

SIGNS, SYMPTOMS CHANGES AND SUCH-P/V DISCHARGE, P/V BLEEDING, PELVIC PAIN, FEVER WITH CHEMO-RADIO THERAPY AND RADIO THERAPY IN THE TREATMENT OF CERVICAL CANCER**H. N. Ashikur Rahaman^{1*} and Shravana Kumar Chinnikatti²**¹Registrar, Dept. of Clinical Oncology, Enam Medical College & Hospital, Savar, Dhaka, Bangladesh.²Senior Consultant, Dept. of Clinical Oncology, Enam Medical College Hospital, Savar, Dhaka, Bangladesh.***Corresponding Author: Dr. H. N. Ashikur Rahaman**

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ABSTRACT

Introduction: Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 representing 6.6% of all female cancers. Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries. The high mortality rate from cervical cancer globally could be reduced through a comprehensive approach that includes prevention, early diagnosis, effective screening and treatment programmes.

Objective: To find out Signs, Symptoms changes and such -P/V discharge, P/V bleeding, pelvic pain, Fever with Chemo-Radiotherapy and Radiotherapy in the Treatment of Cervical Cancer. **Methods and Materials:** The study had conducted in the Department of Radiation Oncology, Enam Medical College Hospital, Savar, Dhaka & in the department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka from July 2018 to June 2019. Experimental study- Randomized Control Clinical Trail. Patients with carcinoma cervix attained at the Radiation Oncology Department of EMCH & NICRH during the study period had included in the study according to inclusion an exclusion criterion. Patients- Clinically diagnosed and histologically proved squamous cell cervical carcinoma. **Results:** A total of 80 patients (40 patients in side A & 40 patients in side B) who have biopsy proven cervical carcinoma with no history of previous treatment were selected from the Department of radiotherapy Enam Medical College Hospital, Savar, Dhaka and in the department of Radiation Oncology, National Institute of Cancer Research & Hospital. All patients in both side received external beam radiation with 50Gy in 25 daily fractions over five weeks. Distribution of study population according to presence of symptoms. Bar chart showed distribution of study population according to presence of symptoms. Almost all the study population had presented with P/V watery discharge with pelvic pain. Majority of the patient presented with P/V bleeding, fever and anorexia. A significant symptomatic improvement was found in side-A, after treatment than side-B. Mildly increases in 2nd week of treatment then decline gradually. Overall treatment related toxicity was more in side-A than side-B. In Grade-I nausea/vomiting and skin reaction in Grade-II were more in side-A. Leukopenia and anaemia II also more in side-A Grade-I and II respectively. Data was analyzed by using chi-square test and result was not significant in nausea/vomiting and skin reaction and significant in leukopenia at p<0.05.

Conclusion: In this study it was observed that patients of carcinoma cervix treated with concurrent chemo radiotherapy was effective for symptomatic improvement and suitable with acceptable toxicity for advanced cancer of the uterine cervix than those with radiation only.

KEYWORDS: cervical cancer, radiation therapy, chemoradiation treatment, randomized trials.

I INTRODUCTION

Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 representing 6.6% of all female cancers. Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries. The high mortality rate from cervical cancer globally could be reduced through a comprehensive approach that includes prevention, early diagnosis, effective screening and treatment programmes. There are currently vaccines that protect against common cancer-causing types of human

papilloma virus and can significantly reduce the risk of cervical cancer (WHO 2018). It is the second-most common cause of female-specific cancer after breast cancer, accounting for around 8% of both total cancer cases and total cancer deaths in women (WHO 2014). About 80% of cervical cancers occur in developing countries.^[1] Most women present with locally advanced stage in developing countries compared with developed countries where most people present with early stage cancer.^[2] In developing and undeveloped countries, a much more severe prevalence of this malignancy is

