ORIGINAL ARTICLE

Cytomorphological patterns in cervical Papanicolaou smear: An analysis based on the 2014 Bethesda system

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Received: 12-02-2024
Accepted: 15-03-2024

How to cite this article:
Singh S, Mhetre SC, Mohan N, Arya A. Cytomorphological patterns in cervical Papanicolaou smear: An analysis based on the 2014 Bethesda system. Int J Adv Integ Med Sci 2024;9(1):9-14.

Source of Support: Nil,
Conflicts of Interest: None declared.

Background: Cervical cancer ranks as the fourth most common cause of death among women globally. In India, it is the leading cause of illness and death among women. This type of cancer is preventable and can be detected early in its pre-cancerous stage through regular and thorough cytological screening using Papanicolaou (Pap) smears. **Aims:** The aim of the study is to observe the pattern of Pap smear in detecting pre-malignant and malignant lesions as well as non-neoplastic lesions of the cervix. **Materials and Methods:** In this retrospective study, 100 Pap smears studied in 6-month duration received in the Department of Pathology. Samples are collected from women between 21 and >71 years presenting for routine screening or with some gynecological problems. Smears were reported as per the 2014 Bethesda system. **Results:** Out of received 100 Pap smears, 55 cases had normal cytology and 22 cases with inflammatory changes. Five cases of unsatisfactory, 10 cases of atypical squamous cells of undetermined significance, three cases of low-grade squamous intraepithelial lesions, three cases of high-grade squamous intraepithelial lesions, one case of atypical glandular cells (not otherwise specified), and one case of squamous cell carcinoma were observed. **Conclusion:** The Pap smear test is a simple, safe, non-invasive, outpatient department-based method to detect extensive cervical epithelial abnormalities. Our study underscores the significance of cervical cytology in identifying pre-cancerous and cancerous lesions. These results emphasize the importance of regular cervical screening through Pap smears, more so at least once in her life before the age of 45 years.

KEY WORDS: Bethesda system, Cervical, Cytology, Pap smear

INTRODUCTION

Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer-related deaths among women globally. In India, it is the second most prevalent cancer, with 123,907 new cases and 77,348 deaths annually.[1]

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Numerous studies indicate that cervical cancer mortality and its burden remain high in developing countries such as India.[2] Cervical cancer is largely preventable due to its long pre-invasive stage.[3] Early changes in cervical epithelial cells can be detected through a Papanicolaou (Pap) smear test, which is the primary screening method for identifying pre-cancerous cervical intraepithelial neoplasia and early invasive cervical cancer.[4] The Pap smear is a highly effective, simple, economical, non-invasive, and safe diagnostic tool for detecting pre-cancerous cervical lesions. It is widely accepted globally and has a specificity of about 95% and a sensitivity ranging from 44% to 78%. However, community awareness about the Pap smear test is very low.[5] Combining Pap screening with a human papillomavirus (HPV) DNA test enhances the sensitivity for early detection of pre-cancerous lesions.[6] According to the American Cancer Society (2012), the Pap smear

test should be conducted every 3 years, and when combined with the HPV DNA test, it is recommended every 5 years.[7]

Several factors have been linked to an increased risk of developing cervical cancer. These include a lack of education, being in a lower economic class, being married for an extended period, experiencing the first menstrual period at a young age, getting married young, having the first child at a young age, having the last child at an older age, having many children, engaging in sexual activity with numerous partners, going through menopause later in life, suffering from infections in the genital area, not maintaining cleanliness of the genital area, using tobacco products or being exposed to second-hand smoke, and using birth control methods.[8]

HPV infection has long been regarded as a crucial factor in the development of most squamous cell cervical carcinomas. There are 13 identified types of HPV with oncogenic potential. Among these, high-risk HPVs play a significant role in cervical cancer development, with types 16 and 18 being the most commonly identified in cervical cancer patients. However, recent data suggest that some cervical tumors, particularly adenocarcinomas, do not contain HPV.[9]

