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Original Article

Prevalence and Factors Associated with Cancer-related Fatigue in Patients Undergoing Cancer Therapy in Eastern India

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Abstract

Background: Cancer-related fatigue (CRF) is a common, debilitating symptom that substantially reduces the quality of life (QoL) in cancer patients. While CRF is well-documented in many countries, data from India remain limited in spite of the potential differences in patient demographics and healthcare context. We conducted the first large cross-sectional study in Eastern India to estimate the prevalence of CRF and identify the clinical factors associated with CRF. **Materials and Methods:** We conducted a cross-sectional study of 320 adults with solid tumors undergoing active anticancer therapy. To minimize confounding from noncancer causes of fatigue, we excluded patients with preexisting comorbidities, including abnormal hematological parameters, renal or hepatic dysfunction, uncontrolled metabolic or endocrine disorders, and major psychiatric illnesses. Fatigue was assessed using the European Organization for Research and Treatment of Cancer FA12 questionnaire, selected for its multidimensional cancer-specific design and compatibility with the QLQ-C30 for QoL. Logistic regression and Pearson correlation analyses were used to identify the factors associated with CRF and assess the fatigue-QoL relationship. **Results:** All 320 patients (median age: 60 years; 55% females) reported some level of fatigue, of which, 26% of patients were classified as having severe fatigue. The median FA12 fatigue score was 47.2 (interquartile range: 26–67). Univariate analysis showed that higher fatigue was associated with older age, advanced cancer stage, worse performance status, and undergoing chemotherapy; in multivariate analysis, advanced stage, older age, and undergoing chemotherapy remained independently associated with higher fatigue. In terms of global QoL, 39.4% of the patients rated as excellent, 31.8% as good, and 28.8% as poor. Fatigue severity showed a strongly significant inverse correlation with global QoL. **Conclusion:** In this large Indian cohort undergoing curative-intent therapy, CRF was essentially universal and often severe. By excluding major medical confounders, we aimed to minimize the noncancer causes of fatigue and improve the attribution to cancer- and treatment-related factors. We confirmed that older age, advanced stage, and chemotherapy were independently associated with higher CRF severity, and that higher fatigue was strongly correlated with poorer QoL. These results underscore the importance of routine, multidimensional fatigue screening, and targeted interventions in Indian oncology practice.

Keywords: Antineoplastic therapy, cancer, cancer-related fatigue, factors associated, quality of life

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Introduction

Cancer-related fatigue (CRF) is one of the most common and debilitating symptoms experienced by cancer patients during active treatment. It is defined as a persistent subjective sense of physical, emotional, and/or cognitive exhaustion that is disproportionate to activity and not relieved by rest. CRF is highly prevalent among the patients undergoing active cancer treatment, with recent meta-analyses reporting an overall fatigue prevalence of approximately 70.7% during chemotherapy, radiotherapy, or combined-modality treatment.[1,2] The consequences are significant, as CRF can severely impair daily functioning, treatment adherence, and overall quality of life (QoL).[3,4]

The pathophysiology of CRF is complex and multifactorial and is thought to involve systemic inflammation, neuroendocrine dysregulation, and altered muscle metabolism.[5-7] Compared with symptoms such as pain or nausea, a significant knowledge gap persists regarding the burden of CRF in low- and middle-income countries (LMICs) such as India.[2,3,8] CRF can further challenge treatment adherence and follow-up, thereby negatively affecting QoL.[3,5,7] Data from India remain limited. Obtaining robust regional estimates and identifying clinical factors associated with CRF are therefore important for developing routine screening protocols and targeted supportive interventions aimed at improving treatment tolerance and patient outcomes.[9]

The primary objective of the present study was to estimate the prevalence of CRF among Indian patients undergoing active cancer treatment (chemotherapy, radiotherapy, or both). Fatigue was assessed using the validated multidimensional European Organization for Research and Treatment of Cancer (EORTC) QLQ-FA12 questionnaire.[10] Prevalidated regional language versions of the FA12 were used in accordance with the EORTC translation requirements to ensure linguistic and cultural relevance. As a secondary objective, we examined clinical and demographic factors associated with CRF severity. We also assessed the relationship between CRF and global QoL using the EORTC QLQ-C30 questionnaire.[11]

The primary contribution of the present study lies in its focus on a predominantly curative-intent cohort, the application of a multidimensional cancer-specific fatigue instrument (EORTC QLQ-FA12) in this treatment setting, and its comparatively large sample size.

