

## A profile of cervical cancer cases in a government medical college hospital

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### **Abstract:**

**Aim:** This is a retrospective profile of new cases of Carcinoma Cervix who presented at the Department of Radiotherapy, Dr.S.N.Medical College, Jodhpur in 2014.

**Methods:** Two hundred and four cases of carcinoma cervix were registered. Detailed clinical examination, history and relevant investigations were undertaken. Staging was by FIGO criteria.150 patients were treated with a curative intent with radical dose of radiation as per the department protocol i.e. both EBRT (with Inj. Cisplatin 40 mg/m<sup>2</sup> weekly) plus Brachytherapy.8 patients received palliative treatment.

**Result:** Most patients were from rural background, mostly in 40-60 year old age group and presented in locally advanced stages.80.67% of patients completed their intended treatment. Disease response (87% overall response) and toxicity were within acceptable limits.

**Conclusion:** Treatment of this common female malignancy was provided at negligible cost to the patient. Increased awareness, HPV vaccination and screening would lead to decrease in incidence of this disease and the trend of late presentation at locally advanced stages.

**Keywords:** Cancer cervix, Locally-advanced, Chemo-Radiation, Tele-cobalt Therapy, Brachytherapy,

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### **I. Introduction**

Cervical cancer is the fourth most common cancer in women worldwide with an estimated 528,000 new cases diagnosed in 2012. South-East Asia contributes to around 175,000 cases of this global burden. About 122,844 new cervical cancer cases are diagnosed annually in India (estimations for 2012). India has a population of 432.2 million women aged 15 years and older who are at risk of developing cancer. Cervical cancer ranks as the 2nd cause of female cancer in India <sup>[1][2]</sup>.

Most cancer cervix cases in India are diagnosed at advanced stages when overall prognosis is poor. The high burden load and the late presentation of this disease can be attributed to various factors like early age of first intercourse, multiple sexual partners, unprotected sex and sex with uncircumcised men, smoking, oral contraceptive use, high parity, and infection with other STDs. Lack of awareness regarding the disease, low educational and socio-economic status, insufficient screening and the tendency to not report to the doctor until significant symptoms arise all lead to cervical cancer presenting in advanced stages <sup>[3]</sup>.

Cervical carcinoma (11.07% of all cancer cases presenting at our department in the year 2014) was the second most common cause of female cancer presenting at the Department of Radiotherapy, Dr. S.N. Medical College, Jodhpur, Rajasthan. Overall it was the third most common cancer after Head and Neck malignancies (52.4%) and Breast cancer (14.5%).

### **II. Materials and methods**

It is a retrospective study conducted from January 2014 to December 2014. During this period, 204 (two hundred and fourteen) biopsy proven cases of carcinoma cervix were registered. 36 patients were post-operative and had been referred to our department for further management. Out of the 204 patients, 150 underwent radiotherapy (teletherapy/ brachytherapy) at our department. 8 patients presented with systematic disease. 46 did not avail any treatment at our department. Pre-treatment evaluation and clinical examination including detailed history along with patient's general, systemic and local examination was done. Laboratory investigations included Complete Blood Counts, Blood Urea, Serum Creatinine, Liver Function Tests (LFT) and Serum Electrolytes. Chest X-Rays and Abdominal Ultrasounds were routinely obtained. Cystoscopy and proctoscopy were performed wherever indicated. CT Scan/MRI was optional. Patients were treated according to the stage of the disease or as per post-operative status.

For those receiving definitive radiation, the treatment was 50Gy to the whole pelvis in 25 fractions over a period of 5 weeks (Monday to Friday of every week) using a Cobalt-60 machine (Theratron780 E) at a source-skin distance of 80 cm by parallel opposing antero-posterior and postero-anterior fields. The upper margin of the External Beam Radiotherapy (EBRT) port was the L4-L5 junction and the lower margin was 2 cm below the

bottom edges of lesions. Lateral margins were 1.5 cm lateral to the bony pelvis. Parametrial boost with midline shielding was as per case basis. Patients received injection Cisplatin 40mg/m<sup>2</sup> intravenous weekly for a total of six courses.

