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# Effect of Pelvic Radiation on Haematopoeitic and Gastrointestinal Syndromes: a Prospective & Observational Study

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## Abstract

***Introduction:*** *Radiotherapy may induce irreversible damage on healthy tissues surrounding the tumor. It has been reported that the majority of patients receiving pelvic radiation therapy show early or late tissue reactions of graded severity as radiotherapy affects not only the targeted tumor cells but also the surrounding healthy tissues.*

***Methods:*** *This prospective, observational study was conducted to observe the effects of pelvic radiation on haematopoeitic and gastrointestinal syndromes. It was done in Radiation Oncology department of National Institute of Cancer Research and Hospital, Dhaka between July 2011 to June 2012. The study participants were all patients getting pelvic radiation in the concerned department. A blood profile was done before radiotherapy. Clinical evaluation as per RTOG Guideline was done to access the gastrointestinal syndromes. Then, pelvic radiation was started and CBC was done and recorded weekly as well as gastrointestinal toxicity grading. Main outcome measures were hemoglobin, TC of WBC, nausea, vomiting, diarrhea.*

***Results:*** *Before treatment the mean hemoglobin % was 11.0±1.1 mg/dl, during 4th week of treatment it 10.37±0.7 mg/dl.The mean TC of WBC was found 11107.4±13481.4 $mm^3$, during 4th week of treatment the mean TC of WBC was found 7550.6±2514.6 $mm^3$.Nausea and vomiting increased upto 3rd week but decline in subsequent follow-up. 42% patients had diarrhea during 2nd and 3rd week of treatment, 20.0% in 4th week and only 2.0% found in 5th week.*

***Conclusion:*** *It can be said that hematopoetic and gastrointestinal syndromes are significantly correlated in patients undergoing pelvic radiation following 4th week of follow up reports.*

***Keywords:*** *pelvic radiation; gastrointestinal & haematopoeitic syndromes.*

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## Introduction

Radiation therapy plays a fundamental role in cancer treatment; although there are some clinical limitations due to its adverse effects. Bone marrow cells are highly sensitive to the effect of radiation and risk for myelosuppression is related directly to the amount of marrow in the treatment field.[1] Generally, bone marrow depletion within the portal is transient under total doses of 4000 cGY and blood counts are affected substantially only when a large proportion of the skeleton is located within the radiation field.[2]

The association between anaemia and poor patient outcome has been assumed to be causal that anaemia leading to an increase in the tumor hypoxic fraction. The assumption of a causal relation had become the rationale for administering blood transfusions to anemic patients prior to and/or during radiotherapy.[4]

In Bangladesh, a least developed country-the patients are very ignorant, reluctant regarding their disease. By knowing the incidence of anemia of pelvic radiation, the severity of anemia and the timing of the onset of anemia we can properly intervene by blood transfusion or haematinics to maintain the blood hemoglobin at a desired level to get the optimum therapeutic outcome.

The primary objective of this study is to observe the impact of pelvic radiation on haematopoetic system such as anaemia, leucopenia, and Gastrointestinal acute

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toxicities like nausea, vomiting, diarrhoea and abdominal cramps.

**Methods:**

This study was a prospective observational study. Study period ranged from 1st July 2011 to 30th June 2012. The study was conducted in National Institute of Cancer Research and Hospital. Respondents were all patients getting pelvic radiation therapy for malignant cases (eg, rectum, urinary bladder, prostate, uterus, cervix) in the Oncology department of the hospital. A total of 50 cases were selected at least who need 50 Gray External Beam Radiotherapy.

**Inclusion criteria:**

The followings are the criteria for accepting patients for the study.

a) Age >18 but < 75 years.

b) Patient getting pelvic Radiation( Malignant cases includes : rectum, urinary bladder, prostate, Uterus, cervix )

c) Karnofsky performance status more than 60.

**Exclusion Criteria:**

a. Karnofsky performance status scale <60

b. Double malignancies.

c. Age >75 years

d. Patients with uncontrolled Diabetes Mellitus or uncontrolled hypertension.

e. Pregnant women.

f. Patients having hematological disease.

After fulfillment of inclusion and exclusion criteria patient were enrolled to the study by giving an ID no. A complete blood profile were done before starting radiotherapy. As well as a clinical evaluation according to RTOG Guideline to access the gastrointestinal system.After this pelvic radiation were started and C.B.C were done and recorded weekly as well as gastrointestinal toxicity grading.Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Main outcome measures were age, sex, occupational status, performance status, haemoglobin, total count of white blood cells, serum creatinine, nausea, vomiting, diarrhoea, proctitis, pelvic pain, serum sodium and electrolyte potassium during different follow-up.

