A Study of the Impact of Pharmaceutical Care on Quality of Life in Carcinoma Cervix Patients treated with Chemo Radiation

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Abstract:
Background: *Aside from clinical variables, the quality of life should be considered in the planning and monitoring of the therapeutic process in patients with cancer. Although it is widely known that this parameter can have a considerable impact on the therapeutic outcome, it is not routinely screened in oncological patients.*
Aim: *The aim of the present study is to evaluate the impact of pharmaceutical care on Quality of life in cervical cancer patients treated with either chemotherapy or radiotherapy.*
Methods: *An observational prospective study was conducted over a period of 6 months on 70 patients in the Department of Radiotherapy, GGH, Guntur. The EORTC QLQ-C30 3.0 version, EORTC QLQ CX24 was used to evaluate the patients' quality of life at three different stages i.e., before treatment, on admission, after treatment, at discharge, and one month after treatment. Cancer Therapy Satisfaction Questionnaire (CTSQ), Patient satisfaction form was assessed at one month after treatment. Patients were counseled about disease & therapy side effects management. Improvement in outcomes was evaluated using one way ANOVA, unpaired t test & Spearman's correlation in graph pad prism version (5.04).*
Results: *Median age of the patients in the study was 51 years (range, 31–71 years). 48(72.72%), 15(22.72%) patients were stage- II & III respectively. Compliance with completion of QOL scores was high. The mean score of global health of cervical cancer patients 1month after treatment was 85.66 ± 12.26, which was significantly higher than the before treatment score 45.88 ± 12.24(P value 0.0001). Function scales like physical function, role function, emotional function, social function and cognitive function, there was also significant improvement. Mean symptoms score 1month after treatment was 6.90 ±23.03 was declined compared to before treatment scores 31.93±23.5 (P value <0.0001). Patients experienced substantial decrease in sexual activity post treatment. The mean scores of the ET, FSE & SWT domain in CTSQ were 34.66 ±13.03, 55.47 ± 15.72 & 47.20 ± 13.24 respectively.*
Conclusion: *Patients of carcinoma cervix have a significant improvement in quality of life following treatment with radiotherapy and chemotherapy along with pharmaceutical care.*
Keywords: *chemoradiation, carcinoma cervix, , EORTC QLQ-C30, EORTC QLQ-CX 24, CTSQ.*

I.   Introduction

Definition of Pharmaceutical Care:

Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life.

These outcomes are
1. Curing a disease,
2. Elimination or reduction of a patients' symptomatology,
3. Arresting or slowing down a disease process, or
4. Preventing a disease or symptomatology.

Pharmaceutical care involves the process through which a pharmacist co-operates with a patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient. This, in turn, involves three major functions:
1. Identifying potential and actual drug-related problems,
2. Resolving actual drug-related problems, and
3. Preventing drug-related problems.

Cervical Cancer
        Cancer is a disease in which cells in the body grow out of control. Cancer is always named for the part of the body where it starts, even if it spreads to other body parts later. When cancer starts in the cervix, it is called *cervical cancer.*
The 2 main types of cells covering the cervix are
* squamous cells (on the exocervix) and
* Glandular cells (on the endocervix).
There are 2 main types of cervical cancer:
* squamous cell carcinoma and
* Adenocarcinoma.
cervical cancer results from genital infection with HPV, which is a virus causing carcinoma cervix in females.

Risk factors for being infected with HPV
* Unprotected sexual intercourse with multiple partners or sexual intercourse with a man who has multiple sex partners.
* Onset of sexual intercourse activity at an early age.
* Multiple pregnancies.
* Poor hygiene.
* Other sexually transmitted genital infections, e.g. *Chlamydia trachomatis* and herpes simplexvirus-2.

Diagnosis:
1. Clinical examination
2. The Pap smeartest
3. Colposcopy
4. Histopathological
5. Routine laboratory examination of blood
6. Medical imaging examinations

Prevention:
Cervical Cancer Screening:
        Screening for cervical cancer has been used to save lives for many years. Screening was first done using only the Pap test. For decades, this was the gold standard test for screening.

Screening Guidelines:

ACOG 2016 Cervical Cancer Screening Guidelines	
Age (years)	**Recommended Screening**
<21	No screening
21 to 29	Pap test every 3 years
30 to 65	Pap test + HPV co-testing every 5 years (preferred) *or* Pap test every 3 years
>65	No screening (if low cancer risk)

QUALITY OF LIFE:
        WHO defines QOL as individual perception of life, values, objectives, standards and interests in the frame work of culture. Cancer is one of the most important health concerns of today and evaluating QOL in cancer patients is an increasingly important issue.

