

# Acute Gastrointestinal radiation toxicities in pelvic radiation therapy; types, grade and frequency

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**Abstract:**

**Background:** quality of life of cancer survivors is adversely impacted by bowel toxicity; result from pelvic radiation therapy. In the UK, 12000 patients are treated with radiation therapy for pelvic cancer, mostly with curative intent; this carries a considerable risk for normal surrounding tissues side effects.

**Objective:** the aim of this study was to determine the frequency, types and grade of acute gastrointestinal toxicity in radical pelvic radiation therapy in our patients so that a comparison could be made with the Western countries.

**Patients and Methods:** a prospective analytic study was carried out in Radiotherapy department / Oncology teaching hospital / Medical city complex, from the 2nd of January to the 30th of April 2016. A total of 53 patients with histologically confirmed uterine, cervical, rectal, urinary bladder or prostatic cancer, treated by radical radiation therapy, were enrolled in the study. Patients were assessed for the frequency, types and grade of acute gastrointestinal toxicities according to grading criteria of CTC (Common Toxicities Criteria), at the start, during and at the end of the treatment. The data was analyzed by the Statistical Package for Social Sciences (SPSS 20).

**Result:** out of 53 patients, 60.37% (32) were female and 39.62% (21) were male. Endometrial cancers represent 30.18% of the cases, cervical cancers were 24.52%, and rectal cancers 11.32%, urinary bladder cancers 24.52% and prostatic cancers were 9.43% of the total cases. Diarrhea was present in 50.9% of the patients; nausea and vomiting were present in 22.6% for each. The majority had grade 1 toxicities and only 2 patients developed grade 3 diarrhea (4.7%).

**Conclusion:** The type and incidence of acute gastrointestinal toxicities in pelvic radiation therapy were mostly related to; Radiation dose, a combined used of chemotherapy with radiation therapy and surgery.

**Key Words:** acute toxicities, radiation therapy, pelvic organ cancer.

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**Introduction:**

Gastrointestinal radiation toxicities from pelvic radiotherapy represent one of the most common acute toxicities that may be indeed affecting the course of the treatment and the patient quality of life. Pelvic radiation therapy had been increasingly used to treat malignancies of genitourinary, gastrointestinal and gynecological system, and the management is categorized according to the stage at presentation, patient performance status. The modern era of cancer therapy is predicated on the safe intensification of radiation therapy, chemotherapy, targeted agents and surgery. This has resulted in a markedly increased survivorship, which now exceeds 64% overall, and for some malignancies, such as breast and prostate cancer, is much higher. Despite the great benefit of these treatment modalities, they do have disadvantage or side effect. And so do radiation therapy. Pelvic radiation therapy had acute and late toxicities on different systems as Genitourinary, Genital system, gastrointestinal system and hemopoietic system. This study is concerned in the acute gastrointestinal radiation toxicities; in general they may include bleeding per-rectum, abdominal pain or cramp, diarrhea or constipation, nausea and

vomiting, mucosal discharge, and also gases distension.

**Aim:** The aim of this study was to determine the frequency and types of acute gastrointestinal toxicity in radical pelvic radiotherapy in our population, which would help us in developing appropriate strategies for its prevention and better management.

**Patients and methods:**

A prospective analytic study was carried out at the Oncology teaching hospital/Radiotherapy department / Baghdad Medical city complex, from the 1st of January to the 30th of April 2016, for 4 months. Patients who were referred for radical pelvic radiotherapy were enrolled into the study on justification of strict inclusion and exclusion criteria after informed consent. All patients received radiation therapy with a minimum dose of 40 Gray (Gy) through External Beam Radiation therapy (EBRT), with average 6 beams radiation fields with no differences in the preparation (maintain empty rectum and comfortable full urinary bladder is mandatory except in cases of urinary bladder cancer where the bladder should be empty) or daily cared was noticed among them. Patients were assessed before commencement of radiotherapy, beginning, during and at the end of treatment for frequency and severity of each

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type of acute gastrointestinal toxicities. Acute gastrointestinal toxicities were assessed according to the Common Toxicities Criteria version 20, and recorded in study preformat.

**Results:**

A total of 53 patients were enrolled in the study, Mean age was 57.3 years for female and 57.9 years for male and their demographic characteristics and treatment specifications are presented in table 1.

