Journal of Complementary and Alternative Medical Research

Volume 20, Issue 4, Page 29-39, 2022; Article no.JOCAMR.96064
ISSN: 2456-6276

Effect of Exercise Program on Cancer Related Fatigue and Quality of Life among Patients Undergoing Cancer Treatment - Pilot Study (Part-2)

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JOCAMR/2022/v20i4422

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/96064

Original Research Article

Received: 28/10/2022
Accepted: 30/12/2022
Published: 31/12/2022

ABSTRACT

Background: Even after effective treatment, cancer-related fatigue (CRF) is the most prevalent and debilitating issue for cancer patients. Daily life, social interactions, reintegration, and general quality of life are all severely impacted by CRF.
Aim: This study was done to determine the effect of exercise program on cancer related fatigue (CRF) and quality of life (QOL) among cancer patients on cancer treatment.

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Materials and Methods: One group before-and-after study was done among patients with breast cancer, gynecological cancers, and head and neck cancers on cancer treatment who were selected by purposive sampling method, in selected hospital. Pretest CRF was assessed using a FACIT-F scale (Functional Assessment of Chronic Illness therapy: Fatigue) and QOL was assessed by FACT-G (Functional Assessment of Cancer Therapy: General) Version 4 scale.
Results: Majority (60%) of the respondents were had >50 years of age. Maximum percentage of the sample (76.7%) were females and rest of them were males. Maximum percentage (33.3%) of the respondents had breast cancer and least percentage (10%) had neck cancer. The pretest fatigue score of the cancer patients (pre-test mean= 26.27) was lower than post-test fatigue scores (post- test1 =25.87, post -test 2 = 27.40 and post- test 3=29.00). Fatigue scores are interpreted as higher the score lower the fatigue level. Similarly, the mean and standard deviation of the QOL score at post -test 2 (48.60±7.152) which was higher than the pre-test mean and standard deviation (45.23±8.029). Repeated measures ANOVA, indicates that exercise programme is effective in reducing CRF and improving QOL(*P*=.05).
Conclusion: As per the study findings exercises shows effective in reducing CRF. Hence exercise programs may be used as adjunct therapy for cancer patients on cancer treatment to reduce CRF.

Keywords: Cancer-related fatigue; quality of life; exercise program; nonpharmacological therapy; home care.

1. INTRODUCTION

A significant amount of disease burden worldwide is caused by cancer, and predictions show that this burden will rise for at least the next two decades [1]. In 2018, worldwide, there were 9.5 million cancer-related deaths and 18.1 million new cases of cancer [2]. In 2020, it was the primary cause of over 10 million deaths, or one in every six deaths, in the world [3]. By 2040, it is predicted that there would be 29.5 million new cases of cancer annually and 16.4 million cancer-related deaths.[2] Eight to nine lakh new cases of cancer are recorded each year in India, making it a serious public health concern. Approximately 25 lakh cancer cases are estimated to be present in the country at any given time, and 4 lakh individuals die from the cancer each year [4]. Due to the prevalence of population ageing and the fact that cancer most frequently affects the elderly, it will continue to be a major worldwide health concern [5].

Typically, systemic therapy (chemotherapy, hormonal treatments, targeted biological therapies), radiation, and/or surgery are used to treat cancer. To obtain the anticipated therapeutic outcome, it is critical to complete the treatment procedure within the allotted time frame. Typically, the main objective is to eradicate the cancer or significantly extend life and to enhance the patient's quality of life [3]. However, the treatments frequently have negative side effects. Just a few of these include fatigue, nausea, vomiting, hair loss, anemia, anorexia, infertility, hemorrhage, mental stress, diarrhoea and constipation and stomatitis. The most typical scenario is when side effects begin during therapy and improve with time. However, some individuals experience severe side effects even months or years after their treatment has ended [6].

Cancer-related fatigue (CRF) is a commonly reported adverse effect of all cancer treatments. Cancer-related fatigue (CRF), also referred to as the fatigue of cancer, is different from general fatigue, [7] according to the National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines. CRF is described as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment that is not proportional to recent activity and significantly interferes with usual functioning"[8].