associated with a generally worse economical and sanitary condition, lack of effective screening, as well as under implemented prevention strategy, where a lot of women were exposed to the risk of, or already affected by, high-risk CC, which remains a major health problem for women in these countries, though important advancement and progress has been witnessed in the last few years.^[3] Carcinoma of cervix is most common in Bangladeshi women comprising of about 25% of all female cancer.^[4] The disease usually occurs in women from a low socioeconomic background, similar to other developing countries of Latin America, Africa etc. Cancer of the cervix is also the commonest cause of cancer related mortality in women of India (age adjusted mortality of 4.3 per 100000 populations per year) and worldwide.^[5] Total number 2805 patients from July 2018 to June 2019 were treated at the department of Radiation Oncology, Enam Medical College Hospital, among them 760 patients were female and 138 patients that means 18.15% of the patients were suffered from carcinoma cervix (Radiotherapy OPD, EMCH 2018-2019). It is common knowledge that the most important cause of cervical cancer is persistent papilloma virus infection. The human papilloma virus (HPV) is detected in 99% of cervical tumors, in particular the oncogenic subtypes such as HPV 16 and 18. While Papanicolaou smears are used in the classical primary screening technique, HPV DNA testing, introduced in 2008, is well diffused in developed countries and is taking off in developing countries with a potentially significant reduction in the numbers of advanced cervical cancers and deaths.^[6] In the HPV vaccination era, we expect that the cervical cancer incidence had reduced, especially in those developed countries where large-scale immunization has been introduced. Most developed countries have introduced IIPV vaccines into routine vaccination programs and more than 60 million doses have already been distributed in 2010, which could guarantee a protection rate of 70%. However, cervical cancer 'still represents a major public health problem even in developed countries.^[7] The disease is extremely rare in virgins. The incidence is higher in married women than single women and increases with the number of pregnancies. There is a fivefold higher incidence among prostitutes. It is commoner in women of lower socioeconomic groups. This is thought to be due to the early age of first intercourse.^[8] Patients with the aforementioned characteristics are at higher risk of recurrence and generally have a shorter survival period. 4-8 primarily applied conventional treatment modality for high-risk CC is radiotherapy (RT) with or without hysterectomy; however. Inefficient local control and lymph node metastasis remain the major causes of treatment failure.^[9, 10, 11] Therefore, treatment strategy combining RT with chemotherapy has been evaluated in a lot of clinical trials, initially in several pilot studies published 15 years ago, most of which were randomized controlled trials (RCTs).^[12,13,8] In these trials, concurrent chemo radiotherapy (CCRT) was the experimental treatment mode most widely assessed. Chemotherapy, at

first, was applied exclusively as palliative care for patients with unfavorable prognosis.

II AIMS AND OBJECTIVE

1. To observe the change of signs, symptoms such - P/V discharge, P/V bleeding, Pelvic pain, Fever etc.

III METHODS AND MATERIALS

Type of study: Experimental study- Randomized Control Clinical Trail.

Place of study: The study had conducted in the Department of Radiation Oncology, Enam Medical College Hospital, Savar, Dhaka & in the department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh.

Period of study: July 2018 to June 2019.

Patient selection: Patients with carcinoma cervix attained at the Radiation Oncology Department of EMCH & NICRH during the study period had included in the study according to inclusion an exclusion criterion.

Inclusion Criteria

1. Patients- Clinically diagnosed and histologically proved squamous cell cervical carcinoma.
2. FIGO stage- Stage IIb to stage IVa.
3. Age group-Less than 60 years.
4. Performance status-Karnofsky performance status score > 60.

Exclusion Criteria

1. Patients- With prior treatment.
2. FIGO stage-Pre-invasive to some case of stage IIa and stage IVb.
3. Age group-More than 60 years.
4. Performance status-Karnofsky performance status score <60.

Study population

The patients who were clinically diagnosed and histologically proved carcinoma cervix (squamous cell carcinoma) attained in the OPD of Radiation Oncology Department EMCH & NICRH.)

