COMPARISON OF QUALITY OF LIFE (QoL) FOR PATIENTS WITH BREAST CANCER RECEIVING ADJUVANT TAC (DOCETAXEL, DOXORUBICIN, CYCLOPHOSPHAMIDE) AND FAC (5-FLUOROURACIL, DOXORUBICIN, CYCLOPHOSPHAMIDE) THERAPY

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ABSTRACT

An important issue in oncology is to evaluate Quality Of Life in breast cancer patients.Due to the lack of a comprehensive reference protocol for the use of adjuvant therapy, various therapeutic regimens have been implemented in the treatment of breast cancer. Thus, this study sought to evaluate the quality of life (QoL) of Breast Cancer patients during chemotherapy. The prospective observational questionnaire based study was conducted in Dept. of Oncology Govt. Medical College; Calicut over a period of 7 months. The quality of life of the patients was analyzed on the basis of European Organisation for Research and Treatment of Cancer QLQ C30 & BR23 questionnaire by using Independent sample T test.The questionnaire comprised of a total of 30 questions with three different scales (functioning scales, symptoms scales and a global health status scale). It measures physical, role, cognitive, emotional and social function in the functioning scale. The symptoms scale includes fatigue, pain, nausea/vomiting, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties. All scales are comprised of multi-item questions except the symptom scales of dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties, which are comprised of single-item questions. Higher functional score indicates better QoL and higher symptom score indicates poor QoL. Total 9 domains were significant for TAC and FAC regimen in 2 questionnaires.The use of FAC as an adjuvant therapy in most aspects was accompanied by better Quality of life than TAC.

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INTRODUCTION

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Breast cancer is a cancer that develops from breast tissue. World statistics on breast cancer shows that about one million women and several thousand men are diagnosed with breast cancer in every year and approximately 60,000 die from it[1]. An increasingly important measure is the quality of life (QoL) in cancer patients as the cancer-specific QoL is related to all stages of the disease. In fact, for all types of cancer patients general QoL instruments can be used to assess the overall impact, however cancer specific instruments assess the impact of a specific cancer on QoL[2]. Due to the lack of a comprehensive reference protocol for the use of adjuvant therapyvarious therapeutic regimens have been implemented in the treatment of breast cancer[3].Most recent methods are the utilization of TAC regimen containing docetaxel, doxorubicin and cyclophosphamide. Another worldwide accepted chemotherapy protocol is FAC which is a combination of doxorubicin, cyclophosphamide and 5-fluorouracil. Using TAC regimen is associated with a higher rate of disease-free periods and an in general survival rate at 5 years. These are significant when compared with other anthracycline-based regimens such as FAC. This is in spite of the fact that TAC has been recognized as having a significantly greater toxicity than FAC. Today, in comparison to FAC, TAC is widely used as an adjuvant therapy. In this study, toxicity and side effects of TAC compared with FAC have been investigated. Each type of combination chemotherapies affects different domains and aspects of health-related quality of life (HRQoL)that can be due to therapy side effects and other mental, social economical factors[2,4]. Previous studies focused on QoL of patients on treatment with TAC and FAC regimens. In some studies it is explained that none of the socio-demographic variables were significantly related to HRQoL: Although patients in TAC groups had lower level of HRQoL over 8 months follow up, they experienced faster improvement than the FAC group[5].The HRQoL of patients treated with TAC is worse than that of those treated with FAC but improves with the addition of Pegfilgrastim, particularly in the final part of chemotherapy treatment[6].Another study explains that in spite of increase in disease-free patients who received TAC regimen and increase their survival rate, there is significant toxicity and decrease in QoL in TAC protocol compare to FAC protocol[7]. Thus, this study sought to evaluate the quality of life of Breast Cancer patients during chemotherapy, seeking support for a more comprehensive and human care. This study is relevant when the increased incidence of cancer in India and how this disease affects the daily lives of patients.