**Table-I**

*Distribution of the respondents by socio-demographic characteristics (n=50)*

| | Frequency | Percentage |
|---|---|---|
| Age (in years) | | |
| ≤30 | 2 | 4 |
| 31-40 | 8 | 16 |
| 41-50 | 18 | 36 |
| 51-60 | 16 | 32 |
| ≥60 | 6 | 12 |
| Mean ± SD | 49.9 ± 10.5 | |
| Range (min-max) | (29-74) | |
| Sex | | |
| Female | 31 | 62 |
| Male | 19 | 38 |
| Occupational Status | | |
| Officials | 11 | 22 |
| Business | 9 | 18 |
| Farmer | 4 | 8 |
| Housewife | 4 | 8 |
| Worker | 2 | 4 |
| Service holder | 1 | 2 |
| Student | 1 | 2 |
| Others | 18 | 36 |

**Results:**

Table 1 shows socio-demographic characteristics of the respondents. For age, majority (36%) belonged to age 41-50 years. The mean age was found to be 49.9 ± 10.5 and range was 29-74 years. In terms of sex, it was seen that maximum respondents (62%) were females. When occupational status was concerned, 11 (22%) patients were officials, 9 (18%) businessmen, and 18 (36%) had various other jobs.

Table 2 shows haemoglobin % of the study patients.It was observed that before treatment majority 43(86.0%) patients had normal (>10 mg/dl) haemoglobin level. Before treatment, the mean hemoglobin % was found 11.0±1.1 mg/dl. 2nd week treatment two third (66.0%) patients had normal (>10 mg/dl) anaemia. After 2nd week treatment the mean hemoglobin % was found 10.7±1.0 mg/dl.4th week treatment, almost two third (62.0%) patients had normal (>10 mg/dl) anaemia. 4th week treatment mean hemoglobin % was found 10.37±0.7 mg/dl.

**Table-II**

*Distribution of the respondents according to their Haemoglobin levels (n=50)*

| HaemoglobinHb % (mg/dl) | Frequency | Percentage |
|---|---|---|
| Before treatment | | |
| Grade 1: <6.5 mg/dl | 0 | 0 |
| Grade 2: 6.5-7.9 mg/dl | 0 | 0 |
| Grade 3: 8-10 mg/dl | 7 | 14 |
| Normal: >10 mg/dl | 43 | 86 |
| Mean ± SD | 11±1.1 | |
| Range (min-max) | (9.1-13.0) | |
| 2nd week | | |
| Grade 1: <6.5 mg/dl | 0 | 0 |
| Grade 2: 6.5-7.9 mg/dl | 0 | 0 |
| Grade 3: 8-10 mg/dl | 17 | 34 |
| Normal: >10 mg/dl | 33 | 66 |
| Mean ± SD | 10.7±1.0 | |
| Range (min-max) | (9.3-12.8) | |
| 4th Week | | |
| Grade 1: <6.5 mg/dl | 0 | 0 |
| Grade 2: 6.5-7.9 mg/dl | 0 | 0 |
| Grade 3: 8-10 mg/dl | 19 | 38 |
| Normal: >10 mg/dl | 31 | 62 |
| Mean ± SD | 10.37±0.7 | |
| Range (min-max) | (9.2-12.0) | |

Table 3 shows TC of WBC of the study patients it was observed that before treatment majority 49(98.0%) patients had TC of WBC (d"16000 $mm^3$). Before treatment mean TC of WBC was found 11107.4±13481.4 $mm^3$. 2nd week treatment majority 29 (58.0%) patients had TC of WBC (≤9000 ($mm^3$). 2nd week treatment mean TC of WBC was found 8204±3006.6 $mm^3$.4th week treatment almost three fourth (74.0%) patients had TC of WBC (d"9000 ($mm^3$). 4th week treatment mean TC of WBC was found 7550.6±2514.6 $mm^3$. Significant platelet count change was not observed within these weekly CBC report so not presented in table.

**Table-III**

*Distribution of the respondents according to their WBC count (n=50)*

| TC of WBC ($mm^3$) | Frequency | Percentage |
|---|---|---|
| Before treatment | | |
| ≤16000 ($mm^3$) | 49 | 98 |
| ≥16000 ($mm^3$) | 1 | 2 |
| Mean ± SD | 11107.4±13481.4 | |
| Range (min-max) | (1200-103000.0) | |
| 2nd Week | | |
| ≤9000 ($mm^3$) | 29 | 58 |
| ≥9000 ($mm^3$) | 21 | 42 |
| Mean ± SD | 8204.2±3006.6 | |
| Range (min-max) | (1000-14000.0) | |
| 4th Week | | |
| ≤9000 ($mm^3$) | 37 | 74 |
| ≥9000 ($mm^3$) | 13 | 26 |
| Mean ± SD | 7550.6±2514.6 | |
| Range (min-max) | (1000-12400.0) | |

Table 4 shows the vomiting pattern of the respondents. It was observed that 6 (12.0%) patients had vomiting in 1st week, 15 (30.0%) in 2nd week, 16 (32.0%) in 3rd week, 10 (20.0%) in 4th week.