Cervical cancer screening options include several methods: (1) Cytology: This involves examining cells from the cervical transformation zone for any abnormalities, (2) HPV testing: Increasingly used as the primary screening method globally, it can also be a follow-up test after an abnormal cytology result (atypical squamous cells of undetermined significance [ASCUS] or higher), or used alongside cytology in co-testing, where both tests are done simultaneously and decisions are based on the combined results, (3) Co-testing: This combines both cytology and HPV testing, (4) Visual inspection tests: An alternative to cytology, these tests use 3–5% acetic acid and/or Lugol's iodine, where abnormal areas appear dense and acetowhite or Lugol's negative, and (5) New strategies: These include high-risk HPV E6/E7 mRNA tests, tests for DNA integration, genome mutation, and DNA methylation.[1]

This study is done to observe the pattern of cervical Pap smear cytology and find the incidence of non-neoplastic and neoplastic lesions of the cervix.

Aims

The aim of the study is to observe the pattern of Pap smear in detecting pre-malignant and malignant lesions as well as non-neoplastic lesions of the cervix.

MATERIALS AND METHODS

The study is a 6-month retrospective observational study conducted in the Department of Pathology to evaluate all the Pap smears. Institutional Ethics Committee approval and implied consent from the patients were taken. Women who visited the gynecology outpatient department with symptoms such as vaginal discharge, bleeding after intercourse, bleeding between periods, and lower abdominal pain underwent a Pap test. Relevant clinical information was recorded. Pap smears were collected from the squamocolumnar junction using Ayre's spatula, which was rotated 360°. The collected material was promptly smeared onto a clean glass slide and immediately fixed in 95% ethyl alcohol. Trained cytotechnologists performed Pap staining, followed by light microscopy and slide interpretation by cytopathologists. The cytological analysis of the smears was conducted according to the Bethesda System 2014.

All the data were manually collected and subsequently analyzed.

Inclusion Criteria

The study included sexually active women aged 21–65 who visited the gynecology department with symptoms such as vaginal discharge, intermenstrual bleeding, post-menopausal bleeding, abdominal pain, irregular menstruation, or a sensation of something protruding from the vagina and who agreed to undergo a Pap smear test.

Exclusion Criteria

Women who were pregnant, known, or treated for cases of epithelial cell abnormality including cancer cervix were excluded from the study.

RESULTS AND OBSERVATION

A total of 100 cases were analyzed. The age of the women ranged from 21 to >71 years. Most of the women were in the age group of 31–40 years [Table 1]. Irregular bleeding per vagina, leukorrhea, abdominal pain, burning micturition, mass p/v, and amenorrhea were the common presenting features [Table 2]. Per speculum examination findings are shown in Figure 1.

Table 1: Age-wise distribution of case

Age (in years)	Number	Percentage
21–30	21	21
31–40	46	46
41–50	26	26
51–60	03	03
61–70	01	1
>70	03	3
Total	100	100

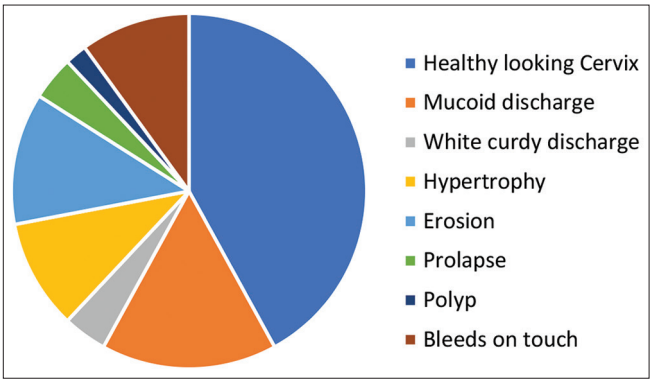

Figure 1: Per speculum examination findings

Table 2: Age-wise distribution of clinical presentation

Age (in years)	White discharge	Abdominal pain	Bleeding P/V	Burning micturition	Amenorrhea	Mass P/V
21–30	13	17	3	14	1	-
31–40	4	22	9	10	14	-
41–50	11	13	16	2	8	6
51–60	4	4	2	2	4	-
61–70	-	-	-	-	2	2
>71	2	2	2	1	3	-
Total	34	58	32	28	32	8

Table 3: Cervicovaginal cytology interpretation/results by the Bethesda System (2014)

