

## ORIGINAL ARTICLE

# Carcinoma Uterine Cervix: Evolving trends and Impact of National Cancer Control Program in India

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### Abstract

**Background:** Globally, cervical cancer is third most common type of cancer after breast and lung cancers among women. In this study, patients treated in 1977, 1997 and 2006 were taken into consideration and data were analysed to see the changes in clinic-pathological profile of the patients over period of time.

**Methods:** This study comprised of 61, 62 and 66 histologically proven patients of carcinoma cervix seen and treated in 1977, 1997 and 2007 respectively in Department of Radiotherapy and Oncology, Christian Medical College, Ludhiana. A detailed analysis was carried out to see the change in demographic profile of the patients, change in treatment modalities and change in treatment related complications.

**Results:** The urban women attendance was increased over years. Premenopausal women percentage was increased from 36% in 1977 to 50% in 2006. Most of the patients were in age-group less than 60 years from 60% to 75%. Mean parity was 5.86, 4.32, 3.62 in 1977, 1997 and 2006 respectively. In early years, patients were presenting in late stages and surgery was not possible in locally advanced cases. Rate of hysterectomy increased from 5% in 1977 to 20% in 2006 due to early presentation. Patients were treated with teletherapy and brachytherapy in 85% and 83% of cases in 1997 and 2006 respectively. In the year 2006, 72% of the cases were treated with chemoradiotherapy. Urinary and rectal complications were decreased from 1997 to 2006 whereas hematological toxicities were increased from 5% in 1997 to 16% in 2006. Patient 5 year survival was 62% in 1997 to 87% in 2006 and follow up was improved significantly over time.

**Conclusions:** The results of this sample study agree with the national data showing down staging and receding prevalence rate. The awareness amongst population about early diagnosis urges us to pass this message to doctors especially gynaecologists and surgeons for the need of judicious application of combined modality treatment in carcinoma cervix in our set up.

**Keywords:** Cervical Cancer, National Cancer Control Program, Evolving trends

### Introduction

Malignant neoplasms remain a leading cause of death worldwide [1]. Globally cervical cancer

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is third most common type of cancer after breast and lung cancers among women [2]. The global burden of cervical cancer is disproportionately high among the developing countries where 85% of the estimated 493,000 new cases and 273,000 deaths occur worldwide [3]. India, which accounts for one sixth of the world's population, also bears one fifth of World's burden of cervical cancer [4]. Over the past 40 years mortality from carcinoma of the cervix has fallen due to improved treatment and the introduction of national screening programs [5].

The treatment of patients with cervical cancer has changed significantly over the last few years. Various new therapeutic options are applied according to tumor stage. Patients with disease of limited volume usually undergo radical hysterectomy [6]. For patients with locally advanced disease, radiotherapy including external pelvic irradiation and brachytherapy has been the standard treatment for several years [7]. More recently, concurrent chemoradiotherapy has become the treatment of choice for the patients with locally advanced cervical cancer and has produced promising results in terms of survival. Neoadjuvant chemotherapy followed by radical surgery has been suggested as an alternative to irradiation [8]. The main reasons for poor survival are inadequate pelvic control and higher incidence of extra pelvic spread as the disease stage progresses [9].

NCI's (National Cancer Institute) Clinical Trials Cooperative Group [10] carried the studies enrolling several hundred women at various stages of the disease, including bulky IB and stages IIB through IVA. NCI's clinical announcement, 1999 [11] states that although

the best chemotherapy regimen for the cervical cancer has not been determined, "Significant results were seen using cisplatin alone or in combination with 5-FU and other agents".

In our set up, bulk of patients (60-70%) belongs to stage III and IV, the real challenge is to achieve loco-regional control. The National Cancer Control Program (NCCP) was launched in 1975-76 with the objectives of primary prevention, early detection, treatment and rehabilitation. During that time, Radical radiotherapy was treatment of choice with or without brachytherapy. This assessment was done to see various aspects related to cervical cancer before implementation of NCCP in India and after 20 years and 30 years to see change in demographic and clinicopathological profile of the patients. This was also to see the impact of NCCP in India based change in various factors.

### **Material and methods**

This study comprised of 61, 62, and 66 histologically proven patients on cervical carcinoma cervix seen and treated in 1977, 1997 and 2006 respectively in department of Radiotherapy and Oncology, Christian Medical College, Ludhiana. A detailed analysis was carried out to see the change in demographic profile of the patients, change in treatment modalities and change in treatment related complications.

These patients have either undergone surgery followed by radiotherapy (EBRT + IVRA) or if locally advanced were treated with radiation alone or with chemoradiotherapy. Radiotherapy was delivered in the form of External Beam Radiotherapy (EBRT) to pelvis or para-aortic region delivering a mid-pelvis

dose of 45-50 Gy in 20-25 fractions over 4-5 weeks by parallel opposed AP: PA fields with a Cobalt 60 Theratron 80 R unit.

