

Spectrum of Abnormal Cervical Cytology in Papanicolaou (PAP) Smears

Ghazala Mudassir, Mariam Abid, Hania Naveed

Department of Pathology, Shifa College of Medicine, Shifa Tameer-e Millat University, Islamabad, Pakistan

Abstract

Background: To determine the frequency of abnormal cytological findings in pap smears of women in a local population in Pakistan.

Methods: In this observational study conventional PAP smear was collected, from squamocolumnar junction, using an Ayer's spatula in clockwise direction for 360° after exposing the cervix by a Cusco speculum. The endocervical smears were made by rotating the endocervical brush. The samples collected were transferred to glass slide and then slides were fixed in 95% ethyl alcohol. The slides were then sent to pathology laboratory for histopathological examination. The adequacy and reporting of pap smears was based on 2001 Bethesda system.

Results: Majority of the patients in the reproductive age group (18- 38 years). Most of the patients (49.6%) had no cervical complaint and they underwent the procedure for screening. In symptomatic patients common presenting complaints were cervicitis (17.1%) and vaginal discharge (11.3%). Out of the total 1984 pap smears, 99.1% were negative for intraepithelial lesion or malignancy. The precursor neoplastic lesions were observed in 0.8%, which included Atypical Squamous Cells of Uncertain Significance (ASCUS) (0.6%), Atypical Glandular Cells of Uncertain Significance (AGUS) (0.2%) and High Grade Squamous Intraepithelial Lesion (HSIL) (0.1%). ASCUS was seen mostly in young age group that is 18- 38 years while HSIL and AGC were identified in patients more than 50 years of age. Non-specific inflammatory pattern was seen in 17.6%. Atrophic pattern was observed in 2.5% smears.

Conclusion- A significant number of abnormal pap smears were negative for intraepithelial lesion or malignancy. Epithelial cell abnormalities, though less prevalent were also seen.

Key Words: Pap smear, Cervical cancer, Intraepithelial lesion, Malignancy

Introduction

Cervical pap smear is an effective screening test for detecting non-neoplastic, precursor neoplastic and neoplastic cervical lesions. Cervical cancer is the fourth most frequently occurring cancer affecting women worldwide after breast, colorectal and lung cancers; it is also the seventh most common type of cancer overall. Worldwide this cancer is responsible for 5% of deaths.¹⁻³ Eighty percent of the cancer cervix is seen in developing countries, where approximately 2-300,000 women die of cervical cancer per year.^{1, 4, 5} In Pakistan it is the third most common cancer after breast and oral cancer.⁶ It has been estimated that an average woman under 40 years of age has 2% chance of developing cervical carcinoma.⁷ Developed countries have focused on cervical cancer screening programs which has resulted in decreased death rate by 50% in the last 30 years.^{1, 8}

Cervical screening is advocated for the early detection of cervical precursor neoplastic lesions so that early therapeutic procedures and surveillance can be planned. The accessibility of the cervix to pap testing and visual examination (colposcopy) as well as the slow progression from precursor lesions to invasive carcinoma (typically over the course of years) provides ample time for screening, detection and preventive therapy. The high burden of cervical cancer in developing countries is due to the lack of effective screening programs.^{7, 9} Failure of screening programs in low socioeconomic status countries is mainly due to inequality of infrastructure, resources and large population to cater for and therefore a heavy burden of cervical pathologies are diagnosed.¹⁰ Most cases of cervical cancer are diagnosed on screening tests only after the onset of symptoms.

Pap smear is an effective test for early detection of cervical cancer. There is a sequential progression in the development of premalignant lesions to malignant ones so it is important to detect precancerous cells in our population so that these cells are either removed or destroyed. Conventional pap smear is an important screening and a diagnostic test.⁷ Masses can be made aware of its importance by proper education done

most effectively via educational documentaries or advertisements.

Patients and Methods

This observational study was conducted in the department of Pathology, Shifa College of Medicine from January 2013 to December 2016. All cervical pap smears received in the pathology department were included. The clinical details of the patients were obtained from the requisition forms. Inadequate smears and patients with total abdominal hysterectomy were excluded from the study. Conventional pap smear was collected with the help of gynaecologists at the squamocolumnar junction using an Ayer’s spatula in clockwise direction for 360° after exposing the cervix by a Cusco speculum. The Endocervical smears were made by rotating the endocervical brush. The samples collected were transferred to glass slide and then slides were fixed in 95% ethyl alcohol. The slides were then sent to pathology laboratory for papanicolaou staining and were later examined. The adequacy and reporting of pap smears was based on 2001 Bethesda system.