After completion of external beam radiotherapy (EBRT), all the cases were examined for fitness for brachytherapy. This consisted of three fractions (7.5Gy each) of High Dose Rate-Intra Cavitory Radiotherapy (HDR-ICRT) with a 5 to 7 days interval between fractions. Applicator insertion was done under conscious intravenous sedation. The vagina was packed with Povidone Iodine-soaked gauze packs to push the bladder and rectum away and to stabilize the applicator. A Foley's catheter was inserted and the balloon was inflated with 7cc of diluted Urograffin to allow identification of the bladder neck region. A rectal marker was inserted in to rectum to visualize the rectal mucosa for rectal points. After applicator insertion, AP and lateral orthogonal marker X-Ray films were taken for dosimetry. Planning was done with the help of HDR Plus Version 2.5.3 treatment planning system. The dose was prescribed to point A. Bladder and rectal reference points were delineated as per the recommendations given in Report 38 of the International Commission for Radiation Units (ICRU). Dose delivered was 22.5Gy to point A in three fractions (per fraction dose was 7.5Gy). Bladder and treatment was delivered rectal doses were limited to 80% of the prescribed point A dose as per the ICRU 38 recommendations<sup>[4]</sup>. Brachytherapy was by HDR remote afterloading unit which used Cobalt-60 (Multisource HDR Brachytherapy, Bebig). The Fletcher suit applicator was used in all patients.

For the post-operative cases, adjuvant radiotherapy (with/without chemotherapy) was based on findings like positive margins, parametrial infiltration, and involvement of pelvic nodes, presence of Lympho Vascular Space Invasion, stromal invasion and size of tumor. For these cases, brachytherapy was considered as per criteria and guidelines given by American Brachytherapy Society<sup>[5]</sup><sup>[6]</sup>. 3 fractions of 5Gy each with dose prescribed to vaginal mucosal surface or at 0.5cm depth was the Departmental Protocol for Post-Operative Brachytherapy.

Patients receiving radiotherapy were assessed weekly for local disease response & development of any acute skin or mucosal reactions, bladder and bowel symptoms. Hematological & Renal function test was evaluated weekly during treatment. Response was evaluated by WHO CRITERIA<sup>[7]</sup>. Grading of normal tissue reactions was done by RTOG (Radiation therapy oncology group) criteria<sup>[8]</sup>.

Patients were evaluated at 1<sup>st</sup> and 3<sup>rd</sup> month after completion of treatment and at 3 monthly intervals subsequently for local disease response, any bladder / bowel symptoms. Hematological & Renal function test were profiled during these follow up visits.

Radiotherapy i.e. both Teletherapy and Brachytherapy in the Department was provided free of cost. Chemotherapeutic agents like Cisplatin and Paclitaxel, basic Laboratory (CBC, LFT, RFT, Serum Electrolytes) and Radiological Investigations (X-Rays and Ultrasonography) were also available free of cost at the Hospital. Weekly Cisplatin injection was administered at our Day Care facility during concurrent Chemo-Radiation treatment. Indoor facilities were available for patients requiring ward care.

### III. Results

The majority of patients were from the 41 – 50 year age group (28.48%) closely followed by those in the 51-60 and 31-40 years age group, attributing to 27.8% and 25.9% of the patients, respectively. 79% of the patients were Hindus, 14.55% Sikhs and 5.7% were Muslims. Majority of the patients were from rural background (85%) and a significant proportion of patients especially those of the elderly age group were illiterate.