In case of large volume treatment, the field was tailored to gross volume after a dose of 40 Gy in 20 fractions over 4 weeks. Intracavitary Radiation Therapy (ICRT) – was delivered after a gap of 3 weeks of EBRT for the reaction to settle, using Cesium-137 with a reference dose of 28-32 Gy to point A. Planning was done using standard isodose charts and dose calculations was done by ICRU 38 [12].

Patients who received chemotherapy did show either as a single agent 5 FU concomitantly with the brachytherapy or as a combination chemotherapy using Cisplatin and 5 FU. Cisplatin was given in a dose of 50 mg/m<sup>2</sup> after necessary hydration and premedication followed by mannitol diuresis, on day 1, 29 and a day prior to ICRT. 5-FU infusion – 500mg in 500ml of normal saline over 6 hours biweekly during 5 weeks of EBRT: radiation fraction was delivered during infusion. 5-FU was also given in dose of 40-45 mg/hour, infused during the whole period of ICRT and 2 hours after its completion. All parameters were entered into a computerized database and comparative evaluation of data was done.

**Statistical analysis:** Data were presented in frequency (%). To see the change in trends in various Clinical-pathological factors over time, Chi-square test with one degree of freedom for linear trend in proportion was applied. Analysis for linear trend in proportions was done in Epi Info Version 6. Other statistical analysis was performed in Stata 12.1. All the p-values less than 0.05 were taken as significant.

## **Results**

We studied the patients who were treated in years 1977, 1997, and 2006 with various treatment modalities i.e. surgery, radiotherapy and chemotherapy in different combination. This study comprised of 61, 62 and 66 histologically proven patients of carcinoma cervix seen and treated in 1977, 1997 and 2006 respectively. The Urban women attendance has increased over years from 32% in 1977 to 50% in 2006. In all cervical cancer patients, 36% patients were premenopausal in 1977 whereas 45% and 50% in 1997 and 2006 respectively. Most of the women were less than 60 years of age who were treated in the department for cervical cancer. In year 1977, 40% of the patients were in age group 61-70 years whereas in year 1997 and 2006, 42% and 33% patients were in age group 51-60 years. Mean parity has decreased over years due to NCCP and effective family planning program. This was 5.86 in 1977 and came down to 4.32 and 3.62 in 1997 and 2006 respectively.

Rate of hysterectomy increased from 5% in 1977 to 20% in 2006. In comparison of 5% of the patients presenting in stage II in 1977, 24% of the patients were in stage II disease in 2006. Although in all these years when assessment was done, majority of the patients presented in stage III cervical cancer. Teletherapy with brachytherapy with or without chemotherapy is treatment of choice for locally advanced cervical cancer. Before 1997, patients were treated with the teletherapy and brachytherapy in 85%, and 83% of cases in 1997 and 2006 respectively. Only EBRT was delivered in 10% and 5% cases due to non-compliance of

**Table 1.** Clinical-pathological profile of the cervical cancer patients

Patient characteristics	Year			*Chi-square	p-value
	1977 (n=61) n(%)	1997 (n=62) n(%)	2006 (n=66) n(%)		
<b>Age (years)</b>					
Mean (Range)	56.4(36-70)	53.8(29-70)	51.3(27-69)	-	-
21-30	0(0)	1(2)	4(6)	4.554	0.033
31-40	6(10)	5(8)	9(14)	0.506	0.477
41-50	9(15)	11(18)	15(23)	1.338	0.247
51-60	21(35)	26(42)	22(33)	0.033	0.879
61-70	25(40)	18(30)	16(24)	4.131	0.042
<b>Area of residence</b>					
Urban	20(33)	28(45)	33(50)	3.774	0.052
Rural	41(67)	34(55)	33(50)		
<b>Menopausal status</b>					
Premenopausal	22(36)	28(45)	33(50)	2.468	0.116
Postmenopausal	39(64)	34(55)	33(50)		
<b>Mean Parity</b>	5.86	4.32	3.62	-	-
<b>Stage at presentation</b>					
I	0(0)	2(3)	4(6)	3.764	0.052
II	3(5)	5(8)	16(24)	10.814	0.001
III	38(62)	43(69)	40(61)	0.049	0.825
IV	20(33)	12(20)	6(9)	10.990	0.001
<b>Treatment</b>					
Surgery only	0(0)	2(3)	2(3)	1.358	0.244
Surgery + IVBT	1(2)	1(2)	2(3)	0.303	0.582
Surgery + EBRT + IVBT	2(3)	4(7)	9(14)	4.679	0.030
EBRT only	6(10)	3(5)	0	6.728	0.009
EBRT + ICRT	52(85)	51(83)	5(8)	79.582	<0.001
EBRT with chemo + ICRT	0(0)	0(0)	48(72)	90.366	<0.001
<b>Treatment complications</b>					
Urinary complications	9(15)	11(18)	4(6)	2.246	0.134
Rectal complications	17(28)	10(16)	3(5)	12.202	0.001
Hematological toxicity	3(5)	3(5)	10(16)	4.376	0.036

