

Evaluation of pre-malignant cervical lesions in females presenting with abnormal pelvic complaints

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Abstract

Objective: To evaluate premalignant cervical lesions by using Papanicolaou smears in females presenting with abnormal pelvic complaints.

Methods: The descriptive cross-sectional study was conducted from June to November 2013 at the Department of Histopathology, Mayo Hospital, Lahore, and comprised female patients aged 25-70 years presenting with abnormal pelvic complaints with no cause in the uterus checked through ultrasonography who were undergoing cervical Papanicolaou smear. The smears were spray-fixed and placed in 95% reagent alcohol and was then stained with haematoxylin and eosin stain. The cytological examination was carried out under light microscope. SPSS 16 was used for data analysis.

Results: There were 210 women with a mean age of 39.51±8.32 years. Vaginal discharge was present in 89(42.4%) women; postcoital bleeding in 12(5.7%), and intermenstrual bleeding was present in 21(10%) women. Dyspareunia was present in 33(15.7%) women, and pelvic pain in 60(28.6%). Overall, premalignant cervical cancer was noted in 17(8.1%) patients. Atypical squamous cells of unknown significance was present in 5(2.4%) women, low-grade squamous intraepithelial lesion (LSIL) in 8(3.8%), and high-grade squamous intraepithelial lesion in 4(1.9%) patients of cervical cancer.

Conclusion: The frequency of premalignant cervical lesions in symptomatic patients was high enough to highlight the importance of early detection of cervical cancer.

Keywords: Pre-malignancy, ASCUS, LSIL, HSIL, Pelvic Pain. (JPMA 70: 272; 2020)
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Introduction

Cervical cancer still continues to be the second commonest female cancer worldwide.¹ Incidence of carcinoma of cervix is 8.9/100000 women.² It accounts for significant morbidity and mortality. Globally, every year around 500,000 women develop cervical cancer and almost 274,000 of them die from the disease.^{3,4} Cervical cancer has been recognised as a rare outcome of a common, sexually transmitted infection. Persistent infection with high-risk oncogenic human papillomavirus (HPV) types is a necessary cause of cervical cancer.⁵

No form of cancer better documents the remarkable effects of early diagnosis, and curative therapy on the mortality rate than does the cervical cancer.⁶ Most cervical lesions do not progress to cancer, and those which do, progress slowly, making cervical cancer largely preventable through effective screening.⁷ This has not been possible in most low-resource settings, including Pakistan, due to ineffective use of Papanicolaou smear which is the foundation of cervical cancer screening and is a powerful tool for early detection of cervical cancer and thus reduces the mortality related to it.⁸

According to Bethesda system, premalignant cervical lesions are classified into the atypical squamous cells of

unknown significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL).⁹

In a study of 300 pap smears, 3.7% smears showed premalignant cervical lesions, 1.3% showed malignant lesions and 95% had benign smears.¹⁰ Another study reported that overall premalignant and malignant lesion prevalence was 1.1%.¹¹

The natural history of HPV infection in Bogota, reported 150 out of 2,110 (7.11%) women having premalignant cervical lesions.¹² A local study reported premalignant cervical lesions as 10 cases out of 280 (3.6%).¹³ In another study, Molano et al. reported results for smears taken as 92.5% benign 0.1% invasive cervical cancer and 1.3% inadequate pap smear (pre-malignant=6.1%).¹⁴ Pakistan, like other developing countries, is undergoing epidemiological transition and has moved from a low-risk to a moderate-risk country for cervical cancer, which is the fourth most common cancer among Pakistani women.¹⁵

The current study was planned to find the frequency of premalignant stage of cervical cancer among patients presenting with abnormal pelvic complaints.

Patients and Methods

The descriptive cross-sectional study was conducted in the Department of Histopathology, King Edward Medical

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University (KEMU) / Mayo Hospital, Lahore, Pakistan, from June to November 2013, after the approval of ERC of College and physician and surgeon Pakistan, CPSP/REU/HSP-2010-066-361 date November 11, 2014.