Results

A total of 1984 cases were analyzed during the study. 6 cases were excluded since they were unsatisfactory for evaluation. The mean age of the patients was 37.7 years. Majority (55.9%) of the patients fell in the reproductive age group (18-38 years) (Table 1). Majority (49.6%) had no cervical complaints and they underwent Pap smear for screening. The rest of the patients showed specific symptoms in which the most common symptom was cervicitis (17.1%). (Table 2; Figure 1,2,3).

Table 1: Age distribution of the patients (n= 1990)

Age groups in years	Number of patients %
18-38	1112 (55.9%)
39-49	633 (31.8%)
50-70	239 (12%)

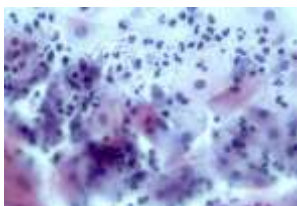


Figure 1: Negative for intraepithelial lesion or malignancy: Candida species (PAP stain;20x)

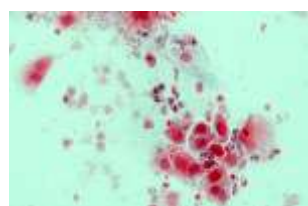


Figure 2: Nucleomegaly 2-3 times the intermediate squamous cell nucleus with regular nuclear membrane and fine chromatin: ASCUS (PAP stain 20x).

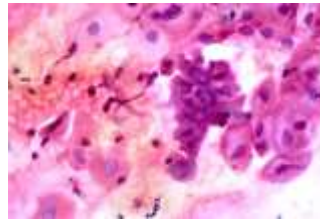


Figure 3: Nucleomegaly 2-3 times the intermediate squamous cell nucleus with regular nuclear membrane and fine chromatin: ASCUS (PAP stain 20x).

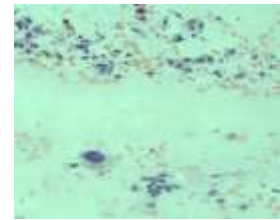


Figure 4: Nuclear enlargement upto 3-5 times the area of normal endocervical nuclei, with mild hyperchromasia, AGUS (Pap stain 20x)

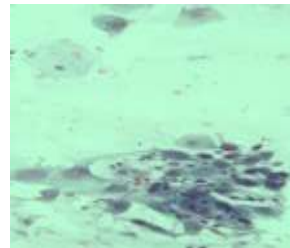


Figure 5: HSIL with marked increase in nuclear/ cytoplasmic ratio, irregular nuclear membrane (Pap stain 20x)

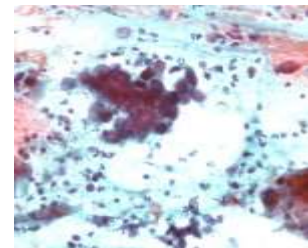


Figure 6: HSIL with marked increase in nuclear/ cytoplasmic ratio, irregular nuclear membrane (Pap stain 20x)

Table 2: Distribution of cytological opinion on Pap smear (n= 1984)

Cytodiagnosis		No	Percentage
NILM		1968	99.1
	Within Normal Limits	1551	77.9
	Inflammatory	351	17.6
	Atrophy	50	2.5
	Candida	9	0.5
	Bacterial vaginosis	5	0.3
	Herpes Simplex Virus	2	0.1
Epithelial cell abnormality		16	0.8
	ASCUS	11	0.6
	AGUS	3	0.2
	HSIL	2	0.1
	LSIL	0	0
Inadequate		7	0.3

NILM- Negative for intraepithelial lesion or malignancy;ASCUS- Atypical squamous cells of uncertain significance;AGUS-Atypical glandular cells of uncertain significance;SIL-Squamous intraepithelial lesion;LSIL-Low grade squamous intraepithelial lesion;HSIL-High grade squamous intraepithelial lesion

LSIL was not observed in any smear. ASCUS was frequently observed in young age group (18-38 years) while HSIL and AGUS were seen mostly in females above 50 years of age. Out of the total cases, 77.9% were within normal limits and 0.3% was unsatisfactory. Non-specific inflammatory pattern was seen in 17.6% smears while fungal infections were seen in 0.5% cases (Figure 4). The atrophic pattern was observed in 2.5% (n= 50) smears.

