

HISTOMORPHOLOGICAL PATTERN OF NON-NEOPLASTIC AND PRE-NEOPLASTIC LESIONS OF CERVIX

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ABSTRACT

BACKGROUND

Specimens from cervix constitute a major contributor of gynaecological tissue received for histomorphological evaluation. Benign lesions presents with varied clinical presentations and age distribution. Lesions such as dysplasia and Cervical Intraepithelial Lesions are a precursor to malignancies which have a high mortality and morbidity among Indian women.

AIMS

To study pattern of non-neoplastic and pre-neoplastic lesions of cervix and their correlation with age, symptoms, gravida, socioeconomic parameters and personal habits.

METHODS AND MATERIAL

A retrospective study was done in Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh from January 2014 to August 2015.

STATISTICAL ANALYSIS

Program epi info and SSPS were used to evaluate data.

RESULTS AND CONCLUSIONS

195 cases were evaluated with peak cases presenting in 4th decade. Chronic nonspecific cervicitis (175 cases) was the most common histomorphological diagnosis and only 5 cases of Cervical Intraepithelial Lesions were reported, though 180 cases of cervical cancers were reported during the same time period highlighting the need to bridge the gap with early diagnosis and treatment of pre-malignant lesions.

KEYWORDS

Benign, Cervix, Histomorphology, Chronic Cervicitis.

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INTRODUCTION

Cervical cancers constitute a major health problem among Indian women. It is preceded by Cervical Intraepithelial Lesions; in fact it is one of the few cancerous lesions in which precursor lesions have been extensively researched and studied. The non- and pre-neoplastic lesions have a wide age distribution and often presents late since most cases are asymptomatic. These lesions are amenable to treatment and early detection of pre-neoplastic cases could reduce the cervical cancers incidence considerably. Cervices from hysterectomies and biopsies constitute the majority of gynaecological specimens, which are received in the Department of Histopathology. Owing to varied frequency of various lesions in different geographic regions within our

country, understanding the histopathological pattern of these lesions will help in the management of the patient. Cytological screening programs for cervical cancers have not yet achieved their goal due to lack of coverage, faulty sampling and processing and paucity of pathologists as well as discordance in reporting of same slide. Therefore, the histopathological examination of the biopsies of cervical lesions is the single best gold standard for the diagnosis of the lesions of the cervix.^[1]

The aim of the following study is to establish the frequency and histopathological types of non-neoplastic and pre-neoplastic cervical lesions of the cervix in our institute. It is hoped that data obtained from our research will be useful in the management of these lesions as well as will serve baseline for further research pertaining to this topic.

MATERIALS AND METHODS

A retrospective study was conducted in the Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh from 1st January 2014 - 31st August 2015.

All the cervical biopsies and hysterectomy specimens with adequate tissue received in Department of Pathology for cervical lesions were evaluated. All non- and pre-neoplastic lesions were included, while all neoplastic cases were excluded from the study. All samples under study were received in 10% formalin, routinely processed according to

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standard techniques after grossing. The wax blocks of tissue were cut using microtome and mounted on slides followed by staining procedure (Haematoxylin and Eosin) and reported by faculty of department. Relevant data like age, clinical history, parity, gravida, menstrual history, personnel hygiene, etc. were obtained from requisition forms as well as case files as and when required. Ethical clearance was received from Institute's Ethical Committee. Statistical Analysis of Data was analysed using appropriate statistical tests using software epi-info and SSPS.

RESULTS

A total of 375 cases were evaluated. Out of these, 195 (52%) cases were in non-neoplastic and pre-neoplastic category and 180 (48%) cases were neoplastic category. Incidence of non-neoplastic lesions was higher than neoplastic lesions. Chronic non-specific cervicitis was the most common histological diagnosis made with 175 cases. Distribution of as in Table 1.

The histomorphological distribution pattern of benign lesions comprising of non-neoplastic and pre-neoplastic (195 cases) was as follows (Table 2).

Thus, non-neoplastic and pre-neoplastic lesions comprised of 176 (90.3%) and 19 (9.7%) cases respectively. Only one case of granulomatous cervicitis was reported, the sections revealed multiple caseating granulomas surrounded by epithelioid cells and mononuclear cells along with fibrin strands. The underlying aetiology was most probably tubercular considering the fact that the patient had history of contact with a known sputum positive tuberculosis cases as well as the geographical and aetiological background of patients in patients reporting in our institute.

