

Pattern of Epithelial Cell Abnormalities on Cervical Papanicolaou Smears in Hospital of North India: A Retrospective Study

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ABSTRACT

Introduction: Cervical cancer is the most common cancer of the female genital tract. India accounts for 25% of the cervical cancer deaths and the incidence is about 23.29%. Pap smear test is considered to be most important test for screening of cervical cancers and is regarded as gold standard for screening program.

Materials and Methods: A retrospective study was carried in Department of Pathology of a Hospital of North India, from June 2014 to Jan2017. Total of 1534 samples were screened. We followed The Bethesda system 2014 for reporting the Pap smears.

Results: Out of 1534 samples, 4.8% were unsatisfactory, 90.6% were NILM, 1.4% were ASCUS, 0.8% each were LSIL, HSIL, and Squamous Cell Carcinoma 0.26% each were AGCUS and ASCH. The commonest age group affected was 30 -50 years.

Conclusion: Pap Screening should focus on the peri-menopausal and the post-menopausal Group as in our study we found that most of the patients belonged to this age group.

Keywords: Pap Smear Screening, Epithelial Cell Abnormalities, Cancer Cervix, The Bethesda System

Introduction

Cervical cancer is the most common cancer of the female genital tract. India accounts for 25% of the cervical cancer deaths and the incidence is about 23.29%,^[1]. Cervical cancer now ranks number two as the cause of female cancer in India, first being carcinoma of the breast,^[2]. The etiological factors of carcinoma of the uterine cervix are early age of marriage, multi parity, early age of sexual intercourse, low socioeconomic status, ignorance and illiteracy, viruses chiefly HPV, HIV, HSV.^[3] Epidemiological studies on cancer cervix suggest that it is very suitable target for primary prevention of the disease by screening^[4]. There are various screening tests for cervical cancer like Pap smear, Liquid based cytology, Visual inspection of the cervix after application of Lugol's iodine, acetic acid application, speculscopy and cervicography.^[5] Pap smear test is considered to be most important test for cervical cancer screening programs. Thus we undertook the present study to study the pattern of epithelial cell abnormalities and cancer cervix and also to assess the age group in which the screening program should be concentrated to bring about a reduction in the incidence of cancer cervix.

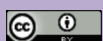
Materials and Methods

A retrospective study was carried in Department of Pathology of a hospital of North Delhi, from June 2014 to

Jan2017. 1534 smears were screened. The patients were in age group ranging from 20 to 80 years, with various complaints of vaginal discharge, abnormal bleeding, bleeding after menopause, PID, unhealthy looking cervix, erosion cervix etc. Patients posted for hysterectomy and vault smears, patients receiving chemotherapy, radiotherapy and known cases of carcinoma cervix were excluded from the study. Smears were taken by senior residents and/ or specialists in the gynecology OPD using modified Ayres spatula. It was inserted and then rotated full 360 degree over the cervix. Both endocervix and ectocervix were sampled. The material obtained was quickly smeared on the glass slides, labelled appropriately and fixed in 95% ethyl alcohol, stained by Papanicolaou stain by the lab technician. The slides were mounted with DPX; and screened by cytopathologist. The Bethesda system 2014 was followed for reporting of Pap smears by the cytopathologists.

Results

Our study showed that 95.2% (1391) smears were benign (NILM) and 4.72% (69) were abnormal smears. 4.8% (74) samples were found to be unsatisfactory (Table 1). Among unsatisfactory smears 30 out of 74 (40.5%) samples belonged to age group of 50-59 and 40-49 years of age (Table 3).



Among the NILM group 69.4% (965) were NOS, 6.4% (62) showed reactive atypia, non-specific inflammation was seen in 81.6% (788), while atrophy was reported in 11.9% (115). (Table2).

Among the specific infections bacterial vaginosis was most common, seen in 264 (18.9%), Candida in 137(9.8%), Trichomonas was reported in 21(1.4%) cases only. Trichomonas with Leptothrix seen in 2 cases (0.14%) and Candida with Leptothrix, and only Actinomyces infection in 1 each constituting 0.07% each.

A total number of 69 cases revealed epithelial abnormalities. The age of the patients with an abnormal smear was **Table. 1 Pap Smear result of the study group.**

Pap Result	No. Of cases	% of total no. of smears
UNSATISFACTORY	74	4.8
NILM	1391	95.21
ASCUS	22	1.5
ASCH	04	0.27
AGC	04	0.27
LSIL	13	0.89
HSIL	13	0.89
SCC	13	0.89
Total	1534	100

Table 2: Non neoplastic cytological diagnosis in pap smear.

