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Comparison of Acute Hematological Toxicities Between Three-Dimensional Conformal Radiotherapy (3DCRT) and Intensity-Modulated Radiotherapy (IMRT) in Locally Advanced Cervical Cancer

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Abstract

Background

Pelvic external beam radiotherapy (EBRT) with concurrent chemoradiotherapy followed by brachytherapy is regarded as the standard treatment for locally advanced cervical cancer. Hematologic toxicities are commonly associated with this treatment. The purpose of this study was to assess and compare acute hematological toxicities between three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT) techniques of EBRT.

Materials and methods

This quasi-experimental study was conducted from October 2021 to September 2022, during which 70 patients with locally advanced squamous cell carcinoma of the uterine cervix were divided into two treatment arms (A and B), 35 patients in each arm, by purposive sampling. Patients in Arm A and Arm B received EBRT by 3DCRT and IMRT techniques, respectively, with concurrent chemotherapy, and the rest of the treatment was the same. All patients were evaluated before starting radiotherapy, weekly during therapy, and after completing treatment. Follow-ups were done after completion of EBRT, then after completion of intracavitary irradiation (ICRT), and finally six weeks after the completion of treatment (EBRT and ICRT) using history, clinical examination, and investigations.

Results

During EBRT, the overall incidence of hematological toxicities was significantly higher in arm A than in arm B (97.14% vs 77.14%, $p = 0.012$). Leukopenia was also significantly more frequent in arm A (65% vs 34%, $p = 0.05$). The incidences of anemia, neutropenia, or thrombocytopenia were not significantly different between the arms. Following completion of ICRT, the overall incidence of hematological toxicity remained significantly higher in Arm A than in Arm B (97.14% vs 71.43%, $p = 0.006$). Among the individual hematological toxicities, only anemia showed a statistically significant difference between the two groups, occurring more frequently in Arm A (85.7% vs 51.4%, $p = 0.002$) in this case. No statistically significant differences were observed in hematologic toxicities between the arms during follow-ups at week 9 and week 15.

Conclusion

The study findings favor the IMRT technique over 3DCRT for decreasing acute hematological toxicities of radiotherapy.

Categories: Radiation Oncology, Oncology

Keywords: acute hematological toxicities, cervical cancer, concurrent chemoradiotherapy, locally advanced cervical cancer, pelvic radiotherapy

Introduction

Cervical cancer is the second most common cancer among Bangladeshi females, the majority of which present at a locally advanced stage [1,2]. The standard treatment for locally advanced cervical cancer typically involves a multimodal approach consisting of external beam radiotherapy (EBRT) with concomitant

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chemotherapy, followed by intracavitary irradiation (ICRT or brachytherapy) [3,4]. Despite its established efficacy, this treatment approach is associated with treatment-related adverse effects in approximately 20%-25% of patients [5].

Three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT) are two standard and widely used techniques to deliver EBRT. IMRT has been proven to be superior to 3DCRT in a number of locations, especially head and neck, central nervous system, lung, and prostate. The benefits were mainly in terms of better dose conformity, reduction of adverse events, improvement in quality of life, and survival benefit [6]. Although the treatment methods are continuously improving, data regarding the advantage of IMRT for treating cervical cancer in terms of outcomes and toxicities are still limited [7].

Radiation-induced acute hematological toxicities are among the most common side effects of pelvic radiotherapy [8]. This is particularly important because the proximal femur, sacrum, ilium, ischium, pubis, and lumbar vertebrae contain more than 50% of the body's active bone marrow [9]. Consequently, a substantial proportion of active bone marrow may be exposed to radiation during pelvic radiotherapy, potentially resulting in hematopoietic suppression. Therefore, the incidence and severity of acute hematological toxicities may be reduced by reducing the irradiated volume of active bone marrow [10]. Dosimetric and early clinical studies have suggested that IMRT technique may be associated with a lower rate of gastrointestinal, genitourinary, and hematological toxicities when compared with conventional 3DCRT technique. Nevertheless, direct comparative clinical data evaluating IMRT and 3DCRT in patients with locally advanced cervical cancer remain limited [11]. The present study was conducted to assess and compare treatment-related acute hematological toxicities among patients with locally advanced cervical cancer treated with 3DCRT or IMRT techniques.

