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ORIGINAL ARTICLE

Frequency and Severity of Acute Perineal Skin Reactions in Rectal Cancer Patients at Completion of Preoperative Pelvic Radiotherapy

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ABSTRACT

Background: The rectum is the lower part of the colon. Its cancer is the third most common cancer worldwide.
Aim: To determine frequency and severity of acute perineal skin reactions in rectal cancer patients at the completion of preoperative pelvic radiotherapy.
Study Design: Descriptive case series.
Methodology: Study conducted at the Department of Clinical Oncology, Shaukat Khanum Memorial Cancer Hospital Multan. Patients (n=96) were enrolled through non-probability consecutive sampling. All patients received neoadjuvant chemotherapy consisting of fluoropyrimidine and oxaliplatin, Radiotherapy planning was carried out for all patients with a dose of 50.4 Gray in 28 fractions through external beam radiotherapy, consisting of concurrent chemotherapy oral capecitabine twice daily. Severity of skin side effects and were evaluated according to toxicity proforma, based on RTOG/EORTC Toxicity criteria. Data was evaluated by using SPSS vr 23. Poststratification Chi-square test was applied with P-value of 0.05 was considered as significant.
Results: Among 96 patients the radiation dermatitis was found in 50(52.08%) patients, grade I treatment toxicity was noted in 27(54%) patients and grade II treatment toxicity was found in 23(46%) patients.
Conclusion: It was concluded that patients of rectal carcinoma showed better response rate to concomitant chemo-radiation using Capecitabine with high radiation induced dermal toxicity.
Keywords: Rectal Cancer, Oral Capecitabine, Concurrent Chemo-Radiation and Skin toxicity.

INTRODUCTION

Rectal cancer is a common health issue with high prevalence worldwide[1]. Approximately 56% of patients with colorectal cancer die from their cancer[2]. In Pakistan its prevalence is found up to 3.6% among all cancer[3]. Prior to the standard use of radiotherapy, treatment of re-current rectal cancer was a big hurdle in its management according to literature review[4,5]. Adenocarcinoma is the predominant histopathology which comprises about 97% of rectal Cancers[6]. Literature review revealed, neo-adjuvant concurrent chemotherapy and Radiotherapy (CCRT) becomes the preferred treatment modality for locally advanced rectal cancers (stage II –III) patients[7-9].

Literature review revealed that increased rates of tumor response with acceptable rates of early toxicity were seen among victims[7]. The tolerance doses for radiotherapy of normal pelvic structures and organs are very well established in guidelines. These guidelines are followed to improve the therapeutic ratio[10]. In spite of all precautionary measures during treatment, the adjacent healthy tissues manifest treatment-related toxicity that adversely affects the quality of life. Acute perineal skin reactions that occur during radiotherapy to pelvis are very common and well established. These reactions are graded according to RTOG/EORTC criteria and common Toxicity Criteria Criteria[11,12].

Keeping these facts in view, we propose to conduct a prospective study in Locally Advanced (Stage II/III) rectal cancer patients to determine the frequency and severity of acute perineal radiation dermatitis at the end of pelvic radiotherapy that are reported at tertiary care Institute, having multidisciplinary team meeting culture. As there was no local data available that specifically addresses the severity of peri-anal side effects involving skin of chemo radiotherapy in advanced rectal cancer patients thus current study was planned to evaluate dermal side effects of radiotherapy among advanced rectal CA patients. Results of present study helped to evaluate the severity of acute skin toxicity due to radiation therapy thus it helped in better management plan in-order to reduce dermal toxicity among rectalcarcinoma patients.