Pap Result	No. of cases	% of cases
NOS Reactive Atypia =6.4% Non Specific Inflammation =81.6% Atrophy =11.9%	965	69.4%
CANDIDA	137	9.8%
B.VAGINOSIS	264	18.95
TRICHOMONAS.VAGINALIS	21	1.4%
ACTINOMYCES	1	.07%
CANDIDA AND LEPTOTHRIX	1	.07%
TRICHOMONAS AND LEPTOTHRIX	2	.14%

Table 3: Cervical epithelial abnormalities in relation to age.

AGE GROUP	UN-SATISFACTORY	%	ASCUS	LSIL	HSIL	SCC	AGC	ASCH %	%
20-29	12	16.21	00	4	0	2	0	00	8.69
30-39	15	20.27	03	3	2	0	2	00	14.49
40-49	17	22.97	06	1	4	1	2	03	24.63
50-59	16	21.62	09	3	4	5	0	01	31.88
60-69	14	18.91	04	2	3	2	0	0	15.94
70-79	0	00	00	0	0	2	0	0	2.89
TOTAL	74	100%	22 (31.88%)	13 (18.84%)	13 (18.84%)	13 (18.84%)	4 (5.79%)	4 (5.79%)	6.79 (100%)

between 20-79 years with the mean age being 52.12 years (Table 3). The most common epithelial abnormality was ASCUS (22 cases) with majority belonging to 30-69 age group. LSIL, HSIL and squamous cell carcinoma were seen in 13 patients each, accounting for 0.89%, collectively contributing to 2.67%. ASCH and AGC were seen in 4 cases each amounting to 0.27% each

Discussion

It is known that the burden of the cervical cancer has declined after the introduction of the screening programmes. [6,7,8] Data from hospital based studies is an important tool to assess the effectiveness of the screening programs. It

Table 4: Results of Pap Smear screening in various parts of India.

Ref.	28, 29	5	30, 31	32	33	34	25	35	
Year	2009	2011	2012	2013	2014	2015	2016	2017	2017
Place	Hyderabad /Lucknow	Gujarat	Punjab /Guwahati	Uttar Pradesh	Mangalore /Ahmedabad	Bhopal	Kerala	Mangalore	Delhi
Sample size	6010/36484	995	300/242	4703	1000/36740	1887	2028	308	1534
Author	MulayK /MisraJS	Patel M	Bal MS /Usha Sarma	Kamna Gupta	Preetha George /Sadhna Kothari	Geeth Katheit	Geethu G Nair	Shashidhar MR	
Prevalence	1.39/7.8%	5.52	5/11.95	3.2	3.5/1.32	1.32	2.42		4.9%
ASCUS	0.64/-	4.1	0.3/1.32	0.52	0.3/0.11	0.48	0.15	1.62	1.5
LSIL	0.22/5.5	0.1	2.7/3.53	1.36	2.0/0.83	0.42	1.58	0.64	0.89
HSIL	0.16/1.6	0.1	0.7/3.53	0.91	0.9/0.31	0.16	0.49	0.00	0.89
SCC	.06/0.6	0.7	1.3/3.53	0.28	0.3/0.05	0.05	0.20	0.64	0.89

also helps to reassess the ongoing programs of screening and develop strategies for implementation, targeting the most vulnerable group. Such data is used for reference and research purposes also. Therefore we carried out a retrospective study in our hospital to find out the pattern of epithelial abnormalities and the target age group where the screening programs should be concentrated.

The Bethesda System for reporting the results of cervical cytology was developed as a uniform system of terminology that aims to provide clear guidelines for clinical management. Pap smear reporting by the use of TBS 2014 has unified various overlapping terminologies and includes specific statements.^[9, 10] Specimen type indicates a conventional smear or a liquid based preparation. Evaluation of specimen adequacy is considered by many to be the most important quality assurance component of TBS. Though the presence of transformation zone is not necessary for adequacy, but its presence or absence should be noted as it may be a quality assurance measure. NILM category includes spectrum of non- neoplastic changes protective and reactive responses to inflammation, hormonal changes, infectious organisms. The (ASC) Atypical Squamous Cells, is now separated in two broad categories ASCUS and ASC-H reflecting the 2 tier reporting for HPV related squamous lesions. The lesions associated with persistent HPV are associated with precancer or invasive cancer, LSIL encompasses mild dysplasia and CIN 1 and HSIL with moderate and severe

dysplasia, CIN 2, CIN3. In our study we have adopted TBS2014 for reporting pap smears^[10].

The most common cause of unsatisfactory smears was scant cellularity 68% (91.89%), mainly blood in 2(2.70%) and 4 (5.41%) smears were obscured by dense inflammation. In our study 30 out of 74 (40.5%) samples belonged to age group of 50 to 59 and 40-49 years of age. Higher age group especially post menopause contributes largely to unsatisfactory smears due to tissue atrophy. Both gynecologists and pathologists should be aware of this and must apply extra efforts to collect the sample with optimal techniques and also counsel the patient if a repeat sample is required.^[11] Many studies recommend second sampling in this age group, extra processing of the smears in the lab and even HPV testing.^[11] In a low resource setting like ours we did not repeat the sample or reprocessed the samples, though in our study the percentage of abnormal smears was highest in this age group.