MATERIALS AND METHODS

A prospective observational study was conducted in 108 patients during 7 months period (February 2016-august 2016) in the department of oncology, Government Medical College, Kozhikode located in Kerala. The study was approved by the Institutional Ethics Committee Reference No GMCKKD/RP 2016/IEC/38. The patients with breast cancer upon treatment with TAC or FAC and aged in between 20 and 60 years were included for the study. The exclusion criteria includes age less than 20, pregnant and lactating women, and patients with any of the following ailments serious infections, end stage disease, blind, psychiatric conditions and Alzheimer's disease. Health-related quality of life was assessed using European organization and cancer treatment quality of life questionnaire EORTC QLQ C-30 and Breast cancer module EORTC QLQ BR 23.Patient's demographic details and social history were collected. A standard quality of life questionnaire (EORTC QLQ C30 and EORTC QLQ BR23 version 3) were used and scores are calculated.Questionnaire was completed by each patient prior to chemotherapy. QLQ C 30 is a cancer specific, self-administered questionnaire. It contains 30 questions (items), 24 of which aggregate in to 9 multi item scale and 6 single items, representing various aspects of QoL. These include 5 functional scales, 3 symptom scales and 1 global scale. Principles of scoring these scale is the same in all cases:-

1. Estimate the average of the items that contribute to the scale; this is the RAW SCORE.
2. Use a linear transformation to standardize the raw score, so that the score ranges from 0 to 100. A higher(better)
level of functioning or a higher (worse) level of symptoms.

STATISTICAL ANALYSIS

Quality of life between the two regimens was done by Independent T test. The level of significance was set at <0.05.

RESULTS

Based on inclusion and exclusion criteria 108 breast cancer patients were included in the study, of which 1 male and 107 were females. In this study population, 66 patients (61.1%) were treated with FAC regimen and 42 patients were treated with TAC regimen (38.9%)

Table 1
Patient Characteristics

SL No	Socio-demographicvariables		Number of patients	Percentage
1	Age	21-30	3	2.8
		31-40	17	15.7
		41-50	29	26.9
		51-60	34	31.5
		61-70	21	19.4
		71-80	3	2.8
		>81	1	0.9
2	Sex	Male	1	0.9
		Female	107	99.1
3	BMI	Under weight	4	3.7
		Normal	78	72.2
		Over weight	18	16.7
		Obesity	8	7.4
4	Menstruation cycle	Nil	1	0.9
		Normal	101	93.5
		Abnormal	6	5.6
5	Educational qualification	Iliterate	12	11.1
		School level	78	72.2
		Graduation	15	13.9
		Post graduation	3	2.8
6	Diet	vegetarian	3	2.8
		Strictly non vegetarian	1	0.9
		Mixed diet	104	96.3
7	Marital status	Married	103	95.4
		Unmarried	5	4.6

According to Age, total populations were divided into seven groups. Out of this, maximum numbers of patients were found to be under the age group of 51-60 (31.5%). Based on BMI, Study populations were classified into four groups. Among this, majority of the patients (72.2%) belong to the normal category. Most of the patients show normal menstruation cycle (93.5%), and very few patients with 'abnormal menstruation cycle'. Based on use of contraception in past, Study populations were classified into two groups. Among this, majority of the patients (83%) have not used contraception in past, only 17% population used contraception in past. Out of 108patients, 95.4% were married and 4.6% were unmarried and no patients were under the category of diverse.According to age of marriage, Total populations were divided into six groups. Out of this, maximum number of patients were found to be under the age group of 16-20 (45.4%) and (29.6%) in 21-25. Based on diet, study populations were classified into three groups. Among this, majority of the patients (96%) belong to the group of mixed diet.In this study population, most of the patients don't have any significant co-morbidities.In the study population, 69.4% of patients did not undergone any surgery, 14.8% of patients undergone hysterectomy (16) and 15.7% of patients undergone other types of minor surgeries.