Cervical cytology finding	No. of cases	Percentage
Unsatisfactory for evaluation	5	5
Negative for intraepithelial lesion	9	9
Negative for an intraepithelial lesion with benign reactive changes	46	46
Bacterial vaginosis	12	12
Atrophic vaginitis/smear	10	10
ASCUS	10	10
LSIL	3	3
HSIL	3	3
SCC	1	1
AGC, NOS	1	1
Total	100	100

ASCUS: Atypical Squamous Cells of Undetermined Significance, LSIL: Low-grade squamous, intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, SCC: Squamous cell carcinoma, AGC: Atypical glandular cells, NOS: Not otherwise specified

DISCUSSION

Cervical cancer is one of the most common malignancies among Indian women. It is considered an ideal gynecological cancer for screening because it has a long latent phase before becoming invasive.[10,11]

Cervical cancer prevention can be categorized into primary and secondary methods.[12] Primary prevention involves modifying sexual behavior and getting vaccinated against human papillomavirus (HPV). Secondary prevention includes techniques such as visual inspection of the cervix (VIA), cervicoscopy, HPV testing, and cytology. The Pap smear test is a secondary preventive measure designed to detect pre-malignant (Figures 2 and 3) and malignant (Figure 4) lesions that may require follow-up or treatment.[13]

The Pap smear test is highly specific, with a 95% specificity rate, but its sensitivity ranges from 44% to 74%.[14] Newer methods, such as liquid-based cytology, help reduce the number of inadequate samples, though they are more costly.[14]

Out of 100 cases, 46 cases were in the fourth decade of life similar to Umarani *et al*.,[15] Vaghela *et al*.,[16] Nikumbh *et al*.,[17] and Pudasaini *et al*.[18] There were three cases of age >71 of which two cases were of atrophic vaginitis and one case of ASCUS (Tables 3 and 4 & Figures 5 and 6).

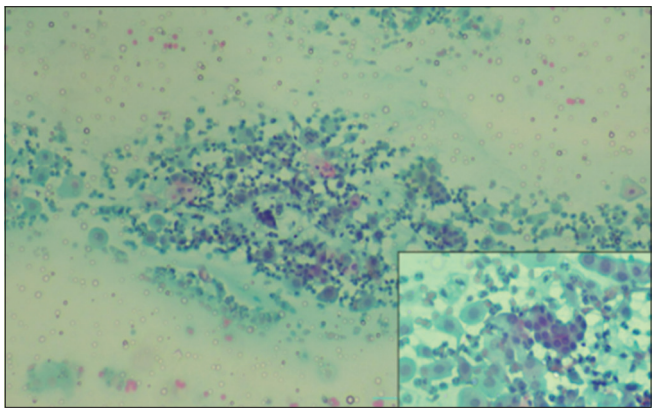

Figure 2: Cytomorphological features of low-grade squamous intraepithelial lesion (Leishman–Giemsa, ×100), Inset-×400

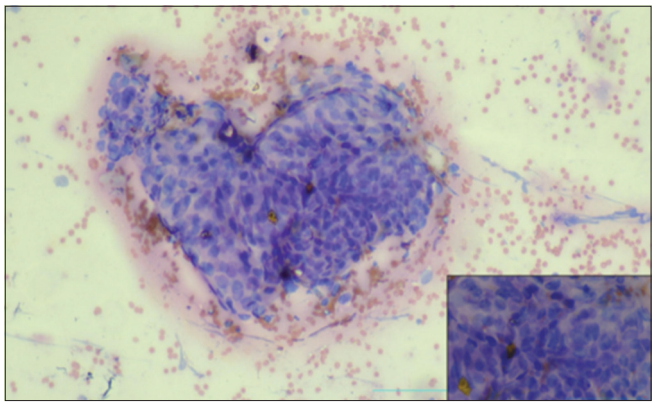

Figure 3: Cytomorphological features of high-grade squamous intraepithelial lesion (Leishman–Giemsa, ×100), Inset-×400

The main symptoms observed were abdominal pain and white discharge, followed by vaginal bleeding and absence of menstruation. Abdominal pain was predominantly noted in individuals in the fourth decade of life. This study was similar to the study conducted by Sachan *et al*.[19] with lower abdominal pain followed by abnormal vaginal bleeding and whitish discharge per vagina. In the majority of cases, no gross pathology was seen on per speculum examination similar to the finding in the studies of Nikumbh *et al*.[17]