CRF is the product of numerous interrelated processes, including changes to an individual's immune system, muscular, endocrine system, and neurochemistry [9]. Most cancer patients (between 25% and 80%) have moderate to severe chronic CRF [10]. Chronic CRF is linked to serious health problems, such as elevated rates of anxiety and depression,[11] poor sleep, and lowered quality of life.[12] Before the start of treatment, fatigue is generally higher and it usually increases during cancer treatment, including chemotherapy and hormonal and/or biological therapies [13]. According to a systematic review, 26-28% of breast cancer

patients experience fatigue after treatment. This fatigue can last up to five years and does not get better in the first two years [14]. CRF is a prevalent and incapacitating condition that can affect a patient's quality of life (QOL) [15].

According to the clinical practice guidelines published by the NCCN in 2015, exercise and physical activity can reduce fatigue before, during, and/or after treatments. A recent meta-analysis demonstrated that while medication had no impact in CRF, exercise and psychological therapies do, with exercise having the most effects during cancer therapy [16]. Exercise and other physical activity release endorphins, a brain chemical that functions as natural painkillers, enhances sleep quality and also lowers stress. It was found by the researchers that regular aerobic exercise has been demonstrated to reduce overall stress levels, enhance and stabilize mood, improve sleep, and boost self-esteem. Aerobic activity for even five minutes can promote relaxation [17].

To reduce fatigue, all forms of exercise are advised, but the more aerobic the activity for example, walking, swimming, cycling, running, or rowing, it is better. For the best physical and psychological results, interval training is recommended. This means that the exercise should be sustained, rhythmic, involve repetitive movements of large muscle groups, include a series of short, intense periods, and be at a moderate intensity (60-85% of the estimated maximum heart rate). A daily exercise log can be quite helpful for setting realistic goals, tracking progress, and motivating someone to take care of their own fatigue [18].

A research on the impact of a walking exercise programme (WEP) on cancer patients' symptom distress, physical functional status, and fatigue brought on by chemotherapy revealed that patients in the three-week WEP group experienced significantly less fatigue than those in the control group [19]. There is significant evidence that suggests exercise is an effective nonpharmacological intervention for cancer patients. Exercise has been found to safely reduce fatigue, improve physical fitness, and improve the quality of life related to health both before and after cancer treatment. Each cancer patient or survivor's needs can be specifically addressed for when designing an exercise programme [20]. While patients is experiencing fatigue, he/she may not be able to perform all the types of exercises. Planning the exercise as per the need and level of fatigue is a major concern. The current study was done to determine the effect of exercise on CRF and quality of life (QOL) in clients undergoing cancer treatment.

2. MATERIALS AND METHODS

This research is a part of the pilot study, "Effect of Multimodal intervention Vs Exercise programme on cancer related fatigue and quality of life among clients undergoing cancer treatment," with the aim to assess the impact of multimodal intervention Vs exercise programme on cancer related fatigue and quality of life among clients receiving cancer treatment. Only one group is analyzed in this study because investigators will collect the data from another group after completion of data collection from first group to prevent contamination.

2.1 Study Design, Settings, Participants

This study was conducted as a pilot study of the above-mentioned study title. In order to achieve the main objectives of the study a quantitative research approach was adopted. Using a one group before-and-after study design, this study was carried out between June 2022 and September 2022 in a chosen hospital in Mangaluru district of Karnataka state, India. Using a purposive sampling technique, 30 cancer patients receiving cancer therapy in particular hospitals were chosen.

2.2 Sample Size

Sample size was calculated for the main study which will be conducted with two groups. Below mentioned sample size calculation was done on the basis of reference study [21].

2.2.1 Sample size formula

$$N=2(Z\alpha+Z\beta)^2 \sigma^2 /d^2$$

Where,

Z_α= 1.96 at 95% confidence level
Z_β= 0.84 at 80% power
σ^2 = Combined standard deviation
d =Mean difference

With the confidence level of 95% and 80% power with reference to the study, sample size was estimated as 90 in each group. With 10% attrition rate sample size for each group was approximated to 100. For pilot study when 1/10 th

of the sample was calculated, it was 10 per group but it was decided to increase to 30 participants in each group for the purpose of accurate statistical analysis. But in the present study only one group is analyzed.

