

Incidence of Fatigue in Patients of Cancer of Head & Neck Region, Receiving Chemotherapy as well as Radiotherapy, and Its Effect on Quality of Life

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ABSTRACT

BACKGROUND

Fatigue has been defined as a feeling of weakness subjectively, also expressed as extreme tiredness and energy loss due to illness or physical or mental exertion. Differences of quality of fatigue between healthy controls and cancer patients have been suggested. Moreover, these are due to heightened degree of expression of fatigue in cancer patients. We wanted to determine the prevalence of fatigue in patients suffering from head & neck cancer and receiving chemotherapy as well as radiotherapy and evaluate the fatigue related impact on quality of life.

METHODS

This is a cross sectional study done among patients of head & neck cancer, receiving chemotherapy and radiotherapy, in the Department of Oncology, Surgery and Pathology, K.D. Medical College Hospital & Research Center, Mathura, Uttar Pradesh. Department of Radiation Oncology, Grecian Superspeciality Hospital, Mohali. PG Department of Radiotherapy, Acharya Harihar Regional Cancer Centre, S.C.B. Medical College & Hospital, Cuttack. Duration of study is 2013 December 2014 November and 2019 March - 2020 July. Forty-one patients were studied.

RESULTS

Out of twenty-four patients who were treated with radiotherapy, nine patients had mild fatigue; fifteen patients had moderate fatigue; and no patient had severe fatigue. Among seventeen patients who received chemotherapy, fourteen patients reported mild fatigue, two reported moderate fatigue, and one patient reported severe fatigue.

CONCLUSIONS

Different anticancer therapies cause Cancer Related Fatigue (CRF); those could be chemotherapy and radiotherapy. Severity of fatigue was more in radiotherapy as compared to chemotherapy group.

KEYWORDS

Cancer, Chemotherapy, Radiotherapy, Fatigue, Quality of Life (QOL)

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BACKGROUND

Fatigue has been defined as weakness feeling subjectively, also expressed as extreme tiredness and energy loss due to illness or physical or mental exertion. fatigue can have different meanings in non-medical setting.¹ In the medical field, for cancer patients, different fatigue definitions have been suggested.² Cancer related fatigue has been defined as a 'upsetting, continuous tiredness and sense of depletion related to cancer or cancer treatment which is even disproportional to recent activity again causing disturbance with usual functioning as per of National Comprehensive Cancer Network.³ The use of the ICD-10 (International Classification of Diseases-10) criteria for the definition of fatigue due to cancer (CRF) requiring, 'diminished energy, significant fatigue or requiring increased rest, disproportionate to any recent change in activity level' to be present in the latest month almost each day till two successive weeks, has been mentioned by the Fatigue coalition.⁴ In all stages of cancer from agile treatment to progressive stages as well as to the state of being survivor, the syndrome of fatigue has been recognized as per the "Diseases-10 criteria of International Classification". Quality of life of head and neck cancer presents some unique and challenging features.⁵ Patients with head and neck cancer are afflicted with a disease that profoundly influences some of the most essential functions of life including breathing, eating and communication. They present with pain, mucositis, dryness of mouth, loss of taste and smell have negative impact on the quality of life of patients may be due to chemotherapy or radiotherapy.

In view of these difficulties, oncologists have increasingly recognized the importance of assessing quality of life. QOL is recognised as an important factor in assessing treatment outcome.⁵ The World Health Organization Quality of Life (WHOQoL) group, in their comprehensive definition of quality of life, describes quality of life as individuals' perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.⁶ Quality of life is a very broad concept, describing a person overall feeling of wellbeing and includes a wide range of both physical and psychological concepts. It has also been defined as "The perceived discrepancy between the realities of what one has and what one wants, or expects or has had". This definition of quality of life is often termed as the gap theory.⁷ The present study is being undertaken to evaluate the factors affecting the quality of life in patients of head and neck cancer treated with radiotherapy or chemotherapy. Cancer Related Fatigue (CRF) is one of the most prevalent symptoms of patients with cancer experience,⁸ both during and after treatment. This is wide spread situation among patients with cancer and troopers of cancer^{9,10,11} that occurs abreast of all sexes, times of detection of cancer, levels of disease, and treatment regimens.¹² Fatigue amalgamated with cancer or its treatment is prominent from the typical fatigue that come across by many people as a result of normal day to day living. CRF is out of proportion to mental and physical effort level and improbable to typical fatigue and is not freed from stress or discomfort by break from