Materials And Methods

We conducted this quasi-experimental study from October 2021 to September 2022 at Bangladesh Medical University or BMU (formerly, Bangabandhu Sheikh Mujib Medical University or BSMMU), Shahbagh, Dhaka. Participants were recruited from three institutions: the Department of Clinical Oncology at BMU; Delta Hospital Limited (DHL), Mirpur, Dhaka; and Ahsania Mission Cancer & General Hospital (AMCGH), Uttara, Dhaka. The study was approved by the Institutional Review Board (IRB) of BMU (approval number: BSMMU/2021/3678) and the Ethical Committees of DHL and AMCGH (approval number: AMCGH/1900/2022-349).

Patients

Seventy female patients were recruited for the study. The sample size was determined at a 5% level of significance and 95% power using the following formula:

$$\sqrt{\frac{p_1(1-p_1) + p_2(1-p_2)}{n}} \times (Z_{\alpha/2} + Z_{\beta}) \sqrt{(p_1-p_2)^2}$$

The inclusion criteria were biopsy-proven squamous cell carcinoma of the cervix in locally advanced stage (FIGO (International Federation of Gynecology and Obstetrics) stage IIB to IVA). Exclusion criteria were ECOG (Eastern Cooperative Oncology Group) performance status [12] score of three or above, prior chemotherapy or pelvic radiotherapy, being pregnant, and serious concomitant medical illness that would make patients ineligible for definitive treatment or chemotherapy (e.g., severe heart or liver disease, chronic kidney disease, uncontrolled diabetes mellitus, or hypertension). An informed written consent was obtained from each participant.

Study design

The seventy patients were divided into two treatment arms (A and B) by purposive sampling according to patients' choice, 35 in each arm. Patients in Arm A and Arm B received EBRT by 3DCRT and IMRT techniques, respectively, using 50 Gy in 25 daily fractions along with I.V. cisplatin 40 mg/m² weekly. This was followed by high-dose-rate intracavitary brachytherapy - three insertions at weekly intervals, 7 Gy each. The patients were planned to receive four to five cycles of cisplatin during EBRT. Cisplatin was not given under the following conditions: white blood cell (WBC) count less than 2000/mm³, neutrophil count less than 1000/mm³, and platelet count less than 50000/mm³.

Radiotherapy planning

Patients underwent CT simulation in a supine position with appropriate immobilization. Standard bladder protocol was maintained for all patients during simulation and treatment. Half an hour before the simulation, patients were instructed to empty their bladder and take 500 mL of water. They were instructed not to void in between. Contrast-enhanced CT simulation was performed after 30 minutes. Planning images were then generated by CT scanning.

Clinical target volume (CTV) and organs at risk were contoured on axial slices. The CTV-T included cervical

tumor, uterus, parametrial tissues, upper vagina, and broad and proximal uterosacral ligaments. The entire uterosacral ligament was included in cases of posterior extension of cervical tumor. CTV-N included regional lymph nodes at risk: common iliac, external iliac, internal iliac, and obturator lymph nodes. The upper presacral nodes were included in cases of posterior extension. A margin of 0.7 cm was added around the vasculature to obtain the nodal margins, excluding bowel, muscles, or bony spaces. Planning target volume (PTV) was defined as the CTV-T plus a 1.5 margin (PTV-T) and CTV-N plus a 0.7 cm margin (PTV-N). PTV-T and PTV-N were merged to obtain the final PTV.

Thirty-five patients in Arm A (50% of the study population) were planned to receive pelvic 3DCRT using the standard four-field technique over five weeks (25 daily fractions). Treatment was delivered using 6-MV photon beams from linear accelerators (LINACs) manufactured by Varian Medical Systems, Inc. (Palo Alto, CA) or Elekta AB (Stockholm, Sweden).

Thirty-five patients in Arm B (50% of the study population) were planned to receive pelvic IMRT at a total dose of 50 Gy in 25 daily fractions over five weeks. IMRT plans were generated using Eclipse™ (Varian Medical Systems, Inc., Palo Alto, CA) or Monaco® (Elekta AB, Stockholm, Sweden) planning software. Five to seven coplanar beams were used to meet the dose objectives. Six-MV photon beams were used for all plans, and dose calculations were performed using the analytical anisotropic algorithm (AAA).