2.3 Eligibility Criteria

The inclusion criteria; Patients with breast cancer, gynecological cancer and head and neck cancers who were undergoing treatment, who were male or female, between the ages of 18 and 65, who were admitted to the hospital for at least three days, who have undergone at least one cycle of cancer treatment and who were able to or willing to perform exercise for three months of period. Patients in any stage of cancer except with bone metastasis were included.

2.4 Exclusion criteria

Patients with active infections, musculoskeletal issues, lower limb amputations, undergoing erythropoietin or blood transfusions, performing intense aerobic exercise already, and neurological or cognitive impairments with functional limitations. Patients with cancer who have been diagnosed with bone metastases, thrombocytopenia, uncontrolled hypertension or diabetes, angina pectoris, diabetes, cardiac insufficiency, lumbar disc osteoarthritis, peripheral artery disease, chronic obstructive pulmonary disease, renal disease and hypothyroidism or hyperthyroidism.

2.5 Intervention

Exercise programme was planned by the investigator with the guidance from the physiotherapist. Video of the exercise performed by the investigator was recorded by the expert videographer for the clarity and validated by the experts. Duration of video is 6 minutes 11 seconds. Exercises were taught by the investigator to the patients individually and redemonstration of exercise by the patients were done in separate room in the hospital for the purpose of privacy. On 3rd day, during data collection, exercise video was uploaded to either patient's or caregiver's smart phone to make it easy for the patient to follow.

2.6 Data Collection Methods

Data was collected by using demographic proforma; consisted of age, gender, marital status, and monthly income. Clinical proforma; consisted of location of cancer, stage of cancer, duration of illness and type of cancer treatment.

FACIT-F and FACT-G scales are standardized scales used to assess fatigue and quality of life respectively. License to use the tools were obtained by the FACIT organization. FACIT-F scale (Functional Assessment of Chronic Illness Therapy: Fatigue) [22] was used to measure the severity of fatigue level among the clients who report fatigue. Questions measure the respondents' fatigue state over the last 7 days. It has 13 items with two positive and 11 negative statements. Each of which is answered using a 5-point Likert scale ranging from 0 (Not at all) to 4 (Very much). Negative statements were scored in reverse order and scores were interpreted as higher the score lesser the fatigue. The FACT-G Version 4 was used to measure the quality of life of cancer patients [23]. It has 27 questions, each of which is answered using a 5-point likert scale ranging from 0 (Not at all) to 4 (Very much). Questions are phrased so that higher numbers indicate a better health state, leading to some items being reverse-scored. Questions measure the respondents' health state over the last 7 days in four subscales: Physical Well-Being (PWB, 7 questions), Social/Family Well-Being (SWB, 7 questions), Emotional Well-Being (EWB, 6 questions), and Functional Well-being (FWB, 7 questions). Scoring the FACT-G is performed through a simple sum of item scores. Each subscale is scored, and a total score for the FACT-G is obtained by adding each of the subscale scores.

Content validity of the sociodemographic proforma, clinical parameters and exercise video were done by giving it to two experts in the field of radiation oncology, one expert in the field of physiotherapy, and six experts in the field of nursing. The tools and interventions were translated into Kannada and retranslated back to English by the language experts. Reliability of the scales were done on 20 cancer patients who were undergoing treatment and yielded a 'r' value 0.763 and 0.965 for FACIT-F scale and FACT-G scale respectively. Reliability was calculated using Cronbach's alpha.

On Day 1 morning; The FACIT-F and FACT-G scales were administered along with the demographic and clinical proformas during the pretest. (Socio demographic proforma, FACIT-F and FACT-G scale were rated by the participants and Clinical proforma was filled by the investigator from the patient record.) This was

finished in 10 to 15 minutes on an average. An exercise programme was offered following the pretest. Five basic exercises, including those for the ankle, knee flexion/extension, static quadriceps, abduction/adduction, and deep breathing, were taught (15-20 minutes).

