



# HISTOPATHOLOGICAL STUDY OF TUMOURS OF CERVIX

Atul Jain<sup>1,\*</sup>, Rachna Jain<sup>1</sup>, Iqbal<sup>2</sup>, Koteeswaran G<sup>3</sup>, Dhannanjay S<sup>3</sup>, Tusar kamble<sup>2</sup> <sup>1</sup>Department of Pathology, MGM Medical College Kamothe, Navi Mumbai <sup>2</sup>Department of Pathology, Dr. D.Y.Patil Medical College Pimpri, Pune <sup>3</sup>Department of Pathology, MGM Medical College, Puducherry

Correspondence should be addressed to **Atul Jain** Received 4 November 2014; Accepted 8 December 2014; Published 28 December 2014

Copyright: © 2014 **Atul Jain** et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

# ABSTRACTS

Carcinoma of cervix is the most common cancer in Indian women and accounts for 20% of all malignant tumours in the females. Squamous cell carcinomas (SCC) account for 75-80%, adenocarcinoma 15-25%, and adenosquamous carcinomas 3-5% of cervical cancers.

**Objectives:** To study histopathology of carcinoma of cervix and to find out the incidence rate, most common type of the carcinoma of cervix and to find out age predilection in various types of carcinoma of cervix.

**Material and Method:** This study was undertaken in the department of pathology over a period of 2 years from May 2010 to April 2012. All Hysterectomy specimens and cervical biopsies were processed routinely and paraffin sections were taken and stained with Haematoxylin and Eosin (H&E) for microscopic examination. Tumours of the cervix were classified and studied according to WHO classification.

**Results:** The most frequent condition diagnosed on cervical biopsies and hysterectomy specimens were benign cervical polyp (66.3%), followed by carcinoma (23.7%) and squamous intraepithelial lesion (0.2%). Out of all benign cervical polyps, occurrence of adenomatous polyp was highest. Incidence of squamous cell carcinoma (19.6%) was more as compared to adenocarcinoma (3.7%). The mean age of the squamous cell carcinoma, adenocarcinoma, squamous intraepithelial lesion and benign cervical polyp was 49.1 years, 43.5 years, 47.7 years and 44.6 years respectively.

**Conclusion:** Incidence of squamous cell carcinoma was more as compared to adenocarcinoma. Occurrence of malignant lesions was earlier during 4<sup>th</sup> decade as compared to benign cervical lesions.

KEYWORDS: Cervical polyp, Carcinoma cervix, Squamous cell carcinoma, Adenocarcinoma

### **INTRODUCTION**

**C**arcinoma of cervix is the most common cancer in Indian women and accounts for 20% of all malignant tumours in the females. [1] Worldwide, invasive cervical cancer is the second most common female malignancy after breast cancer and the fifth most deadly cancer in women.[1] It affects about 16 per 1,00,000 women per year and kills about 9 per 1,00,000 per year. [4] Out of the different histopathological types, squamous cell carcinomas account for 75-80% of cervical cancers, adenocarcinoma 15-25%, and adenosquamous carcinomas 3-5%. [6] Adenocarcinomas have been rising in incidence since the 1970s; especially in women younger than 35 years of age. [7] Part of the increase may be attributable to an increasing prevalence of human papilloma virus (HPV) infection. Cervical carcinomas are classified by WHO classification which is widely accepted.[8]

# MATERIALS AND METHODS

This prospective study was undertaken in the department of pathology in MGM medical college Puducherry India over a period of 2 years from May 2010 to April 2012. All hysterectomy specimens and cervical biopsies (include all polypectomy,punch biopsy, and cone biopsy) were adequately fixed in 10% formalin followed by representative bits (3-5  $\mu$ m thickness) were taken for study from the specimens. The tissues were processed routinely and paraffin sections stained with Haematoxylin and Eosin (H&E) were taken for microscopic examination. Tumours of cervix were classified and studied according to WHO classification (2001).

Statistical Methods-Standard statistical methods were used. Statistical analysis of the data was carried out with SPSS, version 16,A95% confidence interval was used. p<0.05 was considered statistically significant.