Quality Of Life: EORTC QLQ C30

The quality of life analysis was conducted on 108 patients and evaluated by using the EORTC QLQ C30 and QLQ BR 23 version 3 questionnaires. The questionnaire was filled up by interviewing the patient, or by patient itself. The QLQ-C30 is composed of both multi-item scales and single-item measures. These include five functional scales, three symptom scales, a global health status / QoL scale, and six single items. Each of the multi-item scales includes a different set of items - no item occurs in more than one scale.

Table 2
Functional Scale

| Scale Name	Variables	Regimen	Frequency (N)	Mean	Std. Deviation	P Value
Functional Scale	Physical Functioning	FAC	66	35.03	16.211	0.724
		TAC	42	33.98	13.304	
	Role Functioning	FAC	66	43.23	17.917	0.007
		TAC	42	33.50	18.014	
	Emotional Functioning 1	FAC	66	28.712	8.8956	0.000
		TAC	42	44.000	18.4985	
	Cognitive Functioning 1	FAC	66	49.02	22.729	0.147
		TAC	42	41.57	30.046	
	Social Functioning	FAC	66	41.52	28.982	0.000
		TAC	42	21.00	14.528	
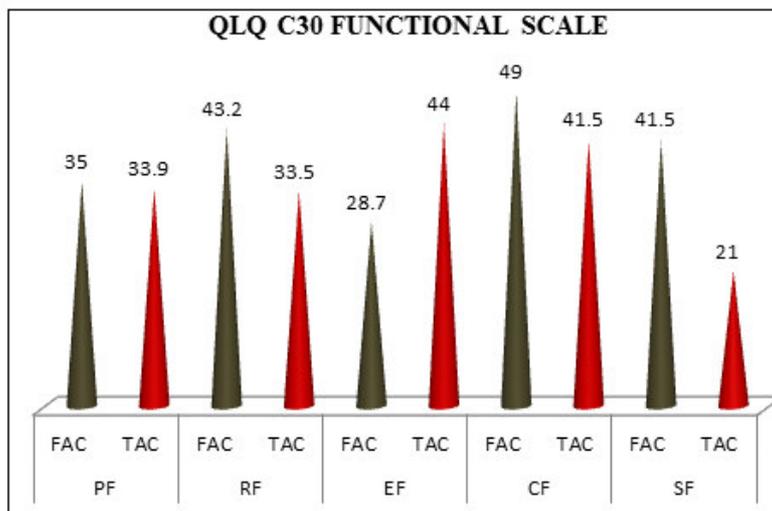
Figure 1
QLQ C30 FUNCTIONAL SCALE

The functional status were categorized into five domains namely physical functioning, Role functioning, Emotional functioning, Cognitive functioning and Social functioning. In this 3 functional scales are significant for both chemotherapy regimens includes Role functioning, Emotional functioning and social functioning. Role functioning (43.23) and Social functioning (41.52) are more significant for FAC patients compared to TAC patients. But Emotional functioning (44) is highly significant for TAC patients.
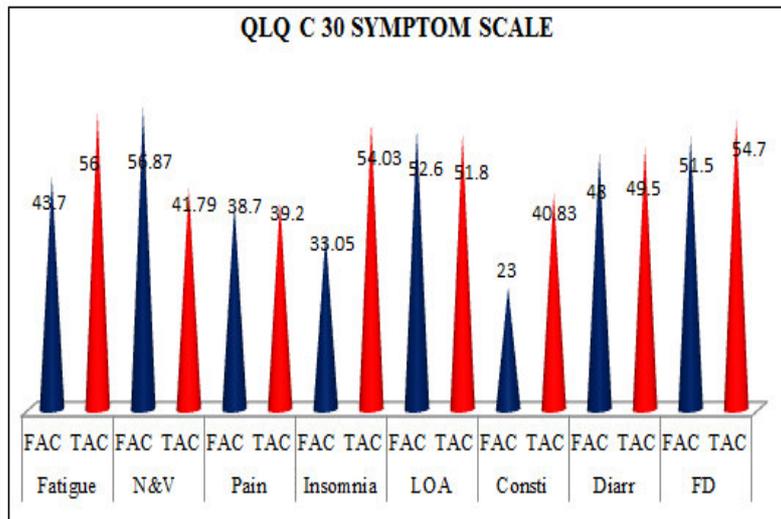
Symptom Scale
Mean score of various symptom scales such as fatigue, nausea and vomiting, Pain, Dyspnoea, insomnia, loss of appetite, Constipation, diarrhoea and financial difficulty were shown in Table 3

