

## A retrospective study of clinicopathological profile of carcinoma cervix and incidence of various postoperative complications

Ravi Iyengar<sup>1\*</sup>, S. Radhika<sup>2</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Professor and HOD, <sup>1</sup>Dept. of Surgical Oncology, <sup>2</sup>Dept. of Gynecology and Obstetrics, Dhanalakshmi Srinivasan Medical College and Hospital, Tamil Nadu, India

\*Corresponding Author: Ravi Iyengar

Email: sraviiyengar@gmail.com

Received: 10<sup>th</sup> May, 2019

Accepted: 15<sup>th</sup> December, 2019

### Abstract

**Introduction:** With the intensified screening and availability of advanced modalities of treatment, the treatment outcomes and the occurrence of various post-operative complications of cervical cancer is constantly changing.

**Materials and Methods:** The current study was a retrospective case record review of all the cervical cancer cases diagnosed in the department of oncology/ gynaecology, Dhana Lakshmi Srinivasan medical college Hospital, Permabalur, South India, diagnosed between January 2016 to December 2017. The socio-demographic, clinical findings, histopathological findings, incidence and management of postoperative complications were documented using a structured proforma. The data were analyzed using IBM SPSS statistical software.

**Results:** A total of 60 cases of cervical cancer were included in the final analysis. The youngest women were 34 years old and mean age was 52.48 ± 10.55 years. The majority (85%) of the women had stage I B, with squamous cell carcinoma as the most common histopathological type in 76.67% of the women. Radical hysterectomy with bilateral pelvic lymph node dissection was performed in 80% of participants. Overall 85% (95% CI 73.89 to 91.9%) of the subjects had postoperative complications. Suprapubic fibrosis (40%) Bilateral Lymphedema (35%), were the commonest post-operative complications. The procedures performed to treat post-operative complications were mesh repair (5%) and USG guided aspiration (5%) Laparotomy with adhesiolysis.

**Conclusions:** The incidence of postoperative complications was very high and a major portion of them can be attributed to radiotherapy. There is a need for further large-scale studies to evaluate the interventions without radiotherapy for their efficacy and safety.

**Keywords:** Carcinoma cervix, Radiotherapy, Clinicopathological profile.

### Introduction

Cervical cancer is the fourth most common cancer and is a major cause of mortality in women and more than a quarter of its global burden is contributed by developing countries.<sup>1</sup> It is relatively less common in the developed world as it accounts for almost 12% of all female cancers.<sup>2</sup> However, it is one of the commonest malignancies and is the principal cause of cancer mortality among Indian women.<sup>3,4</sup> Carcinoma of the cervix is a public health problem in developing countries like India, so much so that India alone accounts for one-quarter of the worldwide burden of cervical cancers.<sup>3,5</sup>

Every year in India, over 1.22 lakh women are diagnosed with cervical cancer and nearly 68 thousand dies from the disease.<sup>6</sup> India has a population of 432.2 million women aged 15 years and older who are at risk of developing cancer. It is the second most common cancer in women aged 15–44 years<sup>6</sup> and has its peak incidence for the age group of 55-59 years.<sup>5</sup> India also has the highest age standardized incidence of cervical cancer in South Asia at 22, compared to 19.2 in Bangladesh, 13 in Sri Lanka, and 2.8 in Iran.

Multiple risk factors have been proposed to play a role in the aetiology of carcinoma of the cervix (CoC). Human papillomavirus, most notably types HPV16 and 18 have been considered the single most important factor,<sup>7-9</sup> in which the association between HPV and CoC has been found to be causal in nature and under optimal testing systems, HPV DNA can be identified in all specimens of invasive cervical cancer. Co-factors that modify the risk among HPV DNA

positive women include the use of oral contraceptives for five or more years, smoking, high parity (five or more full-term pregnancies)<sup>10</sup> and previous exposure to other sexually transmitted diseases such as Chlamydia Trachomatis,<sup>11</sup> Herpes Simplex Virus type 2<sup>12</sup> and Human Immunodeficiency virus.<sup>13</sup>