Simple size calculation for two proportions: n=288

Data analysis: Data analysis was done according to the objectives of the study by using statistical package for social science software program. Statistical significance had taken at $p \leq 0.05$ by using chi-square test.

IV RESULTS

A total number of 80 patients with histological proved cervical carcinoma had selected randomly according to pre-defined inclusion and exclusion criteria and divided into two sides. 40 patients for Side-A (Study group) and 40 patients for Side-B (Control group) had treated by radiotherapy only with a radiation dose- 50 Gy in 25

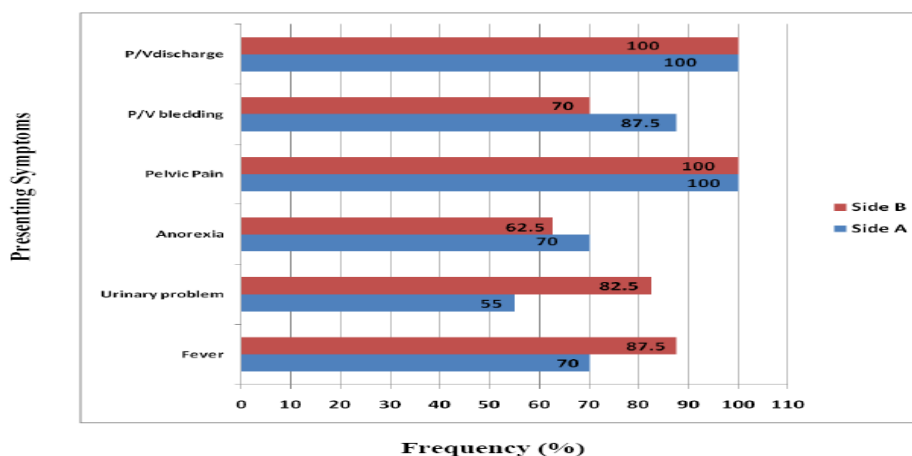
fractions, 2 Gy per day/ fraction, 5 days in a week for 5 weeks by LINAC machine (15 MV photon energy) in SSD & SAD technique, AP, PA, Rt LAT, Lt LAT portal (usually 4 field box) & ICRT-21Gy in 3 insertion, 7 Gy weekly insertion for 3 weeks. All the patients had received weekly till the completion of the treatment, all findings of the local and systemic examination had recorded and to compare with previous findings and had documented.

Table-1: Age distribution of the study of the study population (n=80)

| Sex | Frequency (%) | |
|------------|---------------|--------|
| | Side-A | Side-B |
| 20-30 Yrs. | 12.5 | 7.5 |
| 30-40 Yrs. | 30.0 | 37.5 |
| 40-50 Yrs. | 37.5 | 42.5 |
| 50-60 Yrs. | 20.0 | 12.5 |

Column chart showed the age distribution of the study population. The study populations had divided into 4 age groups. Age ranges from 20-60 years. The pick age incidence of cervical cancer had found in age groups of 40-50 years [Table-1].

Distribution of study population as per the presenting of symptoms (n=80)