Materials and Methods

Study setting and ethical approval

We conducted this descriptive cross-sectional study in the Department of Radiation Oncology, Burdwan Medical College and Hospital, West Bengal, India, from March to June 2025. The Institutional Ethics Committee, Burdwan Medical College, accepted the study protocol (Approval number: BMC/IEC/468 dated 20.3.2025), which complies with the Good Clinical Practice guidelines and Declaration of Helsinki.

As the study was observational and involved no active intervention, trial registration was not mandated. All participants provided written informed consent prior to enrollment.

Study participants

Adults aged 18–80 years with histologically confirmed solid tumors, Stages I–IV (American Joint Committee on Cancer [AJCC] 8th Edition) at the time of assessment, and the Eastern Cooperative Oncology Group performance status (ECOG PS) 0–3 were eligible for selection. All the participants were undergoing active anticancer treatment (chemotherapy, radiotherapy, or concurrent chemoradiotherapy) at the time of questionnaire administration.

To minimize noncancer-related contributors to fatigue, eligibility required adequate baseline laboratory parameters, defined as: hemoglobin - ≥9 g/dL, absolute neutrophil count - ≥1500/μL, platelets - ≥100,000/μL, creatinine clearance - ≥40 mL/min, total bilirubin - ≤1.5× upper limit of normal (ULN), aspartate/alanine transaminase - ≤2× ULN, albumin - ≥3.5 g/dL, and normal thyroid function. These laboratory values were obtained from reports performed within 7 days of enrollment. Patients with synchronous or metachronous double primary malignancies were not included.

Patients were also excluded if they were unable to complete the questionnaires, were receiving systemic corticosteroids at immunosuppressive doses (equivalent to prednisolone ≥10 mg/day) for ≥14 consecutive days within the preceding 4 weeks, were pregnant or lactating, had a body mass index (BMI) <18.5 kg/m², had uncontrolled psychiatric illness, or fulfilled the criteria for metabolic syndrome (defined according to the National Cholesterol Education Program [NCEP ATP III criteria], requiring the presence of at least three of the following five risk factors: [1] waist circumference >102 cm for men or >88 cm for women; [2] triglycerides ≥150 mg/dL; [3] HDL cholesterol <40 mg/dL for men or <50 mg/dL for women; [4] blood pressure ≥130/85 mmHg; and [5] fasting glucose ≥100 mg/dL.[12]).

Study procedures and data collection

Consistent with the cross-sectional design, all screening and data collection occurred during a single visit in the radiation oncology outpatient department. A study physician identified potentially eligible patients, verified inclusion and exclusion criteria through chart review, and assessed their ability to comprehend the study requirements. Clinical stage was recorded as the disease stage at the time of questionnaire administration based on the most recent clinical and imaging assessments. After written informed consent was obtained, demographic and clinical data were collected using a structured pro forma, and physical measurements (height, weight, blood pressure, and waist circumference) were recorded.

The laboratory inclusion criteria were confirmed using reports obtained within 7 days before enrollment. Eligible participants were then self-administered the EORTC QLQ-FA12 and

QLQ-C30 questionnaires in a quiet private setting. Immediately after completion, the questionnaires were reviewed for missing responses. If any item was inadvertently left unanswered, the participant was requested to complete the omitted item(s) during the same visit. No interpretative guidance was provided by the study team to avoid influencing responses. Patients who were unable to understand or comprehend the questionnaire despite assistance with instructions were excluded, as per the exclusion criteria. Patients were instructed not to seek assistance from caregivers during completion to avoid response bias.

Timing of questionnaire administration

To standardize timing within the active treatment, both the QLQ-FA12 and QLQ-C30 were completed during the same study visit. For those undergoing radiotherapy/concurrent chemoradiotherapy, assessment was performed between weeks 3–5, depending on the planned course length, corresponding to the mid-treatment window. For those undergoing chemotherapy, assessment was performed at the midpoint of the intended regimen, with ≥2 cycles completed before assessment (e.g., Cycle 3 of 6 planned cycles or Cycle 4 of 8 planned cycles). Each participant was assessed only once.

Assessment of cancer-related fatigue

CRF was assessed using the EORTC QLQ-FA12,[10] (including socioculturally adapted prevalidated regional language translations) comprising 12 questions marked on a Likert-like scale of 1 (minimum)–4 (maximum). The questionnaire was self-administered, and the patients who had consented were requested to answer the questions in privacy. They were not allowed to discuss the answers with caregivers during the process to avoid any bias. The FA12 comprised physical fatigue (PFA), emotional fatigue (EFA), and cognitive fatigue (CFA) subscales as well as interference with daily life (IDL) and social sequelae (SOC) subscales. Final scores, after transposition of the raw score as per the scoring manual, ranged from 0 to 100, with higher scores denoting greater fatigue. As the FA12 can detect minimal symptom levels, the presence of "any fatigue" may not necessarily indicate clinically significant fatigue. Therefore, fatigue severity was categorized into tertiles as mild (<33), moderate (33–66), and severe (>66) on the 0–100 scale for interpretability. For regression analysis, moderate-to-severe fatigue (FA12 ≥33) was used as the primary outcome.