Normal tissues including bowel, bladder, rectum, and bone marrow were contoured separately for each patient as organs at risk (OAR) or avoidance structures. The whole pelvis was contoured on the planning CT scan for each patient as a surrogate for bone marrow according to the RTOG (Radiation Therapy Oncology Group) contouring atlas. The contour included the L5 vertebral body, entire sacrum, ilium, pubis, ischium, acetabulum, and proximal femurs. Dose volume histograms were constructed for each contoured bone marrow. The volume of each bone marrow receiving 10, 20, and 40 Gy was calculated and denoted as V10, V20, and V40, respectively. For IMRT planning, bone marrow (whole pelvis) dose constraints were V10 < 95% and V20 < 80%. The RTOG consensus contouring guidelines for female pelvis were used as the universal contouring guideline among the three centers participating in this study. An example of bone marrow delineation and its three-dimensional rendering is shown in Figure 1.

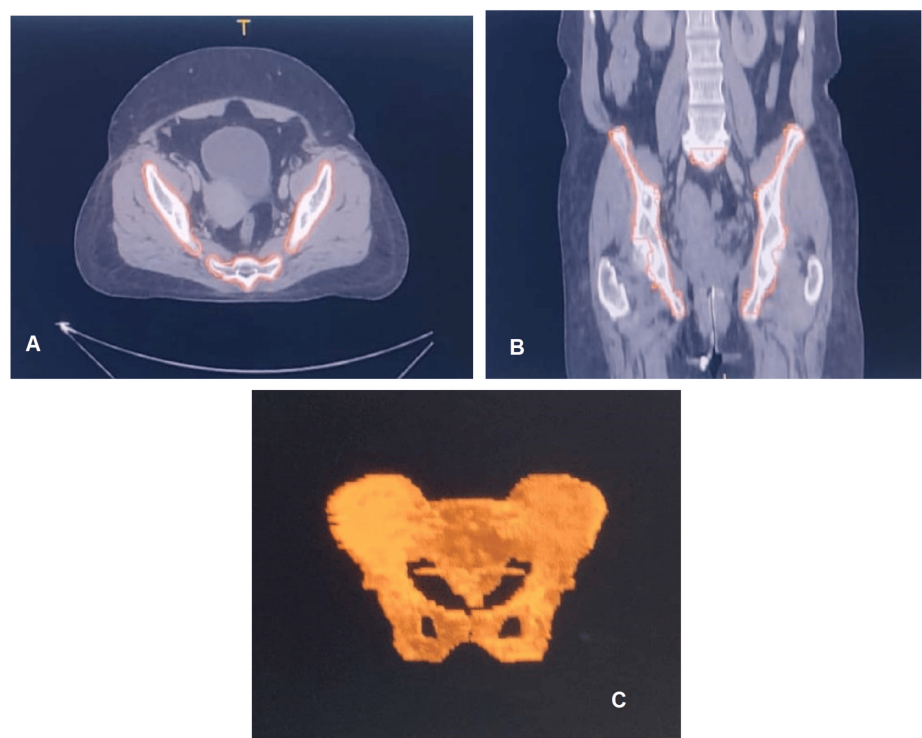


FIGURE 1: Example of delineation of bone marrow in axial plane (A) and coronal plane (B). Panel C shows a three-dimensional rendering of the whole pelvis in TPS.

TPS: Treatment planning system.

Assessment

All patients were evaluated before the initiation of radiotherapy (baseline or week 1) and then weekly throughout the treatment period (weeks 2-8). Complete blood counts, kidney function (serum creatinine), and liver function (serum bilirubin and aspartate aminotransferase (AST)) were assessed weekly. Follow-up assessments were performed at week 9, after completion of ICRT, and at week 15, six weeks later, using history, clinical examination, complete blood count, and serum creatinine measurement.

Acute hematological toxicities, if present, were recorded using the Common Terminology Criteria for Adverse Events, version 5.0 (CTCAE v5.0) [13]. Hematological toxicities were defined as follows: anemia when hemoglobin levels were less than 11 g/dl; neutropenia when neutrophil count was less than $2,000/\text{mm}^3$; leukopenia when WBC count was less than $4,000/\text{mm}^3$; thrombocytopenia when thrombocyte count was less than $150,000/\text{mm}^3$. Data were collected and recorded on a structured data collection sheet.

Statistical analysis

The SPSS (Statistical Package for Social Science) software program for Windows, version 25 (IBM Corp., Armonk, NY), was used for data analysis. Outcomes were compared by the chi-square test, Student's t test, or Fisher's exact test where applicable. A p-value of less than 0.05 was considered statistically significant.