#### RESULTS

During the period of present study, total 1047 specimens (695 hysterectomy specimens and 352 cervical biopsies) received from the gynaecology department were processed and reported by the department of pathology. Out of 1047 cases, 940 were reported as non-neoplastic lesions which we had excluded from our study and 107 cases were reported as neoplastic lesions and these cases were the main study population. Out of total 107 cervical specimens, 80 (74.7%) were cervical biopsy specimens, 27 (25.2%) were hysterectomy specimens. Out of 107 cases, 71 (66.3%) were benign cervical polyp, 11 (10.2%) were squamous intraepithelial lesion and 25 (23.3%) were malignant per Table 1 as

Table 1:	Year wise	distribution	of cervical	lesions
----------	-----------	--------------	-------------	---------

Cervical lesion	2010	2011	2012	Total	Percentage (%)
Benign cervical polyp	28	29	14	71	66.3
Squamous intraepithelial lesion	7	4	0	11	10.2
carcinoma	14	10	1	25	23.3
Total	49	43	15	107	100

Peak incidence of benign cervical polyp was in 5<sup>th</sup> decade, peak incidence of malignant lesions was in 4<sup>th</sup> decade and

squamous intraepithelial lesion in  $6^{th}$  decade as per Table 2.

Age (years)	Polyp	Percentage (%)	Squamous intraepithelial lesion	Percentage (%)	Carcinoma	Percentage (%)
21-30	3	4.2	-	-	-	-
31-40	24	38.8	3	27.2	12	48
41-50	28	39.4	3	27.2	4	16
51-60	12	16.9	5	45.4	8	32
61-70	3	4.2	-	-	-	-
>70	1	1.4	-	-	1	4
Total	71	100	11	100	25	100

Table 2: Age incidence of cervical lesions

The most frequent lesion diagnosed on cervical biopsy and hysterectomy was benign cervical polyp [Figure 1 and Figure 2], followed by malignancy and squamous intracpithelial lesion. Peak incidence of both squamous cell carcinoma and adenocarcinoma occurred in 4<sup>th</sup> decade. The

mean age of the benign cervical polyp, squamous intraepithelial lesion, squamous cell carcinoma, adenocarcinoma, and was 44.6years, 47.7years 49.1 years, and 43.5 years respectively. Incidence of squamous cell carcinoma (19.6%) was more as compared to adenocarcinoma (3.7%) as per Table 3.

Histology type	Cases	Percentage (%)	Mean age (years)
Squamous cell carcinoma	21	19.6	49.1
Adenocarcinoma	4	3.7	43.5
Squamous intraepithelial lesion	11	10.2	47.7
Cervical polyp	71	66.3	44.6
Total	107	100	

Occurrence of large cell non-keratinizing squamous cell carcinoma (SCC) was highest (42.86%), followed by small cell non-keratinizing squamous cell carcinoma (19.05%)

and keratinizing squamous cell carcinoma (38.09) [Figure 3, Figure 4 and Figure 5] as per Table 4.

Table 4: Histological sub-typing of squamous cell carcinoma (SCC) of cervix

Histological sub-typing	Non-keratinizing SCC		Keratinizing SCC	Total
	Large cell	Small cell		
Cases	9	4	8	21
Percentage (%)	42.86	19.05	38.09	100

Occurrence of poorly-differentiated squamous cell carcinoma was highest as compared to well and moderately differentiated squamous cell carcinoma. [Figure 6].

Occurrence of poorly differentiated squamous cell carcinoma was early during  $4^{th}$  decade as compared to well differentiated ( $5^{th}$  decade) and moderately differentiated ( $6^{th}$  decade) squamous cell carcinoma as per Table 5.

Table 5: Age wise distribution	of grading of squamous	s cell carcinoma (SCC)
--------------------------------	------------------------	------------------------

Age (years)	Well differentiated SCC	Moderately differentiated SCC	Poorly differentiated SCC	Total
21-30	-	-	-	-
31-40	2	1	6	9
41-50	3	-	1	4
51-60	-	2	5	7
61-70	-	-	-	-
>70	-	1	-	1

Out of 4 cases of cervical adenocarcinoma, only 1 case was well differentiated [Figure 7 and Figure 8] and rests of 3 cases were with poor differentiation. Out of 11 cases of squamous intraepithelial lesion (10.2%), 5 cases were reported as low grade squamous intraepithelial lesion [LSIL] and 6 cases were reported as high grade squamous intraepithelial lesion [HSIL]. [Figure 9]

Out of all benign cervical polyps, occurrence of adenomatous polyp was highest. Peak incidence of adenomatous, leiomyomatous and inflammatory polyp was in  $5^{th}$  decade as per Table 6.