Table 4: Comparative study of cervicovaginal cytology interpretation

Cervical cytology finding	Our study	Pudasaini *et al*.[18]	Sachan *et al*.[19]	Agrawal *et al*.[20]
Unsatisfactory for evaluation	5 (5)	38 (0.9)	0	10 (4.17)
Negative for intraepithelial lesion	9 (9)	3656 (87.9)	156 (18.8)	60 (25)
Reactive cellular changes	46 (46)	63 (1.5)	576 (69.4)	128 (53.34)
Bacterial vaginosis	12 (12)	220 (5.3)	23 (2.77)	14 (5.83)
Atrophic vaginitis/smear	10 (10)	98 (2.4)	21 (2.53)	10 (4.17)
ASCUS	10 (10)	4 (0.1)	41 (4.94)	5 (2.17)
LSIL	3 (3)	9 (0.2)	11 (1.33)	6 (2.6)
HSIL	3 (3)	9 (0.2)	4 (0.48)	2 (0.86)
SCC	1 (1)	0	2 (0.24)	1 (0.43)
AGC, NOS	1 (1)	0	0	0
Herpes zoster	0	0	1 (0.12)	0
Candidiasis	0	0	52 (6.26)	13 (5.41)
Trichomonas vaginalis	0	63 (1.5)	20 (2.4)	0
Total	100 (100)	4160 (100)	840 (100)	240 (100)

ASCUS: Atypical Squamous Cells of Undetermined Significance, LSIL: Low-grade squamous, intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, SCC: Squamous cell carcinoma, AGC: Atypical glandular cells, NOS: Not otherwise specified

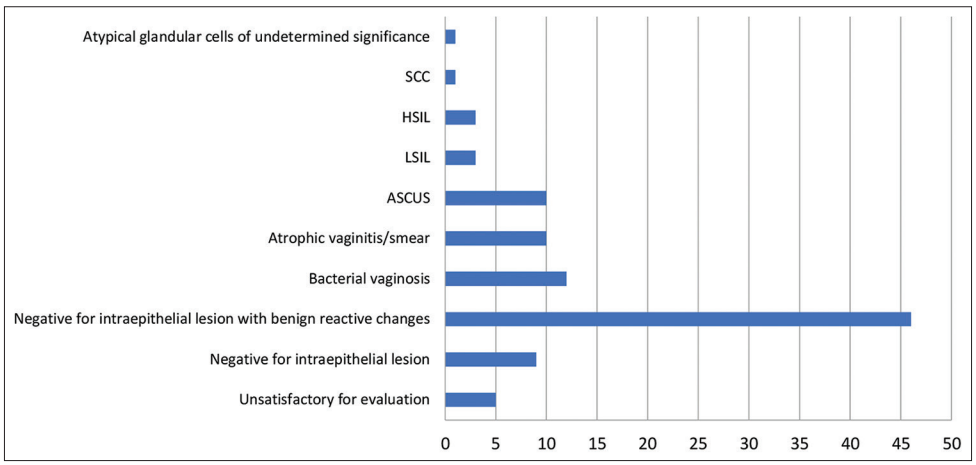

Figure 4: Cervicovaginal cytology interpretation/results by the Bethesda system (2014)