EORTC QLQ-C30:
        The EORTC quality of life questionnaire (QLQ) is an integrated system for assessing the health related quality of life (QOL) of cancer patients participating in international clinical trials. The QLQ-C30 has been used in a wide range of cancer clinical trials.
        The QLQ-C30 incorporates five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status / QoL scale, and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnoea, loss of appetite, insomnia, constipation and diarrhea) and perceived financial impact of the disease. It has four-point scales for the first five Items. These are coded with the same response categories namely "Not at all", "A little", "Quite a bit" and "Very much."Each of the QLQ-C30 domains is scored on a 0–100 scale, with higher scores on the functional scales being indicative of better HRQoL, whereas higher scores on the symptom scales are reflective of worse symptoms [1]

EORTC QLQ-CX 24:

The cervical cancer module is meant for use among cervical cancer patients varying in disease stage and treatment modality (i.e. surgery, chemotherapy, radiotherapy, etc.). It should always be complemented by the QLQ-C30. EORTC QLQ-CX 24 consists of 24 questions (4-Likert scale) including three multi-item scales on symptom experience, body image, and sexual/vaginal functioning and six single-item scales covering statements on lymphedema, peripheral neuropathy, menopausal symptoms, sexual worry, sexual activity, and sexual enjoyment. Each of the QLQ-CX 24 domains is scored on a 0–100 scale, with higher scores on the functional scales being indicative of better HRQoL, whereas higher scores on the symptom scales are reflective of worse symptoms [2]

Cancer Treatment Satisfaction Questionnaire (CTSQ):

The CTSQ contains three domains covering 16 items. Expectations of therapy (ET; five items), feelings about side effects (FSE; four items) and satisfaction with therapy(SWT; seven items). Each item was scored on a scale from one to five with a value of one corresponding with the worst response and a value of five representing the best response. Four items are reverse-coded. Domain score was calculated by the formula: (mean of completed item scores -1) 25.This results in a domain score ranging from 0 to 100, with a higher score representing a better outcome on each domain.[3]

II. Objectives Of The Study
1. To find out the incidence of cervical cancer during the study period.
2. To find out the stages of cancer at which patient mostly get diagnosed.
3. To provide patient counseling to enhance their QOL.
4. To list out most common ADR's observed in cervical cancer patients.
5. To list out the adjuvant drugs used in them.
6. To observe the effectiveness of cisplatin.
7. To evaluate the impact of pharmaceutical care on Quality of life in cervical cancer patients treated with either chemotherapy or radiotherapy or chemoradiation.

III. Materials And Methods
Study Design: In our prospective observational study consist of 70 patients with Carcinoma Cervix with a mean age of 51 years, registered at GGH- Department of Radiotherapy, Guntur Medical College, Andhra Pradesh.

Inclusion Criteria:
• Patients diagnosed with cervical cancer.
• Cervical cancer patients of stages I – IV.
• Patients with or without co morbid conditions.

Exclusion Criteria:
• Pregnant & lactating women.
• Patients with psychiatric illness.
• Patients who are not willing to be consent.

Materials Used:
• Patient consent form
• Data collection form
• Leaflets
• EORTC QLQ C30 questionnaire 3.0 version
• EORTC QLQ CX24
• Cancer Therapy Satisfaction Questionnaire
• Patient satisfaction form
• Graph pad Prism version (5.04)

Study Procedure:

A prior permission was taken from the ethics committee to conduct the study. The whole study was conducted in various steps:

Step 1: Translation of the EORTC QLQ C30 questionnaire 3.0 version, EORTC QLQ CX24 Cancer Therapy Satisfaction Questionnaire, Patient satisfaction form into regional language (Telugu) & their validation by Telugu professionals.

Step 2: Designing & validation of patient information leaflets by medical experts.

Step 3: Selection of subjects based on inclusion and exclusion criteria and an informed consent was taken from the patient and their care giver. Patient demographic details were collected.

Step 4: In selected patients QOL was evaluated by using EORTC QOL-C30 3.0 version & EORTC QOL-CX24 at three different stages:

- Stage 1 - Before treatment, on admission,
- Stage 2 - After treatment, at discharge, and
- Stage 3 - One month after treatment.

Study participants are counseled about disease, life style modifications, diet, side effects occurred during chemotherapy & radiotherapy and its management, importance of adherence to treatment, psychological counseling. Counseled at every stage after assessing the questionnaires.

Step 5: Cancer Therapy Satisfaction Questionnaire, Patient satisfaction form was assessed at stage -3 i.e. one month after treatment.

