

Pattern of Epithelial Cell Abnormalities on Cervical Papanicolaou Smear in a Rural Tertiary Care Centre of Northern India: A Retrospective Analysis

Kumar Naina*, Singh Prem**, Rudra Samar***

Abstract

Background: Cervical cancer is one of most common cancers of women worldwide with high mortality. Early detection and treatment can cure this disease at an early stage which can be achieved by regular screening using conventional Papanicolaou test, an easy, cost-effective method. *Objectives:* To study pattern of epithelial cell abnormalities on cervical Pap smear in rural tertiary centre of Northern India over six years, to know prevalence of abnormal pap smears over that period. *Material and Methods:* Retrospective analysis of conventional Pap smear reports over period of six years was carried out at Obstetrics and Gynecology Department and Pathology Department of rural tertiary centre of Northern India from January 2010-December 2015 after ethical clearance. Case records of 5,725 women aged >21 years, sexually active consulting Gynecology Out Patient Department for different complaints were collected from Pathology Department. Smears were reported as per 2001 Bethesda system. Data was analyzed using SPSS-20 version. *Results:* Of 5725 Pap smears examined retrospectively, majority of women belonged to 41-50 years. 580 (10.13%) cases had abnormal epithelial patterns, 4448 (77.69%) had benign epithelial patterns and remaining 697 (12.17%) were unsatisfactory. Of 4448 benign cases, inflammatory

lesions were most common (38.84%). *Conclusion:* High prevalence of epithelial cell abnormalities (10.13%) as well as squamous cell carcinoma, especially in females >70 years signifies lack of awareness about cervical cancer screening among women of this region. Also women of 41-50 years had maximum number of abnormal epithelial patterns, further indicating need for early, regular screening of women.

Keywords: Carcinoma Cervix; Cytology; Papanicolaou Smear; Screening; Squamous Cell Carcinoma.

Introduction

Worldwide of all cancers in women cervical cancer is fourth most common cancer, with around 5,28,000 new cases and 2,66,000 deaths in 2012 [1]. Also an estimated 86% of these deaths [2] from cancer cervix [3] occur in developing countries. Annually in India around 122,844 women are diagnosed with cervical cancer and an estimated 67,477 die from it [4]. Also it is one of the most common cancers among Indian women aged 15 years or older [4,5] and recent data suggests that around 453.02 million Indian women in this age group are at risk of developing cervical cancer [4]. The age standardized incidence of cervical cancer is also very high in India as compared to other South Asian countries [4]. Unfortunately it is expected that by 2030, cervical cancer will be responsible for 474,000 deaths annually with developing countries responsible for greater than 95% of these mortalities [6].

Despite of high morbidity and mortality related to cervical cancer, it is still one of the few preventable cancers of humans. Its prevention is mainly based on early

*Associate Professor
***Professor and Head,
Department of Obstetrics
and Gynecology,
**Professor, Department of
Pathology, Maharishi
Markandeshwar Institute of
Medical Sciences and
Research, Mullana-133207,
Ambala, Haryana, India.

Naina Kumar, Associate
Professor, Department of
Obstetrics and Gynecology,
Maharishi Markandeshwar
Institute of Medical,
Sciences and Research,
Mullana-133207, Ambala,
Haryana, India.
Email:
drnainakumar@gmail.com

diagnosis of precancerous lesions, treatment of which can completely prevent development of cancer [7]. Also it was reported that incidence of cervical cancer has dramatically reduced by greater than 50% in the last 30 years and this is mainly due to increasing use of cervical cancer screening with cervical cytology [8].

Papanicolaou (Pap) testing is one of few preventive interventions that have received recommendation from the US Preventive Services Task Force (USPSTF) [9]. It was found that screening with Pap smear has drastically reduced the incidence and death from cervical cancer in the United States and other industrialized nations [10]. The updated ACS/ASCCP/ASCP and ACOG guidelines [11,12] recommend that regular screening of all women should begin at 21 years of age and should be repeated every 3 years in females between ages 21 to 29. The new guidelines also recommend that screening should be stopped at 65 years of age [13]-[15].

Hence, Pap smear test is a simple, non-invasive, and cost-effective method for diagnosis of cervical and vaginal precancerous, cancerous lesions [16]. The main purpose of this study is to know the prevalence of cervical cytological abnormalities in rural population of this region of developing country and also to know the pattern of epithelial abnormalities detected by Pap smear.