**Table-IV**

*Table shows the distribution of the respondents according to their vomiting (n=50)*

| Vomiting | Frequency | Percentage |
|---|---|---|
| 1st week | | |
| Positive | 6 | 12 |
| Negative | 44 | 88 |
| 2nd week | | |
| Positive | 15 | 30 |
| Negative | 35 | 70 |
| 3rd week | | |
| Positive | 16 | 32 |
| Negative | 34 | 68 |
| 4th week | | |
| Positive | 10 | 20 |
| Negative | 40 | 80 |
| 5th week | | |
| Positive | 0 | 0 |
| Negative | 50 | 100 |

**Table-V**

*Distribution of the respondents by their diarrhoea pattern (n=50)*

| Diarrhoea | Frequency | Percentage |
|---|---|---|
| 1st week | | |
| Positive | 0 | 0 |
| Negative | 50 | 100 |
| 2nd week | | |
| Positive | 21 | 42 |
| Negative | 29 | 58 |
| 3rd week | | |
| Positive | 21 | 42 |
| Negative | 29 | 58 |
| 4th week | | |
| Positive | 10 | 20 |
| Negative | 40 | 80 |
| 5th week | | |
| Positive | 1 | 2 |
| Negative | 49 | 98 |

Table 3.5 shows pattern of diarrhoea of the study patients it was observed that 21(42.0%) patients had diarrhea in 2nd week, 21(42.0%) in 3rd week, 10(20.0%) in 4th week and only 1(2.0%) in 5th week.Mild abdominal crump found almost full tenure of radiotherapy.

**Discussion**

This prospective observational study was carried out with an aim to observe the effect of pelvic radiation on hematopoetic system and acute effect on gastrointestinal system during pelvic Radiotherapy.

A total of 50 patients received pelvic Radiation under Radiation Oncology departmentof National Institute of Cancer Research & Hospital, Dhaka, during July 2011 to 30 June 2012 (1 year), were included in this prospective observational study. Karnofsky performance status scale <60, double malignancies, patient with uncontrolled Diabetes Mellitus or uncontrolled hypertension, pregnant women and patient having hematological disease were excluded from the study. The present study findings were discussed and compared with previously published relevant studies.

In this series it was observed that more than one third (36.0%) of the patients received pelvic radiation were in 5$^{th}$ decade followed by 32.0% in 6$^{th}$ decade, 16.0% in 4$^{th}$ decade, 12.0% in above 6$^{th}$ decade and only 4.0% in 3$^{rd}$ decade and the mean(±SD) age was 49.9±10.5 years varied from 29 to 74 years. Similarly, Obermairet al.[16] found ages ranging between 25 and 77 years with mean age 49 years, which is closely consistent with the current study. On the other hand, Lundgren et al.[11] showedmean(±SD) age 59.3±12.6 years, which was higher with the current study. The higher mean age range maybe due to increased life expectancy, geographical and racial influences of their patients may have significant impacts on pelvic cancer.

In this study it was observed that 38.0% patients were male and 62.0% were female and male to female ratio was 1:1.6, which indicates that pelvic cancer was more common in female patients, which is closely resembled with Lundgren et al.[11] study, where 68.3% and 31.7% were female and male respectively.

In this present series it was observed that 22.0% patients were officials, followed by 18.0% businessmen, 8.0% farmer, 8.0% housewives, 2.0% service holder, 2.0% student and 36.0% patients involved with profession.

Although anemia is a recognized cancer-related disorder, recent Cella[39], Grogan et al.[40] and Lee et al. [41] studies have focused on its impact rather than its prevalence among patients undergoing radiotherapy. In this present study it was observed that before treatment 14.0% patients had Grade 3 (8-10 mg/dl) anaemia and mean hemoglobin % was 11.0±1.1 mg/dl varied from 9.1 to 13.0 mg/dl. During 2$^{nd}$ week of treatment 34.0% patients had Grade 3 (8-10 mg/dl) anaemia and mean hemoglobin % level was 10.7±1.0 mg/dl varied from 9.3 to 12.8 mg/dl. During 4$^{th}$ week of treatment 38.0% patients had Grade 3 (8-10 mg/dl) anaemia and mean hemoglobin % was 10.37±0.7 mg/dl varied from 9.2 to 12.0mg/dl. The current study finding indicates that grade 3 anaemia increased in subsequent follow-up. In another study, Obermairet al.[16] found the Hb levels at presentation were 12.9 ±1.6 g/dL and 12.1 ±1.4 g/dL in patients who achieved radiation and in patients with treatment failure respectively.