treatment. In the year 2006, 72% of the patients were treated with radiotherapy with concurrent chemotherapy followed by Intracavitary brachytherapy whereas 8% patients were treated with EBRT and brachytherapy in view of medical co-morbidities and advanced age. Treatment related complications were decreased over years. Urinary complications

were associated with 15%, 18% in 1977 and 1997 respectively, that came down to as low as 6% in year 2006. Rectal complications came down from 28% in 1977 and 5% in 2006. Hematological toxicities were increased from 5% in 1977 and 1997 to 16% in 2006 due to addition chemotherapy in treatment. Patient 5 year survival was 62% and 72 % in 1977 and

1997 and that increased to 87% in 2006 and follow up was improved significantly over time.

## **Discussion**

Carcinoma of uterine cervix is the second most common type of female cancer in the world accounting for 15% of all newly diagnosed cases cancel in human [13]. Cervical cancer is an important cause of death in women, especially in developing countries. Cancer cervix occupies either the top rank or second among cancer in woman in developing countries, whereas in affluent countries cancer cervix dose not find a place in top five leading cancer in women [14]. The treatment of patients with cervical cancer has changed significantly over the last few years. For patients with locally advanced disease, radiotherapy including external pelvic irradiation and brachytherapy has been the standard treatment for several years [7]. More recently, concurrent chemoradiotherapy has become the treatment of choice for patients with locally advanced cervical cancer and has produced Promising results in terms of survival.

We studied the patients who were treated in year 1977, 1997 and 2006 with various treatment modalities i.e. surgery, radiotherapy and chemotherapy in different combinations. The urban women attendance has increased over years from 32% in 1977 to 50% in 2006. Mean parity has decreased over years due to NCCP and effective family planning program. This was 5.86 in 1977 and came down to 4.32 and 3.62 in 1997 and 2006 respectively.

In all cervical cancer patients, 36% patients were premenopausal in 1977 whereas 45% and

50% in 1997 and 2006 respectively. Most of the women were less than 60 years of age who were treated in the department for cervical cancer. In year 1977, 40% of the patients were in age group 61–70 years whereas in year 1997 and 2006, 42 % and 33% patients were in age group 51-60 years.

In SEER Cancer Statistics Review, 1975-2008, Howlader et al [15] showed that from 2004-2008; the median age at diagnosis for cancer of the cervix uteri was 48 years of age. Two patients were diagnosed under age 20; 14.3 % between 20 and 34; 25. 8% between 35 and 44; 23.9% between 45 and 54; 16.4 % between 55 and 64; 10.6% between 65 and 74; 6.4 % between 75 and 84; and 2.5 % in 85+ years of age. In a study by Azad and Choudhary [16] on radical radiotherapy of carcinoma uterine cervix using external beam radiotherapy and high dose rate intracavitary radiotherapy on 342 patients, median age was 45 years (range 28-73 years).

In early days, patients presenting in late stage and surgery was not possible in locally advanced cases. In comparison of 5% of the patients presenting in stage II in 1977, 24% of the patients were in stage II disease in 2006. Although in all this years when assessment was done, majority of the patients (61-69%) presented in stage III cervical cancer. Cervical cancer education continues to pose a challenge to the health care system in developing countries and countries with limited resources leading to advanced stage at presentation [17].

In another study on 342 patients of carcinoma uterine cervix, 67.83% patients were stage III followed by 23.98% of stage II, 4.97% and 3.22% patients were in stage IV and stage I respectively [16].

Over the years, due to effective screening program and NCCP, patients started presenting in early stage and rate of hysterectomy increased from 5% in 1977 to 20% in 2006. Teletherapy with brachytherapy with or without chemotherapy is treatment of choice for locally advanced cervical cancer. Before 1997, Patients were treated with teletherapy and brachytherapy in 85%, and 83% of cases in 1997 and 2006 respectively. In the year 2006, 72% of the patients were treated with radiotherapy with concurrent chemotherapy followed by intracavitary brachytherapy whereas 8% patients were treated with EBRT and brachytherapy in view of medical comorbidities and advanced age.