work or slumber.¹³ Fatigue is experienced by approximately 50 – 90 % of cancer patients, that number corresponding with those receiving active anticancer radiotherapy or chemotherapy. Patient's Quality of Life (QOL) and daily activities are very much negatively affected by fatigue. Many cancer individuals experiencing the distress symptoms has been related to QOL. The effectiveness of treatment has been evaluated primarily by QOL in different studies.^{9,10,14,15} This straight away showed that in cancer patients during and after treatment, CRF has been defined as a continuous disabling phenomenon, even after treatment CRF goes on for good number of years.¹² and surely it has intense manifestation on the level of excellence of life. Cancer patient's fatigue was very less noted and so badly managed as common symptoms, like nausea and pain, was focused predominantly.¹⁶

Different treatment modalities such as chemotherapy and radiotherapy, result in CRF, which is reported by many patients as a common symptom.^{17,18} Apparently, it was estimated by researchers that fatigue is experienced by approximately 70 % of patients, suffering from cancer while being treated with Radiotherapy and chemotherapy.¹⁹

Not only QOL's severe impairment, restriction of physical activity, work ability, but also social activities are affected by severe fatigue.²⁰ The characteristics of the patient influences the intensity / type of treatment, the severity and incidence of CRF,²¹ and primary malignancy.²² Therefore in the clinical assessment of cancer patients, CRF assessment and distribution into groups should be the earliest footprint for, appropriate treatment implementation of specific treatment strategy and CRF diagnosis. The patients certainly be scrutinized by means of a self-explanatory concise list of questions like, as Visual Analogue Scale (VAS) otherwise Brief Fatigue Inventory (BFI) for the diagnosis of CRF.^{23,24}

The association of CRF with QOL and its prevalence will provide valid information about CRF.⁸ Moreover, before now for both the therapies fusion or for lone therapy wide extension has been stated formally and studies in academic journals reporting the undivided comparative degree spread of fatigue amidst the two attempted remediations has not been reported until the present time. So measuring the proportion of fatigue among patients suffering from cancer and receiving chemotherapy and radiotherapy, and assessment of its impact relatively on QOL is the purpose of study.²⁵

METHODS

This is a cross-sectional study. By using purposive sampling forty-one (41) cancer patients of head & neck region were selected for the study. The patient sample included seventeen (17) chemotherapy patients and twenty four (24) radiotherapy patients, based on the following criteria.

Inclusion Criteria

1. No history of prior chemotherapy or radiotherapy.
2. Having features which were indications for Radiotherapy.

3. Age more than 15 years.
4. Minimum Haemoglobin level of 10 gm / dL.
5. Karnofsky Performance (KPS) Status of 50 or above
6. Minimum TLC of 4000 per cu mm.
7. Normal biochemical parameters.
8. Those who are willing to provide written informed consent.

Exclusion Criteria

1. Recurrent or second cancers.
2. Evidence of distant metastases by clinical or radiological examination.
3. Severe uncontrolled comorbid conditions like diabetes, hypertension, asthma, neurological abnormalities.
4. Pregnant women.
5. Simultaneous participation in another clinical study.
6. Inability to understand the questionnaire due to cognitive and / or mental impairment.

100	No disease evidence Normal; no complaints; Normal
90	Disease with Minor sign or symptoms; normal activity can be carried on
80	Disease show some sign and symptom; With effort Normal activity
70	Normal activity or active work cannot be carried out; self-care.
60	Able to care for most personal needs; Only occasional assistance required.
50	Frequently medical care is needed; considerable assistance is required.
40	Special care and assistance is required; Disabled.
30	Death not imminent, Hospitalization indicated, Disabled severely.
20	Active support treatment is very much required, Very sick; hospitalization necessary;
10	Rapid progress of Fatal processes, Moribund
0	Dead

Table 1. (K.P.S.) Karnofsky Performance Status

ECOG Performance Scale

1. Asymptomatic, normal activity.
2. Full ambulatory, symptomatic, able to perform activities of daily living.
3. Symptomatic; up and about in bed less than 50 % of time.
4. Symptomatic, capable of only limited self-care, in bed more than 50 % of time.
5. Completely disable, cannot perform any self - care, bed ridden 100 % of time.
6. Dead.