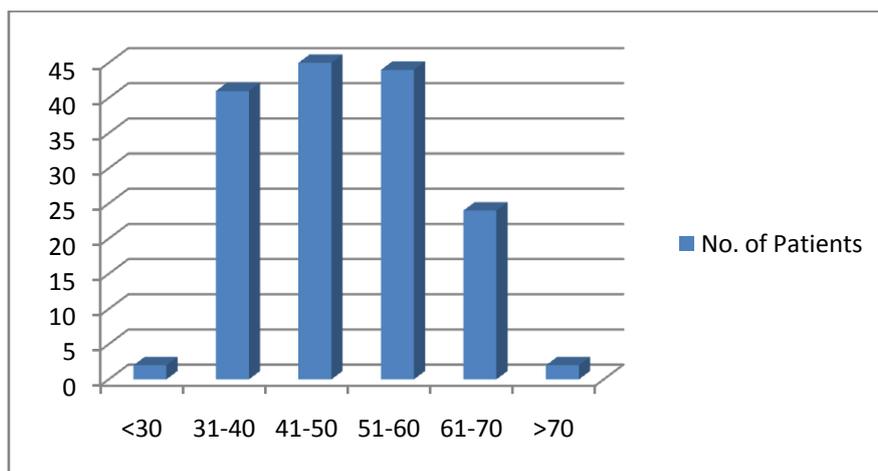


Fig.1. Age Distribution

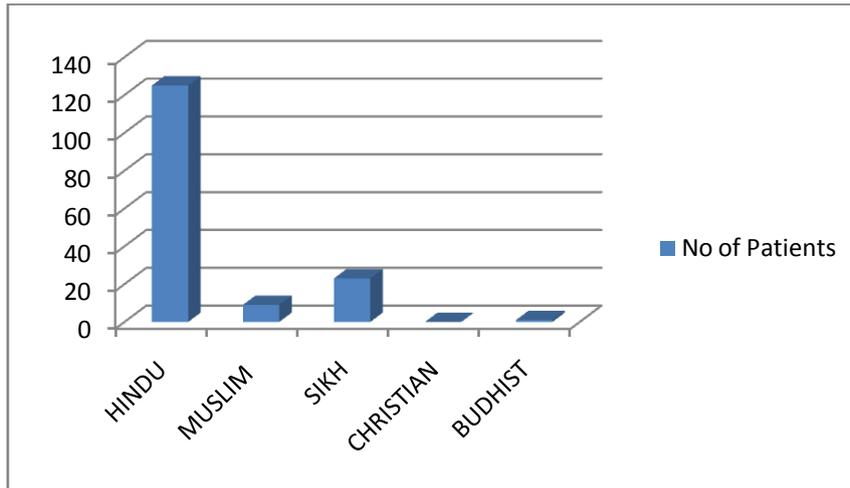


Fig.2. Distribution of patients according to religion

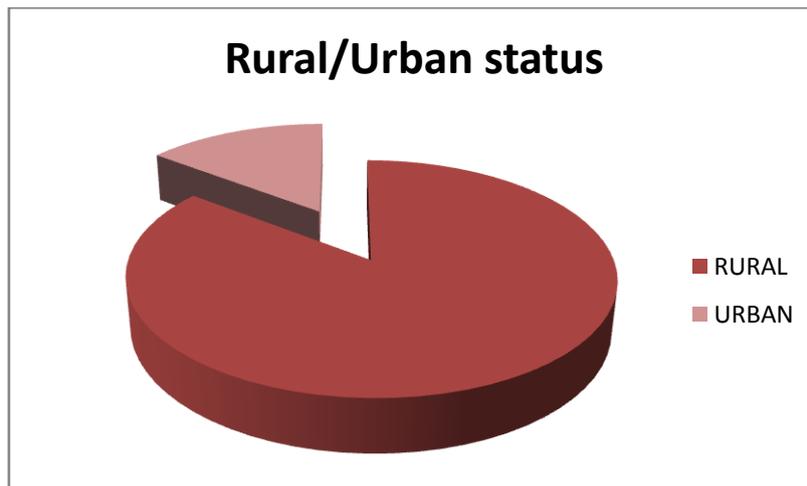


Fig.3. Rural and urban status

Of the 150 cases who received radiotherapy in our department, 36 patients had undergone hysterectomy before reporting to our department and prior staging was available for only 2 of these cases. An overwhelming number of patients presented with FIGO Stage IIIB (40.9%) and Stage IIB (35.24%) disease. 7.3% of patients were of Stage IB and 6.5% were Stage IIA. No patient reported with Stage IA disease. There were 8 cases that presented with distant metastasis (FIGO Stage IVB) and were treated with systemic chemotherapy.