Assessment of quality of life

QoL was assessed using the EORTC QLQ-C30,[11] scored according to the official EORTC scoring manual. Regional language versions of the QLQ-C30, translated and culturally adapted according to EORTC guidelines, were self-administered by the participants in a private setting, just like the FA12 questionnaires.

Sample-size estimation

Assuming a 70% prevalence of CRF (based on previous literature),[13,14] 5% absolute precision and 95% confidence intervals (CIs), the required sample size was 323 [Supplementary Table 1]. The technique employed was convenience sampling.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as medians with interquartile ranges (IQRs), and categorical variables as frequencies and percentages. CRF prevalence was reported with 95% CIs. For regression analysis, fatigue severity was dichotomized into mild fatigue (FA12 <33) versus moderate-to-severe fatigue (FA12 ≥33) based on the predefined cutoff described in the Methods.

Univariate logistic regression was first conducted to identify variables associated with moderate-to-severe fatigue. Variables with $P < 0.20$ in univariate analysis were entered into the multivariable model. Categorical variables (e.g., cancer site, treatment type, stage, and sex) were dummy coded before entry into regression models, with the clinically relevant or most frequent category serving as the reference group. Pearson correlation coefficients were calculated to examine the association between total FA12 scores and global QoL scores from the QLQ-C30. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. Multicollinearity was assessed using the variance inflation factor (VIF). All included variables demonstrated acceptable VIF values (<2.5), indicating no evidence of problematic multicollinearity.

FA12 domain score comparisons

FA12 domain scores (PFA, EFA, CFA, IDL, and SOC) were compared across baseline subgroups using nonparametric tests due to nonnormal distribution of scores. The Mann–Whitney *U* test was used for two-group comparisons (sex), and the Kruskal–Wallis test was used for comparisons involving ≥3 groups (age group, diagnosis, treatment type, stage group, and ECOG PS). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

As the questionnaires were administered in-person during a single study visit and were checked immediately for missing items, no item-level data were missing among the enrolled participants. Therefore, complete-case analysis was performed, and no imputation procedures were required.

Study oversight

No funding or grant support was received for this study. The patient's treatment had no bearing on the conduct of this study or *vice versa*. The manuscript was written principally by the first and corresponding authors. All the authors read and approved the manuscript and vouch for the authenticity of the data presented.

Results

Participant characteristics

Between March and June 2025, a total of 407 patients were screened for the study, of which 320 met the eligibility criteria

and were enrolled [Figure 1]. All the enrolled participants completed both the EORTC QLQ-FA12 and EORTC QLQ-C30 questionnaires, resulting in complete data for this analysis. This was achieved through real-time verification of questionnaire completeness during the study visit, as detailed above. The median time required by the participants to complete the FA12 questionnaire was 12 min (IQR: 8–17), whereas the QLQ-C30 required 21 min (IQR: 20–29). The median age of the cohort was 60 years (range: 18–80 years), and 55% were female. The cohort predominantly comprised patients with head and neck cancer (46.88%), followed by cervical (19.69%), breast (14.69%), colon (5.31%), lung (5.00%), rectal (4.06%), ovarian (1.56%), and gallbladder cancers (1.56%); other sites constituted 1.25%. Most of the patients had early-stage group disease (AJCC Stage Group I/II, 65%) at the time of questionnaire assessment [Table 1], and the most common ECOG PS was 0 (48.8%). The treatment modality at the time of CRF assessment was distributed as follows: Chemotherapy alone (28.1%), radiotherapy alone (29.4%), and concurrent chemoradiotherapy (42.5%) [Table 1].