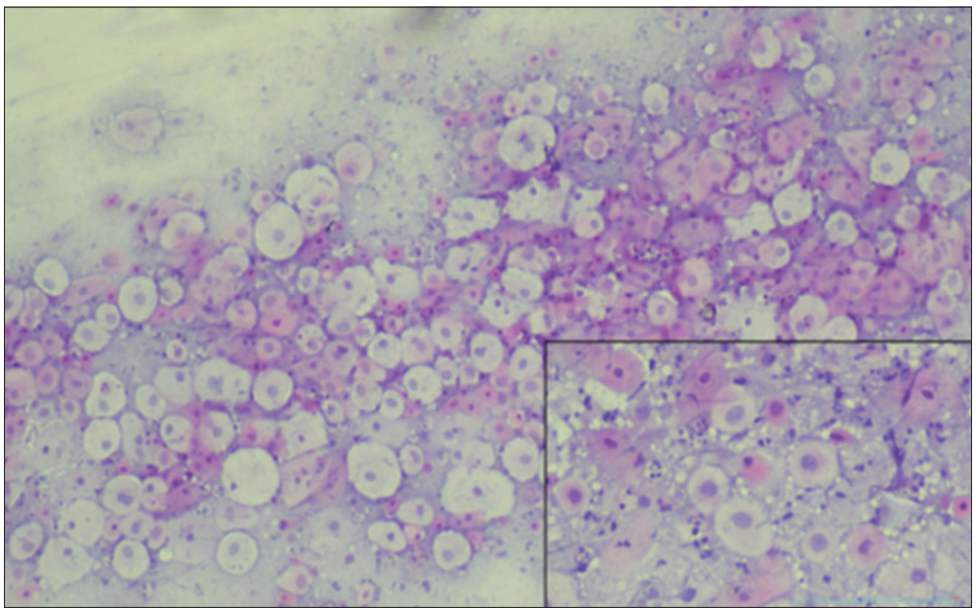

Figure 5: Cytomorphological features of atypical squamous cells of undetermined significance (Leishman-Giemsa, ×100), Inset-×400

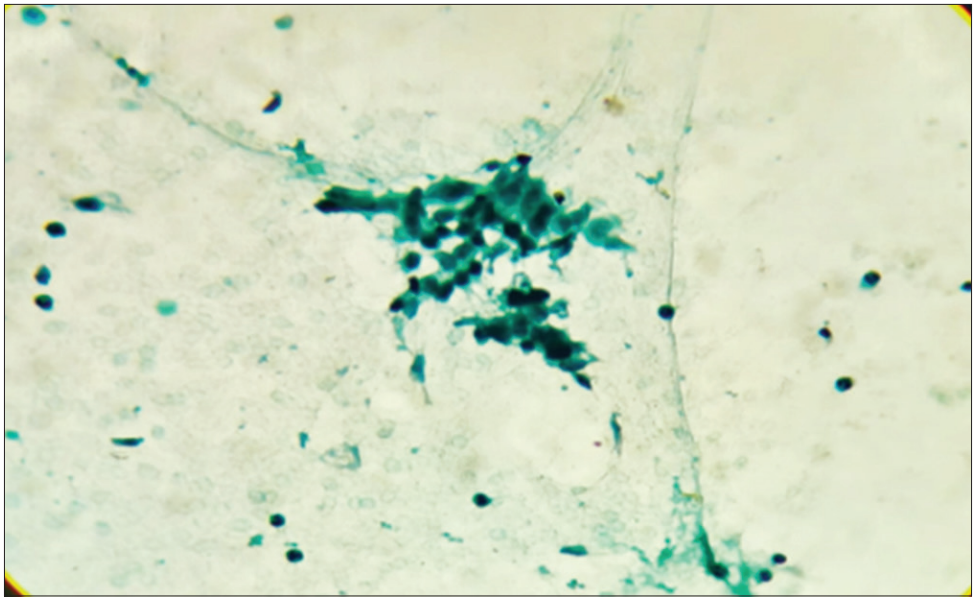

Figure 6: Cytomorphological features of atypical glandular cells of undetermined significance (Leishman–Giemsa, ×100)

Pap smear tests should commence as soon as females become sexually active, regardless of their age, and should be a standard part of gynecological screening. Implementing Pap screening programs across India is crucial for the early detection of cervical pre-cancerous lesions. If abnormal cells are detected in a Pap smear, a colposcopy is often recommended, which may be followed by colposcopic biopsies. Diagnosing and treating cervical cancer pre-cursors can prevent the development of cervical cancer. The detection of squamous cell carcinoma is likely due to the failure of regular screening programs.

CONCLUSION

The Pap smear is an effective screening method for early detection of pre-malignant and malignant cervical lesions. The 2014 Bethesda system for cervical cytology is a standardized procedure that offers descriptive diagnoses, aiding gynecologists in patient care. It is essential for women worldwide to understand the importance and necessity of Pap smears.

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