Material and Methods

The study comprised of retrospective analysis of cervical smear (Pap smear) reports of 5725 women who reported to the Obstetrics and Gynecology outpatient department of a rural tertiary care centre of Northern India during the period January 2010 to December 2015. For Retrospective analysis the data was collected from the record registers of Department of Pathology after proper Institutional ethical clearance from the Ethical Committee. All attempts were made not to disclose the identity of any of the women. All the women of age 21 years or more, married and or sexually active that had undergone Pap smear testing during this period were included in the study. Pap smears were taken for all women who reported to the out-patient department of Obstetrics and Gynecology with complaints of white discharge per vaginum, post-coital bleeding, irregular menses, and pain in lower abdomen as well as those who had no complaints and had come for routine cervical screening and on examination their cervix was found abnormal or eroded. The Pap smears were obtained with the help of Ayer's spatula and cyto-

brush to collect specimen from the squamo-columnar junction. The cellular material obtained on the Ayer's spatula and cyto-brush was then smeared on clean glass slide. The glass slides were fixed immediately by immersing them into coplin jar containing 95% ethyl alcohol. The smears were stained with Papanicolaou stain. After mounting the slides with DPX (Distrene dibutylphthalate xylene), slides were examined under light microscope and were reported according to the Revised Bethesda System of classification 2001 as satisfactory and unsatisfactory. The satisfactory results were further classified as negative for intraepithelial lesion or malignancy (NILM/NILM) and epithelial cell abnormality (ECA). NILM includes infections and other non-neoplastic conditions. ECAs are classified into Atypical squamous cells of undetermined significance (ASC-US), Atypical squamous cells-cannot exclude high grade lesions (ASC-H), Low grade squamous intraepithelial lesion (LSIL), High grade squamous intraepithelial lesion (HSIL), Atypical glandular cells (AGC), Squamous cell carcinoma (SCC), Adenocarcinoma and Other malignancies. Statistical analysis of data was done using SPSS 20 version.

Result

A total of 5725 Pap smear samples were retrospectively analyzed. Majority (37.35%) of the women belonged to 41-50 years age group as shown in Table 1. Of total 5725 samples analyzed, 580 (10.13%) had abnormal epithelial patterns and remaining 4448 (77.69%) had benign epithelial patterns with inflammatory smears being most common finding, accounting for 1728 (30.18%) of total cases (Table 2). The data also revealed that the number of unsatisfactory smears reported with Pap smear were 697 (12.17%). The main causes of inadequate or unsatisfactory smears were obscured films due to red blood cells, necrotic tissue or inflammation.

A total of 580 (10.13%) cases had abnormal epithelial patterns, with Atypical squamous cells of undetermined significance (ASC-US) identified in 45 (0.79%) cases (Figure 1); Atypical squamous cells-cannot exclude HSIL (ASC-H) in 18 (0.31%) (Figure 2); Atypical glandular cells (AGC) in 17 (0.29%) (Figure 3); Low grade squamous intraepithelial lesion (LSIL) in 184 (3.21%) (Figure 4); High grade squamous intraepithelial lesion (HSIL) in 145 (2.53%) (Figure 5); Squamous Cell Carcinoma in 187 (3.27%) (Figure 6); Adenocarcinoma in 2 (0.03%) cases. Also it was found that majority of epithelial cell abnormalities were observed in 41-50 years females with LSIL (1.41%) being most common abnormality in this age

group (Table 3). Maximum cases of squamous cell carcinoma (1.13%) were observed in more than 70 years female who reported to Gynecological OPD with advanced stage of carcinoma cervix (Table 3).

Table 1: Age wise distribution of total number of cases

Age Group (years)	Number of cases	Percentage
21-30	228	3.98%
31-40	1424	24.87%
41-50	2138	37.35%
51-60	1221	21.33%
61-70	455	7.95%
>70	259	4.52%
Total	5725	100%

Table 2: Cytological findings of 5725 conventional smear samples

Finding on Pap Smear	Number of cases (%)
Satisfactory	5028 (87.82%)
Unsatisfactory	697 (12.17%)
Negative for Intraepithelial Lesion or Malignancy	4448 (77.69%)
Normal	855 (14.93%)
Inflammatory	1728 (30.18%)
Infections (Bacterial vaginosis, Candida, etc)	1292 (22.57%)
Atrophic smears	555 (9.69%)
Epithelial cell abnormalities	580 (10.13%)
ASCUS	45 (0.79%)
ASC-H	18 (0.314%)
AGC	17 (0.29%)
LSIL	184 (3.21%)
HSIL	145 (2.53%)
Squamous cell carcinoma	187 (3.27%)
Adenocarcinoma	02 (0.03%)
Total	5725

Abbreviations: ASCUS: Atypical Squamous cells of undetermined significance; ASC-H: Atypical squamous cells-cannot exclude high grade lesions; AGC: Atypical glandular cells; LSIL: Low grade squamous intraepithelial lesion; HSIL: High grade squamous intraepithelial lesion.