Results

Clinical data

The baseline characteristics of patients in the two arms are summarized in Table 1. There was no statistically significant difference in the baseline characteristics between the arms ($p > 0.05$ for all). Among the 70 patients, 33 patients were premenopausal, and 37 were postmenopausal. Excessive per vaginal discharge was the most common presenting complaint, followed by postcoital bleeding. The patients mostly had stage IIB disease with moderate histological differentiation and a good performance status.

	Arm A (3DCRT) (n = 35)	Arm B (IMRT) (n = 35)	Total (n = 70)	p-value*
Age				
Mean (±SD) in years	53.34 (±9.77)	52.06 (±8.71)	52.7 (±9.22)	0.563
FIGO stage				
IIB	20 (57.14%)	19 (54.29%)	39 (55.71%)	0.31
IIIA	0 (0%)	1 (2.86%)	1 (1.43%)	
IIIB	5 (14.3%)	4 (11.43%)	9 (12.86%)	
IIIC	2 (5.7%)	4 (11.43%)	6 (8.57%)	
IVA	8 (22.86%)	7 (20%)	15 (21.43%)	
Histological differentiation				
Well	3 (8.57%)	5 (14.29%)	8 (11.43%)	0.76
Moderate	26 (74.29%)	25 (71.43%)	51 (72.86%)	
Poor	6 (17.14%)	5 (14.29%)	11 (15.71%)	
Performance status				
ECOG 0	25 (71.43%)	27 (77.14%)	52 (74.3%)	0.208
ECOG 1	7 (20%)	8 (22.86%)	15 (21.4%)	
ECOG 2	3 (8.57%)	0 (0%)	3 (4.3%)	
Baseline hemoglobin				
Mean (±SD) in g/dl	12 (± 1.5)	12 (± 1.1)	12 (± 1.7)	0.38
Baseline WBC count				
Mean (±SD) in ×10 ³ cells/mm ³	8.2 (± 2.4)	7.9 (± 3.1)	8.1 (± 1.6)	0.28
Baseline neutrophil count				
Mean (±SD) in ×10 ³ cells/mm ³	4.6 (± 1.3)	5.1 (± 2)	4.8 (± 1.6)	0.43
Baseline platelet count				
Mean (±SD) in ×10 ³ cells/mm ³	311 (± 87)	295 (± 77)	304 (± 71)	0.58

TABLE 1: Baseline characteristics of the patients

* Calculated using the Student's t-test or chi-square (χ^2) test.

SD: Standard deviation; ECOG: Eastern Cooperative Oncology Group (scoring system); WBC: White blood cell; FIGO: International Federation of Gynecology and Obstetrics; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

Hematologic toxicity

There were no significant differences between the two treatment arms in baseline hemoglobin levels or WBC, neutrophil, and platelet counts. All patients underwent complete blood counts at baseline, weekly during treatment (EBRT and ICRT), and six weeks after treatment completion to assess acute hematological toxicities. Figure 2 shows the patterns of anemia and leukopenia during the weeks of EBRT delivery. Most cases of anemia and leukopenia developed from the third week onward. Anemia peaked in the fourth week of treatment, whereas leukopenia peaked in the fifth week.