The cases of chronic cervicitis constituting the majority chunk showed erosion of surface epithelium, congestion, mild inflammatory infiltrate as well as squamous metaplasia in majority of cases.

14 cases of cervical dysplasia were reported along with 5 cases of CIN cases.

Lesions of Cervix and their Correlation with Age

The age distribution for benign cervical lesions peaked in 4th decade with 68 (34.9%) cases. The following observations were made regarding the mean age of patients in 2 broad histological categories in this study (Table 3).

Age distribution of lesions was also studied extensively to infer the pattern and presentations. The mean age of cases increased hierarchically as the spectrum progressed from chronic non-specific cervicitis to CIN. The mean age of chronic non-specific cervicitis was 40.8 years with cases ranging from 22 to 65 years, while that of dysplasia was 47.1 years and range was 33 years to 65 years. Thus dysplasia cases were encountered a decade later than chronic cervicitis. CIN cases had a mean age of 57.2 years and all the cases presented in late 5th and early 6th decade.

Clinical Presentation of Cervical Lesions

The clinical presentation of women was varied. Most common clinical presentation was white discharge with or without lower abdominal pain (47.69%) followed by lower abdominal pain only (26.66%) and abnormal bleeding/spotting (13.84%). Only 10.77% cases had complained of post-menopausal bleeding, while only 1.03% cases presented with

pyometra. Clinical presentation in varied lesions was as in Table 4.

Gravida

Average Gravida of females increased successively from 2.9 in non-neoplastic, 3.47 in pre-neoplastic category. The distribution is as in Table 5.

Abortions

Regarding number of abortions 71.28% had nil abortions, 22.56% had single and a mere 6.15% had 2 or more abortions in their lifetime and were statistically insignificant.

Distribution of Rural and Urban Population

Our study group comprised of population from both rural and urban areas. There was no significant difference in the distribution of cervical diagnosis with regards to area of residence apart from the fact that women of urban area had more accessible health services and better treatment follow-up than their rural counterparts; 97 (49.74%) patients were from rural background.

Other Factors

Majority of females had poor personnel hygiene habits. Only 4% used oral contraceptives, a minority used barrier method, while majority used no contraceptives and underwent total tubectomy after family completion.

Majority of women in our study had menarche at 12-13 years of age and had first sexual exposure before the age of 20 years. A majority of them also had their first conception before reaching 20 years and almost all had completed their family in 2nd decade.

None of the women were immunised with human papilloma virus vaccine. Also, awareness regarding the same was almost non-existent.

Broad Category of Cervical Lesions	No. of Cases	Percentage %
Non-neoplastic	176	90.25%
Pre-neoplastic	19	9.75%
Total	195	100%

Table 1: Distribution Lesions of Cervix

Diagnosis	No. of Cases	Percentage %
Chronic Cervicitis	175	89.74%
Chronic Cervicitis with Dysplasia	14	7.18%
CIN3	2	1.03%
CIN2	2	1.03%
CIN1	1	0.51%
Granulomatous Cervicitis	1	0.51%
Total	195	100.00%

Table 2: Distribution of Benign Lesions of Cervix

Diagnosis	Mean Age (Years)	Standard Deviation
Non-neoplastic	40.72	8.56
Pre-neoplastic	49.79	10.76

Table 3: Mean Age and Standard Deviation of Lesions of Cervix

Symptoms	Chronic Cervicitis	Dysplasia	CIN
White Discharge With/ Without Lower Abdominal Pain	86	5	0
Lower Abdominal Pain	48	4	0
Abnormal Bleeding/Spotting	26	2	1
Post-Menopausal Bleeding	15	3	3
Pyometra	1	0	1

Table 4: Clinical Presentation of Benign Lesions of Cervix

Gravida	Non-Neoplastic	Pre-Neoplastic
0-2	73(41.4%)	6(31.57%)
3-4	89(50.56%)	8(42.1%)
>5(grand multipara)	14(7.9%)	5(26.31%)

