

Prevalence of Cancer Related Fatigue and Associated Factors among Cancer Patients at the Oncology Unit, Bahir Dar, Ethiopia

Belaynew Adugna¹ and Tena Mekonnen^{2*}

¹Department of Physiotherapy, School of Medicine, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia

²Department of Pharmaco-Epidemiology and Social Pharmacy, School of Health Science, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia

Abstract

Background: Cancer related fatigue is one of the most prevalent distressing cancer related symptom. Different studies reported a variety number for its prevalence in cancer patients. However, due to lack of studies, its prevalence and associated factors in developing countries remain ambiguous. Therefore, the aim of this study was to assess the prevalence of cancer related fatigue and associated factors among cancer patients who were visiting the oncology unit of Felege Hiwot Comprehensive Specialized Hospital.

Methods: A cross sectional study design was conducted on 286 participants who were selected using systematic random sampling technique. The collected data was analyzed using SPSS version 23.

Results: The overall prevalence of clinically significant cancer related fatigue was 63.8%. About 36.3% and 27.5% of cancer patients were severe and moderate level of fatigue respectively. The contributing factors were: Age < 40 years [AOR=3.742; 95% CI: 1.157-12.103], BMI < 18.5 [AOR=0.363; 95% CI: 0.154-0.856], Anxiety [AOR=3.548; 95% CI: 1.543-8.159], Pain [AOR=2.718; 95% CI: 1.315-5.618] and Clinical Stage I and Stage II [AOR=4.049; 95% CI: 1.67-9.818] and [AOR=5.715; 95% CI: 2.113-15.460].

Conclusion: The prevalence of clinically significant cancer related fatigue was moderate. Age, BMI, clinical stage, anxiety and pain were factors which had statistically significant association with cancer related fatigue.

Keywords: Cancer related fatigue; Mortality; Patients; Treatment

Corresponding author:

Tena Mekonnen, Department of Pharmaco-Epidemiology and Social Pharmacy, School of Health Science, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia

✉ tenadagim@gmail.com

Citation: Adugna B, Mekonnen T (2021) Prevalence of Cancer Related Fatigue and Associated Factors among Cancer Patients at the Oncology Unit, Bahir Dar, Ethiopia. Am J Pharmacol Pharmacother Vol.8 No.4: 16.

Received: November 19, 2021; **Accepted:** December 03, 2021; **Published:** December 10, 2021

Introduction

Cancer is diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs [1].

It is one of the leading causes of morbidity and mortality worldwide. In 2013 there were 14.9 million incident cancer cases and in 2015 cancer was the second leading cause of death, which was responsible for 8.8 million deaths globally [2]. Around 70% of these deaths from cancer occur in low and middle-income countries [1].

In Addis Ababa, Ethiopia September 2011 to August 2014, a total of 5701 cancer cases were registered [3]. The nationwide incidence of cancer is estimated to be 60,960 cases and responsible for over 44,000 deaths (5.8%) of total national mortality annually [4]. The fast growing population of Ethiopia coupled with lifestyle changes will be the cause for increasing burden of cancer in the country. The number of cancer patients in the country may be

under estimated due to lack of cancer registry and poor reporting system in the country. In the country Ethiopia, oncology services are inadequate, late referrals and only few cancer centers, and a few health care professionals' struggles to serve the entire country [5,6].

Nowadays, with the continued development of cancer diagnostic and therapeutic technologies, patient survival duration has been significantly extended and it is no longer considered to be a death sentence, but rather a disease that patients must manage and live with. Yet, improvements in the Quality Of Life (QOL) of cancer patients have fallen short of expectations because of cancer-related fatigue (CRF) and other cancer related symptoms (CRS) [7,8].

The term Cancer-related fatigue is defined 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'. Compared with the fatigue experienced

by healthy individuals, CRF is more severe, more distressing, and less likely to be relieved by rest [9].

The etiology of CRF is multifactor, several contributing factors are known including, socio-demographic factors, genetic factors, psychosocial factors (e.g. depression) and behavioral factors (e.g. physical inactivity) [10].

Cancer related fatigue is one of the most prevalent distressing CRS both during and after their treatment. It can have a broad impact on physical, emotional and cognitive function of the sufferers and it tends to worsen with the progression of cancer and its treatment [9,11].