It is one of the leading cause of death worldwide, wherein every two minutes a woman dies from the disease, equating to more than 275 thousand cancer deaths annually, of which over 87% occur in developing countries.<sup>14</sup> The deaths of these women who are in their most productive years have overwhelmingly disturbing effects on the well-being of their families and can result in a decrease in school attendance and nutritional status among their children.<sup>15,16</sup> CoC affects women at a time of life when they are critical to social and economic stability. Therefore, the present study aimed to assess the epidemiology, clinical presentation of carcinoma of the cervix in a tertiary hospital in India.

### Objectives

1. To analyse the clinicopathological profile of cervical cancer patients presenting to a tertiary care teaching hospital in south India.
2. To assess the pattern of treatment provided and immediate postoperative complications and their management among the study population.

## Materials and Methods

The current study was retrospective case record review of all the cervical cancer cases diagnosed in the department of oncology/ gynaecology, Dhana Lakshmi Srinivasan medical college Hospital, Permabalur, South India.

The study population included all the histopathologically confirmed cases of cervical cancer between January 2016 to December 2017. The data collection for the study was done in January 2018.

Since the study was a retrospective case record review, no ethical approval was sought. It was also not possible to obtain informed written consent from participants for inclusion in the study. The confidentiality of the study participants was maintained throughout the reporting of the results.

The socio-demographic, clinical, radiological and histopathological findings were retrieved onto a structured proforma. The other details included the type of treatment provided, the occurrence of various post operative complications and the management of the same.

The statistical analysis was carried out by using IBM SPSS version 21.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram, and box plots. Considering the sample size available only descriptive analysis was possible and no inferential statistics or P values were presented.

## Results

A total of 60 cases of cervical cancer were included in the final analysis. The minimum age was 34 years and maximum age was 80 years with a mean age of  $52.48 \pm 10.55$  years in the study population.

There were 5 women (8.33%), who were diagnosed with cervical cancer below 40 years. The proportion of women between 40 to 49, 50 to 59 and above 60 years was 38.33%,

25.00%, and 28.33% respectively. Majority of the women had stage I B disease at the time of diagnosis and remaining 15.00% had stage II A. Squamous cell carcinoma was the most common histological type in 78.33% of cases, followed by adenocarcinoma in 20.00% and only one woman had sarcoma. Pre-operative radiotherapy was provided in 13.34% of the subjects. Radical hysterectomy with bilateral pelvic lymph node dissection was performed in 80% of participants and in remaining 20.00% omentectomy was also performed in addition to it. (Table 1)

Squamous cell carcinoma was the most common histopathological type in 76.67% of the women, followed by adenocarcinoma in 18.34%. The other less common histological types were carcinosarcoma, choriocarcinoma and serous cystadenocarcinoma seen in 1 subject each. The proportion of subjects with node positivity, parametrical involvement, and vaginal involvement were 23.33%, 8.33%, and 11.67% respectively. (Table 2)

A total of 51 subjects received External beam radiotherapy (EBRT) postoperatively, with doses ranging from 40GY to 50 Gy. Post-operative Brachytherapy was given in 24 (40%) subjects in the dose range of 8 to 16 Gy. (Table 3)

In the current study, 85% (95% CI 73.89 to 91.9%) of the subjects had at least 1 postoperative complication. Suprapubic fibrosis was the most common complication seen in 24 (40%) of the subjects postoperatively. Bilateral Lymphedema was seen in 21 (35%), followed by vaginal stenosis in 11 (18.33%) subjects. The other common complications were bilateral lymphedema and incisional hernia in 5 (8.33%) women each. No procedure was required to treat post-operative complications in 46 (76.67%) of the subjects. The common procedures performed to treat post-operative complications were mesh repair and USG guided aspiration in 3 (5%) women each. Laparotomy with adhesiolysis and drainage of lymph cyst under anaesthesia were performed in 2 (3.34%) of the subjects each. (Table 4)

