

Clinicopathological Profile of Cervical Carcinoma: An Experience of Tertiary Care Cancer Centre

Manjit Kaur Rana

Advanced Cancer Institute (Affiliated with Baba Farid University of Health Sciences, Faridkot) Bathinda, India.

Karuna Singh

Advanced Cancer Institute (Affiliated with Baba Farid University of Health Sciences, Faridkot) Bathinda, India.

M K Mahajan

Advanced Cancer Institute (Affiliated with Baba Farid University of Health Sciences, Faridkot) Bathinda, India.

Amrit Pal Singh Rana

Context: Cervical cancer is a malignant neoplasm arising mainly in the transformation zone of the cervix. Cervical cancer is the second most common cancer among women worldwide after breast cancer. Squamous cell carcinoma and adenocarcinoma constitute the greatest burden, globally as well as in India.

Aims: The current study was aimed to assess the histopathological profile and its correlation with clinical findings.

Settings and Design: It was a retrospective analysis of the patients of cervical carcinoma.

Methods and Materials: The retrospective analysis of histopathological patterns of carcinoma cervix was done. A total of 120 cervical biopsies were received, amongst which 5 biopsies were chronic cervicitis, 9 were cervical intraepithelial neoplasia (CIN) and 106 cases were of carcinoma. Further histologic subtyping of cervical carcinoma was done and was correlated with clinical presentations and stage. The collected data were analysed. Statistical analysis used: Analysis of data was done for simple means and percentages.

Results: The most common age group in carcinoma cervix was fifth and sixth decade with history of bleeding per vagina being the most common clinical presentation. Squamous cell carcinoma (SCC) was the most common variant, \geq Stage III case constituted in majority and also showed poor prognosis.

Conclusion: A majority of Indian women presented at later stages of cervical cancer, hence demanding the need of dedicated screening programmes. Many variants present with different clinical findings especially as deep infiltrative growth patterns, hence histologic types should be kept in mind clinically while dealing with unfamiliar clinical presentations. In our experience most of the women presented in later stages and patients with \geq stage III showed poor prognosis.

Introduction

Carcinoma cervix is the second most common cancer of women in India [1]. The incidence of carcinoma is 14% worldwide with 29.1% incidence in Asian countries [2]. It is the most common cause of death among women in the developing countries [3]. The discrepancies in the screening and treatment affects survival rate as the coverage of cervical cancer screening in the developing countries is 19% as compared to 63% in the developed countries [4]. The present study was conducted to determine the clinicopathological profile of cervical cancer patients attending tertiary care cancer hospitals in the developing country.

Materials and Methods

The retrospective analysis of 120 histopathological biopsy specimens received in the Department of Pathology for the evaluation of cervical lesions was done. All the biopsies were performed as outpatient door procedure except for the deeper biopsy which was performed in the minor operation theater. Various parameters such as age, presenting symptoms, duration of disease and staging of the disease were rechecked [5]. Histopathological types and subtypes were analyzed and correlated with clinical parameters.

Histopathological findings of preoperative biopsies were correlated with postoperative hysterectomy specimens in cases where the surgery was performed. The data obtained was analyzed.

Results

Amongst 120 cases, 106 cases were of carcinoma, 2 cases were of CIN II, 7 cases were of CIN III and 5 were of chronic cervicitis. The age group range for carcinoma varied from 33-80 years with mean age of 54.0 ± 10.5 years. Maximum number of patients was in fifth and sixth decade of life (Figure 1).

Figure 1. Agewise distribution of carcinoma cervix patients.

The most common clinical presentation in all histologic types of carcinoma was bleeding per vagina (P/V) (Table 1).

Sr. no	Presenting symptoms	Total cases (%)	Maximum duration	Carcinoma found in cases (%)
1.	Bleeding	95 (79.1%)	<6months	86 (90.5%)
2.	Discharge	10 (8.3%)	>1 year	8 (80%)
3.	Pain abdomen	5 (4.1%)	>1 year	3 (60%)
4.	Others	1(0.8%)	<6months	1 (100%)
5.	Recurrence (suspected)	9 (7.5%)	<6months	8 (88.8%)
		120		

Table 1. Symptomatic profile of cases with cervical lesions.

