretreatment and during the diagnosis of cancer could be another possible reason for CRF.[59]

The odds of having clinically significant fatigue among patients with cancer who had poor sleep quality were three times higher as compared with those who had good sleep quality. The result of this study was in line with previous studies conducted in China,[18 30] Canada[54] and Italy.[55] These associations might be justified by the alterations in cytokine profiles of patients with cancer. Cytokines are molecules that monitor inflammation and have direct effects on the neurobiology of sleep and generation of the circadian rhythm.[56 57] Furthermore, it is postulated that the central molecular clock through the suprachiasmatic nuclei directly influences the activation or inhibition of hypothalamic centres. This effect leads to altered cytokine and hormonal production (melatonin, upsetting physiological balance and resulting in sleep disturbance and fatigue).[58]

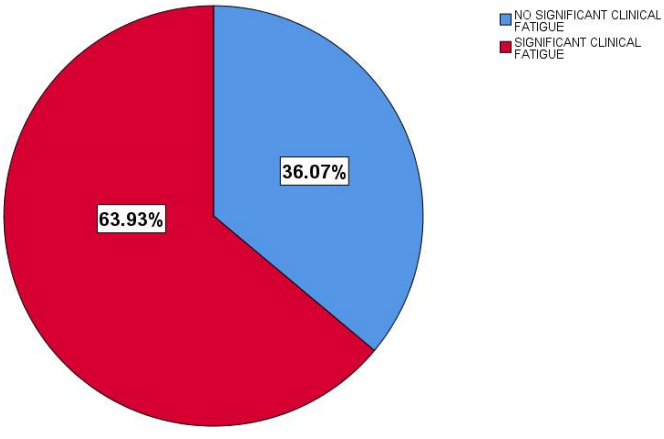

Figure 2 Prevalence of cancer-related fatigue among the study participants attending oncology units in comprehensive specialised hospitals in Amhara region, 2022 (n=305).

Likewise, the odds of having clinically significant fatigue among patients with cancer who had poor performance status were nearly two times higher as compared with those of patients who had good performance status. The current study was in line with previous studies in China,[30] Italy[55] and Taiwan.[59] The possible justification for this association could be that cancer or its treatment can damage the sarcoplasmic reticulum by raising intracellular calcium levels and result in impaired mitochondrial function for regeneration of skeletal muscle, compromising the individual's ability to accomplish physical tasks.[58 60] Dysregulation of the sarcoplasmic reticulum may cause CRF due to lower protein synthesis or accumulation of metabolite. The effect of metabolites can produce metabolic fatigue within the neuromuscular junction or muscle fibres that interferes with the release of calcium from the sarcoplasmic reticulum and reduces the contractile properties of muscles cell actin and myosin, and the performance status of patients with cancer could be compromised.[61]

Regarding the participants' clinical cancer stage, the odds of having clinically significant fatigue among patients with stage 2 cancer were 2.4 times higher as compared with that of patients with stage 1 cancer. In addition to this, the odds of having clinically significant fatigue among patients with cancer who had stage 4 cancer were three times higher as compared with those of patients with stage 1 cancer. Even though contradicting results are available from previous studies with respect to clinical stages of cancer, the current study was in line with studies in Taiwan, China and Ethiopia, where clinical stage 2 and stage 4 cancers were significantly associated with CRF. The possible justification for this association might be when the levels of cancer stage advanced, inflammatory cytokines like interleukin (IL) 1, IL-, IL-5, HT and tumour necrosis factor α (TNFα), and metabolic

Table 3 Multivariable analysis results at the final step of a binary logistic regression model in comprehensive specialised hospitals in Amhara region, 2022 (n=305)

Variable	Category	Cancer-related fatigue		COR (95% CI)	AOR (95% CI)	P value
		No	Yes			
Depression	No	80	86		1	
	Yes	30	109	3.38 (2.03 to 5.60)	1.97 (1.00 to 3.86)	0.04*
Anxiety	No	71	61		1	
	Yes	39	134	3.99 (2.44 to 4.55)	1.32 (0.63 to 2.75)	0.67
Sleep quality	Good	15	6		1	
	Poor	95	189	4.97 (1.87 to 13.23)	3.30 (1.05 to 10.34)	0.04*
Performance status	Good	66	61		1	
	Poor	44	134	3.29 (2.02 to 5.36)	1.98 (1.01 to 3.85)	0.04*
Cancer stage	Stage 1	69	46		1	
	Stage 2	29	83	4.29 (2.44 to 7.54)	2.36 (1.17 to 4.77)	0.01*
	Stage 3	6	31	7.75 (2.99 to 20.04)	2.95(.978 to 8.90)	0.55
	Stage 4	6	35	8.85 (3.40 to 22.46)	3.24 (1.01 to 10.34)	0.04*
Admission status	Outpatient	65	66		1	
	Inpatient	45	129	2.82 (1.74 to 4.57)	2.04 (1.12 to 3.73)	0.02*
Age, years	18–28	18	16		1	
	29–39	29	30	1.16 (.50 to 2.70)	0.70 (0.21 to 2.32)	0.56
	40–50	27	67	2.79 (1.24 to 6.26)	1.32 (0.40 to 4.30)	0.56
	51–60	24	40	1.87 (0.80 to 4.35)	0.91 (0.28 to 2.94)	0.87
	>60	12	42	3.93 (1.55 to 9.98)	2.14 (0.58 to 7.93)	0.25
Antipain medication used	No	32	30		1	
	Yes	78	165	2.25 (1.21 to 3.97)	1.19 (0.53 to 2.70)	0.66
Antiemetic medication used	No	65	67		1	
	Yes	45	128	2.76 (1.70 to 4.46)	0.57 (0.28 to 1.14)	0.77
History of metastasis	No	88	119		1	
	Yes	22	76	2.55 (1.47 to 4.42)	1.51 (0.756 to 3.02)	0.56