It comprised females presenting with abnormal pelvic complaints without any intrauterine cause and undergoing cervical Papanicolaou smear. The sample size was calculated with 95% confidence level, 3.5% margin of error and taking expected percentage of premalignancy as 7.11%.¹¹ The sample was raised using non-probability, purposive sampling. All female patients aged 25-70 years presenting with abnormal pelvic complaints with no cause in uterus on ultrasonography (USG) undergoing cervical Papanicolaou smear were included. Inadequate smears having no endocervical or metaplastic cells, with drying artefacts, haemorrhage and clots masking the underlying morphology were excluded. Inflammatory smear showing dense inflammatory infiltrate obscuring underlying morphology, and infectious smear having pathogenic microorganism were also excluded.

After getting informed consent from the subjects, demographic features were noted. The papanicolaou smears received in the Pathology Department was spray-fixed and placed in 95% reagent alcohol and was then stained with haematoxylin and eosin (H&E) stain. Cytological examination was carried out by a consultant histopathologist under light microscope. According to the Bethesda system,⁹ premalignant smears were further classified into ASCUS, LSIL, HSIL and their frequencies were calculated.

Data was analysed using SPSS 16. Descriptive statistics were used to describe the data. Mean and standard deviation (SD) were calculated for quantitative variables. Frequencies and percentages were used for qualitative variables. Data was stratified for abnormal pelvic complaints to address the effect modifiers.

Results

There were total 210 women with a mean age of 39.51±8.32 years. Vaginal discharge was present in 89(42.4%) women, post-coital bleeding was noted in 12(5.7%), inter-menstrual bleeding was present in 21(10%), dyspareunia in 33(15.7%), pelvic pain in 60(28.6%), and, finally, premalignant cervical cancer was found in 17(8.1%)

Table-1: Distribution of frequency of different signs and symptoms.

	Vaginal Discharge	Post coital bleeding	Menstrual Bleeding	Dyspareunia	Pelvic Pain
Age Mean±SD	39.51±8.32				
Yes n(%)	89 (42.4%)	12 (5.7%)	21 (10%)	33 (15.7%)	60 (28.6%)
No n(%)	121(57.6%)	198 (94.3%)	189 (90%)	177(84.3%)	150 (71.4%)
Total	210	210	210	210	210

Table-2: Distribution according to pre-malignant cervical lesions.

Pre-Malignancy	Frequency	Percentage
Yes	17	8.1
No	193	91.9
Total	210	100

Table-3: Distribution according to type of pre-malignant cervical lesions.

	Frequency	Percent
ASCUS	5	2.4
LSIL	8	3.8
HSIL	4	1.9
No	193	91.9
Total	210	100.0

ASCUS: Atypical squamous cells of unknown significance
 LSIL: Low-grade squamous intraepithelial lesion
 HSIL: High-grade squamous intraepithelial lesion.



Figure-1: Photomicrograph of atypical squamous cells of unknown significance (ASCUS) (Pap stain 40X) revealing slightly abnormal squamous cells, but the changes don't clearly suggesting that precancerous cells are present.

patients. Among them, ASCUS was present in 5(2.4%) patients, LSIL in 8(3.8%) and HSIL in 4(1.9%).

When data was stratified to address the effect modifiers, 6(35.3%) women were found to be having vaginal discharge

Table-4: Stratification with respect to different risk factor.