Table 3
various symptom scales

| Scale Name	Domain		Regimen	Frequency (N)	Mean	Std. Deviation	P Value
Symptom Scale	Fatigue		FAC	66	43.70	26.238	0.015
			TAC	42	56.07	24.194	
	Nausea And Vomiting		FAC	66	56.87	41.089	0.039
			TAC	42	41.79	27.766	
	Pain		FAC	66	38.70	21.640	0.149
			TAC	42	36..48	30.554	
	Insomnia		FAC	66	33.05	25.206	0.000
			TAC	42	54.36	28.294	
	Dyspnoea	n	FAC	66	46.61	28.577	0.876
		1	TAC	42	51.81	20.766	
	Constipation		FAC	66	23.00	15.282	0.000
			TAC	42	40.86	19.019	
	Loss Of Appetite	n	FAC	66	48.00	21.799	0.717
		1	TAC	42	49.57	22.008	
	Diarrhoea	1	FAC	66	51.16	28.720	0.495
			TAC	42	54.74	22.461	
	Financial Difficulty		FAC	66	52.70	22.242	0.734
			TAC	42	54.33	27.22	

QLQ C 30 SYMPTOM SCALE

Higher symptom score indicates poor quality of life. Here, higher symptom score was seen in TAC for fatigue (56.07), Insomnia (51.81), Constipation (49.57).So QoL will be poor. But in Nausea & Vomiting higher symptom score is for FAC (56.87)

Figure 2
QLQ C 30 SYMPTOM SCALE

Table 4
Global Health Status

SCALE NAME	DOMAIN	REGIMEN	FREQUENCY (N)	MEAN	STD. DEVIATION	P VALUE
QOL SCALE	GLOBAL HEALTH STATUS	FAC	66	52.7	22.242	0.734
		TAC	42	54.33	27.220	
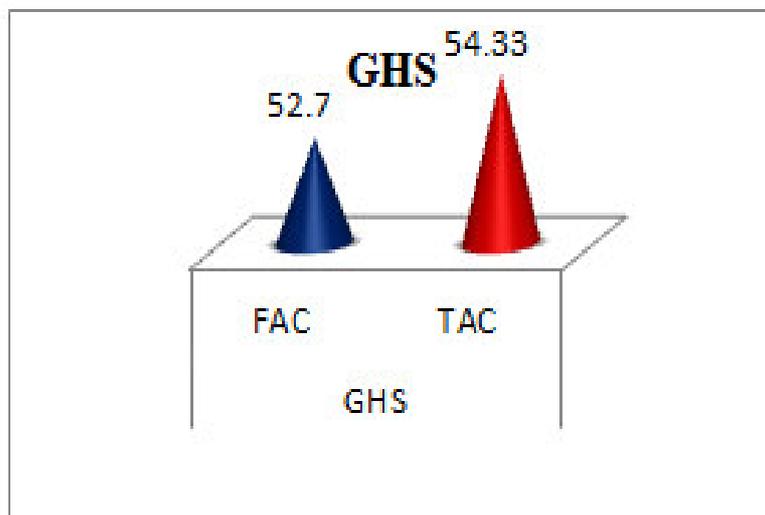
There is no significant difference between FAC and TAC regimen according to Global Health Status.