Measurement Tools

Brief Fatigue Inventory - Fatigue uses BFI as filtering equipment which assesses the seriousness of fatigue since last 24 hours. There are only nine items in BFI, in with the items are measured on a numeric rating scale of 0 - 10. The rate of fatigue severity of patients are determined by three items, which patients are asked at its "now", "worst," and "usual," during normal ambulatory hours, with 10 for "fatigue as unfavorable as we can ween" and 0 for "hardly any or no fatigue" The diverse blees of the patient's life in the span of finished 24 hours are interfered by amount fatigue which are assessed by the six items. The interference items consists of mood, general activity, normal work including house work as well as work outside the home, walking ability, enjoyment of life and relations with other people. The measuring of interference items are

done with a scale of 0 - 10, with 10 being "complete interference and 0 being "no interfere". Categorization of fatigue using the BFI as each non intense / severe (score 0 - 6) or intense (score 7 - 10). The "non intense / severe" again grouped into mild (score 0 - 3) and moderate (score 4 - 6).

Functional Assessment of Cancer Therapy - General (Fact-G) Scale - The health-related Quality Of Life (HRQOL) of patients suffering from cancer is widely being measured by FACT-G. The final form (4) composed of entire 27 Likert-type articles being put in a clear and definite form of statement reduced into different wages: social / family (entities are seven), checkups (entities are seven), emotional (entities are six), and functional (entities are seven) of well-being. For patients, different scores of 0 - 4, where 4 = very much, 3 = quite a bit, 2 = somewhat 1 = a little and 0 = not at all have been assigned for the response of each items. A better quality of life is indicated by higher scores.

Procedure

Written consent over the form was taken from Patients, those who met the inclusion criteria and after the study has been clearly explained to them. Data's like age, gender name along with KPS scores were noted where, for most serious illness, the lower score signifies, the worse survival. Fifty (50) being the cut-off score. Patients were asked to complete the set of questions which are given to cancer patients so that their quality of life and the level of fatigue can be measured by using FACT-G and brief fatigue inventory respectively.

Statistical Analysis

Microsoft Excel work sheet was used to collect raw data. SPSS software was used to analyse the data. Prevalence rate was determined based on the total number of patients within the group of intense / severe, moderate and mild fatigue. The association between the CRF and QOL among the two groups was done by using Spearman correlation coefficient.

RESULTS

The study was conducted in the Department of Oncology, Surgery, Pathology, K.D. Medical College Hospital and Research Center, Mathura, U.P., Gricean Hospital, Department of Radiotherapy, A.H.R.C.C. and SCB Medical College, Cuttack. 41 eligible patients of head and neck cancer, who satisfied the eligibility criteria were accrued during the study period. Out of 41 patients enrolled in the study 2.4 % of the patients were in the age group 15 - 25 years, 9.8 % of the patients were in the age group 26 - 35 years, 26.8 % were in the 36 - 45 years, 29.3 % were in the 46 - 55 years, 24.4 % were in the 56 - 65 years, 4.9 % were in the 66 - 75 years and 2.4 % were in the 76 - 85 years.

Age Ranges (Yrs.)	CT	RT	Total
15 - 25	0 (0.00 %)	1 (4.2 %)	1 (2.4 %)
26 - 35	3 (17.6 %)	1 (4.2 %)	4 (9.8 %)
36 - 45	4 (23.5 %)	7 (29.2 %)	11 (26.8 %)
46 - 55	5 (29.4 %)	5 (20.8 %)	12 (29.3 %)
56 - 65	5 (29.4 %)	5 (20.8 %)	10 (24.4 %)
66 - 75	0 (0.00 %)	2 (8.3 %)	2 (4.9 %)
76 - 85	0 (0.00 %)	1 (4.2 %)	1 (2.4 %)
Total	17 (100 %)	24 (100 %)	41 (100 %)

Table 2. Age Distribution

Majority of the patients in the study were in age group 36 - 65 years. In our study 75.6 % of the study population were male & 24.4 % were female patients. In the present study majority belongs to average income group i.e. 22 patients (53.7 %). Maximum patients (51.2 %) in our study were having KPS 70 – 80.

