ORIGINAL RESEARCH ARTICLE

Incidence and Clinicopathological Correlation of Cervical Cancer in a Tertiary Care Center: A 5-year Retrospective Study

Arshdeep Kaur[1], Amisha Chawla[2], Mridu Manjari[3]

Abstract

Introduction: Cervical carcinoma is the second most common cancer of women in India, with the first being breast carcinoma. In 2018, the age standardized incidence rate in the world was 13.1% and in India was14.7%, with 569,847 new cases and 311,365 deaths in 2018 in the world. Infection by human papillomavirus (HPV) is the most common risk factor for cervical cancer, with more than 99% cases expressing viral sequence. The present study was undertaken to study the incidence, various clinical presentations, and the histological types of cervical carcinoma.

Materials and methods: The study was carried out in a tertiary care center for a period of 5 years (January 2015 to December 2019) on histopathologically diagnosed cases of cervical cancer. A total of 308 cases of cervical carcinoma were studied in this period.

Results: Incidence of cervical cancer in the present study was 2.9%. Maximum number of cases was seen in fifth and sixth decades. The most common clinical presentation was postmenopausal bleeding (78.6%) followed by discharge per vaginam (66.6%). On microscopy, squamous cell carcinoma (SCC)-large-cell nonkeratinizing type was most common (89%) followed by adenocarcinoma (5.5%). Other types were adenosquamous (1.9%) and small cell carcinoma (1.9%), and the least common was SCC-large-cell keratinizing type (1.6%). Of the 308 cases, 164 (53.2%) were in stage II followed by 95 cases (30.2%) in stage I.

Conclusion: In conclusion, the current study stressed the fact that as a majority of Indian women are diagnosed at later stages of cervical cancer rather than in its early treatable stages, so there is a need for strengthening and proper implementation of screening programs. Keeping in mind the incidence, the knowledge of vaccination against HPV for prevention of carcinoma cervix should also be followed.

Keywords: Cervical cancer, Clinicopathological profile, Risk factors.

AMEI's Current Trends in Diagnosis & Treatment (2019): 10.5005/jp-journals-10055-0078

Introduction

Cervical carcinoma is the second most common cancer among women in India, with the first being breast carcinoma. Age standardized incidence rate in 2018 in the world was 13.1% and in India was14.7% with 569,847 new cases, and 311,365 deaths in 2018 in the world.[1] It is the most common cause of death among the developing countries. However, owing to the well-programmed screening procedures in developed countries, the incidence and mortality decreased by 75–80%.[2] Unlike most other malignancies, cancer cervix is easily preventable. Pap smear is easy, simple, and effective screening tool for the detection of early epithelial cell abnormalities.

Human papillomaviruses have emerged as the principal sexually transmitted causal agent in the development of the cancer of uterine cervix in women.[3] The transformation zone of the cervix, specifically that associated with squamocolumnar junction, is vulnerable to HPV. A persistent infection with high-risk HPV is a necessary factor causing cervical carcinogenesis. However, it alone is not sufficient and a variety of cofactors influence development of cervical carcinoma.[4,5] It has been seen that more than 99% cases express the viral sequence. There are more than 150 types of HPV of which more than 14 are cancer causing (also known as high-risk types particularly HPV16 and HPV18). Human papillomavirus is mainly transmitted through sexual contact, and most people are infected with HPV shortly after the onset of sexual activity.[6] Once the HPV infection is established in the cervical epithelial cells of transformation zone, a stepwise progression of the events from preinvasive lesions to invasive malignancy starts gradually. Mass screening at the reproductive age-group helps in detecting early lesions that could be cured easily by complete excision. The other risk factors are early marriage, early age of first sexual intercourse, early age of first pregnancy, multiple pregnancies, increased parity, use of oral contraceptive pills, multiple sexual partners, low socioeconomic status with nutritional and vitamin deficiencies, poor genital hygiene especially penile hygiene of a male partner, women living in rural areas, African-American race, tobacco smoking, sexually transmitted disease, herpes simplex virus infection, coinfection with HIV, immune compromised status (especially in renal transplant cases), and genetic susceptibility.[2] However, the lack of awareness of screening programs, poor

[1–3]Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India

Corresponding Author: Arshdeep Kaur, Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India, Phone: +91 9915865836, e-mail: arshmalhi87@gmail.com

How to cite this article: Kaur A, Chawla A, Manjari M. Incidence and Clinicopathological Correlation of Cervical Cancer in a Tertiary Care Center: A 5-year Retrospective Study. AMEI's Curr Trends Diagn Treat 2019;3(2):64–67.