 Table 6: Age incidence cervical polyp

Age (years)	Adenomatous	Leiomyomatous	Inflammatory	Total
21-30	2	1	-	3
31-40	15	2	7	24
41-50	16	3	10	29
51-60	11	-	1	12
61-70	-	2	-	2
>70	1	-	-	1

#### DISCUSSION

Carcinomas of the female genital tract, particularly cancer of cervix accounts for almost 12% of all cancers in women, and so represents the second most frequent gynaecological malignancy in the world. [9] Cancer of cervix accounts for 4, 70,000 new cases of all cancer each year in the world. [10] Cervical cancer is the third largest cause of cancer mortality in India after cancers of the mouth and oropharynx and oesophagus, accounting for nearly 10% of all cancer related deaths in the country. In India, 90,000 of new cases of cervical cancer occur every year. [11] Cancer that develops in the ectocervix is usually squamous cell carcinoma, and around 80- 90% of cervical cancer cases (more than 90% in India) are of this type. [11] Cancer that develops in the endocervix is usually adenocarcinoma. In addition, small percentages of cervical cancer cases are mixed versions of the above two and are called adenosquamous carcinomas or mixed carcinomas. In our study, percentage of squamous cell carcinoma was more (84%) as compared to adenocarcinoma (16%) which is comparable with study done by Haghdel M. et al., [12] Smith HO et al., [13] and Ijaiya MA et al. [14]

In our study, mean age of squamous cell carcinoma was 49.1 years, adenocarcinoma was 43.55 years and squamous intraepithelial lesion was 47.7 years which are comparable to study done by Nigatu B et al. [15] and Dhakal HP et al. <sup>[16]</sup> In present study, occurrence of squamous cell carcinoma (SCC) and adenocarcinoma was early during 4<sup>th</sup> decade as compared to squamous intraepithelial lesion which was during 6<sup>th</sup> decade. In study done by Dhakal et al., [16] squamous cell carcinoma and adenocarcinoma was during 5<sup>th</sup> decade and highest incidence of squamous intraepithelial lesion was during 5<sup>th</sup> decade and highest incidence of squamous cell carcinoma was 42.86% and small cell keratinizing squamous cell carcinoma (SCC) was 19.05% and keratinizing squamous cell carcinoma (SCC) was 38.09% which is comparable to study done by Omoniyi GOE et al. [17]

In present study, highest occurrence of poorly differentiated squamous cell carcinoma (64%) was noted, while in study done by Husin N et al. <sup>[18]</sup> highest occurrence of moderately differentiated squamous cell carcinoma (44.9%) was noted and in study done by Abudu EK et al. [19] highest occurrence of well differentiated squamous cell carcinoma (39%) was noted..

In our study, highest incidence of cervical polyp was during 5<sup>th</sup> decade which was comparable to study done by Caroti et al. [20] In our study, mean age of cervical polyp was 44.6 years, which was comparable to study done by Schnatz PF et al [21] and Nigatu B et al., [15] who reported the mean age as 48.6 years and 34.8 years respectively.

#### CONCLUSION

Based on the results and the methodology employed, we have concluded that the most common cervical lesion in total cervical biopsies and hysterectomy specimens was benign cervical polyp followed by malignancy and squamous intraepithelial lesion. Incidence of squamous cell carcinoma is more as compared to adenocarcinoma. Highest incidence of both squamous cell carcinoma and adenocarcinoma occurred during 4<sup>th</sup> decade which was earlier as compared to squamous intraepithelial lesion. The mean age of adenocarcinoma was earlier as compared to squamous cell carcinoma. Out of all carcinoma, occurrence of poorly differentiated squamous cell carcinoma was highest as compared to well and moderately differentiated squamous cell carcinoma.

#### REFERENCES

- [1] Cannistra SA, Niloff JM, Cancer of uterine cervix, N Engi j med, 1996; 334: 1030-1038.
- [2] Kristensen GB, Holm R, Abeler VM, Trope CG, Evaluation of the prognostic significance of cathepsin D, Epidermal growth factor receptor, and c-erbB-2 in early cervical squamous cell carcinoma: An immunehistochemical study, Cancer, 1996; 78: 433-440.
- [3] Nair BS, Pillai R, Oncogenesis of squamous carcinoma of the uterine cervix, Int Jgynecol pathol, 1992; 11: 47-47.
- [4] Ferlay J, Bray F, Pisani P, Parkin DM, Cancer incidence, mortality and prevalence worldwide, IARCP press, Lyon, 2001.
- [5] World Health Organization, Fact sheet No. 297: Cancer, February 2006. Retrieved on 2010-12-01.
- [6] Berrington D, Gonzalez A, Green J, Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies, Int J. Cancer, 2007; 120(4): 885-891.
- [7] Grisaru D, Covens A, Chapman B, Shaw P, Colgan T, Murphy J, et al., Does histology influence prognosis in patients with early-stage cervical carcinoma?, Cancer, 2001; 92(12): 2999-3004.
- [8] Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin LH, Parkin DM, Whelan S, International classification of Diseases for oncology (ICD-0), 3<sup>rd</sup> edition, World health organization: Geneva, 2000.
- [9] Hausen HZ, Papilloma viruses and cancer basic studies to clinical application, Nat Rev, 2002; 2: 342.
- [10] Onajole AT, Ajekigbe AT, Bamgbala AO, Odeyemi KA, Ogunnowo BO, Osisanya TF, et al., The sociodermographic characteristics and the level of awareness of the prevention of carcinoma of the cervix among commercial sex workers in Lagos, Nigeria, Medical practitioner, 2004; 45(4): 54-55.
- [11] Panday k., Bhagoliwal A.J., A cancer cervix need for mass surveillance program specially in rural areas, Obstet gynecol India, 2005; 55(5): 436-439.
- [12] Haghdel M, Ardakany MS, Zeighami B, Invasive carcinoma of the uterine cervix in Iran, Int J Gynecol Obstet, 1999; 64: 265-2671.
- [13] Smith HO, Tiffany MF, Qualls CR, Key CR, The rising incidence of adenocarcinoma relative to