Step 6: The data obtained was entered in advanced Microsoft excel spreadsheet & evaluated. One way ANOVA, unpaired t test & Spearman's correlation was used to find statistical significance. Statistical calculations were executed using graph pad prism version (5.04) and the level of statistical significance was set at $P < 0.05$.

Epidemiological Data:

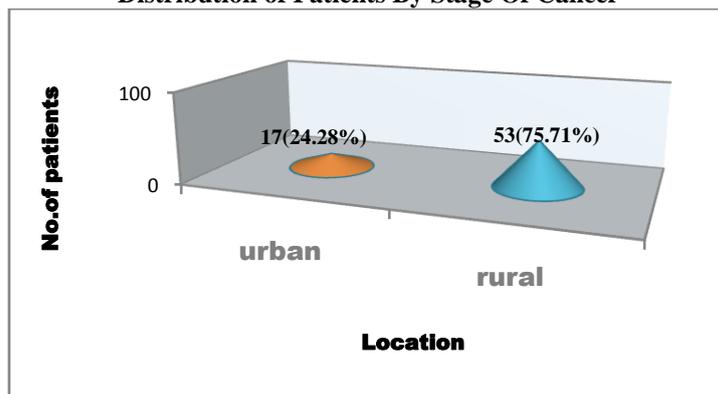| S.no	Stage	No.of Patients	Percentage
1.	I A	2	2.85
2.	II A	17	24.28
3.	II B	33	47.14
4.	IIIA	4	5.71
5.	III B	13	18.57
6.	IV	1	1.42

Area wise Distribution of Patients with Cancer

Area	Number	Percentage (%)
Rural	56	80
Urban	14	20

Age wise Distribution of Patients with Cervical Cancer

S.No	Age Group	Number of Patients	Percentage (%)
1.	31-40	11	15.71
2.	41-50	26	37.14
3.	51-60	24	34.28
4.	61-70	9	12.85

Distribution of Patients By Stage Of Cancer

Area wise Distribution of Patients with Cancer

S. No	location	No. of patients	Percentage (%)
1.	urban	17	24.28
2.	rural	53	75.71

Categorization of Patients Based On Occupational Status

Categorization of Patients Based On Histopathological Class Of Cervical Cancer

S. No	Occupational status	No. of patients	Percentage (%)
1.	Employee	8	11.42
2.	Self employed	11	15.71
3.	Daily wage	27	38.57
4.	Not working	24	34.28

S. No	Histopathological class	No. of patients	Percentage (%)
1.	Squamous cell carcinoma	64	91.42
2.	Adenocarcinoma	6	8.57

Categorization of Patients Based On Mode of Treatment

S.No	Mode of treatment	No.of patients
1.	Radiation+ ICR	12
2.	Concurrent + ICR	58

Mode of treatment

Categorization of patients based on recurrence of cancer

S. No	Recurrence	No. of patients
1.	yes	5
2.	no	65

IV.   Discussion and Results

A total of 70 eligible cervical cancer patients participated in the study. Out of these, majority of patients were in the age group of 41-50 years (n=26, 37.14%). Mean age was 52 years range (31–71 years). Among the eligible patients most of them are from rural areas (n=56, 80%) than from urban areas (n=14, 20%).The majority of cases were squamous cell carcinoma (n=64, 91.42%) followed by adenocarcinoma (n=6, 8.57%). According to International Federation of Gynecology and Obstetrics (FIGO) staging, majority of the patients got diagnosed at stage II B (n=33, 47.14%) and stage II A (n=17, 24.28%). very few patients got diagnosed at stage I (n=2, 2.85%). At stage IV (n=1, 1.42%) was also less. Many of the patients attained menopause (n=55, 83.33%). similar results are observed in other studies. [5] [7] [10] [11] [12] [13] [14] [15] [16]

Overall, 98.39% of patients completed externalbeam, and intracavitary therapy. Few patients (30%) received the planned four courses of weekly cisplatin. A few patients received Radiation + ICR (n= 12, 17.14%). Most common ADRs observed in chemoradiation patients were Nausea & vomiting with highest incidence (n=13, 54.1%). Radiation induced side effects are diarrhea (n=35, 53.03%), fatigue (n=56, 84.84%), nausea (n=12, 18.18%).

Drugs ondansetron (n=52 78.78 %), ranitidine (n=57, 86.36%), Magnesium sulphate (n=22, 33.33%), Potassium chloride (n=22, 33.33%), Mannitol 20% (n=24, 36.36%), Dexamethasone (n=30, 45.45%) are pre medications before administration of cisplatin to overcome side effects.