**Table1: Descriptive analysis of age group in the study population (N=60)**

Age Group	Frequency	Percentage
Up to 39	5	8.33%
40-49	23	38.33%
50-59	15	25.00%
60 and above	17	28.33%
<b>Clinical Stage</b>		
I B	51	85.00%
II A	9	15.00%
<b>Pre-Operative Biopsy</b>		
Squamous cell carcinoma	47	78.33%
Adenocarcinoma	12	20.00%
Sarcoma	1	1.67%
<b>Preoperative Radio Therapy</b>		
Given	8	13.34%
Not Given	52	86.67%
<b>Surgical Procedure</b>		

Radical hysterectomy with bilateral pelvic lymph node dissection	48	80.00%
Radical hysterectomy with bilateral pelvic lymph node dissection with omentunectomy	12	20.00%

**Table 2: Post-operative Histopathological findings (N=60)**

Parameter	Frequency	Percent
<b>Type of a tumour</b>		
Squamous cell carcinoma	46	76.67%
Adenocarcinoma	11	18.34%
Carcinosarcoma	1	1.67%
Choriocarcinoma	1	1.67%
Malignant mixed Mullerian tumor (serous cyst adenocarcinoma)	1	1.67%
<b>Nodes Positivity</b>		
Node-negative	45	76.67%
Node-positive	15	23.33%
<b>Parametrium Involvement</b>		
Present	5	8.33%
Not involved	55	91.67%
<b>Vaginal Involvement</b>		
Present	7	11.67%
Not involved	53	88.33%

**Table 3: Descriptive analysis of postoperative radiotherapy EBRT in the study population (N=60)**

Post op radiotherapy	Frequency	Percentage
<b>External beam radiotherapy (EBRT)</b>		
40GY	33	55.00%
45GY	10	16.67%
50GY	8	13.33%
Not Given	9	15.00%
<b>Brachytherapy</b>		
16GY	22	36.67%
8GY	2	3.33%
Not Given	36	60%

**Table 4: Incidence of various post-operative complications and their treatment (N=60)**

Post-operative events	Number	Percentage
<b>Complication</b>		
No complications	9	15.00%
Suprapubic fibrosis	24	40.00%
B/L lymphedema	21	35.00%
Vaginal stenosis	11	18.33%
Bilateral Lymph cyst	5	8.33%
An incisional hernia	5	8.33%
Vulval and Vaginal stenosis	4	6.67%
Unilateral lymphedema	3	5.00%
Intestinal obstruction	2	3.33%
Left-sided hydronephrosis	1	1.67%
Left pelvic Abscess	1	1.67%
Vesicovaginal fistula	1	1.67%
Repeated cellulitis	1	1.67%
<b>Intervention</b>		
Mesh repair	3	5.00%
USG guided aspiration done twice	3	5.00%
Laparotomy with adhesiolysis	2	3.34%

Drainage of lymph cyst under anaesthesia	2	3.34%
Continuous bladder drainage for eight weeks	1	1.67%
DJ stenting	1	1.67%
Abscess drainage under spinal anaesthesia	1	1.67%
Multiple cycles of IV antibiotics	1	1.67%
No procedure	46	76.67%

## Discussion

Globally, cervical cancer constitutes about 12% of all cancers in women<sup>15</sup> and reflects striking health inequity more than any other cancer. More than 85% of approximately 529 thousand cases diagnosed annually occur in developing countries, a proportion that is expected to increase to 90% by 2020.<sup>14,15</sup> In India, despite such alarming statistics, there has been no synchronized initiative from public health authorities for prevention and control cervical cancer.