Evidences were showing that a patient with CRF has low QOL and poor survival rate [12]. It can also be a barrier to return to work for cancer survivors, thus imposing an enormous burden on the family as well as in the community [13].

Even though, cancer has been increasingly recognized as a critical public health problem in Ethiopia, it gets low public health priority; this is due to high burden of communicable diseases and limited resources [14].

On the other hand, the National Cancer Control Plan (NCCP) of Ethiopia for the years 2015/16 to 2019/20 aims to ensure a better QOL for those living with cancer through innovative research and key thematic interventions such as promoting physical activity [15]. However, studies on the prevalence of CRS including CRF, which affects the QOL of cancer patients directly, were lacking in Ethiopia, this puts questioning the achievement of this goal.

Most of this research has been conducted in developed countries and significant discrepancies exist among studies, as well as due to lack of cancer registry, the exact prevalence and severity of CRF among cancer patients in developing country are not clear. Not only the prevalence but also factors associated with CRF in developing countries including Ethiopia, particularly in the study area, remain unclear. Therefore, this study was designed to assess the prevalence of cancer related fatigue and associated factors among cancer patients who were visiting the oncology unit of Felege Hiwot Comprehensive Specialized Hospital (FHCSH), Bahir Dar town, Ethiopia, from April to May, 2018.

Materials and Methods

Study area and study period

The study was conducted on cancer patients, who were visiting the oncology unit of FHCSH in Bahir Dar, Ethiopia from April to May, 2018. Bahir Dar is the capital city of Amhara national regional state, located in north western part of Ethiopia.

Study design

An institutional based cross sectional study was conducted.

Source population and study population

Source population: All cancer patients who visited the oncology unit of FHCSH were the source population.

Study population: The study population was all sampled cancer patients who visited the oncology unit of FHCSH during the study

period, 2018 and who fulfilled the eligibility criteria.

Inclusion and exclusion criteria

Inclusion criteria: All type of cancer patients who were visiting the oncology unit of FHCSH during the study period was included in the study.

Exclusion criteria: Critically ill patients who were unable to give consent were excluded from the study.

Sample size determination

For the first objective, due to lack of similar study in Ethiopia, the sample size was calculated with the assumption of expected population size=800, expected frequency=0.5, confidence interval=95%, confidence limit=5% and using Epi Info version 7 statistical software to get the optimum sample size. The final sample size was 260 subjects. After adding 10% for non-response rate, the total sample size was 286 cancer patients.

For the second objective, considering exercise as an exposure and setting two sided confidence level of 95%, power=80%, odds ratio=1.45, prevalence of CRF in unexposed group=42.2%, prevalence of CRF in exposed group=62.63% from previous studies and using the Epi Infoversion 7 statistical software to get the optimum sample size, the final calculated sample size was 231 on Fleiss w/CC. After adding 10% for non-response rate and minor adjustment, the total sample size was 255 cancer patients [16].

Therefore, the total sample size of this study was 286 cancer participants.

Operational definition

A. Cancer-related fatigue: is defined 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'. Compared with the fatigue experienced by healthy individuals, CRF is more severe, more distressing, and less likely to be relieved by rest [9].

B. Physical exercise: is any type of regular physical exercise including aerobic exercise, resistance exercise/muscle strengthening, and stretching exercise that has been done by the patient in a regular time interval currently.

C. Sleep quality: to say an individual has a very good quality sleep, he/she has to sleep more time while in bed (at least 85 percent of the total time), falling asleep in 30 minutes or less, waking up no more than once per night; and being awake for 20 minutes or less after initially falling asleep [17].

D. Depression: Everyone feels sad or low sometimes, but these feelings usually pass with a little time. To be diagnosed with depression, symptoms must be present most of the day, nearly every day for at least 2 weeks [18].

E. Interpretation of the BFI result: Brief inventory index=SUM (points for all 9 items)/9 or Brief inventory index=SUM (points for all 9 items)/90* 100 the higher the index, the greater the fatigue [17].

F. Clinically significant fatigue: It is a fatigue greater than or equal to 4 on the numerical rating scale (**Table 1**).

Table 1: Interpretation of brief inventory score.