*indicates a significant factor.
AOR, adjusted OR; COR, crude OR.

by-products could have been accumulated in the blood and cancer treatment could have damaged healthy cells in addition to cancerous cells resulting in fatigue.[57] The possible reason for the association of stage 2 cancer with CRF could be the period, which was very critical for patients to decide and start cancer treatment, adapting to multiple cancer drugs, and facing the adverse effects of chemotherapy and radiotherapy. All this together can cause patients to be more fatigued than patients with stage 1 cancer.[21 30]

Regarding the admission status of the study participants, the odds of having clinically significant fatigue among patients with cancer who were admitted to hospital were two times higher as compared with patients with cancer who were served in the outpatient department. Although this risk factor was not addressed adequately in previous studies, the results of this study are consistent with studies in Brazil and Jordan.[62 63] The possible reason for this association could potentially stem from the fact that hospitalised patients with cancer are more susceptible to infections and are exposed to a greater number of comorbid diseases. In comparison to patients with cancer who are not hospitalised, inpatients may have greater levels of fatigue due to stress, noise and psychological issues.

Strengths and limitations of the study

This study was carried out in four comprehensive specialised hospitals across the Amhara region using a recently validated standardised questionnaire. Hence, it helps to generalise to the regional as well as the national levels. However, because of the cross-sectional nature of the study design, a temporal relationship between the variables could not be established. In addition to this, self-reported questionnaires that measure CRF were prone to recall bias. Despite these limitations, this study clearly showed the magnitude of CRF and risk factors for patients with cancer.

CONCLUSION

In this study, the prevalence of CRF among adult patients with cancer was relatively high as compared with previous studies. Symptoms of depression, poor sleep quality, poor performance status, cancer stages 2 and 4, and hospitalisation were factors significantly associated with CRF.

Recommendations

To Amhara region comprehensive specialised hospitals

The comprehensive specialised hospitals of the Amhara regional state should incorporate screening services for CRF and its risk factors into their regular cancer management programmers.

To healthcare providers

To facilitate and ease cancer treatment and minimise the burden of CRF through early screening, diagnosis and management of CRF, healthcare providers must raise patient-centred awareness about the impact and severity of CRF as well as its associated factors. This will ultimately lead to better health outcomes. For patients with cancer with depression and poor sleep quality, rigorous screening and suitable treatments should be considered throughout the course of therapy.

To policy-makers and programme planners

Policy-makers and programme planners shall design a feasible method of screening and managing CRF and its associated factors and integrate it in the current cancer treatment and palliative care programme. Additionally, they need to consider expanding quality oncology service centres that are equipped with medical equipment along with well-trained healthcare professionals.

To researchers

In order to fully investigate the levels of fatigue of patients with cancer, additional qualitative and longitudinal research is required for integrating variables related to drugs and biomarkers. There are four guidelines on CRF worldwide. Therefore, researchers shall work on updating the guidelines regarding the management and prevention of CRF.

Contributors This study was conceptualised by GZ and refined after discussion with WZW and DA. GZ wrote the proposal and WZW and DA commented on and corrected it. GZ led the data collection process, analysed the data and drafted the manuscript. WZW and DA were also responsible for data analysis and the write-up of the manuscript. GZ, WZW and DA read and approved the final version of the manuscript and agreed to submit the manuscript in this journal. GZ is responsible for the overall content as guarantor.

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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and ethical clearance was obtained from the research and ethical review committee of the University of Gondar, College of Medicine and Health Sciences, School of Nursing on behalf of the Institutional Review Board of the University of Gondar (Ref No. S/N/237/2014). Permission letters were granted from the managements of the respective hospitals. The purpose and importance of the study were explained to the participants. Following that, written informed consent was obtained from each study participant. The confidentiality of the participants was maintained at all times, and the information was kept in a safe, lockable cabin. This study was conducted in accordance with the Declaration of Helsinki. Participants gave informed consent to participate in the study before taking part.

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