Prevalence and severity of fatigue

All 320 patients reported some degree of fatigue on the EORTC QLQ-FA12. Given the symptom burden expected during active anticancer treatment and the ability of the FA12 to capture even low-level symptoms across multiple domains, the finding of "any fatigue" in all the participants should be interpreted cautiously and may reflect a ceiling effect rather than clinically significant fatigue in every patient. Therefore, the clinically meaningful findings are the proportions of patients with moderate-to-severe fatigue and severe fatigue. Of the 320 participants, 112 (35%) reported mild fatigue (FA12 score: <33), 125 (39%) reported moderate fatigue (FA12 score: 33–66), and 83 (26%) reported severe fatigue (FA12 score: >66). The median total FA12 fatigue score was 47.2 (IQR: 26–67), indicating a moderate degree of fatigue. The median subscale scores for each domain were 46.7 (IQR: 40–60) for PFA, 44.4 (IQR: 33.33–66.67) for EFA, 50.0 (IQR: 29.17–66.67) for CFA, 33.3 (IQR: 0–100) for IDL, and 33.3 (IQR: 0–100) for SOC.

Fatigue domain scores by baseline characteristics

FA12 domain scores summarized across baseline characteristics are shown in Table 2. Treatment type and stage group demonstrated statistically significant differences across all five FA12 domains (PFA, EFA, CFA, IDL, and SOC). Age group showed significant differences in EFA, CFA, IDL, and SOC domains, whereas ECOG PS demonstrated significant differences predominantly in CFA, IDL, and SOC domains. Diagnosis showed statistically significant variation only in the SOC domain. Sex did not show statistically significant differences across FA12 domain scores.

Factors associated with fatigue severity

Univariate logistic regression analysis was performed to identify variables associated with moderate-to-severe fatigue. The results showed that diagnosis ($P = 0.0003$), stage group (AJCC Stage Group IV; $P < 0.0001$), ECOG PS ($P < 0.0001$), age group ($P < 0.0001$), and treatment type (chemotherapy; $P < 0.0001$) were significantly associated with higher fatigue severity [Table 3]. Sex was not significantly associated with moderate-to-severe fatigue in univariate analysis ($P = 0.207$). Variables meeting the prespecified threshold on univariate analysis were subsequently included in a multivariable logistic regression model. Multivariable analysis showed that Stage Group IV disease ($P = 0.023$), age >60 years ($P = 0.0035$), and patients undergoing chemotherapy ($P < 0.0001$) remained independently associated with moderate-to-severe

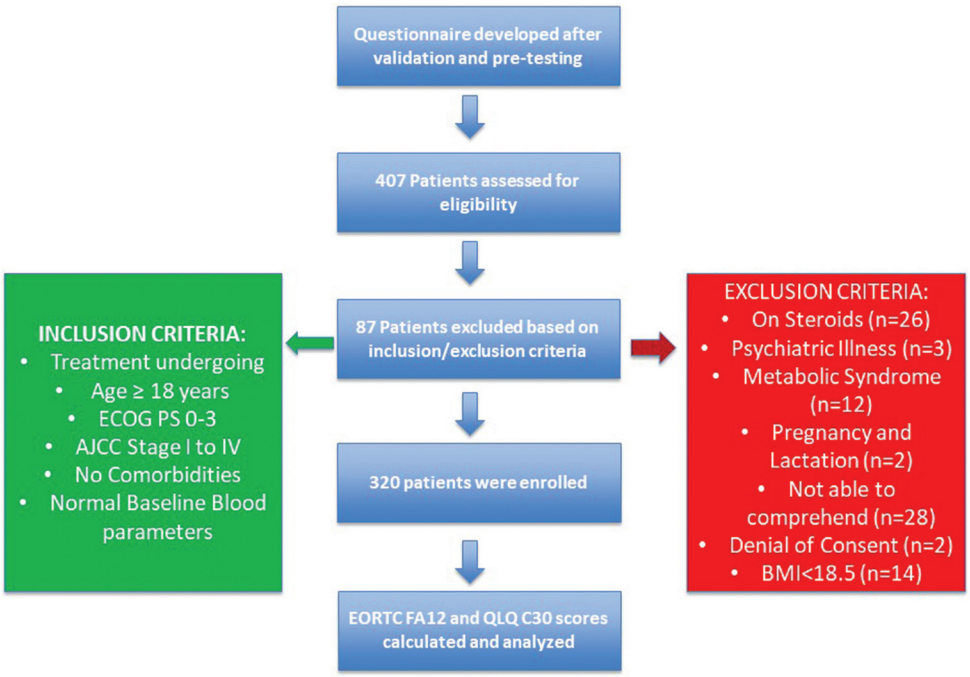

Figure 1: CONSORT diagram

Table 1: Demographic variables of the study participants (*n*=320)

Variable	Category	*n* (%)
Age (years)	Median	60
Sex	Male	144 (45)
	Female	176 (55)
Diagnosis	Head and neck	150 (46.88)
	Cervix	63 (19.69)
	Breast	47 (14.69)
	Colon	17 (5.31)
	Lung	16 (5.00)
	Rectum	13 (4.06)
	Ovary	5 (1.56)
	Gallbladder	5 (1.56)
	Others	4 (1.25)
AJCC stage group	I	108 (33.75)
	II	100 (31.25)
	III	69 (21.56)
	IV	43 (13.44)
ECOG PS	0	156 (48.75)
	1	100 (31.25)
	2	39 (12.19)
	3	25 (7.81)

AJCC: American Joint Committee on Cancer, ECOG PS: Eastern Cooperative Oncology Group performance status

fatigue [Table 4]. No evidence of problematic multicollinearity was observed (all VIF values: <2.5).

