RESEARCH ARTICLE

Assessing fatigue levels in neurological cancer patients of different ages under various anticancer therapies

Bikramaditya Sahoo

ABSTRACT

Background: Cancer-related fatigue (CRF) is now the most specific, recurrent, and challenging phenomenon in people with cancer and a common concern of mental illness that affects patients physically, emotionally, cognitively, socially, and also economically, especially in poor and low-income communities. Therefore, a concise evaluation is crucial for the effective management of this demanding manifestation. The brief fatigue inventory (BFI) was used to assess fatigue in patients with cancer. However, the data on systematic appraisal and gradation of the fatigue level in neurological cancer patients are sparse. *Objective:* The present study aimed to estimate the incidence of CRF in neurological cancer patients and also to find the correlation between the degree of CRF and their quality of life. *Methods:* This study was conducted among 40 neurological cancer patients of both sexes within the 20 to 80 years age group, and the level of fatigue was determined using the BFI. *Results:* It was found that the CRF after the last 24 hours of different modalities of treatment was significantly correlated with general activity, mood, walking ability, normal work, relation with other people, and enjoyment of life. *Conclusion:* The present study indicates that the BFI scale is significantly correlated with neurological CRF. However, the fatigue level is significant in relation to general activity and normal work in daily chores, but not significantly related to mood, walking ability, social interactions, or enjoyment of life.

Keywords: Cancer-related fatigue, Neurological cancer patients, Fatigue level in cancer patients, Brief Fatigue Inventory.

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INTRODUCTION

Cancer is a serious societal, public health, and economic issue in the twenty-first century, leading to about one in every six fatalities (16.8%) and one in every four deaths from non-communicable diseases (22.8%) worldwide. In 2022, there were about 20 million newly identified cases of cancer (including non-melanoma skin cancers), as well as 9.7 million cancer-related fatalities. According to estimates, one in every five men and women will get cancer at some point in their lives, with one in every nine men and one in every twelve women dying from it.[1] The GLOBOCAN 2020 data showed that there were 3,08,102 new cases of brain and other central nervous system tumors and 2,51,329 deaths due to the same. According to the Indian Council of Medical Research (ICMR), Hospital-Based Cancer Registry data (2021), brain tumors accounted for 1.6% relative to all other sites of cancer.[2] Fatigue arises as a necessary sensation in a stable person, encouraging the need to rest and relax. Cancer-related fatigue (CRF) or its management is distinguished from the ordinary fatigue that most people experience as a consequence of daily life.[3] CRF is now the most specific, recurrent, and challenging phenomenon in people with cancer.[4] It is also a common sign of mental illness that affects patients physically, emotionally, cognitively, and socially.[5] According to the International Classification of Diseases, Tenth Revision (ICD-10), CRF is outlined as decreased stamina, growing need for rest, heaviness of the limb, diminished capacity to focus, reduced involvement in daily tasks, sleep disturbance, inertia, emotional accountability, diminished short-term memory, and post-exertional malaise that exceeds many hours, and so on.[6] The afferent sensory nerves in the muscle belly or tendons, and joints produce the sense of fatigue from peripheral to caudal by activating the central pathway in the cerebral cortex.[3,4] It is found that the following factors have an essential role in inducing CRF: condition (cancer) itself, anticancer management, decreased vagal stimulation over muscle tone, disruption of central serotonin (5-HT), ATP disruption, anemia, hypothalamic-pituitary-adrenal axis malfunction, pain, fever, anxiety, distress, insomnia, cachexia, dysfunction of circadian rhythm, proinflammatory cytokines malfunction and prolong immobilization.[3,7,8] CRF is a purely subjective sense of profound exhaustion. Most cancer survivors experience fatigue even after treatment, and others perceive it during radiotherapy or chemotherapy, hospital stays, and in normal daily activities.[7,9] The prevalence of tumors of the CNS in India varies between 5 and 10 per 100,000 population, with the rate growing to 2% of malignancies. They have been found in individuals of all ages, sexes, locations, and tumor

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histologies. The estimated prevalence of fatigue in cancer patients ranges from 20 to 100%.[10,11]

Despite the higher occurrence and effects, comprehensive treatment techniques have not been developed to improve fatigue due to the complexity of the underlying factors in its development and the unknown causes. To enhance fatigue management in cancer patients, data on fatigue prevalence, severity, and its impact on quality of life should be obtained. The effects of various treatments, educational programs, and policy changes aimed at enhancing fatigue management must also be documented.[12,13]