Source of support: Nil

Conflict of interest: None

hygiene, geographical inaccessibility, low socioeconomic status, and failure to attend regular health campaigns are some of the major factors responsible for the rising trends of carcinoma cervix in India.[3] Moreover, the lack of an oncologist and negligence of initial symptoms along with financial constraints are responsible for a late presentation and diagnosis in our country.[7]

In a recent study, it was concluded that cervical cancer incidence could be reduced by 97% in lower-middle-income countries. To achieve this elimination across all lower-middle-income countries, both high HPV vaccination coverage and screening uptake will be necessary, particularly in countries with the highest burden. Considerable international commitment will be required to achieve World Health Organization's (WHO) triple-intervention targets, particularly in these countries where scale-up of vaccination and screening resources are most urgently needed.[8]

Invasive cervical carcinomas may show squamous, columnar, and neuroendocrine differentiation. Other patterns, including adenosquamous, glassy cell, sarcomatoid, lymphoepithelial like, transitional, and undifferentiated, have been described. This spectrum of neoplastic differentiation reflects either specific cell types infected by HPV or pathways of differentiation selected after neoplastic cell transformation.[4]

Pathologic indices like extent of invasion, margin status, and presence of lymphovascular invasion are critical for appropriate management of patients.[9]

This is a retrospective single-center study from northern India conducted over a period of 5 years, with the aim to find the incidence of malignant cervical cancers and to explore the clinical profile and histomorphological subtypes of carcinoma cervix (Fig. 1).

Materials and Methods

The retrospective study was carried out in a tertiary care center for a period of 5 years (January 2015 to December 2019) on histopathologically diagnosed cases of cervical cancer. Ethical clearance was taken from institution's ethical committee. A semi-structured proforma was created in which hospital number and biopsy number were noted, relevant demographic profile like age along with clinical findings, and gross and histopathological findings along with clinical staging were collected from the data available in the department. Histologically the cases were classified as SCC-large-cell nonkeratinizing, SCC-large-cell keratinizing, small cell carcinoma, papillary adenocarcinoma, and adenosquamous types.

Results

In the study period of 5 years, 10,452 total cases of malignancy were reported.

Of the 10,452 cases of malignancy, 308 cases were carcinoma cervix (incidence 2.9%). They constituted 57.7% of the total gynecological malignancies reported in this tertiary care institute over a period of 5 years.

The age range was from 30 to 82 years with a mean age of 55.2 $\pm$ 10.9 years. Maximum cases were seen in fifth and sixth decades (i.e., 58.7%; Table 1).

The most common clinical presentation was postmenopausal bleeding (78.6%) followed by discharge per vaginam (66.6%). Growth cervix followed by bleeding was the most common per speculum findings (Table 2). On microscopy, SCC-large-cell nonkeratinizing type was the most common (89%) followed by adenocarcinoma (5.5%). Other types were adenosquamous (1.9%) and small cell carcinoma (1.9%), and the least common was SCC-large-cell keratinizing type (1.6%; Table 3). Of the 308 cases, 164 (53.2%) were in stage II followed by 95 cases (30.2%) in stage I.

Discussion

Globally 13% of the deaths are due to cancer. Cervical carcinoma is the fifth deadliest cancer, causing 7.5% cancer deaths in the world and 16.2% cancer deaths in India, in 2018. According to the Global Cancer Observatory (WHO), in 2018, India accounted for 17% of the World's cervical cancer cases.[1]

About 80% of new cervical cancer cases occur in developing countries like India.

The incidence in the present study came out to be 2.9%.