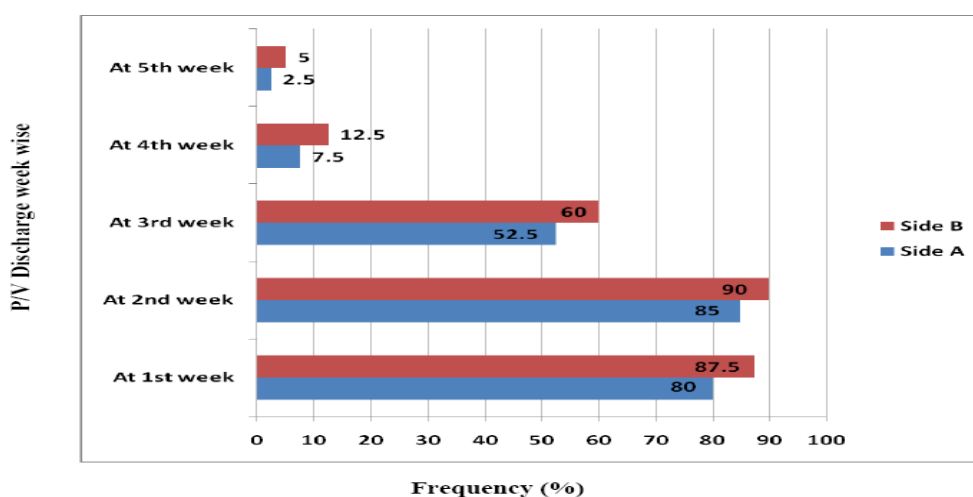
n=no of study population

Figure-1: Distribution of study population according to presence of symptoms (n=80).

Bar chart showed distribution of study population according to presence of symptoms. Bar chart showed distribution of study population according to presence of symptoms. Almost all the study population had presented

with P/V watery discharge with pelvic pain. Majority of the patient presented with P/V bleeding, fever and anorexia [Figure-1].

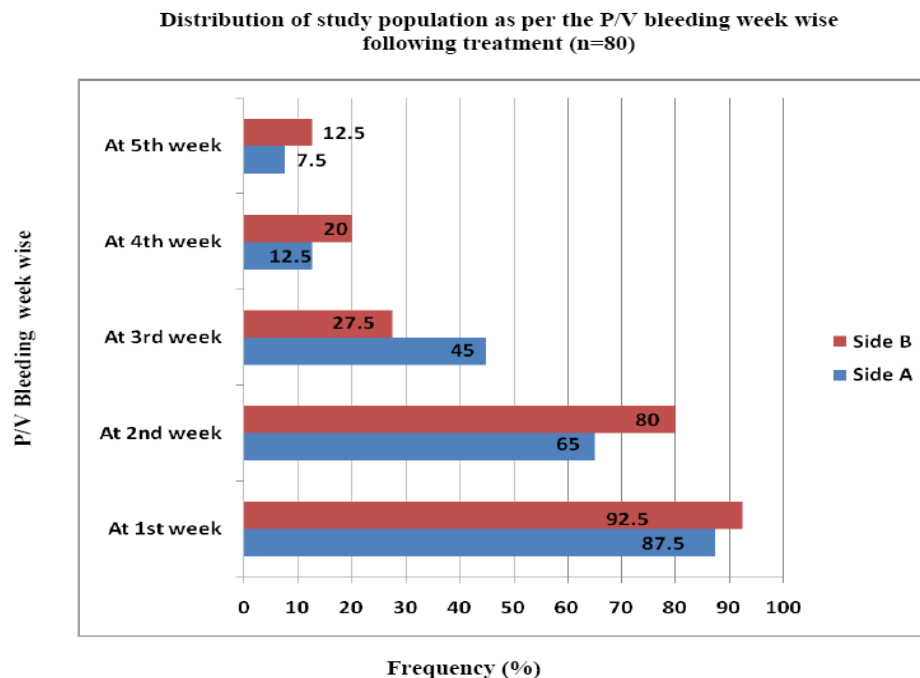
Distribution of study population as per the P/V Discharge week wise following treatment (n=80)



n=no of study population

Figure-2: Distribution of study population according to P/V discharge following treatment (n=80).

