



CLINICO-EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH GYNAECOLOGICAL MALIGNANCIES BEING FOLLOWED-UP AT A RADIATION ONCOLOGY DEPARTMENT OF A TERTIARY CARE GOVERNMENT INSTITUTE OF INDIA

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ABSTRACT **Background:** Gynaecological malignancies constitute a major burden of cancer-related morbidity and mortality amongst females in developing countries including India.

Aims and objectives: The study was conducted to study the clinical and morphological characteristics of patients having gynaecological malignancies and treated by radiotherapy with or without chemotherapy, now under follow-up.

Study design: A retrospective observational study in a tertiary care hospital of government set-up over 2 year period.

Observations: A total of 3120 patients who reported for follow-up were included, of which 394 patients were of gynaecological malignancies. Carcinoma (Ca) Cervix followed by Ca endometrium were the most common sites (76% and 16% respectively). The most common age group was 7th decade. 33% patients with locally advanced cervical cancer were found to have paraaortic lymphadenopathy on presentation warranting extended field radiotherapy (RT). 73% of locally advanced ca cervix patients received 5 or more cycles of weekly chemotherapy (CT) with Cisplatin. 68% patients were disease-free at the time of follow-up. 11% patients were referred for palliative chemotherapy. 17% patients required hospitalization for symptomatic care during followup.

Conclusion: Concurrent chemoradiation is an acceptable and well-tolerated modality of treatment for locally advanced gynaecological malignancies. Multimodal treatment and good collaboration between allied specialists is recommended.

KEYWORDS : Gynaecological malignancies, cancer cervix, radiotherapy (RT), chemoradiotherapy (CRT), toxicities

INTRODUCTION

Cancers of the female reproductive system is a heterogeneous spectrum of entities. Cervical, endometrial, and ovarian cancers are relatively common, and cause significant cancer morbidity and mortality worldwide, whereas vulvar, vaginal, fallopian tube cancers, and choriocarcinomas are very rare [1]. Worldwide among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer for incidence, and vice versa for mortality; cervical cancer ranks fourth for both incidence and mortality worldwide [2]. Gynecological cancers have increased in India and are estimated to be around 182,602 by the year 2020 constituting about 30% of the total cancers among women in India. Among these, cancers of the uterine cervix followed by ovary and corpus uteri are the major contributors [3]. Although cervical cancer is on a declining trend in India, it remains the second most common cancer in women after breast cancer. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from this disease [4].

METHODOLOGY

It was a retrospective observational study where the electronic medical records, medical documents, Radiotherapy treatment charts and allied specialist's notes of female patients with gynaecological malignancies previously treated with radiotherapy (RT) or concurrent chemoradiotherapy (CRT) and now reporting for review were retrieved and studied. All patients were initially worked up as per NCCN guidelines and FIGO staging system wherever indicated including detailed history, general physical examination, gynaecological examination, biopsy of malignant lesion, locoregional imaging, routine hemogram and biochemistry and metastatic workup. The patients who were deemed fit for CRT were treated by external radiotherapy 45-50 Gy at 180-200 cGy per fraction 05 days a week over 05 weeks along with concurrent chemotherapy with Inj Cisplatin 40 mg/m² subjected to tolerance and renal function tests; followed by HDR brachytherapy 07 Gy for 03 fractions. The patients were reviewed weekly during CRT and thereafter, they were followed up 03 monthly during initial 02 years and 06 monthly during another 02 years and annually thereafter. While reporting for follow-up, the patients underwent local and systemic clinical examination, lab studies, Pap smear and imaging as deemed necessary. All pertinent findings were noted in the outdoor case sheets and symptomatic

treatment and further oncological management was recommended as indicated. Those meriting supportive care as indoor patient were admitted for further evaluation and therapeutic interventions.