Index	Level of fatigue
0	None
1 to 3	Mild
4 to 6	Moderate
7 to 10	Severe

Sampling technique/procedure

A systematic random sampling method was employed to draw study subjects from the study population. The sampling interval was calculated using the assumption of expected population size of 800 and the sample size of 286 cancer patients. Considering that, the sampling interval was approximately 3. However, due to time constraint and practical applicability, the first participants were selected randomly by lottery method from the first two cancer patients and then every other patient who was coming to the oncology unit was selected until we reach the optimum sample size of the study.

Data collection procedure

The data were collected by interviewing the participants and reviewing the charts of the patient using a structured questionnaire. Cancer patients who were willing to participate in the study was screened by using the eligibility criteria and after obtaining informed consent, trained data collectors were interviewing the participants who were included in the study. Both in and outpatient were included and measurements like height and weight were measured after the end of the interview. Additional information on clinical stage of the patient, type of the disease and type of treatment used was obtained from the patients chart to reduce potential bias. The data collectors were two nurses working in the oncology unit and the supervisor was a physiotherapist working in FHCSH.

Variables

Dependent variable: Cancer related fatigue (1=Yes, 0=No)

Independent variables: Socio-demographic, personal variables, age, sex, marital status, house hold income, educational level and BMI.

Psychological/behavioral factors

Anxiety, depression, sleeps quality and physical activity

Disease and treatment related factors

Type of cancer, clinical stage and type of the treatment

Co-morbid medical conditions

Pain and anemia

Measurement tool

A structured questionnaire was adapted and modified by the investigator after exhaustive review of previous literatures for both dependent and independent variables.

Demographic information

Personal and psychosocial characteristics (including age, gender, educational level, marital status, household income, BMI, sleep quality, physical activity, anxiety and depression), disease and treatment related information(including disease diagnosis, clinical stage and treatment type) and other medical conditions (including pain and anemia) was collected from the patients interview and from records in the patient chart.

Brief fatigue inventory score

The BFI is a reliable and valid unidimensional measurement tool developed by Mendoza et al. (46). It includes nine items, with the first three assessing the “now,” “usual,” and “worst” levels of fatigue during the past 24 hours. Fatigue severity was evaluated by using an integer scale of 0 (no fatigue) to 10 (fatigue as bad as you can imagine), which was recommended by National Comprehensive Cancer Network (NCCN) guidelines for screening and re-evaluation of CRF, with the cutoff score for clinically significant fatigue being 4[7].The remaining six items assess the extent to which fatigue has interfered with Activity of Daily Life (ADL) during the past 24 hours in terms of general activity, mood, walking ability, normal work, relationships with other people, and enjoyment of life.

Data processing and analysis

The collected data were coded, entered and cleaned using EPI info version 7 and then, exported and analyzed using SPSS version 23. Descriptive statistics including frequency, percentage, mean, median, range and standard deviations was used to describe the findings.

Inferential statistical analysis using multivariable logistic regression was employed to show the relationship between dependent and independent variables. In bivariate logistic regression analyses, variables with P-value <0.25 were considered as potential candidates in the final multivariable logistic regression analysis and P-value <0.05 was considered statistically significant in the multivariable logistic regression. Multi-co linearity and model fitness were checked for the final model fitted. Multivariate analysis was done to control potential confounder variables. Finally, the OR and 95% CI was estimated and interpreted for all predictors that were included in the final model.

Data quality control and management

A valid and reliable instrument was used for the data collection. All data collectors and supervisors were given one-day training on the purpose of the study, details of the data collection instrument(questionnaire), interviewing techniques, importance of privacy and insuring confidentiality of the respondents prior to the actual data collection.

Pretest of the tool was done on 15 (5%) of cancer patients who visited the oncology unit of University of Gondar hospital, to check the understandability, consistency and appropriateness of the questioner. Then the necessary correction and modification of the tool was done before the actual data collection was started.

Daily close supervision at the end of every data collection was

made; the questionnaires were reviewed and checked for completeness, accuracy and consistency by supervisors and investigator to take timely corrective measures.

Results

Socio-demographic and personal characteristics

Among the total 286 study participants, 273 of them completed the interview giving the response rate of 95.5%. The mean age of participants was 46 ± 16 year. The median monthly household income of participants was 2000 and range (200-10000 birr). About 170 (62.5%) of the participants had healthy weight on BMI score (Table 2).

