

Research Article

Cytomorphological evaluation of squamous cell abnormalities observed on cervical smears in government medical college, Jabalpur, India: a five year study

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ABSTRACT

Background: Cervical cancer is the fourth most common cancer affecting women worldwide, the most common cancer in women in several less developed countries, and now the second most common cancer in India. Cervical cytology by papanicolaou (PAP) smear test is an effective tool for detecting abnormal cytology in early stages, thus allowing early detection and treatment. The PAP smear is extremely important for detecting premalignant and malignant conditions of cervix. The study was conducted to determine; (1) Cytomorphologic incidence of various lesions of uterine cervix; (2) Categorization of detected lesions according to Bethesda system; (3) Determination of epithelial abnormalities by cervical cytology.

Methods: The settings and design of this study is a hospital based prospective study from a tertiary care centre in Central India. A total of 5813 conventional pap smear tests collected from January 2010 and December 2014 were analyzed. All patients attending outpatient department of obstetrics and gynecology for complaints of abnormal cervical discharge, dyspareunia, inter-menstrual bleeding, post-coital bleeding and lower abdominal pain were included. Various cervical pap screening camps were also done during this period. Smears were fixed and stained with hematoxylin & eosin (H&E) and papanicolaou stain were done.

Results: The overall frequency of normal, inadequate, inflammatory, and abnormal smears was 11.86%, 5.73%, 74.98% and 13.2% respectively. Atypical squamous cell carcinoma of undermined significance (ASCUS) was seen in 3.61%, squamous intraepithelial lesion (SIL) was seen in 5.36%, low grade squamous intraepithelial lesion (LSIL) was seen in 2.59% while high grade squamous intraepithelial lesion (HSIL) was seen in 2.77%. Invasive carcinoma was seen in 3.69%. The premalignant epithelial abnormalities like ASCUS, LSIL and HSIL were found to be highest in the age group of 31-50 years in our study, which correlated well with other similar studies.

Conclusions: Hence we should advocate regular cervical cytology (PAP) smear study, which can help to treat cervix lesions early before the progress into cervical cancer. Early detection is the only key to saving a woman's life as the later the abnormalities are discovered; mortality, morbidity and treatment cost all increase.

Keywords: PAP smear, Screening, Cervical cancer, Premalignant lesions, ASCUS, LSIL, HSIL, SCC, Bethesda system

INTRODUCTION

Cervical cancer is the fourth most common cancer in women and the seventh overall, with an estimated 528,000 new cases every year. Cancer cervix is the most

common cancer in women in several less developed countries, and now the second most common cancer in India. Almost 70% of the global burden of cervical cancer is in areas with lower levels of development, and more than one fifth of all new cases are diagnosed in

India. About 122,844 new cervical cancer cases are diagnosed annually in India (estimations for 2012). Cervical cancer ranks as the 2nd most common cause of female cancer in women aged 15 to 44 years in India. About 67,477 new cervical cancer deaths occur annually in India, making cervical cancer the 2nd leading cause of cancer deaths in women aged 15 to 44 years in India.¹ Seventy percent or more of these cancers are in stage 3 or higher at the time of diagnosis. This higher rate of mortality is attributed to the late presentation of cervical cancers. However, cervical cancer is a preventable disease if detected in early stage. There are several methods for cervical cancer screening and several studies have established the importance of papanicolaou (PAP) smear as one of the easy and important screening methods for cervical cancer control.² Routine cervical screening programmes by Pap smear has reduced the morbidity and mortality of invasive cervical cancer worldwide.^{3,4} Unfortunately, in India, screening coverage by the existing cancer screening programme is 2.6-5 percent mainly due to inequality between infrastructure, resources and outsized population.⁵⁻⁷ As a result, very often diagnosis of cervical cancer is based on opportunistic screening or after the onset of symptoms. There is an urgent need for initiation of community screening and educational programs for the control and prevention of cervical cancer in India.⁸

This study was conducted to assess the cytomorphological incidence of various lesions of uterine cervix and to determine the importance of conventional pap smears in the diagnosis of various epithelial abnormalities of uterine cervix.