Figure 3
GHS

EORTC QLQ BR 23

The Breast cancer module is meant for use among breast cancer patients varying in disease stage and treatment modality (ie, surgery, Chemotherapy, Radiotherapy and hormonal treatment). It should be always complemented by the QLQ-C30. Twenty three question were evaluated which was specific for the breast cancer, includes functional scale and symptom scale.

Table 5
Functional and Symptom Scales

SACLE NAME	VARIABLE		REGIMEN	N	Mean	Std. Deviation	P Value
FUNCT-IONAL SCALES	BODY IMAGE	n1	FAC	66	26.40	9.891	0.007
			TAC	42	34.45	20.424	
	SEXUAL FUNCTIOING		FAC	66	8.00	21.706	0.910
			TAC	42	8.48	20.606	
	SEXUAL ENJOYMET		FAC	66	4.00	13.594	0.114
			TAC	42	8.64	16.394	
	FUTURE PERSPECTIVE	n1	FAC	66	58.36	22.463	0.000
			TAC	42	35.86	28.670	
SYMPTOM SCALES	SYSTEMIC THERAPY SIDE EFFECTS		FAC	66	35.86	21.477	0.810
			TAC	42	36.83	18.535	
	BREAST SYMPTOM	o	FAC	66	7.88	10.941	0.119
			TAC	42	4.62	9.748	
	ARM SYMPTOM		FAC	66	4.00	12.746	0.095
			TAC	42	8.17	12.163	
	UPSET BY HAIRLOSS	1	FAC	66	33.91	42.661	0.246
			TAC	42	43.21	36.447	

Functional Status

The functional scale were categorized into four domains namely Body image, Sexual functioning, Sexual enjoyment, Future perspective. Among 4 domains assessed, only 2of them got significance (Body image, Future Perspective)
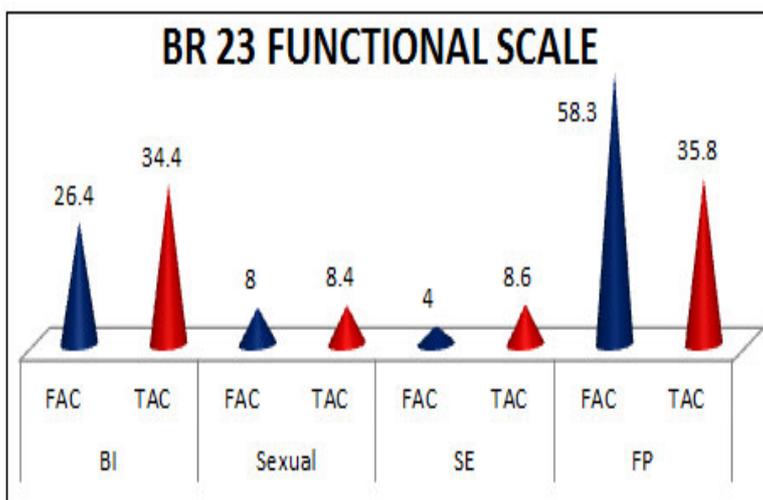
In the case of Body image TAC (34.4) regimen patients have good QoL than FAC (26.4) regimen patients.
But Future perspective is more for FAC (58.3) regimen patients

Figure 4
BR 23 Functional Scale
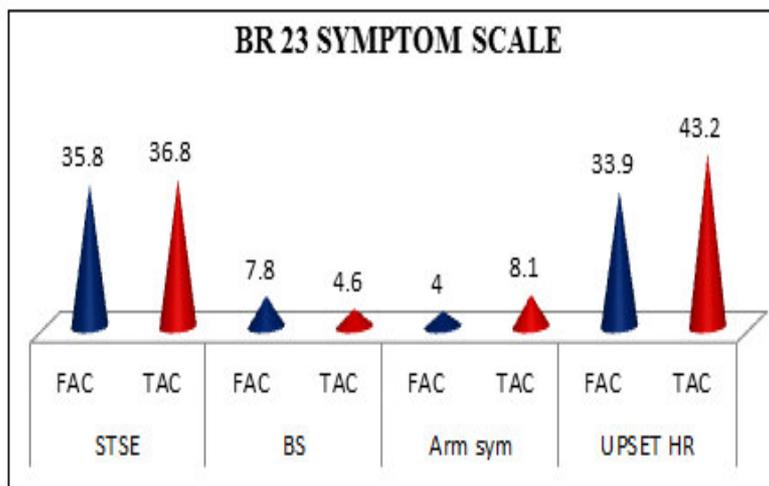
Symptom status