KPS Range	Therapy			Total
	CT	RT		
50 - 70	5.9 %	25.0 %		17.1 %
70 - 80	52.9 %	50.0 %		51.2 %
80 - 100	41.2 %	25.0 %		31.7 %
Total	100.0 %	100.0 %		100.0 %

Table 3. KPS Status in the Study Population

Therapy		Fatigue Score			Total
		Mild	Moderate	Severe	
CT	Count	14	2	1	17
	% Within Therapy	82.4 %	11.8 %	5.9 %	100.0 %
	Count	9	15	0	24
	% Within Therapy	37.5 %	62.5 %	0.0 %	100.0 %
Total	Count	23	17	1	41
	% Within Therapy	56.1 %	41.5 %	2.4 %	100.0 %

Table 4. Fatigue Distribution among Different Therapies

Table showed prevalence of fatigue among patients receiving CT & RT. Out of 24 patients who received RT 37.5 % (9) reported mild fatigue, 62.5 % (15) reported moderate, no severe fatigue. Among patients who received CT (17 patients) 82.4 % (14) reported mild fatigue, 11.8 % (2) reported moderate fatigue. Fatigue Level (BFI) between different therapies.

	CT (^a fq)	RT (^b fq)	
BFI1	Minimum	0	0
	Maximum	7	7
	Mean	2.29	3.79
	SD	2.11	1.44
BFI2	Minimum	0	0
	Maximum	5	7
	Mean	2.24	3.46
	SD	1.52	1.58
BFI3	Minimum	0	0
	Maximum	10	8
	Mean	4.06	5.17
	SD	3.03	2.22

Table 4. Descriptive Statistics in Brief Fatigue Inventory (BFI) for Patients after Being Treated with Radiotherapy and Chemotherapy

Table shows standard deviation and mean for the level of fatigue (^bfq in RT) and (^afq in CT).

In the usual degree of fatigue in finished 24 hours (^bfq₂), of present fatigue (^bfq₁), and worst degree of fatigue in finished 24 hours (^bfq₃) in RT groups, the mean and standard deviation were determined, which was 3.46 ± 1.58, 3.79 ± 1.44 and 5.17 ± 2.22 in the relative manner.

Standard deviation, mean for the, usual level of fatigue in finished 24 hours (^afq₂), of present fatigue (^afq₁), and severe degree of fatigue in finished 24 hours (^afq₃) in patients receiving CT were 2.24 ± 1.52, 2.29 ± 2.11 and 4.06 ± 3.03 respectively.

No. of Subjects	Type of Therapy	Correlation Value (R)	Significance Level
17	CT	r = - 0.842	p < 0.001
24	RT	r = - 0.764	P < 0.001

Table 5. Complementary Relationship between Fatigue and Quality of Life in the Two Therapies

Table 5 shows the correlation analysis of cancer related fatigue and quality of life. Any shoot up in seriousness of the degree of fatigue correlated to worst quality of life. The correlation was separately interpreted for fatigue occurring due to RT and CT with domain of QOL. There is moderate correlation (r = - 0.764 p value < 0.001) between fatigue due to RT and QOL shown in table 5 and graph 2. Correlation analysis of Cancer related fatigue and There is strong (good) correlation (r = - 0.842 at p value < 0.001) between fatigue due to CT & quality of life shown in table 5 & graph 1.

The correlation was separately interpreted for fatigue occurring due to radiotherapy and chemotherapy with domain of life quality. Mediocre complementary relationship (r = - 0.764 at 0.000 significance) between fatigue and QOL seen in radiotherapy exhibited in Table 5 as well as Graph 2. The Complementary relationship between QLF and fatigue in chemotherapy shows strong complementary relationship (r = - 0.842 at 0.000 importance) depicted in no 1 Graph.