Table 3: Age wise distribution of various lesions on Pap smear

Age (yrs) Lesion	21-30	31-40	41-50	51-60	61-70	>70	Total
Normal	53 (0.92%)	255 (4.45%)	351 (6.13%)	180 (3.14%)	14 (0.24%)	02 (0.03%)	855 (14.93%)
Inflammatory	54 (0.94%)	484 (8.45%)	777 (13.57%)	346 (6.04%)	55 (0.96%)	12 (0.20%)	1728 (30.18%)
Infections	93 (1.62%)	467 (8.16%)	521 (9.10%)	184 (3.21%)	22 (0.38%)	05 (0.087%)	1292 (22.57%)
Atrophic	00 (00%)	21 (0.37%)	43 (0.75%)	171 (2.99%)	197 (3.44%)	123 (2.15%)	555 (9.69%)
Epithelial cell abnormalities	05 (0.09%)	74 (1.29%)	199 (3.48%)	150 (2.62%)	86 (1.50%)	84 (1.47%)	580 (10.13%)
ASC-US	00 (00%)	10 (0.17%)	23 (0.40%)	09 (0.16%)	03 (0.05%)	00 (00%)	45 (0.79%)
ASC-H	00 (00%)	02 (0.03%)	06 (0.10%)	08 (0.14%)	02 (0.03%)	00 (00%)	18 (0.31%)
AGC	00 (00%)	01 (0.01%)	02 (0.03%)	03 (0.05%)	05 (0.08%)	06 (0.10%)	17 (0.29%)
LSIL	04 (0.06%)	34 (0.59%)	81 (1.41%)	50 (0.87%)	12 (0.21%)	03 (0.05%)	184 (3.21%)
HSIL	01 (0.01%)	23 (0.40%)	53 (0.92%)	36 (0.63%)	22 (0.38%)	10 (0.17%)	145 (2.53%)
SCC	00 (00%)	04 (0.07%)	33 (0.58%)	43 (0.75%)	42 (0.73%)	65 (1.13%)	187 (3.27%)
Adenocarcinoma	00 (00%)	00 (00%)	01 (0.017%)	01 (0.017%)	00 (00%)	00 (00%)	02 (0.03%)
Unsatisfactory	23 (0.40%)	123 (2.15%)	247 (4.31%)	190 (3.32%)	81 (1.41%)	33 (0.58%)	697 (12.17%)
Total	228 (3.98%)	1424 (24.87%)	2138 (37.35%)	1221 (21.33%)	455 (7.95%)	259 (4.52%)	5725

Abbreviations: ASCUS: Atypical Squamous cells of undetermined significance; ASC-H: Atypical squamous cells-cannot exclude high grade lesions; AGC: Atypical glandular cells; LSIL: Low grade squamous intraepithelial lesion; HSIL: High grade squamous intraepithelial lesion; SCC: Squamous cell carcinoma.

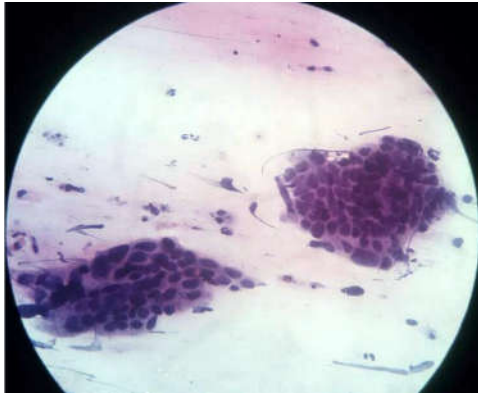


Fig. 1: Atypical squamous cells of undetermined significance (ASC-US) [Pap, 400X]



Fig. 4: Low grade squamous intraepithelial lesion (LSIL) [Pap, 400X]