squamous cell carcinoma of the uterine cervix in the United States: A 24 years population based study, Gynecol Oncol, 2000; 78: 97-105.

- [14] Ijaiya MA, Aboyeji PA, Buhari MO, Cancer of the cervix in Ilorin, Nigeria West, African Journal of Medicin, 2004; 23(4): 25-30.
- [15] Nigatu B, Gebrehiwot Y, Kiros K, Eregete W, A five year analysis of histopathological results of cervical biopsies examined in a pathology department of a teaching hospital, Ethiopian Journal of Reproductive Health, 2010; 4(1): 52-57.
- [16] Dhakal HP, Pradhan M, Histological pattern of gynaecological cancers, J Nepal Med Assoc, 2009; 48(176): 301-305.
- [17] Omoniyi GOE, Olusola BF, Kayode A, Olusegun SO, Histological Pattern of Cervical Malignancies in Southwestern Nigeria, Trop J Obstet Gynaecol, 2004; 21: 118-121.

- [18] Husin N, Helali T, Domi M, Bedri S, Cervical cancer in women diagnosed at the national health laboratory, sudden: A call for screening, Sudan journal of medical science, 2011; (6): 183-190.
- [19] Abudu EK, Banjo AAF, Izegbu MC, J.Agboola AO, Anunobi CC, Jagun OE, Histopathological pattern of carcinoma of cervix in Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria, Nig Ot j Hosp Med, 2006; 16(3): 35-40.
- [20] Caroti S, <u>Siliotti F</u>, Cervical polyps: A colpo-cytohistological study, <u>Clin Exp Obstet Gynecol</u>, 1988; 15(3): 108-115.
- [21] Schnatz PF, Ricci S, O'Sullivan DM, Cervical polyps in postmenopausal women: Is there a difference in risk?, <u>Menopause</u>, 2009; 16(3): 524-528



Figure 1: Gross picture showing cervical polyp



**Figure 2:** Inflammatory Cervical Polyp (H&E 10X) Section shows polypoidal structure lined by cuboidal epithelium with marked acute on chronic inflammatory infiltrate in the underlying tissue



**Figure 3:** CIN 3 (H&E 40X) presence of immature-appearing cells throughout the epithelium. The nuclei are hyperchromatic and have slightly irregular nuclear Outlines with presence of high nuclear/cytoplasmic ratios



Figure 4: Gross picture of squamous cell carcinoma cervix



**Figure 5:** Well Differentiated Squamous Cell Carcinoma (H&E 10X) section shows presence of concentric whorls of cells with central pools of pink cytoplasm (keratinization) along with mild degree of dysplasia and few foci of stromal invasion



Figure 6: Moderately Differentiated Squamous Cell Carcinoma (H&E 40X) section shows fronds of malignant squamous cells pushing in to the stroma with presence of keratinisation



**Figure 7:** Poorly Differentiated Squamous Cell Carcinoma (H&E 10X) section shows highly malignant tumor with loss of differentiation with huge and pleomorphic cells along with abundant abnormal mitosis



Figure 8: Gross picture Adenocarcinoma of Cervix



Figure 9: Microscopic view of well differentiated adenocarcinoma cervix showing malignant endocervical glands (H & E X 10)



**Figure 10:** Moderately differentiated Adenocarcinoma cervix (H&E 20X) showing endocervical glands with dark, elongated, crowded, and stratified nuclei along with abnormal mitosis

8