Table 5: Distribution of Gravida

Study (Place)	Period	Total Cases	Non-Neoplastic Cases (%)	Most Common Non-Neoplastic Lesion-CC Cases (%)	Remarks
			Neoplastic Cases (%)		
Olutoyin ^[2] (Nigeria)	10 yrs. 1900-1999	400	150(32.5%)	123 (82%)	5 cases of granulomatous
			250 (62.5%)		
FN Nwachokor ^[3] (Nigeria)	7 yrs. 2005-2011	176	99(56.3%)	44 (44.44%)	-
			78(43.7%)		
Aravind P (Karnataka)	2 years (2008-10)	1038	1015 (97.8%)	742 (73.2%)	-
			23 (2.21%)		
Naveen BJ ^[4] (Telangana)	2 years (2013-14)	1052	830 (78.89%)	698 (76.79%)	Studied adaptive lesions
			222 (21.1%)		
Srinivani S ^[5] (Tamil Nadu)	3 years (2012-15)	794	633(79.7%)	300 (37.9%)	Included prolapse
			161(20.3%)		
Present study (Madhya Pradesh) (2015)	20 months (Jan 2014 – Aug 2015)	395	195(52%)	175 (46.67%)	Excluded prolapse, one case of granulomatous cervicitis
			180(42%)		

Table 6: Various Studies and their Findings Compared to Present Study

Studies	Peak Decade	Age Range	Mean Age	Most Common Symptom
Olutoyin G ^[2]	4 th (34.5%) followed by 3 rd (30%) & 5 th (18.7%)	20-69	-	-
Aravind P ^[6]	4 th (47%)	-	-	White discharge per vagina (26.6%) followed by mass per vagina (21.08%)
FN Nwachokar ^[3]	4 th (33.7%) followed by 5 th (23.9%) & 3 rd (21.7%)	20-89	54.9+ 4.6	-
Naveen BJ ^[4]	4 th	-	-	Excessive vaginal bleeding (45.7%) followed by mass per vagina (31.8%)
Srivani S ^[5]	5 th	20-79	-	-
Present Study	4 th (40.3%) followed by 3 rd (35.22%) and 5 th (5.58%)	22-65	40.8+8.6	White discharge (47.69%) followed by lower abdominal pain (26.66%)

Table 7: Comparative Evaluation of Age Distribution

DISCUSSION

We observed a wide range of histomorphological lesions among study of benign cervical lesions. In present study, chronic cervicitis and CIN cases had lower reported cases than expected from the population in considering that neoplastic cases were almost equal to non- and pre-neoplastic cases (48% vs 52%) in a period of 20 months. The reason attributed to this is that most cases in our environment go unreported. In addition, it is also important to note that most cases are treated empirically by physicians or by self-medication.

Therefore, only few difficult cases would present at the Gynaecological Clinic for proper evaluation when symptoms are recurrent and/or persistent. Also there is minimal reporting of CIN cases in our scenario due to lack of specific

symptomology in patients, social inhibitions to report gynaecological problems and lack of effective screening program in place. Thus, the gap was quite narrow highlighting the fact that more awareness, screening and regular follow-up could widen the gap and tilt graph favourably more towards the benign spectrum.

With regard to spectrum of lesions Olutoyin G,^[2] FN Nwachokor,^[3] Naveen Kumar BJ^[4] and Srivani Saravanan^[5] reported 38.5%, 56.3%, 78.86% and 79.9% cases of benign lesions respectively among all cervical lesions reported in their respective study groups compared to 52% cases in present study.

The lower proportions of non-neoplastic lesions by Olutoyin G^[2] may be due to the fact that the study was done in

1990s when both education, awareness and health facilities were inadequate compared to present times.

The increased proportion of benign lesions by Srivani Saravanan^[5] and Naveen Kumar BJ^[4] is understood by the fact that both studies were conducted beyond 2010 closer to present study as well as the South Indian population under consideration has better literacy rate, socioeconomic standing and health care facilities than central India, the setting of present study.

Olutoyin G^[2] FN Nwachokor,^[3] Aravind Palladily,^[6] Srivani Saravanan^[5] and Naveen Kumar BJ^[4] observed chronic nonspecific cervicitis as the most common lesion with 82%, 72.2%, 76.79%, 37.9% and 97.3% cases respectively compared to 89.7% cases in present study.

Thus, it was similar to all studies except that by Srivani S et al,^[5] because cervical prolapse was included in their study group unlike the present study which relatively decreased the chronic cervicitis proportions. The increased incidence of chronic cervicitis by Naveen Kumar BJ^[4] may be attributed to increased reporting and awareness among females in present times, especially in South India the study area of aforementioned research.