Green et al.[3] reported in their study that anaemia at presentation is a poor prognostic factor for local control of disease and overall survival. Anaemia leading to an increase in the tumor hypoxic fraction with subsequent relative radio resistance resulting from impaired tumor oxygenation. The assumption of a causal relation had become the rationale for administering blood

transfusions to anemic patients prior to and/or during radiotherapy obtained by Gillian et al.[4] Our results indicate that pelvic radiation induces a loss of fat free mass along with intestinal morphologic and functional changes.

In this current study it was observed that before treatment the mean TC of WBC was found 11107.4±13481.4 $mm^3$ varied from 1200 to 103000 $mm^3$. During 2nd week of treatment, the mean TC of WBC was found 8204±3006.6 $mm^3$ varied from 1000 to 14000 $mm^3$. During 2nd week of treatment, the mean TC of WBC was found 7550.6±2514.6 $mm^3$and varied from 1000 to 12400 $mm^3$. Carr et al.[42] study reported the results of serial observations of simple haematological indices (haemoglobin concentration, white cell count and platelet count) in 25 patients who developed radiation bowel disease as a late complication of pelvic radiotherapy. There is a highly significant elevation of the platelet count at a time when the patients develop radiation bowel disease. The platelet count returns to normal after successful improvement of the disease but the elevation recurs if further radiation disease develops in the urinary or gastrointestinal tracts. It is suggested that the platelet count may have a useful role in the diagnosis of radiation bowel disease. But, in our weekly CBC report Platelet count change was not significantly found.

Lymphocytes demonstrated to be more sensitive to radiation therapy. No alteration was found in leukocyte or platelet counts in correlation with patients' sex or age. Based on the above-mentioned results, weekly leukocyte and platelet counts do not seem to be useful in the assessment patients submitted to conventional radiotherapy for localized cancer.

Side effects from radiation therapy to the stomach and abdomen include nausea, vomiting, or diarrhea. These symptoms will likely disappear when treatment is completed. It was observed that 12.0% patients had vomiting during 1st week of treatment, 30.0% in 2nd week, 32.0% in 3rd week, 20.0% in 4th week and 2.0% in 5th week. Vomiting increase upto 3rd weeks of treatment but decline in subsequent follow-up. Abdominal crump found almost full tenure of radiotherapy.Mitchell [17] had been estimated that approximately 70–80% of patients receiving chemotherapy experience nausea and/or vomiting. It has been reported that the quality of life is impaired due to delayed and anticipatory nausea and vomiting in approximately 40% and 30% of patients, respectively obtained by Morrow et al. [18] and Aaproet al.[19]

Pelvic radiation therapy is used in various clinical settings as an adjuvant or primary treatment for patients with gastrointestinal, gynecologic, genitourinary, or other pelvic cancers. Diarrhea is the major form of acute toxicity for these patients mentioned by Kozelskyet al.[20], Martenson et al. [21], Miller et al.[22], Miller et al.[23] Demers et al.[24] reported that up to 80% of patients receiving radiotherapy will develop acute radiation induced diarrhea. In this present series it was observed that 42.0% patients had diarrhea during 2ndweekof treatment, 42.0% in 3rd week, 20.0% in 4th week and only 2.0% found in 5th week. Pía de la Maza et al. [25] found 86.7% patients presented diarrhea during radiation therapy. After five weeks, intestinal permeability increased, while intestinal transit time decreased. The authors concluded that pelvic radiation induces a loss of fat free mass along with intestinal morphologic and functional changes. This study note that the results do not contradict those of Yavuz et al. [26], where they showed that octreotide was effective for the treatment of radiation-induced diarrhea. Prevention studies and treatment studies inherently study different patient populations.

**Limitations**

- The study population was selected from one selected hospital in Dhaka city, so the results of the study may not reflect the exact picture of the country.
- The present study was conducted at a very short period of time.
- Toxicities not mentioned as per selective disease and mentioned as overall pelvic radiotherapy.
- Small sample size was also a limitation of this study. Therefore, in future, further study may be undertaken with large sample size.

**Conclusion**

Haemoglobin level and TC of WBC declined in subsequent follow-up. Nausea and vomiting increased upto 3rd week but decline in subsequent follow-up. Diarrhea, proctitis and pelvic pain was observed during follow-up.

**Recommendation**

Further studies can be undertaken by including large number of patients.

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