Table 2: Socio-demographic characteristics of cancer patients in FHCSH, April 2018, (n=273).

Variables	Frequency	Percent (%)
Sex		
Female	173	63.4
Male	100	36.6
Age group		
<40	112	41
40-70	119	43.6
>70	42	15.4
Marital status		
Married	187	68.5
Single	33	12.1
Divorced	29	10.6
Widowed	22	8.1
Other	2	0.7
Body Mass Index(BMI)		
<18.5	84	30.8
18.5-24.9	170	62.2
25-30	11	4
>30	8	3
Monthly household income (in Birr)		
<1000	77	28.2
1001-2000	110	40.3
2001-2675	18	6.6
>2676	68	24.9

Psychosocial and comorbid characteristics of cancer patients

Almost half of the participant's experienced bad sleep quality 137 (50.2%) and the majority of the participants were not doing regular physical exercise 248 (90.8%). More than half of them had depression 153 (56%) and about 180 (65.9%) of them had anxiety. One hundred fourteen (41.8%) of study participants were reported that they had anemia and most 159 (58.2%) of them experienced pain (Table 3).

Table 3: Psychosocial and Co-morbid characteristics of cancer patients in FHCSH, April 2018, (n=273).

Variables	Frequency	Percent (%)
Sleep quality		
Good	82	30
Medium	54	19.8
Bad	137	50.2
Physical exercise		
Yes	25	9.2
No	248	90.8

Depression		
Yes	153	56
No	120	44
Anxiety		
Yes	180	65.9
No	93	34.1
Anemia		
Yes	114	41.8
No	159	58.2
Pain		
Yes	159	58.2
No	114	41.8

Disease and treatment related characteristics of cancer patients

The commonly reported type of cancer was Blood cancer 53 (19.4%). Most of the participants were stage IV cancer patients 97 (35.5%). The commonly used treatment was chemotherapy 120 (44%) followed by chemotherapy and surgery 72 (26.4%) (Table 4).

Prevalence of CRF among cancer patients in FHCSH

Out of 273 study participants, 193(70.7%, 95% CI: 65.6%-75.9%) of them have CRF in the last week. Among those, about 174 (63.8%, 95% CI: 58.12% to 69.48%) of cancer patients reported clinically significant fatigue (score 4 and above on BFI).

Factors associated with CRF

Age of the participants, BMI, sleep quality, clinical stage of the patient, physical exercise, history of depression, anxiety, anemia and pain showed significant association with CRF in the bi-variable analysis but only age, BMI, clinical stage, anxiety, and pain showed statistically significant association with CRF during the multivariable analysis.

The result of this study showed that, the odds of being classified as CRF was approximately four times higher in the younger (<40 years' old) than older patients (>70 years' old)[AOR=3.742; 95% CI (1.157-12.103)]. Participants with BMI <18.5 (underweight) had 63.7% extra protection against CRF as compared to those participants with BMI between 18.5-24.9 (healthy weight) [AOR=0.363; 95% CI (0.154-0.856)].

Regarding the clinical stage of the participants, stage I cancer patients were approximately four times more likely to develop CRF and stage II were approximately six times more likely to be fatigue than those patients with clinical stage of IV [AOR=4.049; 95% CI (1.67-9.818)] and[AOR=5.715; 95% CI (2.113-15.46)], respectively.

The odds of being fatigued was about four times higher in cancer patients who had anxiety than who don't [AOR=3.548; 95% CI (1.543-8.159)].

Patients who experienced pain was nearly three times more likely to be affected by CRF than patients who don't experience pain [AOR=2.718; 95% CI (1.315-5.618)] (Table 5).

Table 4: Psychosocial and Co-morbid characteristics of cancer patients in FHCSH, April 2018, (n=273).