CRF has a profoundly negative impact on the standard of living and existence. Quality of life (QOL) is a crucial aspect of clinical neuro-oncology, encompassing a person's multidimensional well-being. Fatigue has multidimensional features, including physical and mental exhaustion, decreased activity, and discouragement. Fatigue has also been associated with physical drops, and psychological and social functioning, which are both major QOL fields.[14]

Accessory medication for cancer patients, like antiepileptic drugs, benzodiazepines, and non-benzodiazepine hypnotics, etc, also harms activities of daily living (ADL).[15]

Researchers and other medical professionals must be able to quantify it in a precise and relevant manner to examine and treat CRF effectively. Standardized measurement tools are necessary for the implementation of process and epidemiological research to compare fatigue characteristics through diseases and therapies and to draw meaningful conclusions from clinical studies of fatigue interventions.[12,13,16]

Several studies have developed valid and reliable tools for evaluating CRF; however, no single tool can be considered the gold standard for assessing CRF to date. Several CRF measurement instruments have been developed in English in various countries around the world, including the Multidimensional Fatigue Inventory, Functional Assessment of Cancer Therapy-Fatigue, Schwartz Cancer Fatigue Scale, Fatigue Symptom Inventory, and Piper Fatigue Scale, among others.[8,12] According to the National Comprehensive Cancer Network (NCCN), evaluation of seven remediable contributing features is – pain, emotional distress, sleep disturbance, anemia, nutrition, activity level, medication side effect profile, and other comorbidities.[17]

A brief questionnaire with suitable psychometric properties is necessary to classify patients with extreme fatigue accurately. The extent of exhaustion must be described in clinical care for clinical purposes. The importance of these baseline limits and the age-gender disparities in fatigue support the rationale for age- and gender-specific usual standards.[18] The Brief Fatigue Inventory (BFI) is a nine-item, self-reported, unidimensional questionnaire to assess the severity and interference of CRF. The BFI was explicitly designed to evaluate fatigue in cancer populations.[8,19] The BFI is a basic fatigue scale that can be quickly applied and ranked. It is validated in numerous languages.[17] BFI consists of three questions to evaluate the extent of fatigue and six questions to assess the effect of fatigue on day-to-day tasks. BFI also measures the harshness and consequences of exhaustion on mood, sleep, daily activity, and so on.

The goal of our study is to assess fatigue levels in neurological cancer patients in India using a simple English version of the BFI to evaluate the CRF. The results shall help us to ascertain the role of fatigue in the progression and recovery of the diseases and may well explain its contribution to the debilitating state of the neurological cancer patient as well.

MATERIALS AND METHODS

This is an exploratory, non-interventional study. The study was approved by the Institutional Ethics Committee (IEC) of Teerthanker Mahaveer University. For this study, the inclusion criteria were age between 20 and 80 years, diagnosed with neurological cancer and receiving various anticancer therapies, and having the ability to fill out the questionnaire. However, patients with cognitive impairments, perceptual disorders, locomotive disabilities, and who were unable to comprehend the purpose of the research were excluded from the study.

After receiving informed consent, the information collection was conducted through a questionnaire-validated BFI. A total of 40 patients participated in the study and were selected based on the above-mentioned inclusion and exclusion criteria.

A questionnaire containing demographics, disease description, and type of treatment (chemotherapy/radiotherapy/surgery, or any combination, etc.) was collected from the patients. The BFI scale questionnaire was used to evaluate fatigue in various aspects of quality of life. Data collection was conducted in two parts. First, demographic information, including age, gender, education, occupation, and cancer-specific data, such as type of cancer, treatment history, and remission status, was collected. Then, a structured questionnaire was taken from a validated BFI scale questionnaire. For the labeling of each question, the term 'Question' has been used in our study to denote the BFI question as Question 1, Question 2, Question 3, and for Question 4 (A, B, C, D, E, and F), there are 6 sub-categories.

Brief Fatigue Inventory (BFI)

This scale includes nine items, starting with a question asking if the patient felt unusually fatigued over the past week. Three questions then assess fatigue severity (right now, usual, and worst in the past 24 hours) on a 0–10 scale. The following six questions measure how fatigue interferes with daily life—activity, mood, walking, work, relationships, and life enjoyment—also on a 0–10 scale. The average of all items gives the global BFI score (0–90), with higher scores showing greater fatigue. The tool has high reliability, with Cronbach's α ranging from 0.82 to 0.97.