METHODS

This was a hospital based cross-sectional study conducted on 5813 Pap smears prepared from women aged 18-70 years coming for this test between January 2010 and December 2014.

Inclusion criteria

Patients presenting with complaints of vaginal discharge, hypogastric pain, backache, dyspareunia, postcoital and intermenstrual bleeding were included in the study, after informed consent.

Exclusion criteria

Pregnant women, menstruating women, women with invasive cervical carcinoma at the time of clinical evaluation and women already treated with cervical carcinoma.

Complete clinical history and relevant information was obtained from the patient and recorded on the proforma. The study was approved by the board of ethical committee. Before taking the Pap smear it was ensured that no local douche, antiseptic cream and no vaginal

medication for the preceding 24 hours was used. Pap smear was taken with a disposable wooden Ayer's spatula. The cellular material was obtained from squamocolumnar junction of cervix, were spread on a glass slide. The glass slide was then immediately dipped in coplin jar containing 95% ethyl alcohol. The slides were sent to pathology department and were stained with hematoxylin and eosin (H&E) stain and rapid papanicolaou stain. The slides were screened and reported by a consultant pathologist. Evaluation of the cervical cells was done using the Bethesda system 2001.⁹

The result of cervical smear was reported as normal smear, inadequate smear, inflammatory smear, atypical squamous cell of undetermined significance (ASCUS), low grade squamous intraepithelial lesion (LSIL) and high grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCC), Adenocarcinoma (ADE) and atypical glandular cell of undetermined significance (AGUS). Data were coded and entered into microsoft excel worksheet. The results were expressed in percentages and proportions.

RESULTS

In the present study 5813 PAP smears were examined in our department of pathology -cytology section. The age range of the patients was 18 to 82 years. The mean age was 36.5±10.73. Majority of cases were in the age group of 30-39 years (45.07%) followed by 23.70% in the age group of 40-49 years, 18.01% in 20-29 years (Table 1). Mean age of patients with low grade intraepithelial lesions (LSIL) was 34.8±10.2, while mean age of HSIL and SCC was 40.9±11.6 and 45.6±10.2 respectively.

Table 1: Distribution of cases according to age (n=5813).

Age in years	No. of cases	Percentage
<20	21	0.36
20-29	1047	18.01
30-39	2620	45.07
40-49	1378	23.70
50-59	466	8.02
60-69	270	4.64
>70	11	0.2

Out of 5813, 5480 (Table 2) smears were satisfactory for evaluation while 333 (5.7%) were inadequate for cytological examination. According to Bethesda system, 4761 (86.88%) smears were negative for intraepithelial lesion (NILM) while epithelial cell abnormalities were seen in 719 (13.12%) smears.

Table 2: Cytological categorization of cases.

Cytological categorization	No. of cases (n=5813)	Percentage
Unsatisfactory for evaluation	333	5.73
Satisfactory for evaluation	5480	94.27

Abnormal vaginal discharge was the commonest complaint among our patients (73.7%) (Table 3), followed by abnormal bleeding in the form of post

menopausal bleeding, intermenstrual bleeding and post coital bleeding.

Table 3: Clinical presentations of the patients.

Complaint	No.of cases	Percentage	NILM	ASCUS	LSIL	HSIL	AGUS	SCC	ADE
White discharge	4043	73.7	3849	75	40	35	10	33	1
Post-menopausal bleeding	260	4.7	127	02	09	19	01	97	5
Inter-menstrual bleeding	320	5.8	205	14	52	24	03	20	2
Post coital bleeding	151	2.7	48	07	17	43	0	32	4
Pain in abdomen	550	10.0	433	64	15	21	10	7	0
Backache	60	1.1	35	16	02	5	0	2	0
Pruritus vulvae	32	0.58	20	7	5	0	0	0	0
Dysuria	12	0.22	6	5	0	1	0	0	0
Something coming out of vagina	52	0.94	38	8	2	4	0	0	0
	5480		4761	198	142	152	24	191	12

80% patients were multiparous. Maximum cases (71%) belonged to low socio-economic group.