Figure 5
BR 23 Symptom Scale

In symptom scale there is no significance for 4 domains between FAC and TAC regimen for breast cancer. By considering mean value 3of 4 domains have higher mean value for TAC [Systemic therapy side effects (36.8), Arm symptoms (8.1), Upset by Hair loss (43.2)] and for Breast symptom FAC (7.8) have high mean.

Higher symptom score indicates poor quality of life. So from this FAC regimen have better QoL than TAC.

Comparison of QoLwith Demographic Variables
By comparing all demographic variables with QoL, only 3 of them were significant.*BMI, UOC in past and special surgeries*

Table 6
QOL and BMI

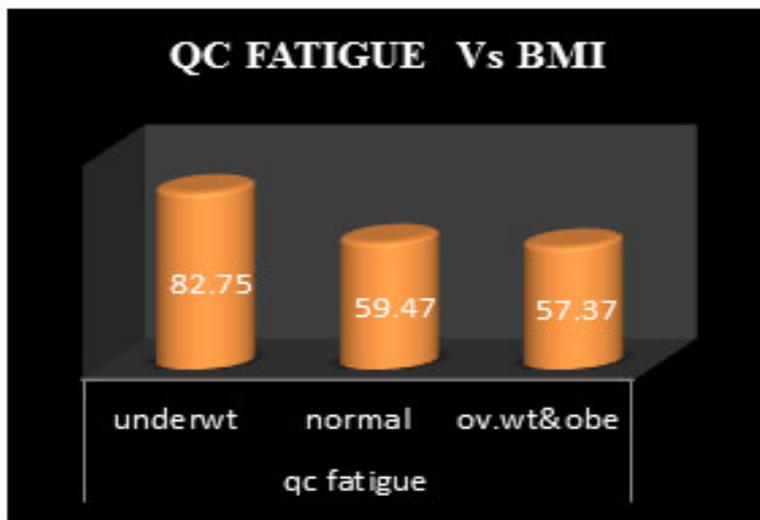| QoLvariable	BMI	frequency	Mean	P value
Qc fatigue	Under wt	4	82.75	
	Normal	78	59.47	
	Over wt& obesity	26	57.37	0.019

Figure 6
QC FATIGUE Vs BMI

BMI is significant with the Qc fatigue variable of QLQ C 30. Since it is a symptom scale, QOL will be better with less mean. From this we can conclude that Underweight, Overweight & obese patients have poor QOL as compared with normal BMI patient.

Table 7
QoL and Use of Contraceptives in past life

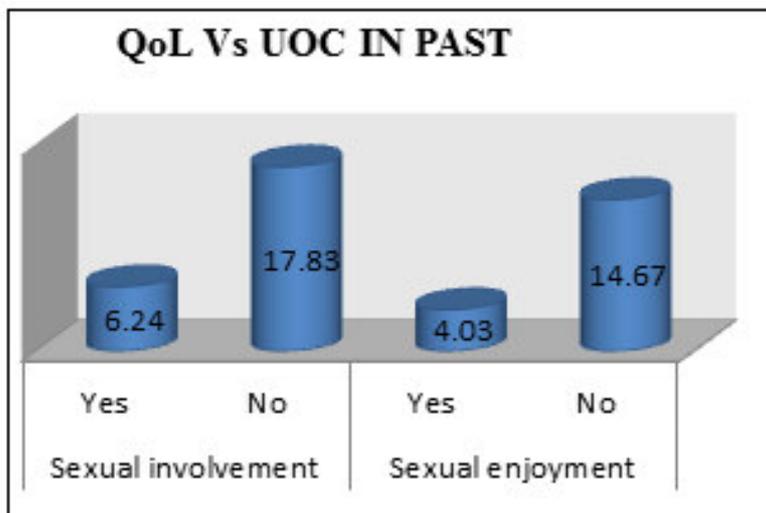| QoL variable	UOC in past	frequency	Mean	P value
Sexual Functioning	Yes	18	6.24	
	No	90	17.83	0.033
Sexual enjoyment	Yes	18	4.03	0.005
	No	90	14.67	