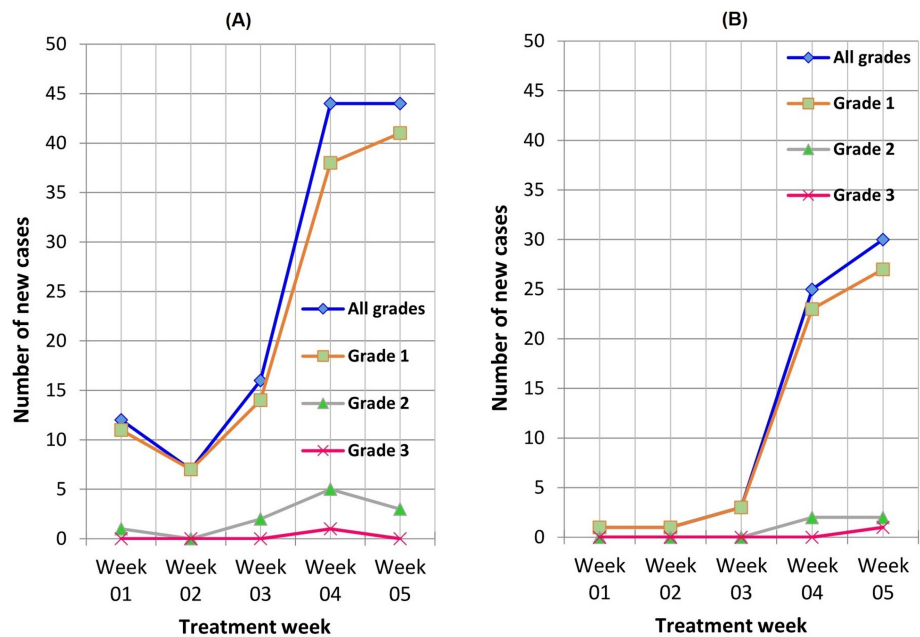


FIGURE 2: Pattern of anemia (A) and leukopenia (B) during EBRT

EBRT: External beam radiotherapy.

Among the 70 study participants, 61 (87%) developed acute hematological toxicities during EBRT, as shown in Table 2. Overall toxicities were significantly higher in Arm A (97.14% vs 77.14%, $p = 0.012$).

Hematological toxicities	Arm A (3DCRT) (n = 35)		Arm B (IMRT) (n = 35)		Total (n = 70)		p-value*
	Number	%	Number	%	Number	%	
Present	34	97.14	27	77.14	61	87.14	0.012
Absent	1	2.86	8	22.86	9	12.86	

TABLE 2: Overall hematological toxicities observed in patients during EBRT

* Calculated using the chi-square test; $\chi^2 = 6.248$, degree of freedom = 1, effect size = 0.299.

EBRT: External beam radiotherapy; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

Table 3 summarizes the individual toxicities. The toxicities were managed accordingly, with blood transfusions and filgrastim injections as needed. Radiotherapy was not discontinued in any patient, as no grade 4 toxicities occurred. Three patients developed grade 3 toxicities, all in Arm A. Chemotherapy was withheld for that week only in these cases, and they all recovered on treatment the following week. There was no significant difference in chemotherapy completion rates between the two arms. The mean number of chemotherapy cycles was 4.9 (± 0.28) in Arm A and 5.0 in Arm B.

	Arm A (3DCRT) (n = 35)	Arm B (IMRT) (n = 35)	Total (n = 70)	p-value*
Anemia				
Grade 0	2 (5.71%)	9 (25.71%)	11 (15.71%)	0.057
Grade 1	26 (74.29%)	24 (68.57%)	50 (71.43%)	
Grade 2	6 (17.14%)	2 (5.71%)	8 (11.43%)	
Grade 3	1 (2.86%)	0 (0%)	1 (1.43%)	
Leukopenia				
Grade 0	12 (34.28%)	23 (65.71%)	35 (50%)	0.05
Grade 1	19 (54.29%)	11 (31.43%)	30 (42.86%)	
Grade 2	3 (8.57%)	1 (2.86%)	4 (5.71%)	
Grade 3	1 (2.86%)	0 (0%)	1 (1.43%)	
Grade 4	0 (0%)	0 (0%)	0 (0%)	
Neutropenia				
Grade 0	31 (88.57%)	33 (94.29%)	64 (91.43%)	0.335
Grade 1	1 (2.86%)	2 (5.71%)	3 (4.28%)	
Grade 2	1 (2.86%)	0 (0%)	1 (1.43%)	
Grade 3	2 (5.71%)	0 (0%)	2 (2.86%)	
Grade 4	0 (0%)	0 (0%)	0 (0%)	
Thrombocytopenia				
Grade 0	33 (94.29%)	35 (100%)	68 (97.14%)	0.15
Grade 1	2 (5.71%)	0 (0%)	2 (2.86%)	
Grade 2	0 (0%)	0 (0%)	0 (0%)	
Grade 3	0 (0%)	0 (0%)	0 (0%)	
Grade 4	0 (0%)	0 (0%)	0 (0%)	

TABLE 3: Individual hematological toxicities between the two arms during EBRT

* Calculated using the chi-square (χ^2) test or Fisher's exact test.

Grade 0 = no toxicity occurred.

For anemia: $\chi^2 = 7.535$, degree of freedom = 3, effect size = 0.328.

For leukopenia: $\chi^2 = 7.590$, degree of freedom = 3, effect size = 0.329.

