



Research Article

CANCER RELATED FATIGUE AMONG PATIENTS WITH GYNECOLOGICAL MALIGNANCIES RECEIVING VARIOUS THERAPIES: AN INSTITUTIONAL EXPERIENCE

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ABSTRACT

Objective: To find out the prevalence of cancer related fatigue (CRF) and its impact on quality of life (QoL) amongst gynecological cancer patients receiving radiotherapy, chemotherapy or concurrent chemo-radiation.

Material and Methods: This study included 194 gynecological cancer patients receiving radiotherapy, chemotherapy or concurrent chemo-radiation who fulfilled the inclusion and exclusion criteria. The patients' fatigue was assessed using Brief Fatigue Inventory (BFI) and quality of life (QoL) was measured using Functional Assessment of Cancer Therapy-General (FACT-G) scale.

Results: Severe fatigue was more prevalent in patients receiving chemotherapy [39/45 (86.66%)], and concurrent chemo-radiation (81/125 (64.8%)) as compared to radiotherapy (Moderate-8/24 (33.33%) and Severe-9/24 (37.5%)). Moderate correlations were exhibited between fatigue due to radiotherapy and QoL ($r = -0.747, P < 0.01$), whereas weak correlation was found between fatigue due to chemotherapy and moderate correlation in concurrent chemo-radiation ($r = -0.311, P < 0.01$ and $r = -0.591, P < 0.01$, respectively).

Conclusion: Severity of fatigue (CRF) was more in chemotherapy and concurrent chemo-radiotherapy patients while QoL was affected more after radiotherapy. CRF is a common and often underestimated distressful phenomenon. Adequate attention should be given from the beginning of treatment to improve the quality of life of cancer patients.

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INTRODUCTION

The definition of Cancer Related Fatigue (CRF) as given by National Comprehensive Cancer Network version 2.2017 is “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”. It is a very common symptom affecting about 80% of cancer patients receiving any type of anti-cancer treatment.[1] CRF has a negative impact on patients' well being and QoL. Despite the high prevalence of CRF and its potential negative impact on patients' QoL and emotional well-being, research in this area is still lagging behind and there are only a few studies available in the literature for Indian population. [2]

CRF is believed to be multifactorial and the causes include the cancer itself and its treatment, anemia, infection, sleep rhythm disturbances, immune activation, pain, psychosocial factors and so on. Various validated tools are available for the measurement of fatigue but there is no gold standard.

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The Brief Fatigue Inventory (BFI) is used as screening tool for fatigue which measures severity of fatigue over the previous 24 hour. The BFI has nine items, with the items measured on 0-10 numeric rating scales. [3] Functional Assessment of Cancer Therapy-General (FACT-G) is an easy to administer questionnaire widely used to measure health-related QoL in cancer patients. Gynecological cancer patients comprise about 18 % of total cancer patients coming to Department of Radiotherapy, SMS Medical College & Attached Hospitals, Jaipur, India. So we decided to study the prevalence and severity of fatigue and its impact on QoL in this patient group.

MATERIALS AND METHODS

A total of 194 cancer patients were selected for this study. Patient characteristics are shown in table 1. The inclusion criteria was as follows: patients with age more than 18 years and less than 70 years, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 to 2, Hemoglobin levels >10gm/dL, patients able to give informed consent. The Exclusion criteria were any patient with known history of psychiatric disorders, neurological impairments, cognitive/perceptual impairments and patients with severe comorbidities. The data was collected from October 2016 to March 2017.

Procedure

Subjects were asked to fill the questionnaire to measure their level of fatigue and QoL by using BFI and FACT-G, respectively. The participants were explained about the questions in their mother tongue and response was noted.

Functional Assessment of Cancer Therapy-General (FACT-G). The latest version 4 consists of a total of 27 Likert-type items formulated into separate subscales: Physical (seven items), emotional (six items), social/family (seven items), and functional (seven items) well-being. Subjects are asked to respond to each item with a score of 0-4, where 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much. A higher score indicates a better quality of life. [4,5]

Brief Fatigue Inventory (BFI). In BFI, three items ask patients to rate the severity of their fatigue at its "worst," "usual," and "now" during normal waking hours, with 0 being "no fatigue" and 10 being "fatigue as bad as you can imagine." Six items assess the amount that fatigue has interfered with different aspects of the patient's life during the past 24 hours. The interference includes general activity, mood, walking ability, normal work, relations with other people and enjoyment of life. The interference items are measured on a 0-10 scale, with 0 being "does not interfere" and 10 being "completely interferes." Fatigue was categorized using the BFI as either severe (score 7-10) or not severe (score 0-6), with the latter further subcategorized into moderate (score 4-6) and mild (score 0-3). [6]

Statistical analysis

All statistical analyses were performed using SPSS for windows, version 20.0 (IBM Corp., Armonk, New York, USA). In all calculations, the significance level was taken as 0.05. Prevalence rate was measured on the basis of number of patients under the category of mild, moderate and severe and their percentage is calculated from the total number of patient in each of three groups, i.e., radiotherapy, chemotherapy, and concurrent chemo-radiation using the descriptive statistics. Pearson product moment correlation was used to find out the association between the CRF and QOL in the all three groups.