The EORTC QLQ-C30 questionnaire (v.3) was used to evaluate the patients' quality of life. The survey was conducted three times: (1) stage 1 - before treatment, on admission, (2) stage 2 - after treatment, at discharge, and (3) stage 3 - 1 month after treatment .*Physical functioning was assessed the worst before the radiation treatment(71.19 ±16.73) and increased gradually throughout* further stages (94.01±8.58) all inter stage differences proved to be significant(p <0.0001). In contrast, emotional functioning was scored the highest

after treatment (94.25±9.67) and was the lowest at initiation of treatment (61.27±17.26) a difference that proved to be significant (p <0.0001). Role functioning was highest immediately after the treatment (93.80±15.46) and the lowest prior to the treatment (69.80±16.26). Differences between stages proved to be significant (p <0.0001).

The overall global health status significantly improved from beginning 45.88 ± 12.24 to 85.66 ± 12.26 at follow up. This is possible by the cancer therapy along with the proper counseling at different stages (p value < 0.0001) [4] [6] [8] [9]

The EORTC QLQ CX-24 cervical cancer specific module was used to evaluate cervical cancer patients at different stages. The patient experienced enhanced body image from 77.26±23.38 at beginning to 97.21 ± 6.77 by stage-3, statistically significant (< 0.0001). The CTSQ was used in the study to assess patient's opinions and feelings concerning their cancer therapy and associated adverse events.

Representation of Overall Global Health Status QOL
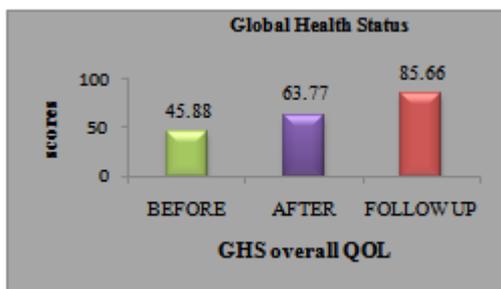
S.No.	Domains	Mean ± Standard Deviation			P Value
		Before Treatment	After Treatment	Follow Up	
1.	GHS	45.88 ± 12.24	63.77 ± 13.34	85.66 ± 12.26	< 0.0001

Functional Scale Domains in EORTC QLQ C-30

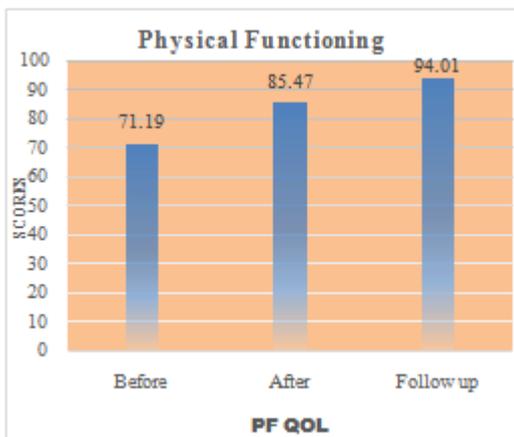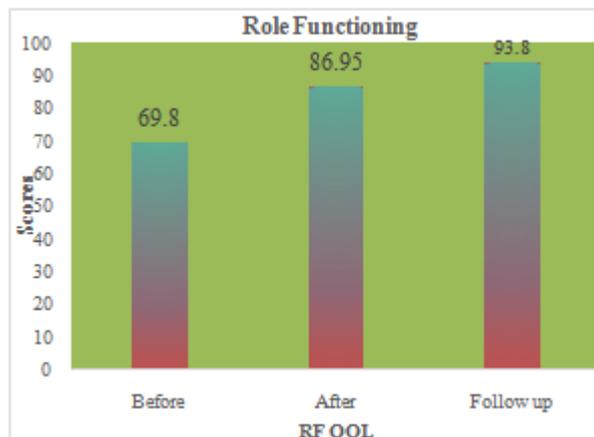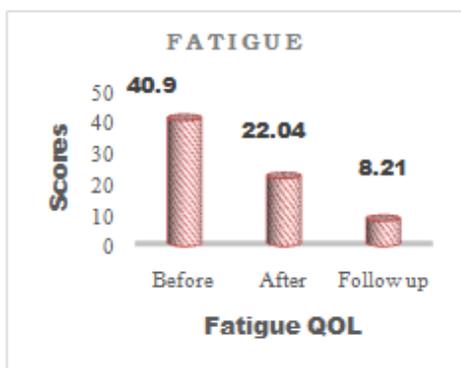| S.No.	Domains	Mean ± Standard Deviation			P Value
		Before Treatment	After Treatment	Follow Up	
1.	Physical Functioning	71.19 ±16.73	85.47±12.87	94.01±8.58	<0.0001
2.	Role Functioning	69.80±16.26	86.95±14.42	93.80±15.46	<0.0001
3.	Emotional Functioning	61.27±17.26	80.95±13.86	94.25±9.67	<0.0001
4.	Cognitive Functioning	75.15 ± 19.27	81.27±18.13	86.27±18.13	0.0030
5.	Social Functioning	65.47±24.9	81.34±19.7	90.37±19.85	<0.0001