DISCUSSION

In cancer patients of head neck region, who received radiation therapy, cytotoxic chemotherapy, or biological response modifiers²⁶, most prevalent phenomenon is Cancer related fatigue (CRF). The act of measurement of the rate of wide extension (spread) of fatigue (seriousness of fatigue) amidst the cancer patients of head as well as neck region, receiving chemotherapy and radiotherapy and it's impacts the QOL is the focus of the current study. Total forty one (41) no. of cancer patients of Head and Neck cancer region were included in our study. Fact-G was used to measure Health related quality of life (HRQOL) in our patients, during the period of treatment where the type of cancer was already diagnosed and in more than half of patients CRF is noted in the immediate vicinity at the treatment beginning. It came out in our study, 62.5 % patients perceived moderate level of fatigue, 37.5 % experienced mild fatigue among 24 patients who received radiotherapy.

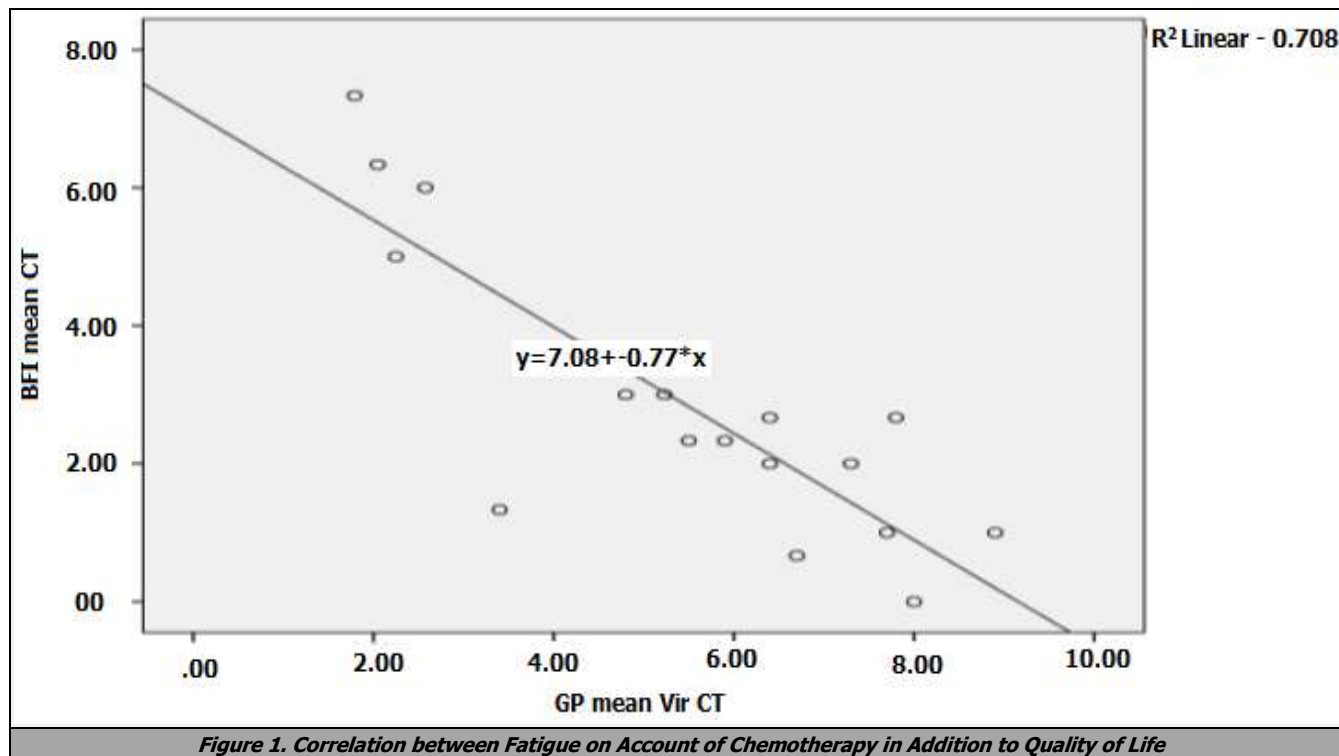


Figure 1. Correlation between Fatigue on Account of Chemotherapy in Addition to Quality of Life