Quality-of-life outcomes

Global QoL was assessed using the EORTC QLQ-C30 questionnaire, and categorized as excellent (>66), good (33–66), or poor (<33). This categorization was used for interpretability on the 0–100 scale and has been applied in prior studies. The QoL was reported to be excellent by 126 (39.4%) patients, good by 102 (31.8%) patients, and poor by 92 (28.8%) patients. Younger patients (20–40 years) had the best QoL profiles, with 30 reporting excellent QoL and only 2 reporting poor QoL. Conversely, the 60–80 years age group had the poorest QoL. Patients receiving radiotherapy alone demonstrated superior QoL outcomes, with 74 patients reporting excellent QoL and only 7 reporting poor QoL, in contrast to those receiving chemotherapy, where 30 patients reported poor QoL. Regarding diagnosis, poor QoL was most frequently reported by patients with head and neck cancer. QoL worsened with advanced stage and ECOG PS, with Stage Group IV and ECOG PS three patients reporting the poorest QoL [Supplementary Table 2].

Correlation between fatigue and quality of life

Pearson correlation analysis demonstrated a strong and statistically significant inverse association between total FA12 score and global QoL score from the QLQ-C30 ($r = –0.82$, $P < 0.0001$). The correlation was further assessed using subgroups of baseline patient characteristics, and the results showed a uniform trend of inverse correlation, especially when poor global QoL (score <33) and the highest fatigue (scores >66) were analyzed. As the severity of fatigue increased, there was a substantial and proportional decline in the overall QoL [Supplementary Table 3].

Discussion

Nearly 25% of Indian cancer patients undergoing treatment in the present study reported severe fatigue, indicating a substantial burden of CRF. These findings are consistent with global research showing that the prevalence of CRF varies from 40% to 90% based on the cancer type, stage, and the modality of the treatment.[1,2,4]

The observed 100% prevalence of "any fatigue" in our study should be interpreted with caution. Fatigue of some degree is expected during active anticancer therapy, and the EORTC QLQ-FA12 is designed to capture a wide range of symptom severity across multiple fatigue domains. Therefore, the clinically meaningful burden in our cohort is reflected by the proportions of patients with moderate-to-severe fatigue (61%) and severe fatigue (26%), rather than the presence of any fatigue symptoms. Similar findings of near-universal fatigue have been reported in other Indian cohorts, including an advanced cancer palliative-care population in which 100% of the patients reported fatigue.[15] Evidence linking age-related physiological decline, comorbidities, and cumulative cytotoxic toxicities to tiredness severity is consistent with the notably high burden among the older persons and chemotherapy patients.

Unlike many earlier investigations that primarily included patients receiving palliative care,[13,15,16] our cohort largely comprised individuals undergoing radical treatment (over 72%).[14] This distinction is important because fatigue in palliative settings is strongly influenced by advanced disease burden, symptom progression, and end-of-life factors. For example, Yennurajalingam *et al*.[17] and Teunissen *et al*.[18] reported CRF prevalence exceeding 80%–90% among terminally ill patients. By contrast, our findings represent one of the first Indian studies to examine CRF predominantly in curative-intent contexts, and the first to apply the EORTC QLQ-FA12 in this population, providing a novel and clinically relevant perspective.

Advanced stage was the factor most consistently associated with severe fatigue in this study, which is biologically reasonable. Prior studies have attributed fatigue in advanced disease to systemic inflammation, metabolic dysregulation, and cachexia, all of which impair energy metabolism and contribute to persistent fatigue.[5,6,17] Our multivariable analysis showed that age, stage, and treatment modality remained independently associated with severe fatigue, reinforcing their value for fatigue risk stratification.

Use of the EORTC QLQ-FA12 also allowed for detailed domain-level assessments. While head and neck cancers showed the highest overall fatigue burden (moderate + severe), gallbladder cancer was associated with the greatest PFA and IDL, and ovarian cancer demonstrated higher EFA and SOC fatigue.