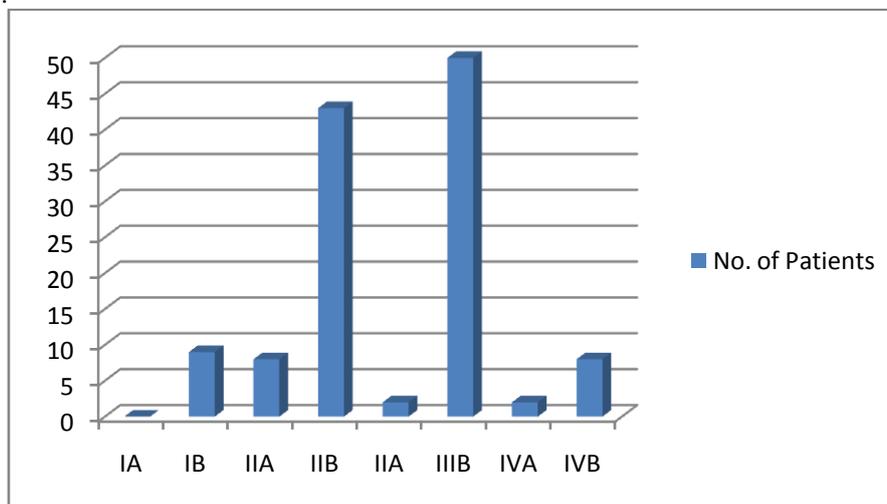


Fig.4. FIGO Stage at presentation

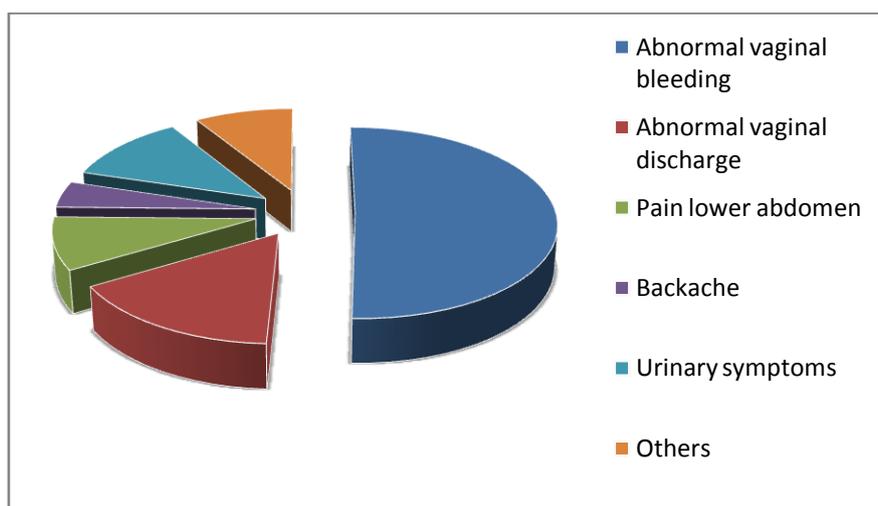


Fig.5. Presenting Complaints

Most of the patients had abnormal vaginal bleeding (51%) as the presenting complaint, followed by abnormal vaginal discharge (16%), urinary symptoms (11%), abdominal pain (9%), and backache (4%). Few patients included generalized weakness, loss of appetite and weight loss among their complaints. At the starting of treatment, 86% of patients had a Performance Score of 1 and 14% had a Performance Score of 2 as per Eastern Cooperative Oncology Group (ECOG) scale.