Amongst the 4761 smears which were negative, 652 (11.89%) showed normal cytological findings and 4109 (74.8%) were inflammatory. Out of inflammatory smears non-specific cellular changes due to inflammation were seen in 3535 (64.50%) and 194 (3.54%) had features of atrophy (Table 4).

Table 4: Categorization of cases according to the results of cervical cytology/ PAP test.

Cytodiagnosis	No. of cases (n= 5480)	Percentage
Negative for intra epithelial lesion	4761	86.88
Normal/Nos	652	11.89
Inflammatory	4109	74.98
i. Organisms	380	6.93
ii. Reactive cellular changes associated with inflammation and repair	3535	64.50
iii. Atrophic	194	3.54
Squamous cell abnormalities	719	13.12
ASCUS	198	3.61
LSIL	142	2.59
HSIL	152	2.77
AGUS	24	0.43
Carcinoma		
Squamous cell carcinoma	191	3.48
Adenocarcinoma	12	0.21

Diagnosis of atypical squamous cells of undetermined significance (ASCUS) was made in 198 (3.6%) cases. Squamous intraepithelial lesion was seen in 284 cases, out of which 142 cases, (2.59%) had low grade squamous intraepithelial lesion (LSIL) showing koilocytosis, hyperchromasia with uniformly distributed and coarsely granular chromatin.

There were 152 smears (2.77%) showing features of high grade squamous intraepithelial lesion (HSIL) which were severely dysplastic cells with hyperchromatic nuclei, irregular nuclear membrane, coarsely clumped chromatin, prominent nucleoli and rounded cell borders. Features of squamous cell carcinoma like numerous dyskaryotic cells along with markedly irregular clumping of chromatin, prominent macronuclei, bizarre shaped cells and tumor diathesis was seen in 191 smears (3.48%) and 12 (0.21%) smears showed features of adenocarcinoma which were malignant cells arranged in sheets and syncytial aggregates along with enlarged, pleomorphic nucleus, irregular nuclear membrane, irregular chromatin distribution and macronucleoli and tumor diathesis. Twelve (0.21%) smears showed features of adenocarcinoma.

DISCUSSION

Cervical cancer is fourth most common cancer affecting women worldwide and now the second most common cancer in India. The literature on cervical cytology is overwhelmed with evidences supporting the importance of early detection of treatable precancerous lesions making cervical cancer unique and subsequent timely treatment would impede progress toward invasive cancer.

More than one fifth of all new cases are diagnosed in India, so the need of the hour is to implement well

planned and systematic cervical cancer screening programs.^{6,10} The best way of preventing and controlling cervical cancer is regular screening and early diagnosis and we all know that the value of Pap smear testing in cervical carcinoma screening is undisputed. Frequently repeated cytology screening programs have led to a large decline in cervical cancer incidence and mortality in developed countries.¹¹

The WHO recommended that in low resources settings, the aim should be to screen every woman once in her life time at an age from 40-45 years, which can significantly reduce the mortality from cervical cancer.¹² It is well established that the rate at which invasive cancer develops from premalignant lesions is usually slow, measured in years. This long natural history provides the opportunity for screening, to effectively detect this process during the pre-invasive phase, thus allowing early treatment and cure and it has been found that the risk of developing cervical cancer is 3-10 times greater in women, who have not been screened before, thus the benefit of conducting screening far exceeds the cost involved.¹³

Amongst the 5,813 cervical smears taken from women attending gynecology OPD between January 2010 and December 2014, only 333 smears (5.73%) of the smears were unsatisfactory for evaluation. Similar studies have shown the percentage of inadequate smears have ranged from 0.2% to 13.94%.¹⁴⁻¹⁶ The proportion of satisfactory samples received was impressively high as in our institute cervical smears were taken by trained gynecologists and then send to department of pathology for analysis, therefore, reducing costs and inconvenience of the patients.