On day 2; The rest of the five exercises were taught: sit-to-stand, inner range quadriceps (sitting on a chair), inner range quadriceps (lying on a bed), and straight leg exercises. In addition to the basic exercises, the patient was instructed to repeat each exercise five times twice a day until the third day.
On day 3*;* patient demonstrated the exercise. Exercise video was uploaded to either patient's or caregiver's smart phone to make it easy for the patient to perform the exercise at home.

From the fourth day onwards, all 10 exercises were done 10 times, twice daily for three months. The client was told to keep an exercise diary noting the date and time. Posttest, fatigue was evaluated three times (7^{th},21^{st} and 90^{th} day) and QOL was evaluated twice (21st and 90th day). Post tests were conducted during their scheduled revisits either in day care visit for chemotherapy, or in the ward when admitted for chemotherapy or radiation therapy or in outpatient department during scheduled follow up visit. No subjects were lost to follow-up due to death or withdrawal from the research.

3. RESULTS

The Statistical Package for Social Sciences SPSS-24 programme was used to analyze the data.

3.1 Sample Characteristics

Table 1 depicts majority (60%) of the respondents were had >50 years of age. Maximum percentage of the sample (76.7%) were females and rest of them were males and equal percentage of respondents (40%) were in the income group of Rs15001-20000 and >20000Rs.

Table 2 reveals the clinical characteristics of the respondents. Maximum percentage (33.3%) of the respondents had breast cancer and least percentage (10%) had neck cancer. Majority (60%) of the patients with cancer were in stage III, majority (56.7%) had illness for >3 months of duration. Maximum (40%) of the respondent underwent surgery and on chemotherapy.

3.2 Effect of Exercise Program on CRF and QOL Scores of Cancer Patients

Table 3 shows the mean and standard deviation of the CRF score at post -test 3 (29.00±5.614) which was higher than the pre-test mean and standard deviation (26.27±5.825). Scores are interpreted as higher the score lower the fatigue level.

Table 3 also shows the mean pretest fatigue score of the cancer patients (pre-test mean= 26.27) was lower than their mean post-test fatigue scores (post- test1 =25.87, post -test 2 = 27.40 and post- test 3=29.00). In the repeated measures ANOVA, *P*-value was less than .05, (*P*=.00) and hence there was a significant difference between the fatigue scores before and after the exercise program.

Table 4 shows the mean and standard deviation of the overall QOL score at post -test 2 (48.60±7.152) which was higher than the pre-test mean and standard deviation (45.23±8.029). Scores are interpreted as higher the score higher the QOL. Table 4 also shows; in the repeated measures ANOVA, *P*-value is less than .05, and hence there was a significant difference between the QOL scores before and after the exercise programme.

3.3 Relationship between Fatigue and Quality of Life of Cancer Patients

Table 5 depicts that there is a significant relationship between fatigue and quality of life as the *P* value is less than .05.

4. DISCUSSION

In contemporary oncologic therapy, supportive care currently places a strong emphasis on CRF identification and treatment. The American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) both recommend screening for CRF at the initial visit, after primary therapy is finished, as clinically indicated (and at least annually) throughout the cancer survivor period, at the time that advanced disease is diagnosed, and at all chemotherapy visits. Patients who have completed primary therapy and are getting posttreatment monitoring should continue to be examined since fatigue may persist after the completion of active treatment [24]. As the number of cancer survivors continues to rise, clinicians are coping with an increasing number

of patients who experience cancer-related fatigue (CRF). Between the patient and the practitioner, there may be a number of potential barriers that could prevent this symptom from being noticed in a cancer survivor. Patients must be checked for fatigue because it greatly affects their day-to-day functioning. The causes of CRF are several. As a result, when trying to treat CRF, the clinician can run across a significant barrier [25]. How fatigue is handled depends on the signs and whether the cause is understood. When the reason of fatigue is unknown, treatment for it is often given to reduce symptoms and teach coping techniques [26].