The patients with age >49 years (n=74, 59.5 ± 7.1) presented with late stage (61.3%) in comparison with patients of age <49years (n=32, 41.3 ± 4.1 years) (52.1%). Only 2.8% cases were underwent Pap smear screening, rest of the cases presented with symptoms of carcinoma. Maximum number of cases presented with stage \geq II in all ages. The most common histopathological type detected was squamous cell carcinoma (SCC) 80.1%, followed by 13.2% adenocarcinoma (AD) (Figure 2).

Figure 2. Histopathological variants of carcinoma a cervix.

Clinical presentation and staging was compared with histopathologic types of carcinoma cervix (Tables 2,3).

Histologic type	1B (P/V)	2D (P/V)	3PA	4Os	5A	6R
SCC	90.5%	3.5%	1.1%	0%	2.3%	5.8%
AD	57.1%	14.2%	7.1%	0%	14.2%	7.1%
*PDC	75%	0%	0%	0%	25%	0%
\$UDC	50%	0%	0%	50%	0%	0%
**CCC	0%	0%	100%	0%	0%	0%

Table 2. Clinicopathological correlation of carcinoma cervix.

*¹Bleeding p/v, ²Discharge p/v, ³Pain abdomen, ⁴Others, ⁵Associated findings, ⁶Recurrence, *Poorly differentiated carcinoma, \$Undifferentiated carcinoma, **Clear cell carcinoma

Histologic type	Stage
	≤II
SCC WD	24
ADWD	6
PD	0
UD	1
CCC	0
Total	31

Table 3. Correlation of histopathologic types with stage of the carcinoma cervix.

One case of well differentiated carcinoma was treated case of carcinoma oesophagus.

Discussion

Cervical carcinoma can occur in of all ages of females, however its usual age at presentation is 35-55 years with the peak age for the incidence varying with populations [6]. In current experience, the mean age was 54.0 ± 10.5 years with majority of cervical cancer cases diagnosed in the sixth decade of life followed by fifth decade. In India, the peak age for carcinoma cervix is 45-54 years, which is parallel to the rest of South Asia [7]. In our experience negligible number of cases (2.8%) were presented through opportunistic screening. In various regions of India opportunistic screening varied from 0.0025% to 6.9% [8][9]. This may be the reason that majority of the cases in the current analysis presented in late stage (80%). The early stages of carcinoma cervix are usually completely asymptomatic followed by bleeding P/V (including intermenstrual, postmenopausal and post coital bleeding), but several times symptoms may be absent until the cancer is in its advanced stages [10]. In the western countries cervical cancer mortality has been reduced due to screening [4]. Late stage cervical cancer can present with weight and appetite loss, fatigue, pelvic pain, heavy bleeding P/V and bone fracture in cases with metastasis. Our study also showed a majority of the patients presenting with late stage disease especially postmenopausal age group. The bleeding P/V

was seen in 81.1% as the most common finding followed by vaginal discharge in 7.5% and pain abdomen in 2.8% as seen in the study done by Mukhtar et al [11][12][13]. The possibility of advanced disease presentation may be the social culture, and lack of awareness, as the maximum duration of symptoms varied from 6 months to years [14]. The most common type of carcinoma was SCC (80.5%) and a wide spectrum of its subtypes was seen. Many studies done in the past showed SCC with its variants and AD as common histologic types of cervical carcinoma [13][15]. SCC was found to be the most common type constituting 58.2% of all the cervical carcinomas. Its different types of differentiation presented with bleeding P/V in all except 0.5% cases of moderately differentiated (MD) SCC. The most common stage at presentation was stage III accounting for 41.6% in MD and 70% in poorly differentiated (PD) type whereas stage I was the common type in well differentiated (WD) SCC. There was no associated specific finding detected in all types except 10% cases SCC PD presenting with brain metastasis. SCC non-keratinizing (NK) type of carcinomas showed mixed variation in presentation being 10% of cases presenting with discharge P/V with 20% cases presenting with stage I disease only [15].

Basaloid SCC is also a rare histologic variant with poor prognosis and it was found in 0.94% of total cases. Due to its rarity much has not been studied about it. In our experience, age affected was <49 years, and clinical features were bleeding and discharge P/V with clinical stage of IIB. No lymph node metastasis was detected except lymphovascular invasion [16].