For neutropenia: $\chi^2 = 3.396$, degree of freedom = 3, effect size = 0.22.

For thrombocytopenia: $\chi^2 = 2.059$, degree of freedom = 1, effect size = 0.171.

EBRT: External beam radiotherapy; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

Participants mostly developed anemia during EBRT treatment. Other cell lines were affected at much lower percentages. Observed differences between the arms were significant only for leukopenia (p = 0.05), where Arm A participants had more toxicities, particularly grade 1 leukopenia. Patients received ICRT after EBRT. Most of them experienced hematological toxicities like EBRT (Table 4).

Hematological toxicities	Arm A (3DCRT) (n = 35)		Arm B (IMRT) (n = 35)		Total (n = 70)		p-value*
	Number	%	Number	%	Number	%	
Present	34	97.14	25	71.43	59	84.3	0.006
Absent	1	2.86	10	28.57	11	15.7	

TABLE 4: Hematological toxicities between the two arms after completion of ICRT

* Calculated using the chi-square test; $\chi^2 = 8.737$, degree of freedom = 1, effect size = 0.353.

ICRT: Intracavitary irradiation; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

Arm A participants had significantly more toxicities compared to Arm B participants. This difference was mostly apparent for anemia, as shown in Table 5. None had grade 2 or higher anemia.

Anemia	Arm A (3DCRT) (n = 35)	Arm B (IMRT) (n = 35)	Total (n = 70)	p-value*
Grade 0	5 (14.29%)	17 (48.57%)	22 (31.43%)	0.002
Grade 1	30 (85.71%)	18 (51.43%)	48 (68.57%)	
Grade 2	0 (0%)	0 (0%)	0 (0%)	
Grade 3	0 (0%)	0 (0%)	0 (0%)	

TABLE 5: Anemia among the study patients between the two arms after ICRT

* Calculated using the chi-square test; $\chi^2 = 9.545$, degree of freedom = 1, effect size = 0.37.

Grade 0 = no toxicity occurred.

ICRT: Intracavitary irradiation; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

During follow-up, acute toxicities were assessed regularly for up to six weeks. The results showed no significant differences between the two arms (Table 6). Most participants had no hematological toxicities. There were also no significant differences in individual toxicities.

Hematological toxicities	Arm A (3DCRT) (n = 35)		Arm B (IMRT) (n = 35)		Total (n = 70)		p-value*
	Number	%	Number	%	Number	%	
Present	9	25.71	6	17.14	15	21.43	0.382
Absent	26	74.29	29	82.86	55	78.57	

TABLE 6: Hematological toxicities observed between the two arms six weeks after completion of EBRT and ICRT

* Calculated using the chi-square test; $\chi^2 = 0.764$, degree of freedom = 1, effect size = 0.104.

EBRT: External beam radiotherapy; ICRT: Intracavitary irradiation; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy.

Discussion

In this study, we compared and analyzed the incidence of acute hematological toxicities in patients receiving pelvic radiotherapy using 3DCRT or IMRT. Patients were evaluated before radiotherapy initiation, weekly

throughout the treatment period, and six weeks after treatment completion. The toxicities assessed included anemia, leukopenia, neutropenia, and thrombocytopenia.

Anemia was the most observed toxicity during EBRT (59 patients, or 84.3%), while the other toxicities occurred in half or fewer than half of patients (leukopenia: 35 patients, or 50%; neutropenia: 6 patients, or 8.57%; and thrombocytopenia: 2 patients, or 3%). However, these findings are contrary to some other studies. Hui et al., Sharma et al., and Erpolat et al. investigated hematological toxicities in 40, 54, and 127 patients with cervical cancer, respectively [14–16]. In contrast to our findings, they all reported that leukopenia and neutropenia were more common than anemia. This discrepancy may be due to a small sample size in our study.