Table 2: Fatigue domains scores according to baseline variables

	Total fatigue score	PFA	EFA	CFA	IDL	SOC
Age group						
20–40	35.30	43.09	40.11	42.68	29.27	20.33
40–60	44.92	48.72	47.71	45.69	42.66	44.29
60–80	52.66	51.57	50.98	49.51	52.94	53.92
P	-	0.3417	**0.0469**	**0.0040**	**0.0028**	**<0.0001**
Treatment type						
Both	48.63	48.63	49.26	48.65	49.02	50.98
Chemo	60.54	53.93	56.67	55.56	60.74	64.81
Radiation	31.60	45.53	38.30	36.17	25.18	18.44
P	-	**0.0088**	**<0.0001**	**0.0001**	**<0.0001**	**<0.0001**
Diagnosis						
Breast	38.21	49.93	45.15	39.36	35.46	24.82
Cervix	47.37	47.83	47.09	50.00	44.44	51.32
Colon	45.27	44.31	49.02	54.90	33.33	47.06
Gallbladder	56.18	64.00	53.33	30.00	86.67	46.67
Head and neck	48.28	49.78	47.85	47.00	46.67	48.67
Lung	61.29	48.33	52.78	62.50	68.75	64.58
Others	51.94	35.00	55.56	62.50	41.67	66.67
Ovary	63.38	54.67	60.00	40.00	66.67	66.67
Rectum	35.06	50.77	51.28	33.33	33.33	10.26
P	-	0.8064	0.1543	0.3921	0.0641	**0.0022**
Gender						
Female	48.15	49.52	49.02	47.24	47.59	46.35
Male	45.33	48.77	46.87	46.49	42.11	43.86
P	-	0.1127	0.1622	0.3251	0.7363	0.3422
Stage						
1	38.03	46.11	45.06	38.73	37.04	29.01
2	43.20	49.53	45.11	46.83	37.00	41.67
3	56.09	50.82	56.36	54.35	64.25	61.35
4	63.61	53.64	49.61	55.81	55.04	68.99
P	-	**0.0030**	**0.0001**	**0.0032**	**<0.0001**	**<0.0001**
ECOG						
0	41.00	46.45	45.44	44.34	36.32	33.97
1	47.11	52.13	47.44	42.83	49.00	47.33
2	59.71	52.14	54.42	58.97	63.25	69.23
3	63.88	50.13	57.78	60.67	58.67	70.67
P	-	0.3463	0.1043	**0.0173**	**<0.0001**	**0.0053**

Values are presented as median. *P* values were calculated using Mann–Whitney *U*-test for two-group comparisons (sex) and Kruskal–Wallis test for ≥3 group comparisons (age group, diagnosis, treatment type, stage group, and ECOG PS). A two-sided $P<0.05$ was considered statistically significant (significant *P* values are highlighted in bold). PFA: Physical fatigue, EFA: Emotional fatigue, CFA: Cognitive fatigue, SOC: Social sequelae, IDL: Interference in daily life, ECOG PS: Eastern Cooperative Oncology Group performance status

Table 3: Univariate logistic regression for high fatigue scores

Variable	*P*	OR	95% CI lower bound (OR)	95% CI upper bound (OR)
Diagnosis	0.0003	1.24	1.11	1.40
Stage	**<0.0001**	7.45	4.89	11.35
ECOG PS	**<0.0001**	2.44	1.85	3.21
Age group	**<0.0001**	4.92	3.18	7.63
Treatment type	**<0.0001**	7.95	5.00	12.62
Gender	0.20713	0.75	0.47	1.18

P values marked in bold are statistically significant. ECOG PS: Eastern Cooperative Oncology Group performance status, OR: Odds ratio, CI: Confidence interval

However, these findings should be interpreted cautiously due to the small sample sizes in these subgroups. This domain-specific variability, often missed by unidimensional measures, underscores the heterogeneity of CRF expression across cancer types. Previous Indian research has been limited in this scope. For example, Agarwal *et al*.[15] examined palliative care patients and linked fatigue to anemia, hypoalbuminemia, BMI, and thyroid dysfunction, but did not explore fatigue domains. Similarly, Prue *et al*.[4] described fatigue prevalence without correlating with treatment or performance status. Our study adds value by offering domain-specific profiling correlated with clinical variables such as age, diagnosis, stage, treatment modality, and ECOG PS.