In the present study, cervical cancer constituted 57.7% of all the gynecological malignancies. Similar finding were also seen in the study done by Kumari et al. who found this percentage to be 52%.[10]

Mean age in the study done by Raju et al. was 54.2 $\pm$ 12 years, which is similar to the mean age in present study, i.e., 55.2 $\pm$ 10.9 years. Jain et al. also observed similar findings in their study.[11]

The studies by Raju et al., Patil et al., and Lakshmi et al. all showed maximum cases in the fifth and sixth decades of life. Similar age distribution was also seen in the present study.[2,12]

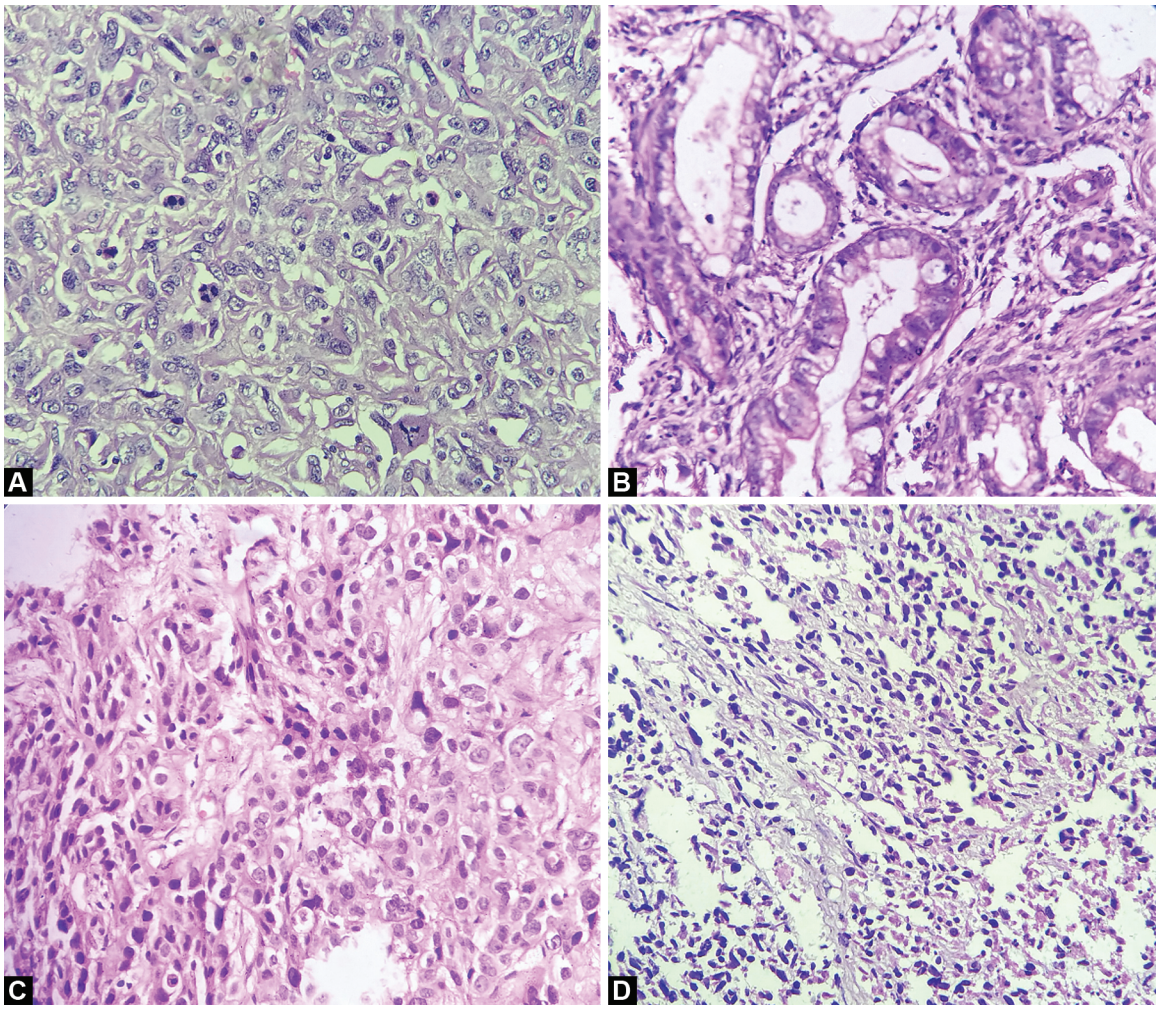
Most of the time, early cervical cancer has no symptoms. Vaginal bleeding, postcoital bleeding, or discharge may be the presenting features. In case of advanced disease, the patient may present with abdominal pain, breathing difficult, and cervical mass. Advanced carcinoma can also present with loss of appetite, weight loss, fatigue, pelvic pain, leg pain, swollen legs, heavy bleeding from vagina, or rarely leakage of urine or feces from the vagina. In present study, postmenopausal bleeding was the most common complaint in more than 70% of the patients followed by discharge (66.6%) and irregular bleeding (33.1%). Raju et al. also noted similar findings, with postmenopausal bleeding in 80% of the cases and discharge in 68% cases. In their study other common complaints were postcoital bleeding (85.7%) and pain in abdomen (53.3%), which were less common in the present study. Jain et al. and Patil et al. also showed similar findings as the present study except for irregular bleeding being a more common presentation than the present study.[2,12]