Statistical analysis

Descriptive statistics compiled baseline demographic data (age, gender, and BFI scoring). Mean and standard deviation were calculated wherever appropriate. BFI scoring and

its relationship to various parameters and demographic characteristics were examined. To determine any correlation between variables, such as fatigue after chemotherapy and radiotherapy, Pearson's correlation coefficient was used. The strength of the correlation between two variables was then tested using Spearman's rho correlation. All statistical analyses were performed using SPSS software version 16.4.

RESULTS

In the present study, 40 patients participated, of whom 17 were female and 23 were male. It was found that the mean age of neurological cancer patients was 51.3 ± 13.2. It was also found that female patients suffered more severe fatigue in comparison to male cancer patients (p <0.05). It was also found that 10% of patients reported overall fatigue of 80%, whereas 2.5% of patients experienced fatigue of 40%, and none reported fatigue below 40%. About 2.5% of patients reported minimal fatigue, with a level of 20% or less, when asked about the fatigue experienced in the past 24 hours. (Figure 1) In contrast, the highest 35% of the population reported fatigue levels of 50% or more. 2.5% of patients' fatigue interference was 90% in their general activities; however, there was no significant change in fatigue level related to mood, walking ability, regular work, or enjoyment of life (Figure 2).

Moreover, the patient's fatigue level did not interfere with mood, social reach, and enjoyment of life. The relation of CRF with BFI under different FLAG Scores is tabulated in Table 1. The correlation of CRF with BFI scores is presented in Table 2. Spearman's rho correlation study established that the FLAG score was significantly correlated with cancer-related fatigue. The *p-value* ($p \leq 0.05$) indicates that individuals with cancer have a severe level of fatigue, which means this correlation is highly significant.

DISCUSSION

The present study explored the relationship between the severity and interference of cancer-related fatigue in patients' daily activities using BFI. The causes of CRF are multidimensional and very challenging for researchers, patients, and physicians. It might be related to the imbalance of biochemical, physiological, and psychological systems. The condition or combination of conditions causing CRF may vary among different individual phases of the condition and the type of management.

The present study has used BFI to assess the CRF. Validity of this scale for cancer was examined by Mystakidou and colleagues, and our study, therefore, adopts a similar perspective, in which it can be presumed that the BFI scale is significantly correlated with neurological cancer-related fatigue, as well as other types of cancer-related fatigue reported by other researchers.[20]

Aprile and colleagues conducted a cross-sectional study on 67 glioma patients (high-grade) to check the incidence and predictors of cancer-related fatigue. Specific scales (Psychological Distress Inventory and BFI) within this main research revealed a clear and essential relationship between distress and fatigue.[21] Our findings align with this study as our results have shown a significant correlation between BFI scores and the severity of CRF.

Another study, Armstrong and colleagues conducted a study on 201 primarily brain tumor patients to evaluate the features related to fatigue. They suggested that moderate to severe fatigue was commonly seen more in female cancer patients in comparison to male patients with cancer.[22] In the present study, the severity of CRF was found to be higher among female patients than among male patients.

Severity of CRF is also found to be directly related to general activities and post-treatment procedures, whereas indirectly affected by mood, social interactions, and enjoyment activities. These findings suggest the positive role of specific activities in combating the CRF. Several studies have suggested some developmental mechanisms of CRF, which may help develop a suitable treatment procedure to combat this debilitating symptom. The most common techniques that help improve fatigue include bodily movements,

Table 1: Characteristics and BFI domain scores of subjects (N = 40)

Variable	*Mean ± SD (Range)*
Age (years)	51.3 ± 13.2
FLAG1: Fatigue "right now"	6.32 ± 0.99
FLAG2: Usual fatigue (past 24 h)	4.97 ± 1.19
FLAG3: Worst fatigue (past 24 h)	2.28 ± 1.19
FLAG4A: Activity interference	5.92 ± 1.02
FLAG4B: Mood interference	1.63 ± 1.29
FLAG4C: Walking interference	5.38 ± 1.71
FLAG4D: Ordinary work interference	6.23 ± 2.07
FLAG4E: Social relationships	2.18 ± 1.74
FLAG4F: Life enjoyment	2.74 ± 1.86