Variables	Frequency	Percent (%)
Type of cancer		
Blood Cancer	53	19.4
Gynecological Cancer	51	18.7
Breast Cancer	48	17.6
Colorectal Cancer	23	8.4
Sarcoma	23	8.4
Esophageal Cancer	20	7.3
Lung Cancer	18	6.6
Gastric Cancer	16	5.9
Hepato cellular carcinoma (HCC)	7	2.6
Other type of Cancer	14	5.1
Clinical stage		
Stage I	58	21.2
Stage II	44	16.1
Stage III	73	26.7
Stage IV	97	35.5
Treatment type		
Chemotherapy	120	43.9
Chemotherapy & Surgery	72	26.4
Surgery	32	11.7
Others	8	3

Table 5: Factors associated with CRF among cancer patients in FHCSH, Bahir Dar, Ethiopia, 2018 (n=273).

Variables	Presence of CRF		Bi-variable		Multivariable	
	Yes	No	COR(95%CI)	P-value	AOR(95%CI)	P-value
Age group						
<40	71(63.4%)	41(36.6%)	1	0.044		
40-70	109(74.1%)	38 (25.9%)	1.656(0.972-2.823)	0.064		
>70	13(92.9%)	1(7.1%)	7.507(0.972-59.49)	0.056		
BMI						
18.5-24.9	118(69.4%)	52(30.6%)	1	0.098	1	
<18.5	66(78.6%)	18(21.4%)	1.616((0.874-2.988) *	0.126	0.363(0.154-0.856) **	0.021
25-30	5(45.5%)	6(54.5%)	0.367(0.107-1.257) *	0.111	1.386(0.329-5.839)	0.656
>30	4(57.1%)	3(42.9%)	0.588(0.127-2.719)	0.496	0.748(0.098-5.710)	0.779
Sleep quality						
Good	46(56.1%)	36(43.9%)	1			
Medium	34(63.0%)	20(37.0%)	0.752(0.372-1.519)	0.427		
Bad	113(82.5%)	24(17.5%)	0.271(0.146-0.504) *	<0.001		
Clinical stage						
Stage I	25(42.4%)	34(57.6%)	7.48(3.513-15.929) *	<0.001	4.049(1.670-9.818) **	0.002
Stage II	21(47.7%)	23(52.3%)	6.2(2.769-13.909) *	<0.001	5.715(2.113-15.460) **	0.001
Stage III	65 (89.1%)	8(10.9%)	0.823(0.338-2.001)	0.667	0.729(0.261-2.032)	0.545
Stage IV	82(84.5%)	15(15.5%)	1		1	
Physical exercise						
Yes	12(48.0%)	13(52.0%)	2.927(1.272-6.733) *	0.012		
No	181(73.0%)	67(27.0%)	1			
Depression						

Yes	131(85.6%)	22(14.4%)	0.180(0.101-0.319) *	<0.001		
No	62(51.7%)	58(48.3%)	1			
Anxiety						
Yes	149(82.8%)	31(17.2%)	0.187(0.107-0.328) *	<0.001	3.548(1.543-8.159) **	0.003
No	44(47.3%)	49(52.7%)	1		1	
Anemia						
Yes	96(84.2%)	18(15.8%)	0.293(0.162-0.532) *	<0.001		
No	97(61.0%)	62(39.0%)	1			
Pain						
Yes	135(84.9%)	24(15.1%)	0.184(0.104-0.325) *	<0.001	2.718(1.315-5.618) **	0.007
No	58(50.9%)	56(49.1%)	1		1	

NB: COR=crude odds ratio, AOR=adjusted odds ratio, *=significant association (on bivariate), **=significant association (on multivariate), 1.00=Reference.

Discussion

About 63.8% of cancer patients reported clinically significant fatigue (score 4 and above on BFI). The contributing factors that had statistically significant association with CRF were: Age, BMI, Clinical stage, Anxiety and Pain.

The prevalence of clinically significant CRF in the current study was higher than the finding of a cohort study done in Norway, 53% (39), China, 52.07% (28), Canada, 29% (24) and Brazil, 25% (12). This observed difference could be due to difference in assessment tool, for example, International Classification of Diseases Ninth Edition (ICD-9) was used in the study of Norway (39) while in Canada, FACT-F (2) and in Brazil EORTC QLQ-C30 was used as an outcome measure (12) which has different cutoff point for clinically significant CRF. The other reason might be due to difference in populations included and data collection method used, in the study of Norway only gynecological cancer patients were included using telephone survey (39) whereas in Canada, post-treatment cancer survivors using self-administered mail based questionnaire [19]. On the other hand, the Brazilian study was done on advanced cancer outpatients using telephone interviews which may reduce finding of the study. The other possible reason also may be due to differences in geographical locations from which the samples were drawn [12].