The most frequent finding was growth, as reported by Raju et al. (65.3%) followed by bleeding and erosion. Similar findings were seen in the present study with growth in 66.2% cases. In a study by Jain et al. the most frequent finding was ulcer (72%) followed by cervical lip hypertrophy (19%) and normal cervix (7%). In the present study, only 1% of the cases had normal cervix.[2,11]

Majority of cervical cancers were SCC. The lesion arises from squamocolumnar junction and may be keratinizing or nonkeratinizing type (well-differentiated or poorly differentiated carcinoma). Studies have shown that 80–90% of cervical carcinoma is SCC and the rest of them constitutes adenocarcinoma. Adenocarcinoma of the uterine cervix arises from the endocervical columnar cells and constitutes about 14% of cervical carcinoma.

In the present study, 92.5% of cases were SCC, of which majority (89%) was SCC large-cell nonkeratinizing type. Adenocarcinoma constituted only 3.6% cases (Table 4).

In the present study, all of the cases that were clinically diagnosed as cervical cancer were confirmed by histopathology, 53.2% of the patient were in stage II (IIA comprising 36%) followed by stage I. In contrast to our results, Patil et al. and



Figs 1A to D: Photomicrographs show: (A) Squamous cell carcinoma (H&E, 400X); (B) Adenocarcinoma (H&E, 400X); (C) Adenosquamous carcinoma (H&E, 400X); (D) Small cell carcinoma (H&E, 400X)

Table 1: Age distribution of cases

Age range (years)	*Cases (%)*
30–39	21 (6.8)
40–49	90 (29.2)
50–59	91 (29.5)
60–69	74 (24)
70–79	30 (9.7)
80–89	2 (0.6)

Table 2: Per speculum findings of cases

Per speculum findings	*Cases (%)*
Growth	204 (66.2)
Bleeding	34 (11.0)
Erosion	33 (10.7)
Restricted uterine mobility	26 (8.4)
Firm cervix	11 (3.6)
Cervical lip hypertrophy	4 (1.3)
Normal	3 (1)

Raju et al. reported maximum cases in stage III (i.e., 65.3% and 40%, respectively). Results of study by Jain et al. coincided with the present study (Table 5).

Table 3: Histological types of cases

Histological type	*Cases (%)*
Squamous cell carcinoma-large-cell nonkeratinizing type	274 (89)
Squamous cell carcinoma-large-cell keratinizing type	5 (1.6)
Small cell carcinoma	6 (1.9)
Adenocarcinoma	11 (3.6)
Papillary adenocarcinoma	6 (1.9)
Adenosquamous carcinoma	6 (1.9)

In conclusion, the current study stressed the fact that as a majority of Indian women are diagnosed at later stages of cervical cancer rather than in its early treatable stages, there is a need for strengthening and proper implementation of screening programs. Although clinical management and treatment of carcinoma cervix are not much relied upon histopathological types and variants, there are many variants with different clinical presentations and specific light microscopic features that need to be considered clinically while dealing with unusual clinical presentations. At the same time, keeping in mind the incidence, the knowledge of vaccination at younger age for prevention of carcinoma cervix should also be followed aggressively.