Table 4: Multivariate logistic regression by high fatigue scores

Variable	*P*	OR	95% CI lower bound (OR)	95% CI upper bound (OR)
Diagnosis	0.5549	1.04	0.91	1.19
Stage	**0.023**	1.53	1.07	2.20
ECOG PS	0.7524	1.06	0.75	1.50
Age group	**0.0035**	1.88	1.23	2.88
Treatment type	**<0.0001**	2.80	1.88	4.18

P values marked in bold are statistically significant. ECOG PS: Eastern Cooperative Oncology Group performance status, OR: Odds ratio, CI: Confidence interval

To improve internal validity, patients with established CRF predictors such as anemia, hypoalbuminemia, uncontrolled thyroid dysfunction, and organ dysfunction were excluded from this study. This design choice reduced potential confounding from noncancer causes of fatigue and improved interpretability of associations with cancer- and treatment-related variables. Importantly, fatigue remained prevalent even among early-stage, curatively treated patients, highlighting its clinical significance across the disease trajectory.

When measured with the EORTC QLQ-C30, QoL was considerably lower in older patients, patients undergoing chemotherapy, patients with advanced disease, and patients with poor ECOG status. Patients who only underwent radiotherapy reported the best QoL, probably as a result of lower systemic toxicity. There was a significant inverse relationship between QoL and fatigue, which is in line with findings by Xu *et al*.[19] and other studies. Elevated CRF scores were noted across all FA12 domains (PFA, EFA, CFA, IDL, and SOC), reaffirming CRF as a multidimensional burden.[20] The National Comprehensive Cancer Network (NCCN) recommendations (Version 2.2025)[21] describe CRF as a "distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness related to cancer or its treatment that interferes with usual functioning."

The NCCN recommendations emphasize an integrated approach, including routine screening, education, and correction of reversible causes such as anemia, depression, and thyroid dysfunction (excluded in this study). Nonpharmacologic interventions – particularly aerobic and resistance exercise – are strongly supported, with additional evidence for yoga, mindfulness-based stress reduction, and cognitive behavioral therapy.[21-23] Pharmacologic strategies (e.g., psychostimulants, antidepressants) may benefit select refractory cases, whereas nutrition counseling, sleep hygiene, and psychosocial support remain vital elements of comprehensive care. Our findings support the routine use of multidimensional tools such as the FA12 to guide early interventions aimed at improving treatment adherence and QoL.

Strengths of the study

To the best of our knowledge, this is the first and largest Indian study to assess CRF with the EORTC FA12 in patients undergoing radical treatment. Concentrating on fatigue related to cancer and its treatment and excluding known physiological and biochemical confounders improved the methodological rigor. Individual fatigue dimensions were analyzed with respect to baseline data (age, sex, cancer subtype, stage group, and ECOG PS), which allowed for linkage with QoL and granular insights. The findings in LMIC settings are more applicable because of the strong representation of head and neck cancers. The clinical necessity of routine tiredness screening during curative-intent therapy is further highlighted by the inverse relationship between fatigue and QoL shown in our results.

Limitations of the study

Despite these strengths, several limitations should be acknowledged. First, reliance on self-reported questionnaires may have introduced reporting bias and contributed to the overestimation of low-level fatigue symptoms (ceiling effect). Second, convenience sampling and the single-center setting may limit the representativeness and generalizability of this study. Third, given the cross-sectional design, temporality and causality cannot be inferred. Residual confounding is possible due to unmeasured factors such as objective biomarkers (e.g., IL-6/CRP), sleep quality, detailed comorbidity and nutritional parameters, and enteral feeding support (NG/PEG/jejunostomy), which is particularly relevant in head and neck cancers; however, we attempted to minimize nutritional confounding by excluding underweight patients and requiring adequate serum albumin. Socioeconomic status was also not formally assessed using a standardized scale. Cancer site-specific domain comparisons for less frequent malignancies were limited by small subgroup sizes and should be interpreted as exploratory. Finally, cumulative treatment exposure (e.g., exact chemotherapy cycle number or radiotherapy fractions completed) was not modeled as a continuous variable and may have influenced fatigue severity.

Future directions

This study focuses on an understudied population and highlights the burden, prognosis, and complex impacts of CRF in Indian patients undergoing radical treatment. Future research to track the course of CRF from diagnosis to survivorship and palliative treatment should prioritize prospective longitudinal designs. Multicentric research is necessary to develop risk models, identify novel CRF biomarkers, and validate associated factors. Early screening techniques, customized treatment plans, and high-risk population strategies should receive special attention. Research frameworks should include a thorough assessment of fatigue-management techniques, such as physical activity, psychosocial support, and medication, in order to improve evidence-based clinical practice.