**Table 1: distribution of study group according to several parameters under study**

	Number	%	
Stage of cancer	IA	5	9.4%
	IB	12	22.6%
	IB2	8	15.1%
	II	16	30.2%
	II A	1	1.9%
	II B	1	1.9%
	III	4	7.5%
	III B	1	1.9%
	IV	5	9.4%
Age groups/years	≤50	12	22.6%
	>50	41	77.4%
History of surgery	yes	24	45.3%
	no	29	54.7%
Chemotherapy status -used/not	yes	27	50.9%
	no	26	49.1%
Dose of radiation/Gray	≤50	28	52.8%
	>50	25	47.2%

Five different tumor sites were included, the most common observed tumor for the study group was endometrial cancer with 50.0% followed by cervical cancer with 40.6% among female patients, while prostatic cancers were 23.8% among male patients, and bladder and rectal cancers were 60.2% and 25.2% respectively among both female and male patients together. On initial evaluation 6 female patients were found to have constipation for more than 5 days so they were excluded from the constipation analysis. The most frequently observed acute gastrointestinal radiation toxicities was diarrhea in 50.9% (n=27/53) followed by pain in 28.3% (n=15/53) while constipation and nausea and vomiting were 22.6% (n=12/53) each. The majority had grade 1 toxicities and only 2 patients developed grade 3 diarrhea (4.7%), this is shown in table 2.

**Table 2: frequency, grade and time of development of symptoms of gastrointestinal toxicities**

Types of radiotherapy adverse events	Number	Percentage	Grade	Time of development	Percentage per week	
Diarrhea	yes	27	50.9%	G1=12(44.4%) G2=13(48.1%), G3=2(4.7%)	1st week 2nd week, 3rd week	14(51.9%) 11(40.7%) 2(7.4%)
	no	26	49.1%			
Constipation	yes	12	22.6%	G1=12(100%)	1st week 2nd week	11(91.7%) 1(8.3%)
	no	41	77.4%			
Nausea and vomiting	yes	12	22.6%	G1=12(100%)	1st week	12(100%)
	no	41	77.4%			
Bleeding	yes	5	9.4%	G1=5(100%)	1st Week	5(100%)
	no	48	90.6%			
Anorexia	yes	3	5.7%	G1=3(100%)	1st week	3(100%)
	no	50	94.3%			
Proctitis	yes	8	15.1%	G1=7(87.5%) G2=1(12.5%)	1st week 2nd week	7(87.5%) 1(12.5%)
	no	45	84.9%			
Abdominal pain	yes	15	28.3%	G1=14(93.3%) G2=1(6.7%)	1st week 2nd week	14(93.3%) 1(6.7%)
	no	38	71.7%			
Distention	yes	8	15.1%	G1=7(87.5%) G2=1(12.5%)	1st week	8(100%)
	no	45	84.9%			
Flatulence	yes	3	5.7%	G1=3(100%)	1st week	3(100%)
	no	50	94.3%			

A radiation dose also show association on acute gastrointestinal toxicities, mostly observed with diarrhea, dose >50 Gy was associated with 55.6% (n=15) compared with 44.4% (n=12) with dose <50 Gy, p-value =0.2. While nausea and vomiting was 66.7% (n=8) with dose >50 Gy vs. 33.3% (n=4) with dose <50 Gy (p-value=0.1). Table 3 show the radiation dose impact on the toxicities.

**Table 3: distribution of symptoms of toxicity according to dose of radiation.**

		surgery				p-value
		Yes		No		
		Count	%	Count	%	
Diarrhea	yes	14	51.9%	13	48.1%	0.3
	no	10	38.5%	16	61.5%	
Constipation	yes	4	33.3%	8	66.7%	0.3
	no	20	48.8%	21	51.2%	
Nausea and vomiting	yes	5	41.7%	7	58.3%	0.7
	no	19	46.3%	22	53.7%	
Bleeding	yes	1	20.0%	4	80.0%	0.2
	no	23	47.9%	25	52.1%	
Anorexia	yes	1	33.3%	2	66.7%	0.6
	no	23	46.0%	27	54.0%	
Proctitis	yes	4	50.0%	4	50.0%	0.7
	no	20	44.4%	25	55.6%	
Abdominal pain	yes	6	40.0%	9	60.0%	0.6
	no	18	47.4%	20	52.6%	
Distention	yes	5	62.5%	3	37.5%	0.2
	no	19	42.2%	26	57.8%	
Flatulence	yes	1	33.3%	2	66.7%	0.6
	no	23	46.0%	27	54.0%	

There is a clinically established relationship between surgery and the development of toxicities in this study (table 4), diarrhea developed in 51.9% (n=14) of patients undergoing surgery compared to 48.1% (n=13) with no surgery.