Different studies have shown a wide range of prevalence of epithelial cell abnormalities ranging from 1.14% in Nepal,^[12] to 14.52% in Iran.^[13] In our study we found them to be 4.72%. ASCUS was the commonest accounting for 1.5% cases, the commonest age group in which it was reported was 50 -59 years of age. ASCUS progresses to LSIL, HSIL, SCC. AGUS progresses to adenocarcinoma.^[14]

Comparisons between the labs have shown that diagnostic frequency of ASCUS is variable ranging from 1.6% to 9%.

[15,16] Gerber et al detected ASCUS in 5% (1387) out of total 29,827 patients in their study. Guerreni et al reclassified 107 patients with a diagnosis of ASCUS and found 78.5% of them to be reactive and 21.5% to be probably neoplastic. The absence of well-defined criteria, as well as subjectivity of the diagnosis may account for the variation.^[17] In our study of 22 cases, 12 came for follow up, 8 came out to be NILM, 3 showed reactive atypia and 1 was labelled LSIL. The criterion for ASCUS may differ subtly among labs, reflecting differences in staining and techniques for slide preparation.^[10] According to Barcelos M et al who performed a clinical study on ASCUS as per The Bethesda classification and association with HPV; they observed that the number of cytological diagnoses of ASCUS in their service was equivalent to 1.3 times the frequency of LSIL^[18]. In majority of the US labs, the ratio between ASCUS and LSIL is in the range of 2;1^[19]. Nascimento, et al used ASCUS/SIL ratio for cytopathologists as quality control measure. The value of ASCUS/SIL ratio was calculated every 6 months for 3.5 years and a feedback was provided to 10 cytopathologists. When they analyzed the initial and final ratio for individual cytopathologists and also for entire group, the ratio showed a downward trend from 2.05 to 1.73^[20]. Juskevicius R, et al analyzed the factors that influence the ASUS/SIL ratio of pathologists. They provided a confidential feedback every six months and also introduced thin layer technology as an alternative to conventional smears. They found a significant reduction in the mean ASUS/SIL ratio, which declined from 2.92 to 1.87^[21]. In present study, 22 cases of ASCUS were reported which is less than 2 times that of LSIL (13 Cases).

LSIL, HSIL and squamous cell carcinoma were seen in 13 patients each, accounting for 0.89%, Collectively contributing to 2.67%. ASCH and AGC was seen in 4 cases each amounting to 0.27% each. Nuclear abnormalities are required to make a diagnosis of LSIL. Cytopathic effect of HPV in form of peri-nuclear cytoplasmic halo is not a prerequisite for its diagnosis. According to Stoler MH et al (ALTS) Group inter observer reproducibility of LSIL on cytology is much more than LSIL on histology.^[22] Since the HPV Status of our patients was unknown, a repeat cytology was recommended in 12 months as per ASCCP management guidelines 2012.^[23] In our study HSIL and invasive carcinoma was 0.89% of total epithelial lesions. Except for Pakistan, South Africa and Bangladesh prevalence of HSIL is less than 1% as found in our study also.^[24]

In our study, epithelial abnormality was more prevalent in post-menopausal group (50-59) with 31.8% followed

by 24.6% in 40-49 years age group. This is slightly lower than studies by Bukhari et al and Geethu Nair et al in which 44.9% cases belonged to this age group^[25-26]. (Table 4). This fact strongly highlights the need to create awareness about pap screening programs in this age group and to motivate them to attend cervical cancer screening programs. In a study conducted by Naseema et al among health care workers in a government medical college Calicut shows 46.7% of them had never heard of the pap smears, and 30.7% had undergone pap only once.^[27]

Limitations of the study were lack of follow up of majority of the patients. HPV –DNA testing could not be done on the patients, Liquid based cytology, though can have an impact on reducing the number of unsatisfactory smears, but is not -feasible in our set up, owing to cost constraints.

Conclusions

Cervical cancer is a leading cause of death in India. Pap smear is a very simple, cost effective method to detect cervical epithelial cell abnormalities. Hence as a routine procedure all females above 40 should undergo this test as per WHO guidelines. It should especially focus on the peri-menopausal and the post-menopausal group as in our study most of the patients belong to this age group. Our study supports other studies for the need to have more awareness programs through Pap smear screening camps, female health fairs, linking ADHAAR number and sending educational messages for awareness, motivation and better follow up.

Larger studies are required to know the pattern of abnormalities and also study into the socio-cultural, economic as well as psychological aspects which prevent the females from attending the Pap screening programs.

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