With respect to granulomatous lesions only Olutoyin G^[2] reported 5 cases in Nigeria compared to 1 case in present study. These were most probably due to tuberculosis, which had a high prevalence of 250/1 lakh population in Nigeria and 10th rank among the 22 high-burden TB countries in the world.^[7]

Also tuberculosis is seldom known to infect cervix, though fallopian tubes are its common site. Though central India has high rate of tuberculosis particularly in association with HIV, it seldom comes to notice as other health problems mask its incidence.

Comparative evaluation has been tabulated in Table 6 and Table 7.

For benign lesions of cervix, the peak age group was 4th decade in studies by Olutoyin G,^[2] FN Nwachokar,^[3] Aravind P^[6] and Naveen BJ^[4] similar to present study barring that by Srivani S^[5] observed peak in 5th decade. This can be explained by the fact that she included cervical prolapse in study group, which might have skewed the peak to 5th decade.

In our study, the mean age of non-neoplastic lesions was 40.7 years compared to 49.7 in pre-neoplastic group almost a decade later. We inferred that women are increasingly being health conscious and awareness regarding gynaecological treatment has increased significantly among the relatively younger generation. Though social and economic barriers still hound many to seek health care facilities apart from obstetric causes

The most common clinical presentation was white discharge per vaginum similar to Aravind P,^[6] and in contrast to that of Naveen BJ^[4] - abnormal bleeding. We could not explain the reason for this contrast. However, findings of present study were consistent with symptomology mentioned in standard literature.

Benign lesions of cervix consisting mainly of chronic cervicitis is a precursor for carcinogenesis, as repeated and persistence insult to cervical epithelium leads to metaplasia and subsequently neoplasia as well, thus screening and early detection of same is pertinent for control of cancers of cervix uteri.

There is an urgent need for regular and effective cervical screening program as well as HPV vaccination should be included in universal immunization program in India. Vaccine is expensive and cytology based screening is resource intensive in terms of infrastructure, equipment and manpower. As a result, death and disability from this cancer are high including India.^[8]

Women being the main caretaker of children as well as an almost equal economical contributor in current era need to be properly screened for malignancies and detecting cases in pre-neoplastic and curable stage will go a long way in reducing morbidity and mortality.

We observed that women were reluctant in approaching health clinics for gynaecological symptoms. Also none of the cases had HPV vaccination before the first sexual encounter. Though awareness regarding the same is increasing, cost and social stigma are the main deterrent factors for females in current scenario. History regarding number of sex partners and sexual history of their male counterparts was also unreliable in our study group.

Though there are many national programs successfully running for obstetrics cases, same is lacking for gynaecological problems.

The WHO recommended target group for HPV vaccination is 9–13 year old girls who have not yet become sexually active.^[9] Including school girls in HPV vaccination program in future will help reduce the burden of cervical lesions. Sensitisation of parents is essential for undertaking such programs and large scale awareness programs need to be implemented highlighting its long-term health benefits. Especially designed messages are essential to educate communities keeping in mind social yardsticks and education of people. Parents, specifically illiterates need to be sensitively communicated the reason for targeting girl child. Subsequently, non-school going girls should be included more so because low socioeconomic and poor hygiene is a known risk factor for cervical pathologies.

Early screening of the disease through cytology has considerably reduced morbidity and mortality from the disease in the developed world.^[10] Cervical cancer causes loss of productive life both due to early death as well as prolonged disability. Additionally, the high medical costs that are incurred by families due to cervical cancer (especially since most cases in developing countries are diagnosed at advanced stages when treatment is costly but prognosis poor), further impoverish individuals and communities.^[11] Thus, detecting precursor lesions in nascent stage could reduce the cancer burden considerably.

In finance constrained setting like ours, cost of vaccine as well as operational cost for delivery need also to be taken into consideration during planning process itself and will be a critical step in the decision-making process.

Due to difficulties of access and affordability, compliance to and follow-up of treatment is much worse for women of low socioeconomic strata leading to further morbidity and mortality from the disease.

CONCLUSION

Large scale screening programs for target populations should be organised to reduce the long-term morbidity, mortality and socioeconomic burden related with cervical lesions.

Also increasing literacy rate, personnel hygiene, socioeconomic strata, use of contraceptive measures to reduce parity will be highly instrumental in tackling the current and future burden of cervical cancers.

We hope and recommend that this study will lay the foundation for policy makers to effectively prevent and control cervical cancers in future as well as improve the present scenario.

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ABBREVIATIONS

CIN - Cervical Intraepithelial Lesions.

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