AD of the cervix was seen in 14% of the cases, and presented in stage II and III. Discharge P/V was more commonly seen associated with AD than SCC and the recurrence rate was higher than SCC as seen in current analysis (7.1%) [12][13]. As it is mentioned in the literature that there is no significant difference in the prognosis between AD and SCC. The prognostic significance of AD histology remains unclear [17][18]. As seen in our experience majority of the AD presents with classically endophytic growths (Figure 3) and tend to show deep infiltration of the cervix except in the cases where AD presented in the long standing endocervical polyps (Figure 4).

Figure 3. Gross specimen of adenocarcinoma cervix.

Figure 4. Adenocarcinoma arising in the polyp (H&E stained section 20X).

A timely and accurate diagnosis is the key to its successful management [14].

The papillary SCC of the cervix is also a rare variant of SCC. In our experience 2.9 % of the cases were identified and presented with locally advanced disease. In the review of literature, papillary SCC is a disease of old aged and is a distinct type of carcinoma. Due to the indolent course of the variant, clinical presentation may vary and preoperative biopsy may be misleading due to pattern of growth both grossly as well as microscopically (Figure 5).

Figure 5. Papillary squamous cell carcinoma cervix (H& E stained sections 20X).

As seen in current study, no clinically visible growth or bleeding/ Discharge P/V were seen except pain abdomen. Radiological findings suggested fibroid cervix. Histopathology revealed CIN III on preoperative biopsied and invasive papillary SCC was detected on hysterectomy with invasion of deeper stroma upto paracervical tissue microscopically [19][20].

In this study the least common variant, a type of adenosquamous cell carcinoma (glassy cell carcinoma) was recognized accounting for 0.97% of total cervical carcinomas and presented with

metastasis to solid organs. It is an aggressive tumour of the cervix accounting for 0.2%-9.3% of all uterine cervixes. This histologic type has the high incidence of early distant metastasis leading to fatal clinical outcome and minimal chances of survival, hence the treatment strategies are variable compared to the other subtypes [21]. Other least common types identified were neuroendocrine type (1.8%) and undifferentiated type (1.9%) [13][22]. The patients presenting with \leq Stage II of carcinoma cervix responded well to treatment and showed good prognosis irrespective of type. However the patients with \geq Stage III showed poor prognosis [23][24]. This study highlights a range of histopathological subtypes and variation in clinical presentation of carcinoma cervix in a small study population.

In conclusion, the current study stressed the fact that 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 of screening programmes. Although clinical management and treatment of carcinoma cervix are not much relied upon a histopathological type and variants but there are many variants with different clinical presentations and specific light microscopic features which need to be considered clinically while dealing with unusual clinical presentations and supposed to be mentioned in the histopathology reports.

References

References

1. Mishra Gauravi A., Pimple Sharmila A., Shastri Surendra S.. Prevention of Cervix Cancer in India. *Oncology*. 2016; 91(1)[DOI](#)
2. Ferlay Jacques, Soerjomataram Isabelle, Dikshit Rajesh, Eser Sultan, Mathers Colin, Rebelo Marise, Parkin Donald Maxwell, Forman David, Bray Freddie. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer*. 2014; 136(5)[DOI](#)
3. Denny L. Cervical cancer: prevention and treatment. *Discov Med*. 2012; 14:125-131.
4. Gakidou Emmanuela, Nordhagen Stella, Obermeyer Ziad. Coverage of Cervical Cancer Screening in 57 Countries: Low Average Levels and Large Inequalities. *PLoS Medicine*. 2008; 5(6)[DOI](#)
5. Padubidri VG, Daftary SN. Shaw's Textbook of Gynecology. 15th ed. New Delhi: Elsevier; 2011.
6. Zeller JL, Lynn C, Glass RM. Carcinoma of the cervix. *JAMA*. 2007; 298:2336.
7. WHO/ICO. Human Papillomavirus and Related Cancers in India. Summary Report 2009. Information Centre on Human Papilloma Virus (HPV) and Cervical Cancer (a) 2009.
8. Aswathy S, Quereshi MA, Kurian B, Leelamoni K. Cervical cancer screening: current knowledge and practice among women in a rural population of Kerala, India. *Indian J Med Res*. 2012; 136:205-210.
9. Sankaranarayanan Rengaswamy, Esmy Pulikkottil Okkuru, Rajkumar Rajamanickam, Muwonge Richard, Swaminathan Rajaraman, Shanthakumari Sivanandam, Fayette Jean-Marie, Cherian Jacob. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *The Lancet*. 2007; 370(9585)[DOI](#)
10. Kulkarni Vaman, Sharma Aadhy, Bhaskaran Unnikrishnan, Singha Meher, Mujtahedi Saad, Chatrath Anshul, Sridhar Mallika, Thapar Rekha, Mithra PPrasanna, Kumar Nithin, Holla Ramesh, Darshan BB, Kumar Avinash. Profile of cervical cancer patients attending Tertiary Care Hospitals of Mangalore, Karnataka: A 4 year retrospective study. *Journal of Natural Science, Biology and Medicine*. 2017; 8(1)[DOI](#)
11. VALLIKAD E. Cervical Cancer: The Indian Perspective. *International Journal of Gynecology & Obstetrics*. 2006; 95[DOI](#)
12. Kaku M, Mathew A, Rajan B. Impact of socio-economic factors in delayed reporting and late-stage presentation among patients with cervix cancer in a major cancer hospital in South