Discussion

The incidence of cervical cancer has decreased more than 50% in the last 30 years due to use of pap smear as a screening test.¹¹ Out of 1984 cases subjected to pap smear, majority (55.9%) of the patients were in the reproductive age group (18- 38 years). This is in accordance with a study done in Nepal . They also found the majority of the patients (87%) fell in the age range of 20-45 years.¹ Present study had 0.4% of the

cases below 20 years of age however, a study conducted in a hospital of Hyderabad had seen a considerably higher percentage of female (11.7%) under 20 years of age undergoing pap smear.¹²

Majority of the patients did not have any cervical complaints and they underwent pap smear for screening purpose while the frequent cervical complaint noted was cervicitis (17.1%), followed by vaginal discharge(11.3%) and irregular bleeding (7.1%). Bamanikar conducted a study in a tertiary care hospital of India found that vaginal discharge was the commonest complaint(51.8%), followed by abdominal pain (40 .8%) and post-menopausal bleeding(7.8%).⁹

In the present study, majority of the cases 99.1% (n= 1968) were negative for intraepithelial lesion or malignancy. This is in accordance with the study done by Pudasaini who also found out that most of his subjects 87.9% were negative of any precursor lesion. Bamanikar et al have also mentioned similar results (88.93%) in their study.¹⁹ Present study showing majority of the cases negative for intraepithelial lesion or malignancy may be due to the fact that most the patients underwent pap smear for screening purpose.

Epithelial cell abnormality was only 0.8 % (n= 16) of the total pap smears collected over a four year period in the present study that included both the squamous and glandular abnormalities. Variable incidence of ECA has been published in various studies. A study conducted in Bangladesh has revealed epithelial cell abnormality of about 1.6% including ASCUS, AGUS, LSIL, HSIL and SCC as 0.2%, 0.6%, 0.2%, 0.3% and 0.4% respectively.^{13, 14} Although another study from the

same region have shown a high prevalence of ECA (8.18%) with Low grade squamous intraepithelial lesion (LSIL) being the most frequent abnormality. This result was explained on the basis that these patients did not visit the tertiary health institute for screening purpose but rather for specific gynaecological complaints such as something coming down per vaginum, abnormal vaginal bleeding or discharge.⁷

The most frequent epithelial cell abnormality encountered in the present study was ASCUS comprising of 0.6% (n= 11) of the total cases, observed in young patients (18-38 years). This is in accordance with the reported incidence of ASCUS in various studies. Tailor in his study have reported an incidence of 0.77% of ASCUS in a local population of India¹⁵. Bal MS have also reported 0.3% of ASCUS in his study.¹⁶ High grade squamous intraepithelial lesion comprises of 0.1% .Similar results have been shown various studies as well.^{1, 6} The incidence of atypical glandular cells of undetermined significance has been noted to be 0.2 % in our study. Various studies have also shown low incidence of atypical glandular cells, ranging from 0.05% to 2.1%.¹⁷

Atrophic changes were seen in 2.5% of the subjects and it was frequently observed in patients older than 50 years of age. Similar findings were observed by Pudasaini (2.5%) and Khan MS (3.1%).¹⁸ Candida infections were observed in 0.5% cases. This is in contrast to various studies. Malkawi SR in his study of 1176 pap smear observed Candida Albicans infection in 1.2% cases while Avwioro O G showed 7.6% of smears positive for Candida species.^{19, 20}

In Pakistan cervical cancer is the third most common cancer after breast and oral cancer.^{21, 22} Lack of awareness, cultural barriers and economic factors prevent women from seeking timely care which is increasing the incidence of cervical cancer in developing countries. Therefore pap smear examination should be done as a routine examination in patients visiting gynaecology OPD regardless of the age, for timely detection and treatment of cervical carcinoma.^{23, 24, 25, 26}

Conclusion

1. Pap smear is a simple, safe and effective test to detect premalignant and malignant lesions of the cervix at an early age, and thus helps the clinicians in early and more efficient management of the patients
2. As conventional cervical screening remains the most dependable screening and diagnostic test which are cost effective with benefits outweighing expenses, it should be implemented at the government level. Many

precious lives can be saved by identifying and treating the precancerous stage..