Hemoglobin (gm %)	No. of Patients	Percentage
<10	70	44%
10 - 12	46	29%
> 12	42	27%
Total	158	100%

Table 1 shows the hemoglobin distribution of patients in gm%

Regarding histology of the disease, 93% were squamous cell carcinoma (well differentiated 20%, moderately differentiated 48% and poorly differentiated 25%), adenocarcinoma constituted 4%, there was one case each of adenosquamous and small cell carcinoma cervix.

6 patients out of the 150 did not complete their intended schedule of External Beam Radiotherapy (EBRT). Regarding Brachytherapy, 5 cases were not considered fit for the intra-cavitary application process. 10 patients refused or did not come for the process. 8 patients did not complete all the intended fractions of Brachytherapy. 121 (80.67%) of the 150 patients completed the intended treatment. 46 (22.1%) patients who were registered as biopsy proven cases of carcinoma cervix either did not complete pre-treatment evaluation or pursue the treatment advised to them. There were cases 8 (3.8%) cases that presented with systemic metastasis and were treated with palliative intent. This study was a profile of new cases of carcinoma cervix presenting to our Department in the year 2014 and therefore we have not included those patients who had been treated earlier at our department/other centre and were now presenting with local or systemic failure.

Disease local response was as follows. By end of 2<sup>nd</sup> week of radiotherapy, 37% of patients had Partial Response (PR), 63% had Stable Disease (SD). By 5<sup>th</sup> week, 84% had PR, 16% had SD. At end of treatment (after brachytherapy), 19% had Complete Response (CR), 65% had PR and 16% had SD. At 1 month follow up, 57% had CR, 31% PR and 12% SD. At 3 months, 69% had CR, 19% PR and 8% SD. At 6 months, 72% had CR, 15% PR and 8% SD. So, overall response at 6 months was 87%.

Regarding Skin reactions during Radiotherapy, 6% of patients developed Grade 1 skin toxicity by the end of 2<sup>nd</sup> week. By 5<sup>th</sup> week, 38% had Grade 1, 48% had Grade 2 and 12% had Grade 3 skin reactions. At 3 months post radiotherapy, skin reactions had subsided to 28% Grade 1 reactions. By 6 months, no patient had any recognizable skin reactions.

Grade 1 diarrhea developed in 20% of patients by end of 2<sup>nd</sup> week of radiotherapy. . By 5<sup>th</sup> week, 32% had Grade 1, 8% had Grade 2 and 4% had Grade 3 diarrhea. At 3 months post radiotherapy, diarrhea had subsided to 4% Grade 1 and no patient in higher grades. By 6 months, no patient had diarrheal symptoms.

No patient developed Grade 4 toxicity during treatment or in the follow up period. Cisplatin related nausea and vomiting, hematological toxicity and nephrotoxicity were within acceptable limits.

#### **IV. Discussion**

Cervical cancer is one of the most common cancers among women worldwide. The prevalence and burden of cervical cancer is much higher among women of low Socio Economic Status and among rural women in India. This is also reflected in our study where 85% of patients belonged to rural backgrounds. A significant percentage of our patients were of lower income group and illiterate. Lack of access to screening and health services, and lack of awareness of the risk factors of cervical cancer are the problems faced by such women. HPV infection and precancerous lesions go unnoticed and develop into full blown cancer before women realize they need to go for medical help. Moreover, due to difficulties of access and affordability, compliance to, and follow up of, treatment is much worse for women of low Socio Economic Status, leading to further morbidity and mortality from the disease<sup>[3]</sup>. A huge proportion of our patients presented in the Locally Advanced Stages (79%).

70 (44%) of our patients had presented with hemoglobin levels (Hb) <10gm%. 29% of patients had Hb levels between 10-12gm% and 27% had levels >12gm%. Dunst et al.<sup>[9]</sup> showed that pretreatment anemia had a significant impact on 3-year relapse rates (6% in 20 patients with Hb of >13 g/dL, 15% in 47 with Hb between 11 and 13 g/dL, and 67% in 20 with Hb of <11 g/dL). The 3-year survival rate was 38% in patients with poorly oxygenated tumors, compared to 68% in patients with higher Po<sub>2</sub> (p = .02). Munstedt et al.,<sup>[10]</sup> in a study of 183 patients who received adjuvant RT after radical surgery, noted that those with Hb of <11 g/dL had lower recurrence-free and overall survival rates, primarily in a subgroup of women who had inadequate surgery.