**Table 4: distribution of symptoms of toxicity according to surgery status**

		Dose category/Gray				p-value
		≤50		>50		
		Number	%	Number	%	
Diarrhea	yes	12	44.4%	15	55.6%	0.2
	no	16	61.5%	10	38.5%	
Constipation	yes	7	58.3%	5	41.7%	0.6
	no	21	51.2%	20	48.8%	
Nausea and vomiting	yes	4	33.3%	8	66.7%	0.1
	no	24	58.5%	17	41.5%	
Bleeding	yes	3	60.0%	2	40.0%	0.7
	no	25	52.1%	23	47.9%	
Anorexia	yes	1	33.3%	2	66.7%	0.8
	no	27	54.0%	23	46.0%	
Proctitis	yes	4	50.0%	4	50.0%	0.9
	no	24	53.3%	21	46.7%	
Abdominal pain	yes	8	53.3%	7	46.7%	0.5
	no	20	52.6%	18	47.4%	
Distention	yes	5	62.5%	3	37.5%	0.5
	no	23	51.1%	22	48.9%	
Flatulence	yes	3	100.0%	0	0.0%	0.09
	no	25	50.0%	25	50.0%	

**Discussion:**

Radiation dose required for tumor eradication in the management of different pelvic cancers usually exceed the tolerance of the normal structures that surround the tumor, leading to toxicity both acute as well as late that affects patient's quality of life. Therefore, evaluation of the toxicity has been a part of good clinical trials. Among acute gastrointestinal toxicities, diarrhea was the most commonly observed 50.9% (n=27/53) in this study with grade 1 (44.4%), grade 2 (48.1%) and grade 3 (4.7%). This finding was specifically focused on different trials, since it represents the most common toxicities in pelvic radiation therapy. Jereczek-Fossa et al. also reported that gastrointestinal symptoms were the most common complaints, i.e. 76% in pelvic radiotherapy for endometrial cancer.1 The grade of toxicities increased with increasing the dose, diarrhea was observed in 55.6% in dose >50 Gy compared to 44.4% in dose <50 Gy; thus grade 2 was seen in 48.1% more in the 2nd week compared to grade 1 was more in the 1st week in 44.4%, but with the proper management of the patients, together with continuous education regarding dietary habit, resulting in decrease the frequency and severity of diarrhea. The combination of chemotherapeutic drugs with radiation perhaps had one of the strongest impacts on current

cancer radiation therapy practice.<sup>2</sup> However; these benefits are achieved at the expense of increased acute as well as late toxicity. Roberts et al. reported the interim result of a phase III trial in which patients with cervical cancer were randomized to chemoradiation versus radiotherapy alone. He found that toxicities increased with the addition of chemotherapy.<sup>3</sup> Similar finding were observed in patients who were treated with chemoradiation, developed more toxicity. Nausea and vomiting were increase from 25% of cases in non-chemotherapy patients to 75% in chemotherapy patients. Volume of the radiation field is directly correlated with the tumor stage, also presence and absence of surgery may affect the irradiated normal tissue volume due to the postoperative anatomical changes such as increased volume of intestine in the pelvis, adhesion of the bowel to the surrounding structures resulting in reduced motility, therefore, more exposure to radiotherapy.<sup>4</sup> Small-bowel tolerance to ionizing radiation is one of the dose-limiting factors in abdominal–pelvic radiotherapy. The small bowel can be considered an organ with a significant correlation between irradiated volume and the probability of acute toxicity, independent of the dose received.<sup>5</sup> This is well observed in this study by increase rate of diarrhea in patients cases treated with surgery compared to non-surgical cases, 51.9% vs. 48.1% respectively. Similar data was reported by Keys et al.<sup>6</sup>, the acute toxicity of pelvic RT after surgery in endometrial cancer patients. The incidence of hematological, gastrointestinal and urinary toxicity were found to be 35.3% (G1-2=35%, G3=0.5%), 68% (G1- 2=63%, G3 and 4=5%) and 30% (G1-2=30%, G3=0%) respectively as compared to RT alone as 9.9% (G1- 2=9.9%, G3=0.9%), 7% (G1=5%, G2=2%), 7.9% (G1=4.5%, G2=3.4%) respectively.<sup>6</sup> There are certain limitations of this study. First, the small sample size may adversely affect the results and their statistical value because of the short duration of data collection. Secondly, accurate comparison of radiation therapy complications from literature is difficult because most radiation therapy centers used advanced radiation therapy technique.

#### **Conclusion:**

The type and incidence of acute gastrointestinal toxicities in pelvic radiation therapy were mostly related to; Radiation dose, as the dose of radiation therapy increase the incidence and severity of toxicities increase, certain toxicities are significantly observed with the combined used of chemotherapy with radiation therapy and since surgery is a leading cause of increase radiation volume, toxicities were more.

#### **Authers contributions:**

Hadeel M. Ali Rasheed: Student

Khudair J. Sabeeh Al-Rawaq: Supervisor

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