RESULTS

The details regarding age, ECOG PS, concurrent disease and location of cancer for various patients receiving anticancer treatment is given in Table 1.

Table 1 Patient and disease characteristics.

| Characteristics | RT | CT | CT-RT |
|---------------------|----|----|-------|
| Age (Median) | 54 | 52 | 46 |
| ECOG PS | | | |
| 0 | - | - | 2 |
| 1 | 11 | 16 | 49 |
| 2 | 13 | 29 | 74 |
| Cancer type (Total) | | | |
| Cervix (131) | 7 | 14 | 110 |
| Uterus (21) | 13 | 1 | 7 |
| Ovary (29) | 0 | 29 | 0 |
| Vagina (9) | 3 | 1 | 5 |
| Vulva (4) | 1 | 0 | 3 |

RT = Radiotherapy, CT = Chemotherapy, CT-RT = Concurrent chemoradiotherapy
 ECOG = Eastern Cooperative Oncology Group PS = Performance Status

Table 2 Fatigue distribution

| Treatment | Number of patients (n) | No fatigue | Mild fatigue (%) | Moderate fatigue (%) | Severe fatigue (%) |
|-----------|------------------------|------------|------------------|----------------------|--------------------|
| RT | 24 | 2 (8.33%) | 5 (20.83%) | 8 (33.33%) | 9 (37.50%) |
| CT | 45 | - | 3 (6.66%) | 3 (6.66%) | 39 (86.66%) |
| CT-RT | 125 | - | 10 (8%) | 34 (27.2%) | 81 (64.8%) |

RT = Radiotherapy, CT = Chemotherapy, CT-RT = Concurrent chemoradiotherapy

Table 2 describes the prevalence of fatigue among the patients receiving the various therapies. Out of 24 patients who received radiotherapy, 8.33% (2 patients) reported mild fatigue, 33.33% (8 patients) reported moderate, and 37.5% (9 patients) reported severe fatigue. Among patients who received chemotherapy 3 patients (6.66%) reported moderate fatigue, while overwhelming majority of 39 patients (86.66%) reported severe fatigue. Among patients who received concurrent chemo-radiation, 10 patients reported (8%) mild fatigue and 34 patients reported moderate fatigue (27.2%) and 81 patients experienced severe fatigue (64.8%).

The mean and standard deviation for the level of present fatigue (Q1), usual level of fatigue in past 24 hours (Q2), and the worst level of fatigue in past 24 hours (Q3) in radiotherapy group were 5.21 ± 2.943 , 5.09 ± 2.875 , and 5.15 ± 2.954 , respectively. The mean and standard deviation for the level of present fatigue (Q1), usual level of fatigue in past 24 hours (Q2) and the worst level of fatigue in past 24 hours (Q3) in chemotherapy group were 6.51 ± 2.324 , 6.87 ± 2.097 , and 6.92 ± 2.014 , respectively. The mean and standard deviation for the level of Present fatigue (Q1), usual level of fatigue in past 24 hours (Q2) and the worst level of fatigue in past 24 hours (Q3) in concurrent chemo-radiation group were 5.632 ± 2.791 , 5.602 ± 2.658 , and 5.607 ± 2.768 , respectively.

Table 3 Correlation between fatigue and quality of life

| Treatment | No of patients | Correlation coefficient (R) | Significance level (p) |
|----------------------------|----------------|-----------------------------|------------------------|
| Radiotherapy | 24 | $r = -0.747$ | <0.01 |
| Chemotherapy | 45 | $r = -0.311$ | <0.01 |
| Concurrent chemo-radiation | 125 | $r = -0.591$ | <0.01 |

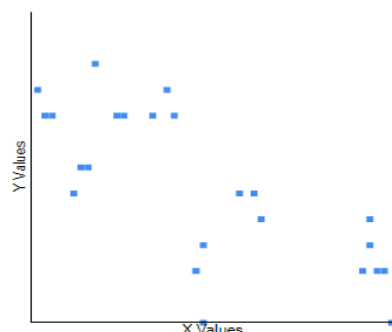


Figure 1 Correlation of fatigue due to Radiotherapy and Quality of Life (QoL) $r = -0.747$ revealing strong negative correlation.