The average time of completion of radiotherapy was 57.64 days, with maximum 81 days and minimum 43 days. Several studies described lower pelvic tumor control and survival rates in invasive carcinoma of the uterine cervix when the overall time in a course of irradiation is prolonged<sup>[11][12]</sup>. Chatani et al.,<sup>[13]</sup> in 216 patients with stage IIB to III cervical carcinoma treated with a combination of external-beam and HDR brachytherapy, noted that overall treatment time was the most highly significant factor for local tumor control in multivariate analysis (p = .0005). For relapse-free survival, stage classification (p = .0001), overall treatment time (p = .0035), and hemoglobin level (p = .0174) were the three most important prognostic factors; there was no relationship between treatment time and late complications.

The primary treatment for early-stage cervical cancer is either surgery or radiation therapy (RT). Both these modalities have equivalent results in early stage disease<sup>[14]</sup>. For locally advanced stages, concurrent chemo-radiation is the treatment of choice as per recent guidelines. The result of five randomized studies which included nearly 2,000 patients were published in 1999, demonstrating that survival rate with concomitant chemotherapy based on cisplatin was superior to that obtained with radiation alone<sup>[15-19]</sup>. Afterwards, a meta-analysis based on 19 trials (17 published and two unpublished) including 4,580 patients corroborated these findings, confirming that chemoradiation offers an absolute survival benefit of 12% at 5 years<sup>[20]</sup>. Thus, cisplatin-based chemoradiation was largely accepted as the standard of care for patients with cervical cancer whose treatment required radiation, except for patients with co-morbidities who are radiated for stage IB1 or less. For early stages (FIGO Stage IA<sub>1</sub>, IA<sub>2</sub> and IB<sub>1</sub> with tumor size <2cm) fertility sparing procedures can be given for those wishing so. These include cone excision, radical trachelectomy and pelvic lymph node dissection. When fertility is not an issue, Stage IA<sub>1</sub> can be managed by cone excision, simple or modified radical hysterectomy and pelvic lymph node dissection. Radical hysterectomy and bilateral pelvic node dissection is the preferred surgical approach for FIGO Stage IA<sub>2</sub> to IIA. Radical hysterectomy is preferred over simple hysterectomy because of its wider margins of resection that includes aspects of cardinal and uterosacral ligaments, upper vagina, and pelvic nodes. Adjuvant radiotherapy (with/without chemotherapy) is based on findings like positive margins, parametrial infiltration, and involvement of pelvic nodes and Sedlis criteria (presence of Lympho Vascular Space Invasion, stromal invasion and size of tumor). Alternatively these patients can be managed by definitive radiotherapy (with concurrent chemotherapy for IB and IIA patients). For those with FIGO stage IIB or greater cancers definitive chemo-radiation is preferred over radical surgery<sup>[21]</sup>.

Among the post-operative cases (36 in total) who presented to our department, 14 had undergone a Wertheim's procedure and pre-operative staging was available for only 2 patients. Details of the surgical procedure and histo-pathology report findings were considered for adjuvant radiotherapy.

#### **V. Conclusion**

We were able to achieve good local response with acceptable toxicity levels during the treatment which was provided at negligible costs to our patients, the majority of whom came from poor rural backgrounds. It is hoped that with increased awareness of the disease, screening programs and HPV (Human Papilloma Virus) vaccination services, there will be a decrease in the incidence of this disease and the trend of late presentation at locally advanced stages. Effective counseling of patients and relatives about the disease and treatment modalities/associated complications before, during and after treatment would lead to a decrease in the number of defaulters and those lost during follow up.

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