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METHODOLOGY

It was a descriptive case series conducted at the Department of Clinical Oncology, Shaukat Khanum Memorial Cancer Hospital Multan. After IRB permission. Patients (n=96) were enrolled through non-probability consecutive sampling. All patients received neoadjuvant chemotherapy consisting of fluoropyrimidine and oxaliplatin, Radiotherapy planning was carried out for all patients with a dose of 50.4 Gray in 28 fractions through external beam radiotherapy, consisting of concurrent chemotherapy oral capecitabine (500mg) twice daily for 28 days of radiotherapy. Patients were evaluated before, during and at the end of treatment by radiotherapy while using toxicity Performa, based on RTOG/EORTC Toxicity criteria attached at the end. Complete history and physical examination and workup were performed before treatment including CBC, Serum Creatinine and LFTs. X-ray chest was performed to exclude lung metastasis. Patients of either gender with age (18-70 years) with non-metastatic disease as assessed by complete metastatic workup including CT chest abdomen pelvis were included. Patients with distant metastases with recurrent disease were excluded.
Statistical analysis: Data will be entered and analyzed in SPSS version 23.0. Age was presented as mean and SD. Qualitative variables like severity of acute perineal skin reactions were presented as percentage and frequencies. Post stratification chi-square test was applied with P-value of 0.05 was considered as significant.

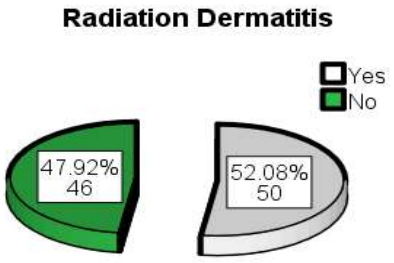
RESULTS

Mean age of the patients was 43.88±14.38 years (Table-1, Figure-1). According to this study the mean BMI of the patients was 21.03±2.53 kg/m^2 with minimum and maximum BMI of 17.33 & 25.84 kg/m^2 respectively as shown in table-1. Parameters like gender and radiation dermatitis distribution were summarized in table-1. Figure-1 showed graphical presentation of radiation dermatitis among enrolled patients.

Table-1: Baseline parameters of enrolled population (n=96)

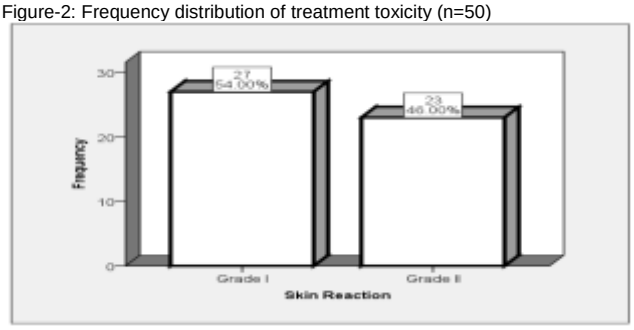
Characteristics	Frequency & Percentage
Gender	
Males	65 (67.71%)
Females	31 (32.29%)
Radiation Dermatitis	
Yes	50 (52.08%)
No	46 (47.92%)
Mean ± SD	
Age (years)	43.88±14.38
BMI (Kg/m^2)	21.03±2.53

Figure-1: Frequency distribution of radiation dermatitis



Grade I treatment toxicity was noted in 27(54%) patients and grade II treatment toxicity was found in 23(46%) patients that was summarized in figure-2.

Figure-2: Frequency distribution of treatment toxicity (n=50)



Radiation dermatitis was stratified with age among enrolled patients. Results showed significant difference with p-value (0.027) as shown by table-2.

Table-2: Comparison of radiation dermatitis between age groups

Age (Years)	Radiation Dermatitis		Total	p-value
	Yes	No		
≤ 40	17	26	43	0.027*
	39.5%	60.5%	100.0%	
>40	33	20	53	
	62.3%	37.7%	100.0%	
Total	50	46	96	
	52.1%	47.9%	100.0%	

*Statistically significant

In patients having age ≤40 years grade I treatment toxicity was found in 11(64.7%) and in patients having age >40 years the grade I treatment toxicity was found in 16(48.5%) patients. Similarly, in patients having age ≤40 years grade II treatment toxicity was found in 6(35.3%) and in patients having age >40 years the grade II treatment toxicity was found in 17(51.5%) patients with insignificant p-value (0.276) as shown in table-3.