Table 2: Spearman correlations

Fatigue Measure	r_s	*pvalue*
Present fatigue (FLAG1)	–0.46	0.003
Past 24 h fatigue (FLAG2)	–0.32	0.028*
Worst fatigue (past 24 h) FLAG3	–0.29	0.049*
FLAG4A	–0.40	0.010
FLAG4B	–0.18	0.26
FLAG4C	–0.35	0.022*
FLAG4D	–0.45	0.002
FLAG4E	–0.20	0.22
FLAG4F	–0.25	0.12

Note: r_s = Spearman's rho (correlation coefficient); Level of Significance* for $p < 0.05$

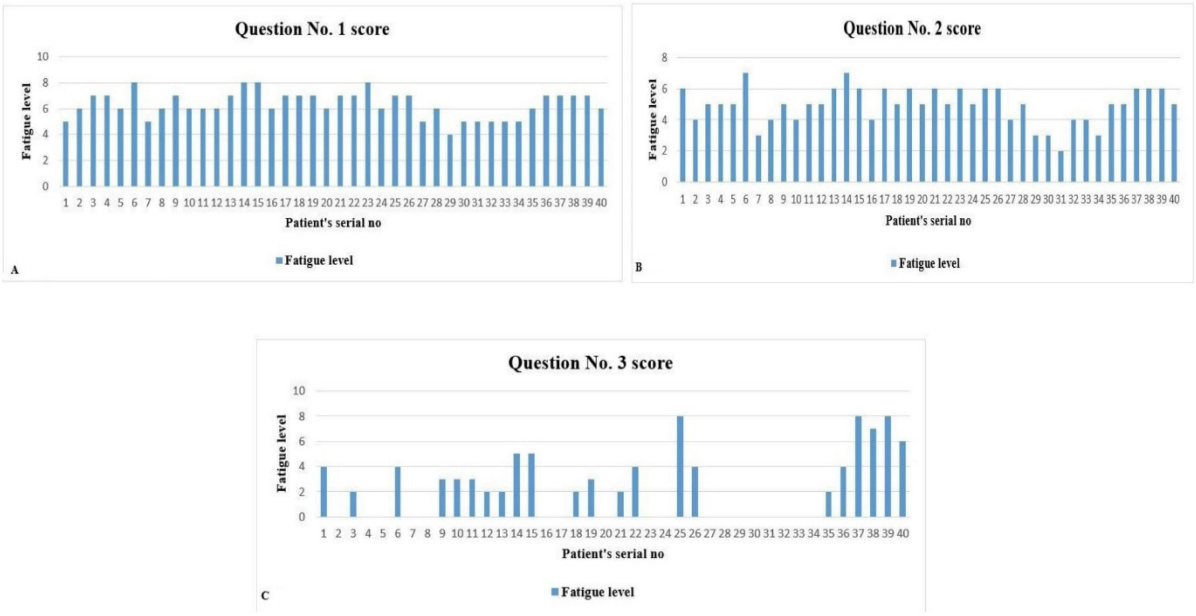

Figure 1: Fatigue level about duration. (A – Fatigue level immediately after the treatment. B – Usual level of fatigue after 24 hours of treatment. C - Worst level of fatigue after 24 hours of treatment.