OBSERVATIONS AND RESULTS

A total of 3120 patients reported for followup in the OPD during the study period including 1810 males and 1310 females; of which 394 patients were of gynaecological malignancies, forming approximately 12.6% of total cases. Out of these 394 patients, 298 patients (76%) had cancer cervix, 64 had cancer endometrium (16%), 24 had carcinoma of vagina/vaginal vault (6%) and 8 patients (2%) were uncommon variants. The age-wise distribution is as given in Table-1, the most common age group was 7th decade followed by 6th decade, as seen in 33% and 24% patients respectively.

Table-1: Age-wise distribution (n=394)

Sr No	Age-group	Number of patients	Percentage (n=394)
1	< 30 years	5	1
2	30-40 years	20	5
3	40-50 years	56	14
4	50-60 years	94	24
5	60-70 years	129	33
6	70-80 years	82	21
7	> 80 years	8	2

Moderately differentiated squamous cell carcinoma was the most common histopathology of the primary site, seen in about 68% of cancer cervix cases. The shortest time of follow-up post completion of treatment was 06 weeks and longest was 64 months, average being 14 months. 99 patients with locally advanced cervical cancer were found to have paraaortic lymphadenopathy (PALN) on imaging studies during initial workup, forming about 33% of total cervix cases. These patients received extended field RT along with concurrent CT. 267 patients (68% of gynaecological malignancies) were disease-free at the time of follow-up, while the rest (32%) had residual disease, locoregional recurrence, paraaortic nodal metastasis and other sites of distant metastases. 42 patients (11%) were referred for palliative CT.

67/394 patients (17%) were admitted for management of complications, distribution of which is given in Table-2. Among these

patients meriting hospitalization, 36 patients (54% of total admitted patients) were elderly female over 60 years. In our study, 14 patients developed Grade III or more radiation cystitis, most of whom responded well to conservative management including bladder irrigation and hyperbaric oxygen therapy, but warranted intermittent admissions. **In our study, 218 patients of locally advanced ca cervix (73% of all cervix cases) were planned for Cisplatin based weekly CT subjected to renal parameters and general performance status.**

Table-2: Indications for hospitalization while on follow-up

Sr No	Indication of hospitalization	Number of patients
1	Generalized weaken// cachexia	13
2	Hematological toxicities	12
3	Radiation cystitis	14
4	Radiation proctitis	6
5	Delayed enteritis	6
6	Renal complications	8
7	Others (fever, medical comorbid conditions, dyselectrolytemia etc)	9

DISCUSSION

Cervical cancer (Ca Cx) is the second most fatal cancer contributing to 14% of all cancers in Indian females, which account for 25.4% and 26.5% of the global burden of CaCx prevalence and mortality, respectively [5]. In view of paucity of uniform treatment protocols for various stages of cervical cancer in India and the need to optimize treatment paradigms for the Indian population, three expert panel meetings of 15 oncologists from various allied subspecialties were held in different regions of India from 2016 to 2017. The panel concluded that a uniform, multi-disciplinary treatment approach across patient care centers is ideal but not realistic due to cost implications specially in absence of robust insurance schemes. Preventative strategies including visual inspection with acetic acid to screen for precursor lesions (i.e., cervical intraepithelial neoplasia) with immediate referral for cervical cryotherapy and possible large-scale roll-out of the HPV vaccine in the near future can be expected to reduce mortality rates significantly in this country [6].

In our study, carcinoma endometrium was the second most common gynaecological cancer after cervical cancer treated by external RT and/or vault brachytherapy, constituting 16% of the followed-up gynaecological cancers. Carcinoma endometrium is the most common gynecological malignancy in the developed countries. In developing countries, cervical cancer still remains the leading cause of gynecological cancers, but there is a recent increase in the incidence of endometrial cancer. The age standardized incidence rate of endometrial cancer in India is 2.1/100,000 women. About 12,335 cases are diagnosed every year and 4773 cases die of this malignancy. The declining incidence of cervical cancer and the predicted rise of endometrial cancer mean that endometrial cancer will be a significant issue in India. The rise is mainly attributed to the changing trends in the lifestyle and reproductive profile of women especially in urban areas [7,8].