The current finding was relatively comparable with the finding of a study done in China, where the prevalence of CRF was reported as 60%. This likeness could be due to the similarity in the study design and the outcome measure used [20].

However, the prevalence of CRF in this study was relatively lower than the finding of studies done in USA, 75.0% (23), Bangladesh, 79.4% (29), South Africa, 80% (30) India, 83.3% (34) and Switzerland, 87% (15). This difference may be due to the sampling technique, in South Africa; purposive sampling technique was used (30) whereas in Switzerland, they used convenience

sampling (15). The additional possible explanation is that due to difference in definition of CRF, result from the study done in India reported prevalence of fatigue whereas we reported clinically significant fatigue [21]. On the other hand, the study in USA used retrospective chart review in emergency care and all these reasons may have the capacity to inflate the finding of those studies [22].

In the current study, the odd of being classified as fatigued was four times higher in the younger patient's older one. This finding was in line with a study in Germany, where the odds of being classified as fatigued was four times higher in the younger patients who were <40 years' old than in the older patients who were >60 years' old cancer patients [23]. Likewise, a study in Brazil (35) and Switzerland (15) reported that, younger cancer patients were experiencing more fatigue than older one. Understanding the relationship between age and fatigue has some challenges. But some of the possible explanations for this finding are that younger patients may find it more difficult to accept a cancer diagnosis and they view cancer as a greater threat to their lives as well as they have fewer coping strategies than older patients (48). In addition, younger patients perceive a larger discrepancy between themselves and their peers in the general population or between their current level of energy and their previous situation [24]. The other reason might be that, in contrast to their older counterparts, young patients must deal simultaneously with their illness and their social and vocational developments crucial to establishing their adult lives (4).

In this study underweight participants had 63.7% extra protection for CRF than those who had healthy weight. On the contrary, a study among Brazilian cancer patient reported that patients with CRF had lower scores of BMI [12]. On the other hand, the study done in China reported that, obese women have experienced clinically significant fatigue [25]. These three studies have different findings and this observed difference may be due to difference in study area, clinical stage and difference in diagnosis of the participants, the study in Brazil was done on advanced cancer outpatients who were under palliative care [12]. In the same way, the study done in China was focused on breast cancer patients undergoing endocrine therapy, which has an impact

on BMI due to changes in hormone levels and altered eating behaviors of the patients [25].

Regarding the clinical stage of the participants, in the current study, stage I and stage II cancer patients had higher risk for CRF as compared with cancer patients who had clinical stage of IV. On the contrary, the result of the study in China reported that, patients with higher clinical stage of cancer were more likely affected by CRF than patients with lower clinical stage [26]. The result of a meta-analysis of studies on BCS also reported that, survivors with stage II or III cancer were at higher risk developing severe fatigue than survivors with stage 0 or I cancer [21]. These two studies were performed on women's living with breast cancer and this may be one of the reasons for the observed difference with our study. The other reason can be, Stage I and II were most common period for patients to be aware of their condition and start Chemotherapy in our study area. Together with psychological distress can cause patients to be more fatigued than stage IV patients were they may complete their treatment and become free from its short term effect.

In our study, the prevalence of CRF was four times higher in cancer patients who had anxiety than patients without anxiety. Studies have consistently reported a strong relationship between anxiety and CRF, which is in accord with our results. In a population based survey in China reported that, cancer patients who had a history of anxiety were significantly associated with fatigue than patients with no history of anxiety [27]. Correspondingly, a cross-sectional study on gynecological cancer patients showed that, cancer patients who had CRF reported higher levels of anxiety than patients without CRF [28]. Regardless of their difference in methodology and study participants, all of this study agreed that, anxiety was significantly associated with fatigue. This could be due to the capacity of psychological distress to increase the physical distress of individuals, which can cause fatigue, and can reduce coping capacity of individuals. However, the possible relationship and the direction of causality of fatigue and anxiety are still unclear, despite a recent increase in research interest [29].