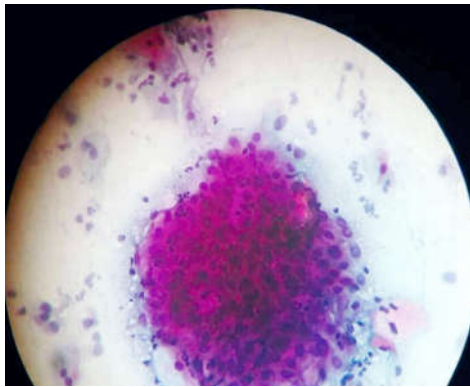


Fig. 2: Atypical squamous cells-cannot exclude HSIL (ASC-H) [Pap, 400X]

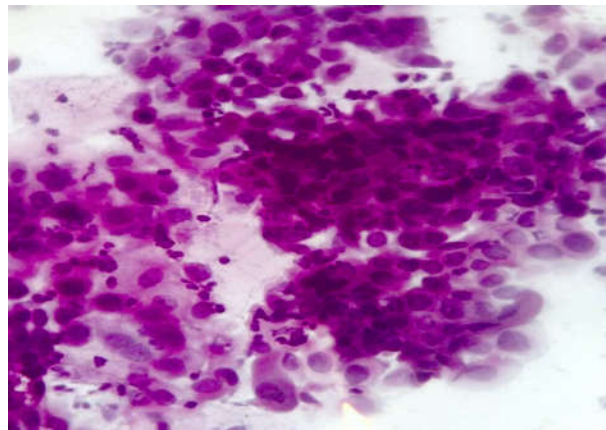


Fig. 5: High grade squamous intraepithelial lesion (HSIL) [Pap, 400X]

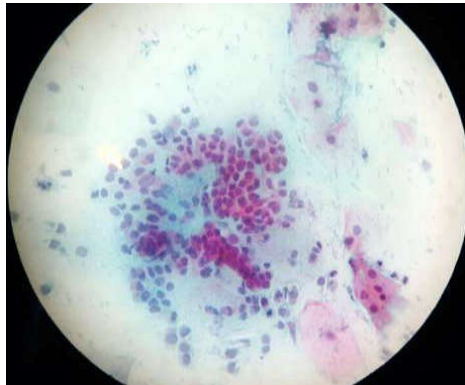


Fig. 3(A): Atypical glandular cells (AGC) [Pap, 400X]

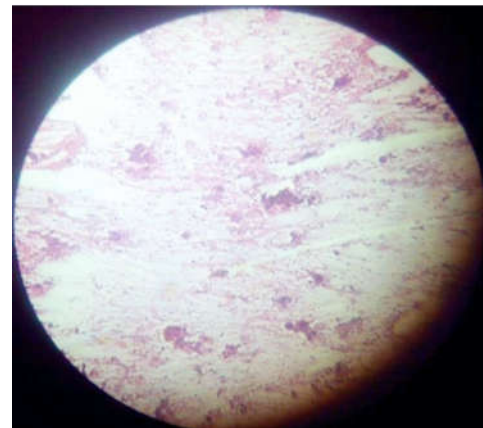


Fig. 6: Squamous Cell Carcinoma showing tumor diathesis [Pap, 400X]

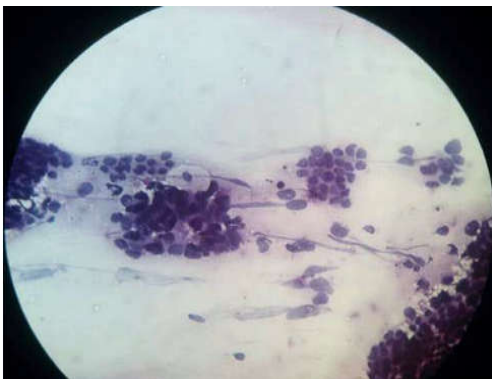


Fig. 3(B): Atypical glandular cell favoring neoplasia [Pap, 400X]

Discussion

In India cancer cervix is second most common cause of mortality in 15-44 years women accounting for thousands of deaths annually [4]. One out of every five women in world suffering from carcinoma cervix belongs to India which has the maximum burden of this disease [17]. Cervical cancer is one of the cancers

that can be easily prevented by early diagnosis and treatment using various screening techniques, of which conventional Pap smear is the most commonly used method because of its cost effectiveness and easy technique, which a trained nursing staff can also do.