Table-3: Comparison of treatment toxicity between age groups

Age (Years)	Treatment Toxicity		Total	p-value
	Grade I	Grade II		
≤ 40	11	6	17	0.276
	64.7%	35.3%	100.0%	
>40	16	17	33	
	48.5%	51.5%	100.0%	
Total	27	23	50	
	54.0%	46.0%	100.0%	

In male patients the radiation dermatitis was noted in 33(50.8%) patients and in female patients the radiation dermatitis was noted in 17(54.8%) patients. This difference was statistically insignificant i.e. p-value=0.709 as shown in table-4.

Table-4: Comparison of radiation dermatitis between gender

Gender	Radiation Dermatitis		Total	p-value
	Yes	No		
Male	33	32	65	0.709
	50.8%	49.2%	100.0%	
Female	17	14	31	
	54.8%	45.2%	100.0%	
Total	50	46	96	
	52.1%	47.9%	100.0%	

In male patients grade-I treatment toxicity was found in 17(51.5%) and in female patients the grade-I treatment toxicity was found in 10(58.8%) patients. Similarly, in male patients grade-II treatment toxicity was found in 16(48.5%) and in female patients the grade-II treatment toxicity was found in 7(41.2%) patients. This difference was statistically insignificant i.e. p-value=0.623 as shown in table-5.

Table-5: Comparison of treatment toxicity between gender

Gender	Treatment Toxicity		Total	p-value
	Grade I	Grade II		
Male	17	16	33	0.623
	51.5%	48.5%	100.0%	
Female	10	7	17	
	58.8%	41.2%	100.0%	
Total	27	23	50	
	54.0%	46.0%	100.0%	

DISCUSSION

In this study the among 96 patients the radiation dermatitis was found in 50 (52.08%) patients in which grade I treatment toxicity was noted in 27(54%) patients and grade II treatment toxicity was found in 23(46%) patients. German rectal cancer trial has established the acute Grade I and II perineal skin toxicity due to radiotherapy in 49% of patients.[13] Results of STAR -01 randomized phase III trial reports 40% of grade I and II acute radiation-related skin toxicity with neoadjuvant CCRT in rectal cancer patients[14].

Severity of acute organ toxicity was significantly higher in female patients, for the entire cohort ($p < 0.001$) i.e., male grade I (35.2%), female grade I (28.7%) while in male grade II (13.7%) and female grade II (18.8%). Our results were similar to the results of one study that evaluated primary tumor response to preoperative chemo-radiation with or without oxaliplatin in locally advanced rectal cancer[15].

One study evaluated the efficacy of preoperative CCRT and demonstrated 25% of acute perineal skin toxicities of grade I/II.[16] Another study reported that most common non-hematologic toxicity was grade I and II Radiation Dermatitis (54%) in locally advanced rectal cancers patients with preoperative CCRT[17].

One local study evaluated safety and efficacy of potent v/s mild topical corticosteroids were compared in patients with acute radiation dermatitis. They also labeled acute radiation dermatitis as

one of the common side effect of radiotherapy resulting in treatment interruptions[18].

In present study, total dose used was 44 Gy in 2.2 Gy/fraction, which is equivalent to 45 Gy in 1.8 Gy/fraction, assuming an α/β of 10 for tumor control. It was followed by a cycle of capecitabine for two weeks after the end of chemo-radiation. Similar dosage and regimen was used in other study with mild modifications[19].

Limitations of study: Treatment planning system facility is not available at our Institute which is mandatory for optimization of dose distribution in the treatment volume. Financial constrains and limited resources with no genetic workup and long follow-ups added to limitations.

CONCLUSIONS

It was concluded that patients of rectal carcinoma showed better response rate to concomitant chemo-radiation using Capecitabine with high radiation induced dermal toxicity. Thus better treatment strategies either with reduced .radiation dose are required for less side effects.

Author's contribution: SM&AB: Overall supervision, write up and literature review. **MHAQ:** Analysis literature review, help in write up, **AA:** Literature review help in write-up.

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