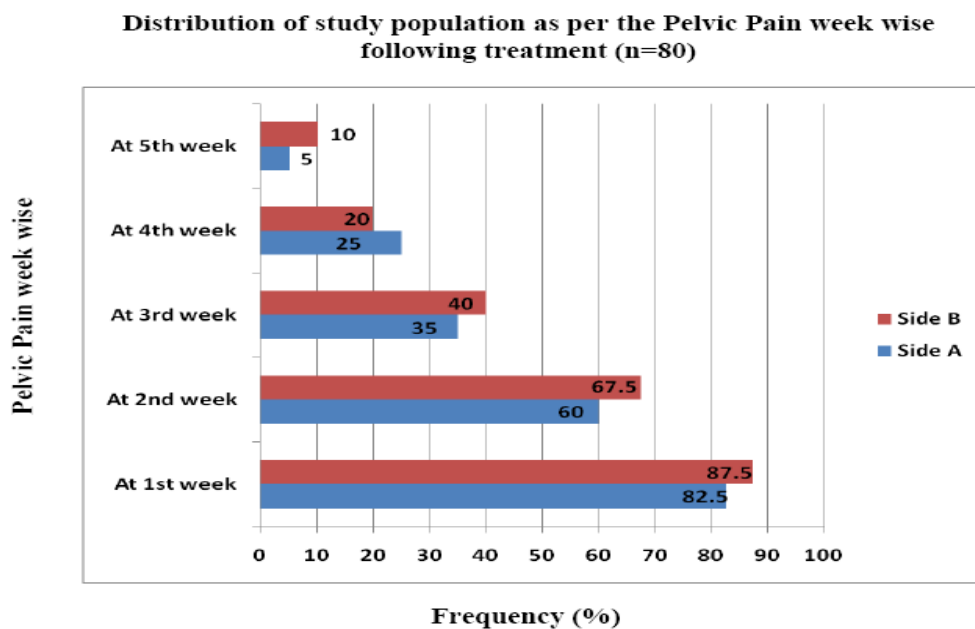
Bar chart showed discharge mildly increases in 2nd week of treatment then decline gradually [Figure-2].



n=no of study population

Figure-3: Distribution of study population according to P/V bleeding following treatment (n=80).

Bar chart showed P/V bleeding decline gradually following treatment [Figure-3].



n=no of study population

Figure-4: Distribution of study population according to pelvic pain following treatment (n=80).

Bar chart showed pelvic pain decline gradually following treatment [Figure-4].

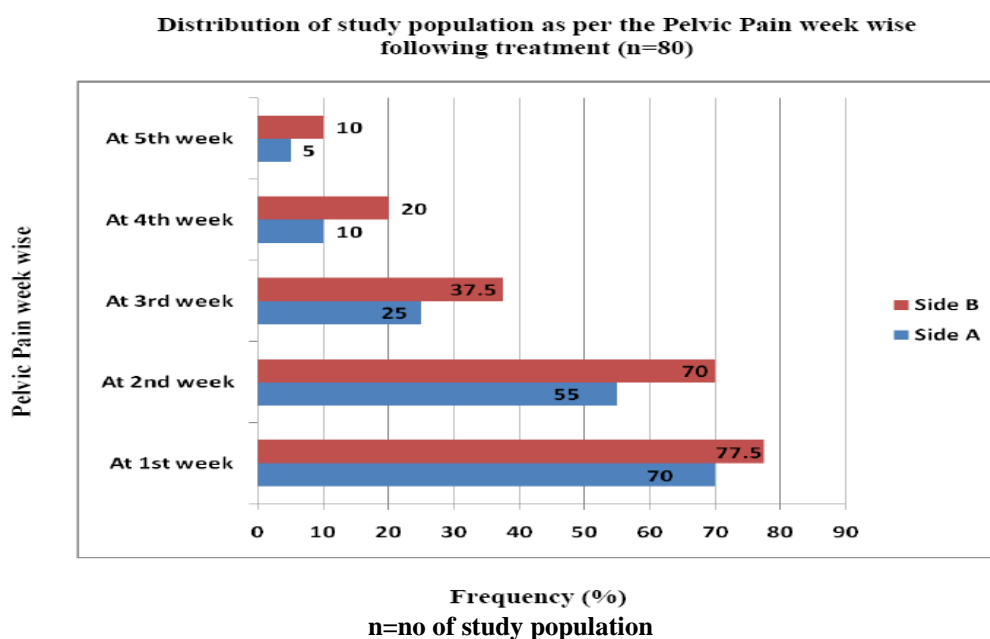


Figure-5: Distribution of study population according to fever following treatment (n=80).