Cancer patients who were experiencing pain were three times more likely to be affected with CRF than patients who were not experiencing pain in the current study. This was supported by a study done in Brazil, which reported that, the presence of pain on cancer patients was significantly associated (four times) with the development of CRF [30]. Likewise, the study in University of Texas showed that, the occurrence of moderate to severe fatigue was positively associated with moderate to severe reports of pain [31]. Another study in similar setting also reported that, patients with severe pain were two times more likely to experience severe fatigue than patients with mild pain [23]. Pain, which had a direct effect on fatigue, in cancer patients can occur secondary to cancer treatment, such as surgery and radiotherapy or the presence of lymph edema and may cause fatigue experience [11,32]. However, differentiating cancer and non-cancer pain is still very complex and need further investigation to provide better understanding and development of specific prevention and treatment [33]. On the other hand, pain in cancer patients require use of opioid

medication for pain control, which may cause patients to be fatigued by itself and needs another investigation [34].

Conclusion

The present findings suggest that the prevalence of clinically significant CRF was moderate, (63.8%), where 36.3% of them were severely fatigued and 27.5% were moderately fatigued. Age, BMI, clinical stage, anxiety, and pain showed statistically significant association with CRF in the final binary logistic model.

Data Availability

The authors confirm that data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

"The author(s) declare(s) that there is no conflict of interest regarding the publication of this article."

Funding Statement

The research did not receive specific funding, but was performed as part of the employment of the authors in Bahir Dar University.

Ethical Statement

The ethical approval was obtained from the Research and Ethical Review Committee and Institutional Review Board of Mekelle University, College of Health Sciences. Permission to conduct the study was obtained from Felege Hiwot comprehensive specialized hospital and the oncology unit.

Participation was completely voluntary and participants were informed that, they had the right to refuse or participate in the study after purpose, duration, benefit and possible risks of participation was presented for each participant. Data anonymity and confidentiality was kept throughout the study. Moreover, both written and verbal informed consent was obtained prior to collect data. The collected data were used only for the intended purpose of the study.

References

1. WHO Cancer (2018).
2. The Global Burden of Cancer 2013. *JAMA Oncol* (2015) 4:505-27.
3. Addis Ababa City Cancer Registry (2018).
4. Globocan 2012 (2018).
5. Woldeamanuel YW, Girma B, Teklu AM (2013) Cancer in Ethiopia. *Lancet Oncol* 14(4):289-90.
6. Tadele N (2015) Evaluation of quality of life of adult cancer patients attending Tikur Anbessa specialized referral hospital, Addis Ababa Ethiopia. *Ethiop J Health Sci* 25(1):53.
7. Berger AM, Abernethy AP, Atkinson A, Barsevick AM, Breitbart WS, et al. (2010) NCCN Clinical practice guidelines cancer-related fatigue. *J Natl Compr Cancer Netw* 8(8):904-31.