Table 4: Histological type in various studies compared to the present study

Histological type	*Rana et al.,*[13] *(%)*	*Lakshmi et al.,*[14] *(%)*	*Patil et al.,*[12] *(%)*	*Jain et al.,*[11] *(%)*	*Gupta et al.,*[15] *(%)*	*Present study (%)*	
Squamous cell carcinoma-large-cell nonkeratinizing type	80.1	85	96	89.1	47.3	89	90.6
Squamous cell carcinoma-large-cell keratinizing type					37.8	1.6	
Small cell carcinoma	1.8				5.4	1.9	
Adenocarcinoma	14	9.7	4	9	8.1	3.6	
Papillary adenocarcinoma						1.9	
Adenosquamous carcinoma	0.97				1.35	1.9	
Others	3.1	4.8		1.9			

Table 5: Clinical stage in various studies compared to the present study

Clinical stage	*Raju et al.,*[2] *(%)*	*Patil et al.,*[11] *(%)*	*Jain et al.,*[12] *(%)*	*Present study (%)*	
IA	8	4.6		5.2	30.8
IB				25	
IIA	32	26.6	80	36	53.2
IIB				17.2	
III	40	65.3	20	12.3	
IV	20	33.3		4.2	

References

1. Gco.iarc.fr. 2020. Cancer Today. [online] Available at: http://gco.iarc.fr/today/online-analysis.
2. Raju K, Raghuveer CV, Sheela SR. Clinico pathological correlation of invasive squamous cell carcinoma of uterine cervix: a cross sectional study. Biomed Res Ther 6(11):3443–3451. DOI: 10.15419/bmrat.v6i11.573.
3. Dikshit R, Gupta PC, Ramasundarahettige C, et al. Cancer mortality in India: a nationally representative survey. Lancet 2012;379(9828): 1807–1816. DOI: 10.1016/S0140-6736(12)60358-4.
4. Wang T, Chen B, Yang Y, et al. Histologic and immunophenotypic classification of cervical carcinomas by expression of the p53 homologue p63: a study of 250 cases. Hum Pathol 2001;32(5): 479–486. DOI: 10.1053/hupa.2001.24324.
5. Burd EM. Human papillomavirus and cervical cancer. Clin Microbiol Rev 2003;16(1):1–17. DOI: 10.1128/cmr.16.1.1-17.2003.
6. Human papillomavirus (HPV) and cervical cancer [Internet]. Who.int.2020. Available from https://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer.
7. Gundrajakuppam L, Vissa S, Nandam MR, et al. Clinic pathological correlation of cervical carcinoma by pap smear. J Biosci Tech 2011;2:439–445.
8. Brisson M, Kim JJ, Canfell K, et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. The Lancet 2020;395(10224):575–590. DOI: 10.1016/S0140-6736(20)30068-4.
9. Park KJ, Soslow RA. Current concepts in cervical pathology. Arch Pathol Lab Med 2009;133(5):729–738. DOI: 10.1043/1543-2165-133.5.729.
10. Kumari A, Pankaj S, Choudhary V, et al. Retrospective analysis of patients of cervical cancer a tertiary center in Bihar. Indian J Cancer 2018;55(1):70–73. DOI: 10.4103/ijc.IJC_482_17.
11. Jain DK, Shukla P, Gupta V. Clinicopathological survey of carcinoma uterine cervix in patients attending tertiary care hospital of central Uttar Pradesh. IJRPM 2019;3(2):14–17.
12. Patil N, Deshmukh V, Rathid A, et al. ClinicoPathological correlation of cervical carcinoma: a tertiary hospital-based study int. J Sci Stud 2019;6(10):1–4.
13. Rana MK, Singh K, Mahajan MK, et al. Clinicopathological profile of cervical carcinoma: an experience of tertiary care cancer centre. Asian Pac J Cancer Care 2019;4(3):83–86. DOI: 10.31557/apjcc.2019.4.3.83-86.
14. Lakshmi V, Prakash HM, Jyothi BL, et al. Retrospective histopathological analysis of cervical cancer: our experience. Aerchives of Cytology and Histopathology Research 2016;1(1):28–31.
15. Gupta M, Basavaraj PK. Histopathological spectrum of premalignant and malignant lesions of uterine cervix. national journal of laboratory medicine. 2018;7(1):PO19–PO26.