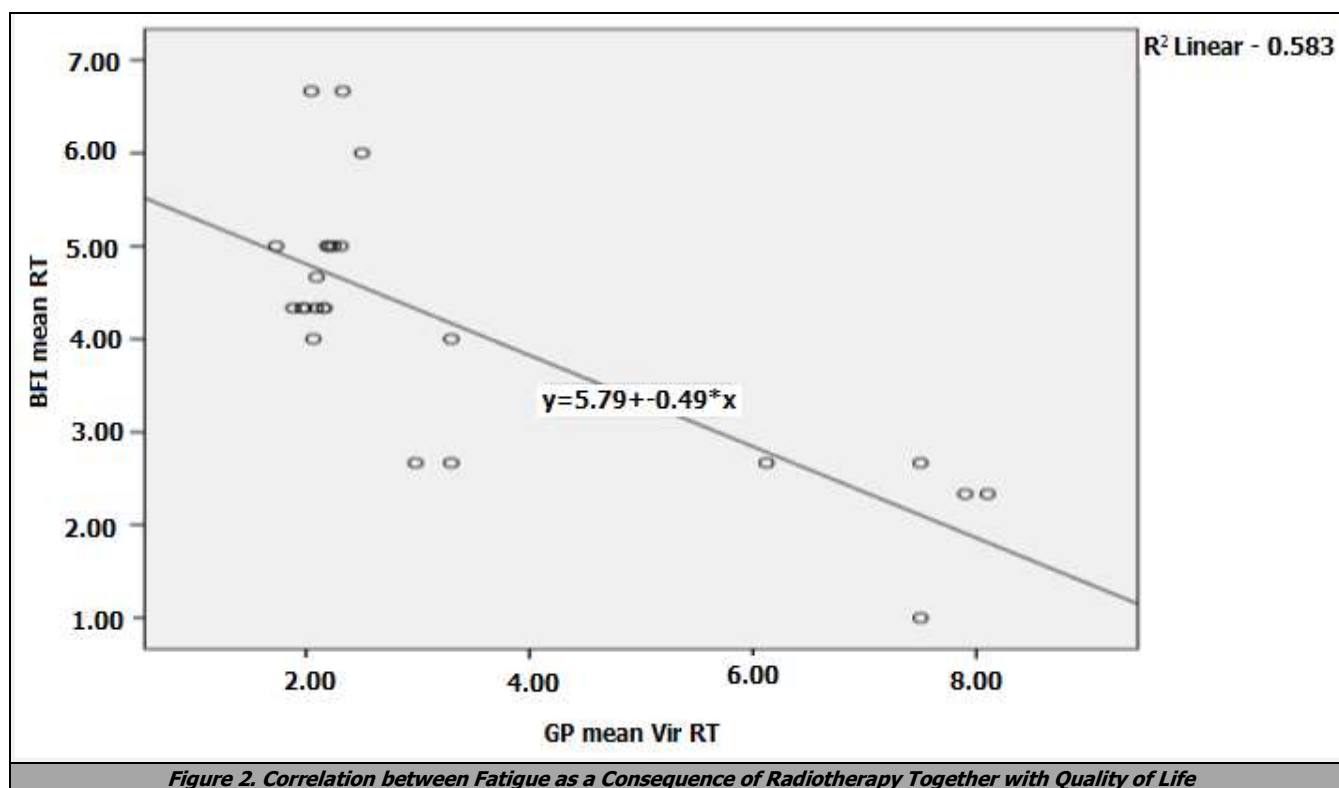


Figure 2. Correlation between Fatigue as a Consequence of Radiotherapy Together with Quality of Life

Initial shoot up of degree of fatigue and then a comparative stable level of fatigue at sennight 4 in a radiotherapy orderly government that prevailed for 6 to 9 sennights, further discovered in other studies.^{27,28} Transient increase in the fatigue is caused by radiotherapy in which the fatigue accumulates over weeks and at one month after completion of treatment the fatigue reaches to the pretreatment level.²⁹ For a duration of many weeks the patients were receiving Radiotherapy and the fatigue was measured between 16th to 20th session of radiotherapy treatment in this study also. intense radiation unlimited

consequences were also observed that might down regulate the nourishment of patient and other health distinguishing features preceding to fatigue intensification. Fatigue is one of the commonest side effects, in chemotherapy.