Figure 7
QoL Vs UOC IN PAST

In order for Sexual functioning (BRSEF) and Sexual enjoyment (BRSEE) to be interpreted as functional scales (i.e. higher score is better), they should be scored according to the symptom scale algorithm. So use of contraceptives in past patients has poor QoL as compared to category B.

Table 8
QoL and special surgeries

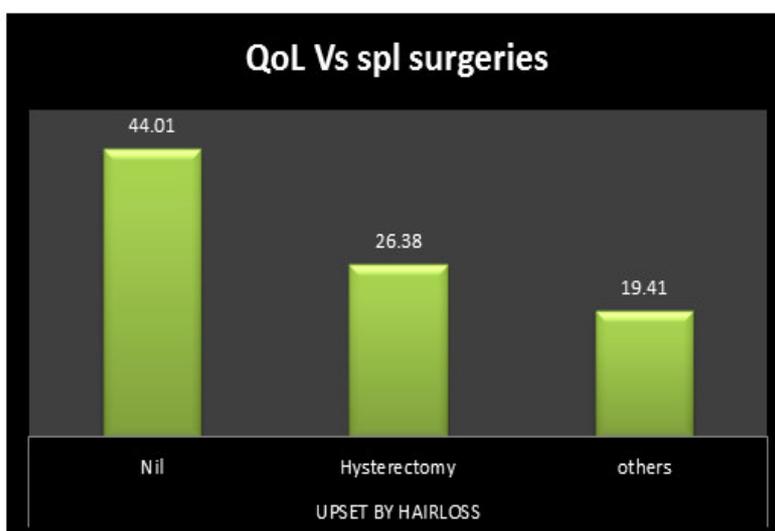| QoL variable	Special surgery	frequency	Mean	P value
Upset by hairloss	Nil	75	44.01	
	Hysterectomy	16	26.38	
	Others	17	19.41	0.036

Figure 8
QoL Vs spl surgeries

The patients who do not undergo any surgeries have high mean value for BRHL QoL. Since it is a symptom scale high mean value denote poor QoL. , i.e. the patients who had undergone any type of surgery in their life feel that hair loss is not a solid reason for upset.

DISCUSSION

Among 108 patients, 107 patients (99.1%) were female and 1 patient (0.9%) is male.Breast cancer is the most common malignancy amongst women in both developed and developing countries[8].Lal p *et al*[9] point out that, in females, breast cancer accounts for about 22% which is more than twice the prevalence of cancer at any other site. High incidence of Breast cancer and ADR were observed in patients under the age group of 51-60. (Range 40-70) i.e., elderly patients encountered majority of the ADRs. Similar results of incidence in elderly groups were seen in studies carried out by Amartya *et al*[10], Anju Prasad *et al*[11], Guyatt *et al*[12] and Ali Dehkordi *et al*.[8] These results were analogous to the study conducted by Thalyta Cristina Mansano-Schlosser *et al*.