A total of 60 cases of cervical cancer were included in the final analysis. The mean age of the patients was 52.48 ± 10.55 years, belonging to the range of 34-80 years. Almost all of the patients were aged above 40 years, with the majority (23: 38.33%) of the patients belonged to 40-49 year group while 17(28.33%) were aged 60 years and above. Concurring these findings, in their six-year, follow up of 61 patients, Eze et al<sup>17</sup> reported the mean age of their patients as being 54 years, with an age range of 32-78 years and most of the subjects belonged to 40 years and above, with 26.2% 40-49 year group. These findings further assert strongly that cervical cancer affects women at a time when they are vital to social and economic stability.<sup>18</sup>

Regarding the stage of CoC, most (51: 85.00%) of them had clinical stage were clinical stage in I B, and the remaining (9: 15.00%) were II A. Contrastingly, Eze et al<sup>17</sup> found most of their patients had advanced stages of CoC, with stage III (36.6%) or stage II (34.1%) and only 9.8% of them had stage I cancer.

In the current study, the minimum age was 34 years and maximum age was 80 years with a mean age of 52.48 ± 10.55 years Suprasert P., et al.<sup>19</sup> have reported a mean age of 44 years at the diagnosis, which was lower than the current study.

In the current study, Squamous cell carcinoma was the most common histopathological type in 76.67% of the women, followed by adenocarcinoma in 15%. The proportion of subjects with node positivity, parametrial involvement, and vaginal involvement were 23.33%, 8.33% and 11.67% respectively. Majority of the women had stage I B disease at the time of diagnosis and remaining 15.00% had to stage II A. As in the current study, Suprasert P., et al.<sup>19</sup> have reported most common histology as squamous cell carcinoma (67%) followed by adenocarcinoma (23%). The distribution of FIGO staging was: stage IA 8.7%; stage IB 15.8%; stage IB1 61%; stage IB2 6.2%; and stage IIA 8.5%. Pelvic nodes, parametrial and vaginal margin involvement were detected in 15.9%, 10.7% and 3.8% of the patients, respectively. A total of 66.5% of patients underwent RHPL without adjuvant treatment; 12.1% received neoadjuvant chemotherapy.

Evidence suggests that cervical cancer patients present very late to tertiary hospitals in developing countries including India, which could be related to patients' delay in seeking healthcare and care providers' delay in referring patients to a tertiary hospital.

Poverty, early marriage, polygamy, grand multiparity, and illiteracy have all been found to be significantly associated with increased risk of occurrence of cervical cancer and could contribute to the high incidence of late presentation.<sup>20</sup>

In the current study, 85% of the subjected had at least one postoperative complication. Suprapubic fibrosis was the most common complication seen in 24 (40%), followed by Bilateral Lymphedema was seen in 21 (35%), and vaginal stenosis in 11 (18.33%) subjects. The other common complications were bilateral lymphedema and incisional hernia in 5 (8.33%) women each. No procedure was required to treat post-operative complications in 46 (76.67%) of the subjects. The common procedures performed to treat post-operative complications were mesh repair and USG guided aspiration in 3 (5%) women each. Laparotomy with adhesiolysis and drainage of lymph cyst under anaesthesia were performed in 2 (3.34%) of the subjects each. Savino, L., et al.<sup>19</sup> have reported lymphocytes in 10% cases and ureteral stenosis in 2% and ureterovaginal fistula, in 2% of subjects. All complications occurred in patients who received radiotherapy or chemotherapy preoperatively.

Wu, K., et al.<sup>19</sup> have reported the development of postoperative complications in 22.4% of cases of early carcinoma cervix treated with radical hysterectomy and pelvic lymph nodal dissection. The common complications reported in this study were bladder dysfunction (10.0%), lymphocytes (7.8%), wound infection (6.8%); hydronephrosis (1.4%) and formation of ureteral fistulas (0.5%). The postoperative complication incidence in the patients who had preoperative neoadjuvant chemotherapy through an intra-arterial catheter or radical radiotherapy were 50.0% (2/4) and 100.0%. In a study by Suprasert, P., et al.<sup>19</sup>, the most common long-term complication was lymphoedema.