Correlation analysis of CRF and QOL revealed negative correlation which meant that any increase in severity of the level of fatigue, worst for the QOL. The correlation was interpreted separately for fatigue occurring due to radiotherapy, chemotherapy, and concurrent chemo-radiation

with quality of life domains. There is moderate correlation ($r = -0.747$ at 0.01 significance) between fatigue due to radiotherapy and QOL shown in [Table 3] and Figure 1. Correlation between fatigue due to chemotherapy and QOL reveals weak correlation ($r = -0.311$ at 0.01 significance). Correlation between fatigue due to concurrent chemo-radiation and QOL reveals negative and moderate correlation ($r = -0.591$ at 0.01 significance).

DISCUSSION

CRF is a common phenomenon in individuals with cancer who receive radiation therapy, cytotoxic chemotherapy. [7] It is a multi-factorial, multidimensional phenomenon, which consists of physical, psychological, social, cognitive, and behavioral aspects [8] [9]. In spite of growing evidence regarding the fatigue occurring due to various anticancer treatments and how CRF affect patient's quality of life, still determining its severity is underestimated. The current study stressed on measuring the prevalence rate of fatigue (and its severity) among the gynecological cancer patients receiving the various anticancer treatments, and how it impacts the QOL.

Radiotherapy causes transient increase in the fatigue which accumulates over weeks. It comes back to the pretreatment level at one month after completion of treatment. Fatigue during radiotherapy is unique as the treatment is stretched over many weeks. Fatigue was measured in the third week of radiotherapy treatment. This is also associated with significant acute radiation side effects which may alter the patient's nutrition, blood parameters leading to aggravation of the fatigue [10]. Furthermore, Radiotherapy related fatigue starts increasing from second week onwards coinciding with the beginning of radiation reactions. This may explain the reason for lesser level of fatigue in this study as the fatigue measurement was taken only once, during the third week of radiotherapy.

Fatigue is one of the most prevalent side effects during cancer chemotherapy. It usually persists for more than two weeks [2]. It has been observed that during the first 24 to 48 hours of chemotherapy, there is a spiked rise in fatigue levels [11,12]. Fatigue level was measured here when the patients were receiving the second or third session of chemotherapy treatment. In this study, among 45 patients who were receiving chemotherapy, 39 patients experienced severe level of fatigue (86.66%). So the magnitude of fatigue after chemotherapy is more than that of radiotherapy treatment.

Furthermore, patients receiving a combination of chemotherapy and radiotherapy have reported higher levels of fatigue compared to those receiving a single therapy [13,14]. In our study, among the 42 patients receiving concurrent chemo-radiation in this study, 9.52% reported mild fatigue, 11.90% documented moderate level of fatigue, and 78.57% reported severe level of fatigue. So the magnitude of fatigue resulted after the concurrent chemo-radiation is more than that of radiotherapy alone and little lesser than that of chemotherapy alone in this study. Schmidt *et al* [15] also found that fatigue level substantially increased during chemotherapy and radiotherapy and among the patients who received both therapies it was 61.4% higher, 30% same, and 8.6% lower fatigue level during chemotherapy. This study also documented that the severity of fatigue was more in patient receiving concurrent chemo-radiation and chemotherapy as compare to those who receiving the

radiotherapy alone. A meta-analysis [16] also supported the fact that women receiving both CT + RT reported significantly more fatigue.

Correlation analyses of our study suggested that there is moderate correlation ($r = -0.71$ at 0.01 significance) between fatigue due to radiotherapy and QOL. At the same time, correlation between the fatigue due to chemotherapy and concurrent chemo-radiation and QOL reveals weak correlation ($r = -0.361$ at 0.01 significance, $r = -0.453$ at 0.001 significance, respectively). But the severity of fatigue was found more in concurrent chemo-radiation and chemotherapy group as compare to the radiotherapy group. Dagnelie *et al.*[17] found in their study that the fatigue showed by far the strongest univariate correlation with overall QOL ($r = -0.76, P < 0.001$).

While addressing the issue of CRF, we need to consider the issue from both the patients' and clinicians' perspective. Patients usually do not complain of symptoms of fatigue even if it is severe. [1] This can be circumvented by taking proper history and encouraging patients to share their psychosocial problem with the physician besides the physical complaints. The physician should be trained regarding the use of non-pharmacological therapies such as cognitive behavior therapy, graded exercise therapy, pacing besides the use of pharmacological management like antidepressants and psycho stimulants. Furthermore, a patient and compassionate approach would greatly help to address this issue.

CONCLUSION

Severity of fatigue (CRF) was more in chemotherapy and concurrent chemo-radiotherapy patients while QoL was affected more after radiotherapy. CRF is a common and often underestimated distressful phenomenon. Adequate attention should be given from the beginning of treatment to improve the quality of life of cancer patients.

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