Table 1. Distribution of patients based on the demographic characteristics

Demographic characteristics		f	%
Age	a) ≤50	12	40.0%
	b) > 50	18	60.0%
Gender	a) Male	7	23.3%
	b) Female	23	76.7%
Marital Status	a) Married	25	83.3%
	b) Unmarried	-	--
	c)Divorced/Separated	2	6.7%
	d)Widow/Widower	3	10.0%
Income/	a) <10000	-	-
Month	b) 10000-15000	6	20.0%
in Rupees	c) 15001-20000	12	40.0%
	d) >20000	12	40.0%

Table 2. Distribution of patients based on clinical characteristics

Clinical characteristics		
Location of cancer	**F**	**%**
a) Breast cancer	10	33.3
b) Gynecological cancer	8	26.7
c) Head	9	30.0
d) Neck	3	10.0
Stage of Cancer		
a) Stage I	0	0.0
b) Stage II	10	33.3
c) Stage III	18	60.0
d) Stage IV	2	6.7
Duration of illness		
a) 1-3 months	13	43.3
b) >3months	17	56.7
Type of cancer treatment currently receiving		
a) Chemotherapy	7	23.3%
b) Radiation	1	3.3%
c) Surgery	-	-
d) Both a) & c)	10	33.3%
e) Both b) & c)	12	40.0%

Table 3. Effect of exercise on CRF among cancer patients by using repeated measures analysis of variance (ANOVA)

Pre/Post tests	Mean fatigue scores	Std. Deviation	F Value	*P* Value
Pre	26.27	5.825		
Post 1	25.87	5.643		
Post 2	27.40	4.854	9.200	.00*
Post 3	29.00	5.614		

**Significant (P < .05)*

Table 4. Effect of exercise on QOL of cancer patients by using repeated measures analysis of variance (ANOVA)

Areas of QOL	Pre/Post Tests	Mean QOL scores	Std. Deviation	F	*P*
Physical wellbeing	Pre	13.00	3.414	85.138	.00*
	Post 1	13.00	2.924		
	Post 2	15.67	2.758		
Social wellbeing	Pre	13.67	2.339		
	Post 1	13.57	2.269	0.592	.44*
	Post 2	13.57	2.402		
Emotional wellbeing	Pre	12.80	2.058		
	Post 1	12.53	2.161	1.613	.21*
	Post 2	13.03	2.141		
Functional Wellbeing	Pre	5.77	2.315		
	Post 1	5.70	2.395	2.509	.12*
	Post 2	6.33	2.928		
Over all QOL	Pre	45.23	8.029		
	Post 1	44.80	7.467	53.895	
	Post 2	48.60	7.152		.00*

**Significant (P < .05)*

Table 5. Showing the relationship between fatigue and quality of life of cancer clients

Areas of QOL	Pearson Correlation	*P*
Physical welbeing-Pre	0.825**	.00
Social welbeing-Pre	0.670**	.00
Emotional welbeing-Pre	0.640**	.00
Functional Welbeing-Pre	0.637**	.00
Over all QOL-Pre	0.894**	.00

***Significant (P< .05)*

According to the Brief Fatigue Inventory (BFI) scale, 83.3% of the patients in cross-sectional research in Punjab reported feeling fatigued [27]. Another observational study done in Japan had a mean global fatigue score of 4.1 and divided the patients' fatigue severity into four categories: none (score 0), mild (score 1-3), moderate (score 4-6), and severe (7-10)[28]. In the current study mean pretest score was 26.27 (maximum possible score was 52 and interpreted as higher the score lesser the fatigue).

CRF is a common and debilitating disorder which affects patients' quality of life [29]. Because of the severe nature of the treatment, the quality of life continues to diminish following the cancer diagnosis [30]. The complex interplay between these variables and the patients' degrees of emotional distress, as well as their physical, mental, and functional well-being, have an effect on their quality of life [29]. A prospective study held with 40 patients with nasopharyngeal cancer aimed to evaluate the fatigue levels during radiation therapy and the possible causes of the symptom. As a result, the study identified that 60% of patients had acute fatigue during treatment, which persisted after its term. The research associated as possible causes for fatigue induced by radiation the toxicity caused by the treatment, as the increased production of pro-inflammatory cytokines [31]. A cross sectional, descriptive and hospital-based study conducted for the duration of 6 months, in Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India, among 84 breast cancer patients with mean age 43.32±10.2 in which data were collected by interview using validated questionnaire, noted that 20.2% had average QOL, 51.2% had below average and 28.6% had significantly poor QOL [32].