In our study, 67 patients were admitted for management of complications, of which 54% patients were elderly female over 60 years. Wang YM et al., [9] evaluated the differences in the treatment outcomes and complications between elderly patients and younger patients with uterine cervical cancer who underwent definitive RT/CTRT. The overall survival (OS), cancer-specific survival (CSS), local failure (LF), distant failure (DF), late proctitis, and cystitis were compared between the age groups. In this study; there was a significant difference in the 5-year overall survival between the Elderly and Young groups. Significant differences between the Elderly and Young groups were observed in the 5-year cumulative grade 2 proctitis (39.7% and 17.2%, respectively; $p=0.015$) and grade 3 proctitis (18.1% and 6.2%, respectively; $p=0.040$). The authors concluded that elderly patients tended to have higher radiation-related proctitis than younger patients.

In our study, 33% of patients with locally advanced cervical cancer were found to have PALN on imaging studies at presentation, of which 30% later metastasized or had locoregional recurrence. PALN metastases affect around 20% of all stage IB2–IVA, although other studies claim considerably higher rates up to 40% [10]. Masaharu H et al., [11] evaluated the efficacy of radiation therapy for PALN metastases from uterine cervical cancer and attempted to identify an optimal radiation regimen. The 3-year lymph node progression-free

rates were 78% in the cohort of 22 patients and 89% considering all 80 metastatic lymph. The authors concluded that RT can effectively control PALN metastases in patients with uterine cervical cancer. A total dose of 50.4 Gy in 1.8 Gy fractions is sufficient to control metastatic lymph nodes ≤ 25 mm in diameter, whereas a higher dose (approximately 55.8 Gy) may be required for larger nodes.

In our study, 14 patients (4.7% of total cervix cases treated) developed Grade III or more radiation cystitis, most of whom responded well to conservative management including bladder irrigation and hyperbaric oxygen therapy, but warranted intermittent admissions. Radiation cystitis is a recognised complication of pelvic radiotherapy. Incidence of radiation cystitis ranges from 23 to 80% and the incidence of severe haematuria ranges from 5 to 8%. Treatment modalities are subclassified into systemic therapies, intravesical therapies, and hyperbaric oxygen and interventional procedures. Ultimately, most patients require multimodal treatment for curative purposes [12]. Barua SK et al; [13] retrospective studied cervical cancer patients with intractable haematuria due to radiation cystitis. Irrigation with 0.9% saline, hem coagulase and subsequently 1% alum irrigation were given. Of the 34 patients 20 (64.51%) patients showed complete response, 4 (12.9%) patients showed partial response and 7 (22.58%) patients had no response to alum irrigation and cystoscopic fulguration were done in these cases. The authors concluded that no standard of care therapy is presently available for such patients; and 1% alum irrigation is safe and efficacious for these patients although normal renal function is a prerequisite.

In 1999, the National Cancer Institute mailed a clinical announcement to thousands of physicians stating that strong consideration would be given to adding chemotherapy to radiation in the treatment of invasive cervical cancer based on the results of five randomized clinical trials [14]. **In our study, 73% patients of locally advanced ca cervix were offered Cisplatin based weekly chemotherapy.** In a phase 3 open-label randomized clinical trial of 850 women in Mumbai, India, with FIGO stage IIIB squamous cell carcinoma of the uterine cervix suitable for concurrent cisplatin chemotherapy were randomly assigned to CTRT and RT only arms. Five-year disease-free and overall survival was significantly higher for women who received CTRT vs those who received RT alone. This study provided level 1 evidence in the largest clinical trial reported so far in favor of concurrent weekly cisplatin based CT in this setting [15].

SHORTCOMINGS OF THE STUDY

The main shortcomings of this study were that it included patients of gynaecological cancers reporting for follow-up in a single Radiotherapy OPD of a hospital over two year period. The data could not be collated with that from allied Oncological specialties due to technical reasons. Details of the patients who were lost to follow-up or who died due to disease/medical comorbidities was not included.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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