References

1. Pudasaini S, Prasad KBR . Cervical pap smear- A prospective study in a tertiary hospital. *Journal of pathology of Nepal* 2015; 5: 820-23.
2. Parkin DM, BrayF, FerlayJ, Pisani P. Global cancer statistics 2002. *CA CancerJ Clin* 2005;55:
3. Renuka N, Sultana A. Cytopathological study of pap smear: A hospital based retrospective study. *Medical Journal of Islamic world academy of sciences* 2014;22:42-49.
4. Tamboli GD. Accuracy of cytological findings in abnormal cervical smear by cytohistological comparison. *Journal of Medical Education & Research*.2013; 3(2):19-24.
5. Tewari R, Chaudhary A. Atypical Squamous Cells of Undetermined Significance : A Follow up Study. *Med J Armed Forces India* 2010;66(3):225-27.
6. Banik U, Bhattacharjee P, Ahamad SU, Rahman Z. Pattern of epithelial cell abnormality in Pap smear: A clinicopathological and demographic correlation. *Cytojournal*2011;8:8.
7. Balaha MH, Al Moghannum MS, Al Ghowinem N, Al Omran S. Cytological pattern of cervical Papanicolaou smear in eastern region of Saudi Arabia. *Journal of Cytology / Indian Academy of Cytologists*. 2011;28(4):173-77.
8. Richart RM. A modified terminology for cervical intraepithelial neoplasia. *Obst Gynecol* 1990;75:131-33.
9. Bamanikar SA, Bravkar DS . Study of cervical pap smears in a tertiary hospital. *Indian Medical Gazette* 2014); 250-54.
10. Bruni L, Rosas B. ICO information center onHPV and cancer (HPV information center). Human papilloma virus and related diseases in India. Summary Report 2014;08-22. Available from www.hpvcntr.net
11. Vaghela BK, Vaghela VK . Analysis of abnormal cervical cytology in papanicolaou smear in a tertiary care center- a retrospective study. *IJBAR* 2014;5:47-49
12. Haider G, Parveen Z, Anjum F, Munir A. Pap smear an important screening tool to detect precancerous stage of carcinoma of cervix. *J Ayub Med Coll Abbottabad* 2013;25(1-2):26-29
13. Yeasmin S, Begum T . PAP- Smear study and its utility in cervical cancer screening in a tertiary care hospital in Chittagong, Bangladesh. *ChattagramMaa-O-Shishu Hospital Medical College Journal* 2014;13(1):110-14
14. Mehnaz N . Evaluation of conventional pap smear for cervical intraepithelial lesions and cancer in a tertiary hospital of Bangladesh. *ChattagramMaa-O-Shishu Hospital Medical College journal*. 2013;12(2):
15. Tailor HJ, Patel RD. Study of cervical pap smears in tertiary care hospital of South Gujrat India. *Int J Res Med Sci* 2016;4;286-88.
16. Bal MS, Goyal R, Suri AK, Mohi MK. Detection of abnormal cervical cytology in Papanicolaou smears. *J Cytol*. 2012 ;29(1):45-47.
17. Marques JP, Costa LB, Pinto AP, Lima AF, Duarte ME. Atypical glandular cells and cervical cancer: systematic review. *Rev Assoc Med Bras* 2011;57(2):234-38.
18. Khan MS, Raja FY, Ishfaq G . Pap smear screening for precancerous conditions of the cervical cancer. *Pak J Med Res* 2005;44:111-13
19. Malkawi SR¹, Abu Hazeem RM, Hajjat BM, Hajjiri FK. Evaluation of cervical smears at King Hussein Medical Centre, Jordan, over three and a half years. *East Mediterr Health J* 2004 ; 10(4-5):676-79.
20. Og A, Oe O, To A. Sensitivity of a papanicolaou smear in the diagnosis of candida albicans infection of the cervix. *N Am J Med Sci*. 2010 ;2(2):97-99.
21. Atla BL, Uma P . Cytological patterns of cervical pap smears with histopathological correlation. *International Journal of Research in Medical Sciences* 2015;3(8): 1911-16.
22. BhurgriY, Bhurgri A, Rahim A, Bhutto K, PinjaniPK, Usman A. The pattern of malignancies in Karachi(1995-96). *J Pak Med Assoc* 1999;49:157-61.
23. Bukhari MH, Saba K. Clinicopathological importance of papanicolaou smears for the diagnosis of premalignant and malignant lesions of cervix. *J Cytol* 2012;29:20-25.
24. Stjernward J, Eddy D, Luthra U, Stanley K. Cervical cancer screening in developing countries. *National Health* 1995;11(2):42-44.
25. Mufti Sh T, Altaf FJ. Changing pattern of epithelial cell abnormalities using revised Bethesda system. *Iran J Basic Med Sci* 2014; 17:779-84.
26. Saudi Cancer Registry cancer incidence and survival reports Saudi Arabia 2007. National Saudi Cancer Registry. Riyadh (ksa): Ministry of Health. Available at: <http://www.scr.org.sa/reports/SCR2007.pdf> website