- India. *Asian Pac J Cancer Prev*. 2008; 9:589-94.
13. Mukhtar R, Mehmood R, Parveen SH, Mukhtar H. Prevalence of Cervical Cancer in Developing Country: Pakistan. *Global Journal of Medical Research*. 2015; 15:12-7.
14. Ali F, Kuelker R, Wassie B. Understanding cervical cancer in the context of developing countries. *Ann Trop Med Public Health*. 2012; 5:3-15.
15. Jin J. Screening for cervical cancer. *JAMA*. 2014; 312(21):2302.
16. Kwon Yong Soon, Kim Yong Man, Choi Ga Won, Kim Young Tak, Nam Joo-Hyun. Pure Basaloid Squamous Cell Carcinoma of the Uterine Cervix: A Case Report. *Journal of Korean Medical Science*. 2009; 24(3)[DOI](#)
17. Fregnani José H.T.G., Soares Fernando A., Novik Pablo R., Lopes Ademar, Latorre Maria R.D.O.. Comparison of biological behavior between early-stage adenocarcinoma and squamous cell carcinoma of the uterine cervix. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2008; 136(2)[DOI](#)
18. Kasamatsu T, Onda T, Sawada M, Kato T, Ikeda S, Sasajima Y, Tsuda H. Radical hysterectomy for FIGO stage I-IIB adenocarcinoma of the uterine cervix. *British Journal of Cancer*. 2009; 100(9)[DOI](#)
19. Nagura Michikazu, Koshiyama Masafumi, Matsumura Noriomi, Kido Aki, Baba Tsukasa, Abiko Kaoru, Hamanishi Junzo, Yamaguchi Ken, Mikami Yoshiki, Konishi Ikuo. Clinical approaches to treating papillary squamous cell carcinoma of the uterine cervix. *BMC Cancer*. 2014; 14(1)[DOI](#)
20. Odida M. Papillary squamous cell carcinoma of the cervix in Uganda: A report of 20 cases. *African health sciences*. 2005; 5:291-294.
21. Guitarte Camilla, Alagkiozidis Ioannis, Mize Benjamin, Stevens Erin, Salame Ghadir, Lee Yi-Chun. Glassy cell carcinoma of the cervix: A systematic review and meta-analysis. *Gynecologic Oncology*. 2014; 133(2)[DOI](#)
22. Tempfer Clemens B., Tischoff Iris, Dogan Askin, Hilal Ziad, Schultheis Beate, Kern Peter, Rezniczek Günther A.. Neuroendocrine carcinoma of the cervix: a systematic review of the literature. *BMC Cancer*. 2018; 18(1)[DOI](#)
23. Horiot Jean-Claude, Pigneux Jacques, Pourquier Henri, Schraub Simon, Achille Emmanuel, Keiling Roger, Combes Pierre, Rozan Raymond, Vrousos Constantin, Daly Nicolas. Radiotherapy alone in carcinoma of the intact uterine cervix according to G. H. Fletcher guidelines: A french cooperative study of 1383 cases. *International Journal of Radiation Oncology*Biophysics*. 1988; 14(4)[DOI](#)
24. Montana Gustavo S., Fowler Wesley C., Varia Mahesh A., Walton Leslie A., Mack Yvonne, Shemanski Lynn. Carcinoma of the cervix, stage III. Results of radiation therapy. *Cancer*. 1986; 57(1)[DOI](#)