Abnormal vaginal discharge was the commonest compliant among our patients (73.7%). Present study

emphasized the significance of vaginal discharge and its association with neoplastic changes in the cervix. Other studies by Kenneth et al, Khattak et al, Pradhan et al and Bal et al, found vaginal discharge as the commonest presentation.¹⁷⁻²⁰

In our present study, 74.98% of the smears showed non-specific inflammation. Studies in populations carried out by Patel et al, Mulay et al and Bal et al have observed inflammation in smears in 19.6%, 57.48% and 74.3%, respectively.²⁰⁻²² It is likely that the poor socio-economic status and unhygienic conditions of the women in our study was responsible for the higher percentage.

The detection of cervical epithelial abnormalities in routine Pap (cervical) smear examinations does not show any consistent pattern in both the developed and developing countries around the world. The prevalence in epithelial cell abnormalities in previously published various studies, from around the world has shown a wide range from as low as 0.98% to as high as 15.5%.^{23,24} Of the 5813 cervical smears included in this study 86.88% (n=4761) were negative for any intraepithelial lesion with 13.12% (n=719) have epithelial abnormalities. The prevalence of various epithelial abnormalities in our study showed ASCUS - 3.6%, LSIL - 2.59%, HSIL - 2.77% and SCC - 3.48%. The prevalence rates of cervical dysplasia in India range from 1.392-7.8% while in our study it was 13.12%.^{14,21,22,30} Prevalence of epithelial abnormalities in different studies were represented in Table 5. The result of the current study is quiet high in comparison to some of the available literature. The reason may be that the study was conducted in a tertiary care hospital, which is a referral centre for symptomatic as well as clinically suspicious patients, thus more cases of positive results.

Table 5: Prevalence of epithelial abnormalities in different studies.

	Gupta et al ²⁵	Mulay et al ²²	Ranabhat et al ²⁶	Bal et al ²⁰	Saha et al ²⁷	Patel et al ²⁸	Bukhari et al ²⁹	Present study
Epithelial cell abnormalities	5.64%	1.39%	1.7%	5%	10.3%	12.98%	10.2%	13.12%
ASCUS	3.36%	0.64%	0.23%	0.3%	2.6%	1.66%	9.8%	3.61%
LSIL	1%	0.21%	0.34%	2.7%	3.5%	8.33%	45%	2.59%
HSIL	0.34%	0.16%	0.68%	0.3% %	2.1%	2.66%	21.8%	2.77%
SCC	0.41%	0.06%	0.23%	1%	1.2%	-	13.7%	3.48%

In present study, incidence of ASC-US/SIL ratio was 0.67. The ASC-US/SIL ratio is a quality indicator of reporting quality of Pap smears and should be less than 1.5:1 for satisfactory reporting quality. In present study the ASC-US/SIL ratio, indicates that the reporting quality was optimal.

CONCLUSION

This study has shown a high prevalence of epithelial cell abnormalities in cervical smears in our set up. Pap smear examination is widely accepted screening method. Even though there was steady increase in number of Pap smear tests over the years indicating awareness and importance

of Pap smear screening, but there was low Pap smear self-request indicating need for increased public education and awareness about the disease. If morbidity and mortality from cancer of the cervix are to be further reduced it is the pre and post-menopausal women of the population that must be reached and persuaded to participate in the screening programme.

Thus, cervical cytology screening by Pap smear is a simple, safe, quick and effective test to identify cervical intraepithelial neoplasia (CIN) and carcinoma of cervix at an early stage; thereby helps the gynecologists in early and more efficient management of the patients.

In countries like India with predominant rural population, having low socio-economic status, marriage at an early age and poor medical facility, Pap smear examination should begin at 30 years and it should be subsequently followed with HPV-DNA testing at higher centers which will increase the sensitivity.

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