[9] According to BMI, 72.2% patients are under normal category followed by overweight 16.7%.The present study shows majority of patients have their body surface area 1.6m^2. (47%), followed by 1.7m^2 (28%). G. Berclaz*et al*[13] and Isabella Romieu I[14]explains that BMI is a dependent prognostic factor for overall survival in patients with breast cancer. In this study 95.45% patients were married and only 4.6% were unmarried. From this result it was found that, our observation was similar to the study conducted by MinoriYokoo*et al*[15]. Almost 96.3% patients consuming mixed diet includes both vegetarian and non vegetarian foods. It is similar to the study of Isabella Romieu I[14]. In the study population, 69.4% of patients did not undergone any surgery, 14.8% of patients undergone hysterectomy and 15.7% of patients undergone other types of minor surgeries. From the study of Ritta Luoto*et al*[16] it is explained that hysterectomy is not associated with any substantial protective or promoting effect on cancers in general, which is comparable with this study, that hysterectomy is not associated with breast cancer. This study observed in great detail, the patient's QoL in two chemotherapy regimens: TAC and FAC. The results show that, the use of TAC as an adjuvant therapy in most aspects was accompanied by more side effects. These TAC patients had a higher range of side effects which includedamenorrhea, anemia, febrile neutropenia, hyper pigmentation and nail disorder, neurologic toxicity, edema, fatigue, pain, insomnia and diarrhoea. These effects may be attributed to the lower mean score regarding QoL in TAC arm during chemotherapy cycles.This was the same as Martin M *et al*[7] on node-positive breast cancer that indicated every type of chemotherapy decreases the domain of HRQoL during the chemotherapy cycle but this fact in TAC regimen was more because of more severe and common side effects in this protocol. Furthermore, this result was reported in the study of Martin in 2005 in which the primary mean score of QoL in node-positive breast cancer with EORTC QLQ-C30 questionnaire in both groups was 72 out of 100. This result at the sixth session of chemotherapy became 62 in TAC compared with 69 in FAC (95% CI) but when the treatment continued after the first session of follow-up, the level of the scores returned to 76 for TAC and 75 for FAC that was even higher than the initial score before adjuvant therapy[17].In the study of Martin et al[7]carried out on 1,056 patients with node-negative, the above results of QoL were confirmed so that during the chemotherapy cycle the scores of QoL in TAC arm were lower than FAC (95%). But after finishing the chemotherapy cycle, there were no statistically significant differences between their QoL between two groups. BMI is significant with the fatigue variable of QoL. underweight, overweight and obese patients have poor QoL as compared with normal BMI patients from this study. This result is comparable with the study conducted by Berclaz*et al*[13].Use of contraceptives in past patients has poor QoL as compared to the patients not used. This result is comparable with the David J. Hunter *et al*[18].

CONCLUSION

Total 9 domains were significant for TAC and FAC regimen in EORTC QLQ C30 and EORTC QLQ BR23. Role functioning (43.23) and Social functioning (41.52) is significant for FAC. Emotional functioning (44) is highly significant for TAC patients. In symptom scale higher symptom score was seen in TAC for fatigue (56.07), Insomnia (51.81), Constipation (49.57). But in nausea and vomiting higher symptom score is for FAC (56.87). In EORTC QLQ BR 23 Future perspective is more for FAC (58.3). By considering 3 domains have higher mean value for TAC includes Systemic therapy side effects (36.8), Arm symptoms (8.1), Upset by Hair loss (43.2) and for Breast symptom FAC (7.8) have high mean. Higher symptom score indicates poor quality of life. The use of FAC as an adjuvant therapy in most aspects was accompanied by better Quality of life than TAC. This study was performed in a Government tertiary care hospital where majority of the patients were from rural areas and economically backward society. So this study could give only a partial reflection of the whole society.The score calculated for various parameters were based on the response obtained from the patient or caregivers, which may be subjected to many biases.The study would be more effective; if the study population was divided into control and intervention group. But due to ethical considerations, control group were not able to be implementedDespite the limitations, the present study represents an attempt to understand the complicated interaction of cancer patients undergoing chemotherapy and their response to QoL domains. This study is the first of its type which assessed in depth chemotherapy response in terms of improvement in QoL in an area where the breast cancer incidence is alarmingly high.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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