During the second or third session of chemotherapy treatment of the cancer patient fatigue level was measured here. Fourteen (14) no of patient had mild level of fatigue, One patient experienced severe level of fatigue, 2 no of patient had moderate level of fatigue amongst total 17 patients who were receiving chemotherapy in this study. So the extent of fatigue after radiotherapy treatment is more

than that of chemotherapy treatment. The measurement of fatigue was done only once when they were receiving the treatment in this study and also at the same time the population was not specific to one type of cancer, while it was measured only in breast cancer patients in case of Donovan et al. It was also found by Schmidt et al that there is substantial level of increase of fatigue in cancer patients during Radiotherapy and chemotherapy those treated with each of the therapies. It was 30 % same, 61.4 % elevated and 8.6 % underslung fatigue degree throughout chemotherapy. The fatigue severity was more in patients receiving radiotherapy in comparison to those who receiving alone the chemotherapy, was documented in this study.

So to say patients treated with radiotherapy in the early part of treatment were anticipated to report underslung fatigue degree and causing more unrest than patients taking chemotherapy in their early treatment. The perception that it was "not as bad" or "no greater" than the chemotherapy fatigue experienced, have influenced severity of fatigue during subsequent radiotherapy. QOL was the significant determining factor for entire Fatigue, displaying a polynomial complementary relationship with entire QOL, 0.76. Like the former studies had recounted such CRF had an impact on the QOL, in our study the correlation analyses implied that there is mediocre complementary relationship ($r = -0.764$ at $p < 0.001$ importance) amid fatigue as a consequence of radiotherapy as well as QOL.

Simultaneously, complementary relationship between the fatigue caused by chemotherapy and QOL uncovers strong (good) reciprocal relationship ($r = -0.842$ at $p < 0.001$ significance). The fatigue severity was found more in radiotherapy group as compare to the chemotherapy group. The fatigue showed by far the strongest univariate correlation with overall QOL ($r = -0.76$, $p < 0.001$), as showed by Dagnelie et al.³⁰

Patient present indoor and outdoor area of home, earnestly desirous and melancholic symptoms were alike in radiotherapy and chemotherapy. The relationship between CRF and QOL was not fully recognized in our study because of smaller number of specimens in each collection ("r" value as well as p value responsive to specimen magnitude) though it is prudently pointed out that there is noticeable intense reciprocal relationship between CRF and QOL. Material world responsibilities, functions related to intellectual and society were made smaller for all of the interval of radiation therapy management which after one month of follow up returns to baseline level, has been found by Janakietal.³¹ Furthermore, the wide extension or spread rate of fatigue amidst population of India for cancer patient treated with the radiotherapy, chemotherapy has been measured in this study, which is reported in only few literature. The cancer patient can be helped by the beneficiary health care persons for improving their QOL by assessing the different parameters. Additionally, Prior to and later in time the beginning of anticancer management, CRF should be assessed. The association between CRF because of radiotherapy as well as chemotherapies and QOL has not been fully justifiable in our study. CRF have intellectually deep manifestation on general wellbeing (quality) of life, the actual instance of CRF on account of diverse anticancer

management is not a lone foreteller for influencing QOL have clearly been documented in earlier studies. Moreover exploration should be concentrated upon cancer tiers in reference to preliminary location as well as specific type of cancer. Above things would have given superior introspect for management as well as into the range of values of fatigue in cases where greater degree concentrated remedy (management) is given to cancer patient. There were certain limitations in terms of size of the sample owing to relatively smaller groups and inequality between the groups in this group. Another limitation of the study is potential correctable etiologies for patient's fatigue were not examined. Further studies should be done to know fatigue distribution precisely, and longitudinally how long its impact remains.

CONCLUSIONS

Different anticancer therapies such as chemotherapy and radiotherapy can lead to cancer related fatigue (CRF) and the CRF prevalence rate among the anticancer treatments given to patients suffering from cancer varies widely. Degree of seriousness of exhaustion was less in chemotherapy group as compared to radiotherapy group. Strong correlation was found between CRF and Quality of Life (QOL) among the patients receiving chemotherapy; and in radiotherapy group moderate correlation was found between CRF and SOL. Hence, as soon as the patient suffering from cancer is confirmed and prior to the initiation of anticancer remedy (management), CRF assessment should start. Additionally, examining CRF prior to and following treatment will be an assistance. The health care professional should, evaluate CRF before and after treatment so that prevention and treatment of severe distress symptoms can be accomplished.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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