Similarly in the current study mean overall QOL was 45.23 (maximum possible score was 108 and interpreted as higher the score higher the

QOL). It indicates that cancer patients experience fatigue during and followed by treatment and it declines the QOL of patients which needs preventive strategies to overcome.

Many studies have attempted various nonpharmacological approaches for treating cancer-related fatigue as a single therapy or combination of therapies. Few investigators have conducted a trial among the patients receiving single type of treatment either chemotherapy or radiation therapy and few have conducted with patients receiving combination of therapies. In this study intervention included an exercise program and patients receiving chemotherapy, radiation and surgery were included.

A study conducted to evaluate the effects of aerobic exercise on cancer-related fatigue in patients of the solid tumor after chemotherapy and radiotherapy in Gujarat among 34 patients between ages 35 and 70 years, the intervention group received aerobic exercise program which included treadmill walking with low to moderate intensity (50%–70% of maximum heart rate), for 20–40 min/day for 5 days/week, control group were taught stretching exercises of hamstrings, gastrocnemius, and soleus (to be done at home) and were encouraged to remain active, study showed a significant reduction in cancer-related fatigue and significant improvement in the physical performance and quality of life [33].

A randomized controlled trial (RCT) done in South India to determine the effectiveness of pranayama on CRF among breast cancer patients receiving radiation therapy which has enrolled the patients who were having locally advanced breast cancer and who underwent modified radical mastectomy or breast conserving surgery, followed by eight cycles of chemotherapy, have reported the reduction in CRF experienced by the women who practiced pranayama than the women who had undergone radiation therapy alone [34].

As mentioned in above studies, interventions were provided during the cancer treatment [34] as well as continued after the treatment also. [33] In this study intervention was provided during the treatment and followed up even after the completion of the treatment. This study findings were in consistent with above study findings that there was a reduction in the level of fatigue after the intervention. Study finding is also consistent with the study mentioned above [33] that there was improvement in quality of life after 21 days and 3 months of intervention. Participants reported continued maintenance of QOL at 3months. Current study findings also indicate that even a simple exercise with low intensity is sufficient to reduce the CRF.

The improvement in understanding of the impacts of cancer and its treatment-related side effects on patients' overall QoL is emphasized by the rise in survival time. To effectively manage CRF and lessen its detrimental effect on quality of life, its complex etiology, which can be related to both the disease itself and its treatment as well as to a wide range of physical and psychological comorbidities, must be better understood. An observational study carried out among 30 breast cancer patients who were receiving third cycle of chemotherapy from the cancer hospital, Ahmedabad in which Facet fatigue questionnaire, FACT B questionnaire and 6-minute walk test (6MWT) was used for the assessment purpose of fatigue, QOL and functional capacity, respectively. The Spearman’s correlation confirmed that the fatigue is having strong association with quality of life and moderate effect with functional capacity in these patients. [35]The current study findings also reveals significant correlation between CRF and QOL of the cancer patients. This indicates the need for proper rehabilitation to maintain the optimum level of quality of life in these patients.

5. CONCLUSION

Regardless of mechanism of occurrence of fatigue, most patients living with cancer suffer with persistent cancer-related fatigue. Yet it is often not assessed, has limited treatment options, there is a need to assess the state of fatigue in cancer patients. They do need intervention to reduce the fatigue and to improve quality of life. Nonpharmacological therapies could be used to manage the fatigue among cancer patients without any safety issue could be practiced at patient’s own setting and exercise may be utilized as an adjunct in the management of cancer patients to alleviate the CRF and to maintain the QOL.

6. LIMITATIONS

This study has been conducted among different types of cancer patients and without control group. Hence magnitude of effect of exercise alone may not be measurable and also the effect of time may also influence the severity of fatigue.

Hence findings of the study may not be generalizable.

ETHICAL APPROVAL AND CONSENT

Institutional Ethics Committee approval was received (AJEC/REV/292/2019). The hospital's concerned administrators and the oncology department head (HOD) gave their prior written consent. Participants in the study were given their informed permission after being informed of its objectives.

ACKNOWLEDGEMENTS

The authors sincerely acknowledge the patients for their participation in the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/96064