Figure-32: Representation of PF QOL



Figure-33: Representation of RF QOL

Symptom Scale Domains in EORTC QLQ C-30

S.No.	Domains	Mean ± Standard Deviation			P Value
		Before Treatment	After Treatment	Follow Up	
1.	Fatigue	40.98±20.67	22.04±17.74	8.21±21.29	<0.0001
2.	Nausea & Vomiting	4.53±12.21	13.13±19.72	1.25±6.71	<0.0001
3.	Pain	34.62±22.2	21.49±25.27	7.65±22.4	<0.0001
4.	Dyspnea	15.87±30.49	14.36±31.49	11.86±28.33	0.7401
5.	Insomnia	33.26±30.36	26.29±28.34	11.30±25.01	<0.0001
6.	Appetite Loss	38.35±26.3	26.71±24.94	10.77±22.75	<0.0001
7.	Constipation	9.27±22.7	12.64±45.11	4.24±18.03	0.3181
8.	Diarrhea	1.50±6.96	20.68±21.66	2.01±7.98	<0.0001
9.	Financial	26.73±26.27	15.79±25.61	5.63±16.19	<0.0001

Representation of Fatigue QOL
EORTC CX-24– Quality Of Life

Functional Scales

S.No.	Domains	Mean ± Standard Deviation			P Value
		Before Treatment	After Treatment	1st Follow Up	
1.	Body image	77.26±23.38	89.93 ± 16.4	97.21 ± 6.77	<0.0001
2.	Sexual activity	67.03±24.97	60.00±20.88	65.63 ± 36.49	<0.0001
3.	Sexual enjoyment	64.68±24.84	-	-	<0.0001(t –test)
4.	Sexual /vaginal functioning	88.89±16.99	-	-	<0.0001(t-test)
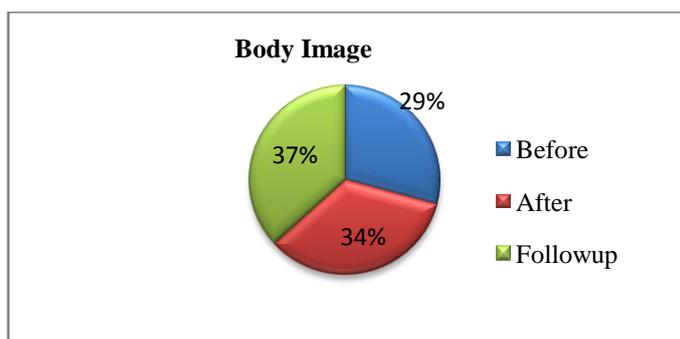
At before treatment, after treatment, and at follow up the scores of the questions related to domain Body image were 77.26, 89.93, and 97.21 respectively. The scores were gradually increased at follow up.

Cancer Treatment Satisfaction Questionnaire (CTSQ)

Domains	Expectations Of Therapy	Feelings About Side Effects	Satisfaction With Therapy
Global Health Status	0.05	-0.009	0.19
Physical Functioning	0.16	-0.06	0.25
Role Functioning	0.02	0.12	0.08
Emotional Functioning	-0.82	0.29	0.37
Cognitive Functioning	-0.19	0.4	0.5
Social Functioning	-0.09	0.15	0.08
Fatigue	0.11	0.1	0.06
Nausea & Vomiting	-0.03	-0.09	-0.15
Pain	0.05	0.06	-0.21
Dyspnea	0.04	0.03	-0.19
Insomnia	0.003	0.002	-0.12
Loss Of Appetite	-0.03	-0.17	0.018
Constipation	0.005	0.07	0.08
Diarrhoea	0.22	0.07	0.15

V. Conclusion

Our study has shown that most common cancer among Rural women was cervical cancer. Majority of the patients in the study are unaware about disease signs & symptoms, etiology, risk factors& preventive measures. Screening campaigns as the most effective means for reducing cervical cancer morbidity & mortality. Initially the patients QOL was worse, which was gradually improved after treatment & effective patient counseling and pharmaceutical care. Pre medication is required before chemotherapy administration. Radiation induced side effects like bowel & bladder problems are most common. These problems can be overcome by using modernized radiation emitting machines and effective pharmaceutical care.

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