The introduction of Pap test led to significant reduction in mortality and morbidity in developed countries by 68% to 84% [18]-[20]. On the other hand, the coverage of screening programs in Asian countries is low and varies from 50% in Singapore to 2.6-5% in India [19,21]. This disparity in screening coverage in India is mainly due to poor infrastructure, low resources and very huge at risk population [17].

The present study highlights the abnormalities seen on conventional Pap smear reports of rural women of Northern part of Country. In our study, majority of patients with abnormal smears belonged to 41-50 years age group. Similar findings were reported by a study conducted in Guntur city in which the epithelial abnormalities were also most commonly seen among 41-50 years females [22]. Another similar study reported that majority (97.9%) of women with epithelial cell abnormalities were between 20-59 years [23].

The present study of retrospective analysis of Pap smear reports revealed that of total 5725 cases, 4448 (77.69%) reports were Negative for Intraepithelial Lesion or Malignancy and remaining 580 (10.13%) cases had some or other Epithelial cell abnormalities, with ASC-US accounting for 0.79%, ASC-H for 0.31%, AGC 0.29%, LSIL 3.21%, HSIL 2.53%, SCC 3.27% and Adenocarcinoma 0.03% of total cases observed. A similar study on Pap smear reports from Andhra Pradesh revealed epithelial cell abnormalities in 16.1% smears and negative for intraepithelial lesion in the remaining 83.9% [23].

According to most of studies the ECA rate varied between 1.5 and 12.60% [24]-[27] on conventional Pap smear screening. Another study by Bamanikar et al. [28] also reported ECA rate of 5.36%. In a similar study conducted by Urmila Banik et al. [29] the ECA rate was found to be 8.18% of all cases analyzed. Another study conducted in Surat city of Gujarat reported that out of total 995 women screened by Pap smear, 940 showed inflammation and other benign lesions (94.5%), 55 women showed premalignant and malignant lesions (5.5%). Premalignant lesions were present mostly in 30-50 year age group. They also reported that of 5.5% women with epithelial cell abnormalities; 4.1% showed ASC-US, 0.5% AGC, 0.1% LSIL, 0.1% HSIL and 0.7% Squamous cell carcinoma [26].

In another similar study by Bajpai [30] it was found that of total smears analyzed; 33.3% had normal

smears, 11.3% inadequate cytology reports, 9.0% had atrophic changes, 2.0% were ASCUS, 0.3% had AGC and SCC respectively, whereas HSIL were 0.6 % and LSIL 1.3%. According to another study it was reported that the most common type of lesions on Pap smear were inflammatory (76.9%), followed by normal smears (17.14%) and epithelial abnormalities (5.71%) [22] which is similar to our findings.

On contrary to our findings a study by Tailor et al. reported that of total 1425 patients screened; there were 72.56% abnormal Pap smears, with 24.84% normal cases and 2.59% unsatisfactory samples. Total 1.89% cases showed epithelial cell abnormalities with ASC-US being most common finding (40.74%) [31].

Hence, it is evident from the present study that unlike in developed parts of world, Pap smear based screening is not well-planned in India with very less coverage. Those who report for screening in OPD are the symptomatic ones only; asymptomatic women rarely turn up for screening because of lack of knowledge, infrastructure, illiteracy, etc. Therefore, it is need of the hour that cytological screening facilities should be extended up to all health care levels for 100% coverage of women and also in addition to doctors the nursing staff and midwives should be trained, so as to reduce the overall burden of this dreadful disease.

Conclusion

The present study emphasized the need for regular and early screening of women with Pap smear to detect the cervical epithelial cell abnormalities at an early stage, so that the development of cervical cancer can be prevented. It was observed that the major burden of abnormal epithelial patterns was borne by 41-50 years females signifying that these women are among the under users of Pap screening. Also the maximum number of cases of Squamous cell carcinoma of cervix were observed in >70 years females, further indicating the need for regular screening. Hence, women should be efficiently motivated for cervical cancer screening at regular intervals, so as to reduce the overall incidence of cervical cancer in near future.

Limitations

The present study was a retrospective analysis of Pap smear reports in a rural tertiary care centre which has referral from many areas; hence the results obtained cannot be applied on general population. In near future we will try to conduct a prospective

study with the aim of screening all the women >21 years of age in this region of India. This will help in knowing the exact burden of abnormal epithelial patterns and will also help in screening and treating every female at an early stage and prevent development of carcinoma cervix in this region of India.

Conflicts of Interest

There are no conflicts of Interest.

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