Although the differences were not statistically significant for all types, hematological toxicities occurred predominantly in the 3DCRT arm (Arm A) during EBRT across all cell lines. Anemia was observed in 33 (94.3%) patients in Arm A versus 26 (74.3%) patients in Arm B ($p = 0.057$). Similarly, leukopenia developed in 23 (65.7%) versus 12 (34.3%) patients ($p = 0.05$), neutropenia developed in 4 (11.43%) versus 2 (5.7%) patients ($p = 0.335$), and thrombocytopenia developed in 2 (5.7%) versus 0 (0%) patients ($p = 0.15$) in Arms A and B, respectively. The difference in the incidence of leukopenia was statistically significant according to the predefined criteria. However, we acknowledge that the p -value was borderline and that there was no significant difference in the incidence of neutropenia between the arms. These findings are consistent with those of Sharma et al. [15]. They reported a significant increase in anemia (44.4% vs. 33.3%, $p = 0.034$) and neutropenia (59.26% vs. 37.04%, $p = 0.039$) in the 3DCRT arm, especially grade 1 anemia and neutropenia. They also observed less thrombocytopenia in the IMRT arm, although the difference was not significant. Erpolat et al. reported a similar pattern [16]. In contrast, Hui et al. reported slightly more leukopenia in the IMRT arm, although this was also not statistically significant [14].

The IMRT arm showed fewer toxicities across all grades. While only two (5.71%) patients had grade 2 or higher anemia and one (2.86%) patient had grade 2 or higher leukopenia in the IMRT arm, the corresponding numbers in the 3DCRT arm were seven (20%) and four (11.43%), respectively. Arm A had three (8.57%) patients with grade 2 or higher neutropenia, whereas Arm B had none. Erpolat et al. reported that grade 2 or higher anemia and leukopenia were more common in the 3DCRT arm, but neutropenia and thrombocytopenia were more common in the IMRT arm [16]. Sharma et al. also reported higher incidences of grade 2 or higher neutropenia and thrombocytopenia in the IMRT arm of their study [15].

We observed a few grade 3 toxicities in Arm A but none in Arm B. The incidence of grade 3 toxicities was much higher in the study conducted by Hui et al., although the differences were not statistically significant [14]. In their study, grade 3 leukopenia and neutropenia occurred in 60% (12) and 30% (6) of patients, respectively, in the 3DCRT group, compared with 10% (2) and 0% (0), respectively, in the IMRT group [14]. Sharma et al. also reported a few cases of grade 3 neutropenia and thrombocytopenia among patients receiving IMRT [15]. The low incidence of grade 3 hematological toxicities in our study could be attributed to improved dose distribution and more advanced dose calculation algorithms in the latest radiotherapy machines. The volume of the whole pelvis receiving 40 Gy (V40) was significantly lower with IMRT planning than with 3DCRT planning (61.64% vs. 52.43%, $p = 0.00048$). There were no statistically significant differences in V10 or V20 between the arms.

These conflicting results may have resulted from small sample sizes. All these diverse data suggest that well-designed studies with larger sample sizes are needed to reach definitive conclusions. However, all these studies concur that acute hematological toxicities are more frequent with 3DCRT than with IMRT.

As with EBRT, anemia was the most prevalent toxicity after ICRT. It developed at a significantly higher rate in Arm A patients than in Arm B patients (30 or 85.7% vs 18 or 51.4%, $p = 0.002$). However, during the follow-up period, all these differences evened out, and the overall hematologic toxicity profiles became similar between the arms.

This study had several limitations. Selection bias could not be avoided because the study was unblinded and non-randomized. Patients were recruited from three centers in Dhaka, Bangladesh; therefore, the findings may not reflect the nationwide situation. Another key limitation was the short study duration, which precluded the evaluation of overall survival and late toxicities. We intend to investigate these outcomes in future research. The association between human papillomavirus (HPV) and carcinoma could not be ascertained because of limited logistical support. Future research should involve larger sample sizes, longer follow-up periods, and stratified data collection.

Conclusions

As per this study, IMRT decreases acute hematological toxicities during the treatment delivery period. However, the toxicity outcomes became similar between the two arms during follow-up. The clinical benefits of IMRT in reducing hematological toxicities need to be further confirmed in prospective, randomized studies.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Md Masudur Rahman, Shahrin Jahan, Mohammad A. Bari, Khandokar Samsujjaman, Mohammad Jahan Shams, Afsana Sharmin

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Concept and design: Shahrin Jahan, Mohammad A. Bari

Supervision: Mohammad A. Bari

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Review Board of Bangladesh Medical University (BMU) and Ethical Committees of Delta Hospital Limited (DHL) and Ahsania Mission Cancer & General Hospital (AMCGH) issued approval (approval number: BSMMU/2021/3678 and AMCGH/1900/2022-349, respectively). **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** The BSMMU (Bangladesh Medical University) Research Grant Committee provided partial funding for this study. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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