Conclusion

All patients in this study reported some degree of CRF, with severe fatigue observed in approximately one-quarter of the participants. Higher fatigue severity was independently associated with patients undergoing chemotherapy, the

advanced stage group, and older age. As the first Indian study to apply the EORTC QLQ-FA12 in this treatment setting, our findings highlight the need for routine multidimensional fatigue screening and targeted supportive interventions for patient groups with a higher fatigue burden. Future prospective studies should evaluate evidence-based fatigue management strategies and their integration into routine oncology care to improve QoL and treatment adherence.

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Author contributions

A.B. was associated with conceptualization, methodology, validation, resources, data curation, writing-original draft, writing-review and editing, visualization, supervision, project administration. A.M. was associated with conceptualization, methodology, formal analysis, investigation validation, resources, data collection, data curation, writing-original draft. S.G.R. was associated with conceptualization, methodology, formal analysis, data curation, writing-review and editing, supervision. The manuscript has been read and approved by all the authors.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Sample size calculation

Parameter	Value
Expected prevalence of CRF	70%
Confidence level	95%
Absolute precision (margin of error)	5%
Z-score for 95% confidence	1.96
Formula used	$n=Z^2 \times P \times (1-p)/d^2$
Calculated sample size	323

The sample size was calculated based on the assumptions for estimating the prevalence of cancer-related fatigue (CRF) in cancer patients undergoing treatment

Supplementary Table 2: Quality of life outcomes

Parameter	Groups	QoL scores (by tertiles)		
		Excellent (>66)	Good (33–66)	Poor (<33)
Age Group	20–40 years	30	9	2
	40–60 years	63	48	32
	60–80 years	33	45	58
Treatment Type	Chemo	41	65	30
	Both	11	24	55
	Radiation	74	13	7
Diagnosis	Breast	31	8	8
	Cervix	20	33	10
	Colon	8	5	4
	GB	1	2	2
	Head & Neck	52	47	51
	Lungs	3	5	8
	Others	1	1	2
	Ovary	1	0	4
	Rectum	9	1	3
Gender	Female	69	62	56
	Male	57	40	36
Stage group	I	61	40	7
	II	52	22	26
	III	8	31	30
	IV	5	9	29
ECOG PS	0	84	50	22
	1	37	34	29
	2	2	14	23
	3	3	4	18

QoL: Quality of life, ECOG PS: Eastern Cooperative Oncology Group performance status

Supplemental Table 3: Fatigue and quality of life score correlation

Parameter	Group	Fatigue scores in patients (numbers)			QoL scores in patients (numbers)			Correlation	
		Mild (<33)	Moderate (33–66)	Severe (>66)	Excellent (>66)	Good (33–66)	Poor (<33)	Pearson's Coefficient*	*P*
Age	20–40 years	12	29	0	30	9	2	-0.552	<0.0001
	40–60 years	39	93	11	63	48	32	-0.804	<0.0001
	60–80 years	22	95	19	33	45	58	-0.855	<0.0001
Treatment Type	Chemotherapy	11	49	30	41	65	30	-0.813	<0.0001
	Both	3	133	0	11	24	55	-0.668	<0.0001
	Radiation	59	35	0	74	13	7	-0.738	<0.0001
Diagnosis	Breast	23	20	4	31	8	8	-0.860	<0.0001
	Cervix	5	55	3	20	33	10	-0.703	<0.0001
	Colon	7	9	1	8	5	4	-0.862	<0.0001
	GB	1	4	0	1	2	2	-0.948	0.014
	Head & Neck	27	111	12	52	47	51	-0.813	<0.0001
	Lungs	1	10	5	3	5	8	-0.924	<0.0001
	Others	1	3	0	1	1	2	-0.973	0.027
	Ovary	1	1	3	1	0	4	-0.921	0.026
	Rectum	7	4	2	9	1	3	-0.863	<0.0001
Gender	Female	38	126	23	69	62	56	-0.614	<0.0001
	Male	35	91	7	57	40	36	-0.745	<0.0001
Stage group	1	43	65	0	61	40	7	-0.616	<0.0001
	2	30	64	6	52	22	26	-0.683	<0.0001
	3	0	60	9	8	31	30	-0.612	<0.0001
	4	0	28	15	5	9	29	-0.787	0.007
ECOG PS	0	52	98	6	84	50	22	-0.700	<0.0001
	1	19	75	6	37	34	29	-0.548	<0.0001
	2	1	31	7	2	14	23	-0.420	0.093
	3	1	13	11	3	4	18	-0.777	<0.0001

* - A negative value indicates inverse correlation whereas a value closer to unity indicates stronger correlation. QoL: Quality of life, ECOG PS: Eastern Cooperative Oncology Group performance status.