## Conclusions

The current study has found a high incidence of postoperative complications. Majority of the complications (suprapubic fibrosis, followed by lymphedema and vaginal stenosis etc) can be attributed to the policy of adjuvant radiotherapy. There is a need to reconsider the policy of the administration of radiotherapy for stage IB and II cervical cancer and need for further large-scale studies to generate quality evidence on the subject.

**Conflict of Interest:** None.

## References

1. Ferlay J SI, Dikshit R, Eser S, Mathers C, Rebelo M et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136(5):E359-86.
2. L D. Cervical cancer: prevention and treatment. *Discov Med* 2012;14:125-31.
3. 2012-2014 T-YRoPBCR. Incidence, Distribution, Trends in Incidence Rates and Projections of Burden of Cancer. Bengaluru: National Centre for Disease Informatics and Research National Cancer Registry Program (ICMR); 2016.
4. Arbyn M CX, de Sanjosé S, Bruni L, Saraiya M, Bray F et al. Worldwide burden of cervical cancer. *Ann Oncol*. 2011;22(12):2675-86.
5. N K. Breast and cervical cancer in 187 countries between 1980 and 2010. *Lancet* 2012;379:1391-2.
6. Sankaranarayanan R FJ. Worldwide burden of gynecological cancer: The size of the problem. *Best Pract Res Clin Obstet Gynaecol* 2006;20:207-25.
7. Munoz N BF, de Sanjose S, Shah KV. The role of HPV in the etiology of cervical cancer. *Mutat Res* 1994;305:293-301.
8. Clifford GM GS, Herrero R, Muñoz N, Snijders PJ, Vaccarella S et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. *Lancet* 2005;366(9490):991-8.
9. Khan MJ1 CP, Lorincz AT, Wacholder S, Sherman M, Scott DR et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst* 2005;97(14):1072-9.
10. Castellsagué X MN. Chapter 3: Cofactors in human papillomavirus carcinogenesis--role of parity, oral contraceptives, and tobacco smoking. *J Natl Cancer Inst Monogr* 2003;31:20-8.
11. Castellsagué X PR, Franceschi S, de Sanjosé S, Smith JS, Albero G et al. Chlamydia trachomatis infection in female partners of circumcised and uncircumcised adult men. *Am J Epidemiol* 2005;162(9):907-16.
12. Smith JS HR, Boretti C, Muñoz N, Bosch FX, Eluf-Neto J et al. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. *J Natl Cancer Inst*. 2002;94(21):1604-13.
13. Palefsky JM HE. Chapter 6: Immunosuppression and co-infection with HIV. *J Natl Cancer Inst Monogr* 2003;31:41-6.
14. Jemal A BF, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61(2):69-90.
15. Agosti JM GS. Introducing HPV vaccine in developing countries— key challenges and issues. *N Engl J Med* 2007;356(19):1908-10.
16. Saleh JA YH, Zailani SB, Aji BM. Role of HPV vaccine in the prevention of cervical cancer. *J Interdiscipl Histopathol* 2013;1(4):2146-8362.
17. Eze JN E-IE, Edegbé FO. A Six-Year Study of the Clinical Presentation of Cervical Cancer and the Management Challenges Encountered at a State Teaching Hospital in Southeast Nigeria. *Clin Med Insights Oncol* 2013;7:151-8.
18. RI A. Cervical cancer: the sub-saharan African perspective. *Reprod Health Matters* 2008;16(32):41-9.
19. Prakash GT, Das AK, Habeebullah S, Bhat V, Shamanna SB. Maternal and Neonatal Outcome in Mothers with Gestational Diabetes Mellitus. *Indian J Endocrinol Metab* 2017;21(6):854-8.
20. Ketiku KK OE, Ekanem EE. Cancer of the cervix in Nigeria: A case-control study of some epidemiological factors. *NQJHM* 2004;14(2):161-5.

**How to cite this article:** Iyengar R, Radhika S. A retrospective study of clinicopathological profile of carcinoma cervix and incidence of various postoperative complications. *Indian J Pathol Oncol* 2019;6(2):218-22.