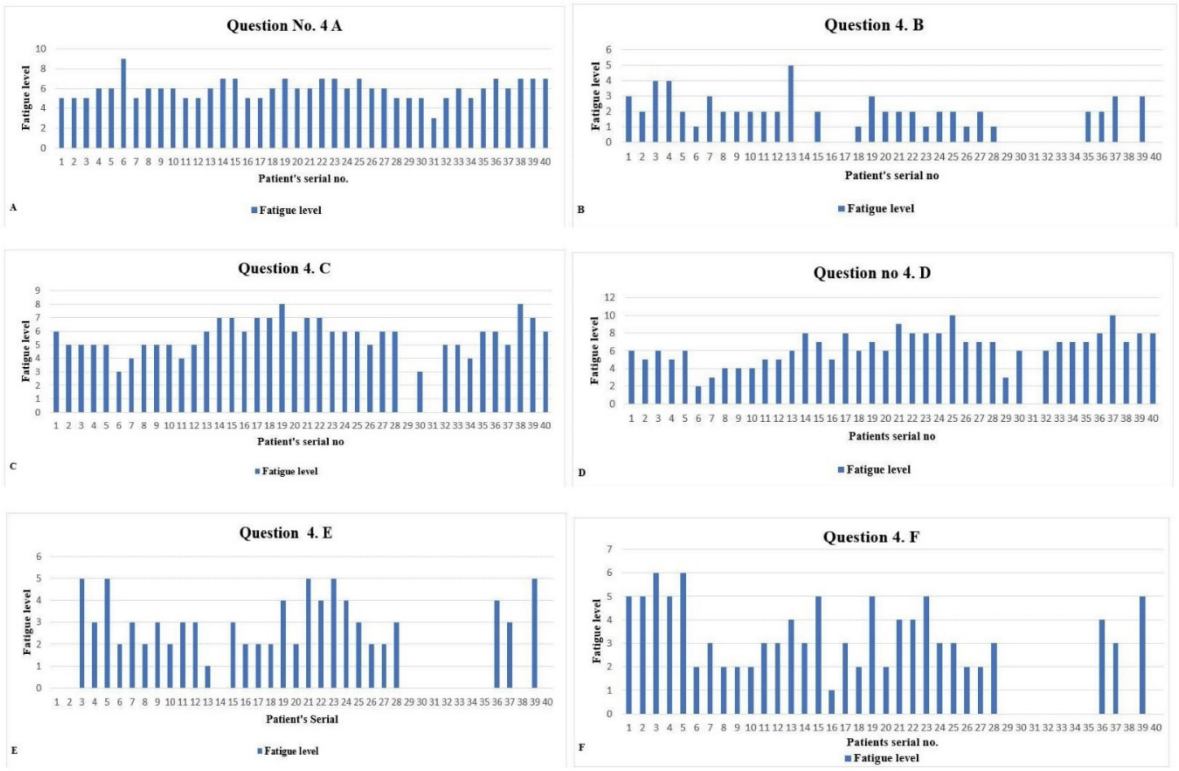

Figure 2: Fatigue level about different activities and states. A – Fatigue interference with general activity. B – Fatigue interference with mood. C – Fatigue interference with walking ability. D – Fatigue interference with work outside home and daily chores. E – Fatigue interference in relations with other people. F – Fatigue interference with enjoyment of life

psychosocial rehabilitation (which provides for educational management, complete relaxation, attention therapies, work management, and rest periods), and cognitive behavioral therapy. Among psychosocial rehabilitation methods (evaluation, education, and support groups), cognitive behavioral therapy and educational management have shown remarkable improvements in brain tumor patients. A study by Levin and colleagues suggested that exercise (without contraindication) helped in improving mental health, curtailing morbidity, and had a positive effect on the overall treatment of brain tumor patients.[23]

Neurological cancer and its management procedure have a remarkable adverse effect on QOL. Anticancer treatments, such as radiation therapy, chemotherapy, and surgery, may improve a patient's functional status and health-related quality of life, while also extending life expectancy.[24] Early assessment can play an essential role in preventing and better management of CRF One such study by Jones and colleagues assessed 35 newly diagnosed post-surgical malignant glioma patients to find out the usefulness of longitudinal evaluation of functional status. They revealed that a longitudinal quantitative assessment of functional performance is secure and beneficial among glioma patients undergoing chemotherapy and radiation.[25]

The study had a few limitations. The sample size was small. BFI is only a single-dimensional scale and it cannot assess the quality of life of patients. It is recommended that these points be considered in future studies.

CONCLUSION

CRF happens owing to multiple anticancer managements such as radiation therapy, chemotherapy, and simultaneous chemoradiation, but the incidence level differs commonly among all cancer patient therapies. We observed that CRF is the most wearing symptom that most cancer patients experience, regardless of the diagnosis or type of treatment they receive. CRF was discovered to be mildly linked to QOL among radiotherapy patients and to be poorly associated with chemotherapy and concurrent chemotherapy groups. The evaluation of CRF should therefore start once the patient has been identified with cancer and before the therapy for anticancer treatment has begun. In addition, pre- and post-treatment evaluation of CRF will assist healthcare practitioners in preventing and treating this serious symptom of distress.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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PEER-REVIEWED CERTIFICATION

During the review of this manuscript, a double-blind peer-review policy has been followed. The author(s) of this manuscript received review comments from a minimum of two peer-reviewers. Author(s) submitted revised manuscript as per the comments of the assigned reviewers. On the basis of revision(s) done by the author(s) and compliance to the Reviewers' comments on the manuscript, Editor(s) has approved the revised manuscript for final publication.