8. Bartsch HH, Weis J, Moser MT (2003) Cancer-related fatigue in patients attending oncological rehabilitation programs: prevalence, patterns and predictors. *Oncol Res Treat* 26(1):51-7.
9. Butt Z, Rosenbloom SK, Abernethy AP, Beaumont JL, Paul D, et al. (2008) Fatigue is the most important symptom for advanced cancer patients who have had chemotherapy. *J Natl Compr Cancer Netw* 6(5):448-55.
10. Bower JE (2014) Cancer-related fatigue: Mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol* 11(10):597-609.
11. Horneber M, Fischer I, Dimeo F, Ruffer JU, Weis J (2012) Cancer-Related Fatigue. *Dtsch Arztebl Int* 109(9):161-72.
12. Paiva CE, Paiva BSR (2013) Prevalence, predictors, and prognostic impact of fatigue among Brazilian outpatients with advanced cancers. *Support Care Cancer* 21(4):1053-60.
13. Islam T, Dahlui M, Majid HA, Nahar AM, Taib NAM, et al. (2014) Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Pub Health*. 14(3):8.
14. Wagner LI, Cella D (2004) Fatigue and cancer: Causes, prevalence and treatment approaches. *Bri J Cancer* 91(5):822-8.
15. Spichiger E, Müller-Fröhlich C, Denhaerynck K, Stoll H, Hantikainen V, et al. (2012) Prevalence and contributors to fatigue in individuals hospitalized with advanced cancer: A prospective, observational study. *Int J Nurs Stud* 49(9):1146-54.
16. Andrykowski MA, Donovan KA, Laronga C, Jacobsen PB (2010) Prevalence, predictors, and characteristics of off-treatment fatigue in breast cancer survivors. *Cancer* 116(24):5740-8.
17. Forlenza MJ, Hall P, Lichtenstein P, Evengard B, Sullivan PF (2005) Epidemiology of cancer-related fatigue in the Swedish twin registry. *Cancer* 104(9):2022-31.
18. Patrick DL, Ferketich SL, Frame PS, Harris JJ, Hendricks CB, et al (2003) National Institutes of Health State-of-the-Science conference statement: Symptom management in cancer: Pain, depression, and fatigue, July 15-17, 2002. *J Natl Cancer Inst* 95(15):1110-7.
19. Singer S, Kuhnt S, Zwerenz R, Eckert K, Hofmeister D, et al. (2011) Age- and sex-standardised prevalence rates of fatigue in a large hospital-based sample of cancer patients. *Bri J Cancer* 105(3):445-51.
20. Wang XS, Zhao F, Fisch MJ, O'Mara AM, Cella D, et al. (2014) Prevalence and characteristics of moderate-to-severe fatigue: a multicenter study in cancer patients and survivors. *Cancer* 120(3):425-32.
21. Banipal RPS, Singh H, Singh B (2017) Assessment of cancer-related fatigue among cancer patients receiving various therapies: A cross-sectional observational study. *Indian J Palliat Care* 23(2):207.
22. Escalante CP, Manzullo EF, Lam TP, Ensor JE, Valdres RU, et al. (2008) Fatigue and its risk factors in cancer patients who seek emergency care. *J Pain Symptom Manage* 36(4):358-66.
23. Peters MEWJ, Goedendorp MM, Verhagen CAHHVM, Graaf WTA van der, Bleijenberg G (2014) Severe fatigue during the palliative treatment phase of cancer: an exploratory study. *Cancer Nurs* 37(2):139-45.
24. Wondemagegnehu T (2015) Pattern of cancer in Tikur Anbessa specialized hospital oncology center in Ethiopia from 1998 to 2010. *Int J Cancer Res Mol Mech* 1(1).
25. NCCP Ethiopia Final 261015 (2018).
26. Eshita I (2017) Assessment of cancer-related fatigue on the lives of patients.
27. Respini D, Jacobsen PB, Thors C, Tralongo P, Balducci L (2003) The prevalence and correlates of fatigue in older cancer patients. *Crit Rev Oncol Hematol* 47(3):273-9.
28. Storey DJ, Waters RA, Hibberd CJ, Rush RW, Cargill AT, et al. (2007) Clinically relevant fatigue in cancer outpatients: the Edinburgh Cancer Centre symptom study. *Ann Oncol* 18(11):1861-9.
29. Purell A, Fleming J, Haines T, Bennett S (2009) Cancer-Related Fatigue: A review and a conceptual framework to guide therapists' understanding. *Bri J Occup Ther* 72(2):79-86.
30. Hwang IC, Yun YH, Kim Y-W, Ryu KW, Kim YA, et al. (2014) Factors related to clinically relevant fatigue in disease-free stomach cancer survivors and expectation-outcome consistency. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer* 22(6):1453-60.
31. Abrahams HJG, Gielissen MFM, Schmits IC, Verhagen C A. HHVM, et al. (2016) Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. *Ann Oncol Off J Eur Soc Med Oncol* 27(6):965-74.
32. Wang XS, Giral SA, Mendoza TR, Engstrom MC, Johnson BA, et al. (2002) Clinical factors associated with cancer-related fatigue in patients being treated for leukemia and non-Hodgkin's lymphoma. *J Clin Oncol* 20(5):1319-28.
33. Banthia R, Malcarne VL, Ko CM, Varni JW, Sadler GR (2019) Fatigued Breast Cancer Survivors: The role of sleep quality, depressed mood, stage, and age. *Psychol Health* 24(8):965-80.
34. Akechi T, Kugaya A, Okamura H, Yamawaki S, Uchitomi Y (1999) Fatigue and its associated factors in ambulatory cancer patients: a preliminary study. *J Pain Symptom Manage* 17(1):42-8.