Treatment related complications were decreased over years. Urinary complication were associated with 15%, 18% in 1977 and 1997 respectively that came down to as low as 6% in 2006. Rectal complication came down from 28% in 1977 and 5% in 2006. Hematological toxicities were increased from 5% in 1977 and 1997 to 16% in 2006 due to addition of chemotherapy in treatment. A study by Azad and Choudhary (16) on 342 patients reported late complications involving the bowel and bladder in 62 (18.12%) patients. Bladder complications were seen in 21(6.14%) patients, and rectal complications in 32 (9.35%) patients. One patient had grade 3 radiation cystitis and 2 had grade 3 proctitis. Hydronephrosis with uremia were seen in 7 (2.04%) of patients whereas 2 (0.58%) patients had acute intestinal obstruction. Jensen et al [18] found that women treated with Radiation therapy had more sexual dysfunction at 2 - years follow up, with 85% of women reporting no interest in sex, 55% having dyspareunia, and 50% having vaginal shortening.

Patient 5 year survival was in 62% and 72% in 1977 and 1997 and that increased to 87% in 2006 and follow-up was improved significantly over time.

## **Conclusion**

The results of this sample study agree with the national data showing down staging and receding prevalence rate. The awareness amongst population about early diagnosis urges us to pass this message to doctor specially gynecologist and surgeons for the need of judicious application of combined modality treatment in carcinoma cervix in our set up.

## **References:**

1. Shankar A, Roy S, Malik A, Julka PK, Rath GK. Prevention of Chemotherapy-Induced Nausea and Vomiting. **Asian Pac J Cancer Prev.** 2015; 16 (15): 6207-13.
2. Sugukpinar N, Karaca Saydam B, Ozturk Can H, et al. Assessment of cervical cancer risk in women between 15 and 49 years of age: case of Izmir. **Asian Pac J cancer Prev** 2013; 14:2119-25.
3. Ali F Kuelker R, Wassie B. Understanding cervical cancer in the context of developing countries. **Ann Trop Med Public Health** 2012; 5:3-15.
4. Barillot I, Horiot JC Maingon P, et al. Impact on treatment outcome and late effects of customized treatment planning in cervix carcinoma: baseline results to compare new strategies. **Int J Radiat Oncol Biol Phys** 2000; 48 :189–200.
5. Davidson SE, Burns M, and Routledge J, et al. Short report: morbidity scoring scheme for clinical oncology practice: questionnaire produced from the LENT SOMA scoring system. **Clin Oncol** 2002; 14:68-9.
6. Perez CA Grigsby PW, Nene SM, et al. Effect of tumor size on the prognosis of

- carcinoma of the uterine cervix treated with irradiation alone. **Cancer** 1992; 69:2796-2806.
7. Keys H, Gibbons SK. Optimal management of locally advanced cervical carcinoma. **J Natl Cancer Inst Monogr.** 1996;89-92.
  8. Green JA, Kirwan JM, Tierney JF, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. **Lancet.** 2001; 385: 781-786.
  9. Jones WB, Singelton HM , Russel A. Patterns of care study for invasive cervical cancer. Results of national survey of 1984 and 1990. **Cancer** 1995; 76: 1934-1947.
  10. Peter W et al. Five cervical studies show Cisplatin-Based Chemoradiation reduces deaths. **JNCI J Natl Cancer Inst** 1999; 91 (6): 501.
  11. NCI issues clinical announcement on Cervical Cancer: Chemotherapy plus radiation improves survival. **JNCI Press office** (301) 1999; 496 6641.
  12. ICRU Report number 38. Dose and volume specifications for reporting intracavitary therapy in Gynaecology, ICRU: **Bethesda**, 1985.
  13. Boyle P, Ferely J. Cancer incidence and mortality in Europe, 2004. **Ann Oncol** 2005; 16: 481-488.
  14. Shanta V, Krishnamurthy S, Gajalakshmi CK, Swaminathan R, Ravichandran K . Epidemiology of cancer of the cervix: Global and national perspective. **J Indian Med Assoc** 2000; 98: 49-52.
  15. Howlader N, Ries LAG, Mariotto AB, Reichman ME, Ruhl J, Cronin KA. Improved estimates of cancer-specific survival rates from population-based data. **J Natl Cancer Inst** 2010; 102: 1-15.
  16. Azad SK, Choudhary V. Treatment results of radical radiotherapy of carcinoma uterine cervix using external beam radiotherapy and high dose rate intracavitary radiotherapy. **J Can Res Ther** 2010; 6: 482-486.
  17. Shankar A, Rath GK, Roy S, Malik A, Bhandari R et al. Level of awareness of cervical and breast cancer risk factors and safe practices among college teachers of different states in India: do awareness programmes have an impact on adoption of safe practices? **Asian Pac J Cancer Prev** 2015; 16(3): 927-32.
  18. Jensen PT, Groenvold M, Klee MC, Thranov I, Petersen MA, Machin D. References- longitudinal study of sexual function and vaginal change after radiotherapy for cervical cancer. **Radiat Oncol Biol Phys** 2003; 56: 937-949.