Bar chart showed fever decline gradually following treatment [Figure-5].

A significant symptomatic improvement was found in side-A, after treatment than side-B [Figure-2, 3, 4, 5]. Overall treatment related toxicity was more in side-A than side-B. In Grade-I nausea/vomiting and skin reaction in Grade-II were more in side-A. Leukopenia and anaemia II also more in side-A Grade-I and II respectively. Data was analyzed by using chi-square test and result was not significant in nausea/vomiting and skin reaction and significant in leukopenia at $p < 0.05$.

V DISCUSSION

It was an empirical study done on patients with of carcinoma cervix attained at the Radiation Oncology Department of NICRH & EMCH during the study period. The pick age incidence of cervical cancer had found. Majority of the patients in this study were in age groups of 40-50 years in both sides (37.5% and 42.5% respectively). Bellow 30% of the cases were found in between 30-40 years in both sides and lesser number cases found in the age groups 20-30 years. A study by showed 51.1% cases had got chemo-radiation in between 41-50 years. So these observations were in conformity with that the present study.^[15] Most of the populations in both sides were in poor group followed by middle class. Studied had found that patients with low socioeconomic condition were at a higher risk of in-hospital mortality due to the cervical cancer.^[16] In this study more than 30% patient were belonged to illiterate, 45% to 50 % had primary education and bellow 5 patients have found to have HSC in both sides. Previous study found that quite a greater number of the interviewees who received chemo-radiation, 68.3% were literates, whereas the other 31.7% were illiterates. That was not largely different from reports of our studies.^[17] These clinical findings were almost similar with previous studies.^[18] A significant symptomatic improvement was found in side-A after treatment than side-B which was similar to

observations made in several other studies.^[19, 20] Overall treatment related toxicity was more in side-A than side-B. One GOG (Gynecologic Oncology Group) trial with weekly cisplatin combination radiation in IIB-IIB cervical cancer showed 5 years survival rate.^[21, 22, 8] Among the drugs used for chemotherapy in advanced CC, Cisplatin was one of the most effective agents.^[23] However, no significant benefits in favor of DDP-CCRT concerning survival outcomes and toxicity profile were revealed in two other studies.^[13] These differences might be attributed to different study designs, subjects enrolled, control settings, regimens used, and duration of follow-up. A meta-analysis summarized these pilot studies, which presented positive results and comments recognizing improved outcomes achieved by DDP-CCRT, as well as evident toxic effects possibly enhanced by treatment combination.^[23] However, the results of the meta-analysis showed that interventions for control groups were not totally consistent among the included studies.^[12, 13, 8] Without considering surgical treatment performed in two studies as part of the local interventions for both experimental and control arm^[24, 25], exclusive RT were set as control in four studies;^[12, 13] however in another two studies^[8], hydroxyurea, a widely used cytotoxic agent with antitumor-activity-targeting a variety of malignancies, was combined with RT as control group treatment. Afterward, several similar studies comparing DDP-CCRT with RT alone were conducted, with different results reported.^[14, 26, 27, 28, 29] Most recently, an RCT conducted in Brazil again evaluated the difference in treatment effects between DDP-CCRT and exclusive RT in advanced CC, using patients with International Federation of Gynecology and Obstetrics (FIGO) Stage III disease as the targeted population.^[26] With accumulated and updated data from relevant studies available for a new pooled analysis, we performed this study with refined design and analytical

methods to provide more definitive evidence for clinical guidance.

VI CONCLUSION

In this study it was observed that patients of carcinoma cervix treated with concurrent chemo radiotherapy was effective for symptomatic improvement and suitable with acceptable toxicity for advanced cancer of the uterine cervix than those with radiation only. Almost all the study population had presented with P/V watery discharge with pelvic pain. Majority of the patient presented with P/V bleeding, fever and anorexia. A significant symptomatic improvement was found in side-A, after treatment than side-B. Mildly increases in 2nd week of treatment then decline gradually.

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