	Post Coital Bleeding		Inter Menstrual Bleeding		Dyspareunia		Pelvic pain		
	Yes	Yes	Yes	No	No	No	Yes	No	
Pre-malignant cervical lesions	17 (100.0%)	3 (17.6%)	4 (23.5%)	8 (47.1%)	9 (52.9%)	13 (76.5%)	14 (82.4%)	8 (47.1%)	9 (52.9%)
	193 (100.0%)	9 (4.7%)	29 (15.0%)	52 (26.9%)	141 (73.1%)	164 (85.0%)	184 (95.3%)	52 (26.9%)	141 (73.1%)
Total	210 (100.0%)	12 (5.7%)	33 (15.7%)	60 (28.6%)	150 (71.4%)	177 (84.3%)	198 (94.3%)	60 (28.6%)	150 (71.4%)

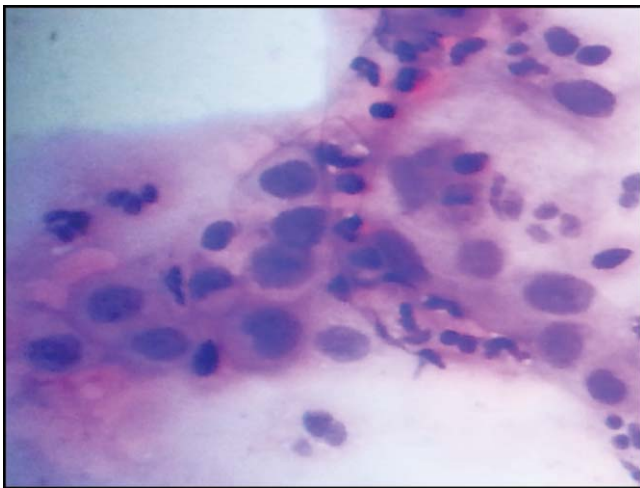


Figure-2: Photomicrograph (Pap stain 40X) low-grade squamous intraepithelial lesion (LSIL), revealing sheets of cells (The changes in cells with intermediate and superficial-type cytoplasm). There koilocytic change and nuclear enlargement (>3x normal intermediate cell), with slightly increased N:C and variable nuclear hyperchromasia.

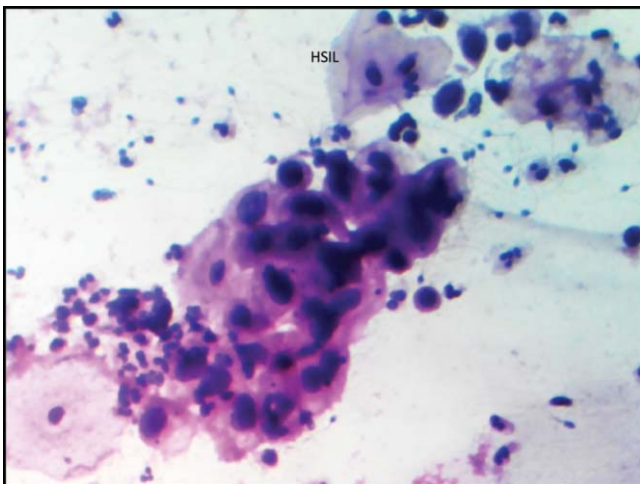


Figure-3: Photomicrograph (Pap stain 40X) showing single, loose sheets of cells with hyperchromatic nuclei, high nuclear to cytoplasmic ratio, irregular nuclear membranes, coarse chromatin and indistinct or absent nucleoli.

along with premalignant cervical lesions, post-coital bleeding 3(17.6%), inter-menstrual bleeding in 6(35.3%), dyspareunia in 4(23.5%), and 13(76.5%) had premalignant cervical lesion without dyspareunia. Pelvic pain was the

complaint in 8(47.1%) cases of premalignancy and 9(52.9%) were free from pelvic pain (Table-1,4; Figure-1,3).

Discussion

Pre-malignant cervical lesions were noted in 8.1% women which is higher than results reported from Bogota, and Latin-American figures but lower than some others.^{16,17}

The difference may be due to poor health condition and lack of education. ASCUS prevalence (2.4%) was approximately the same as reported in the United States where it has been found to be closer to 2.1% or to even reach 9.0% in the high-risk population. Molano et al. have reported results for smears taken at recruitment in their HPV study in Bogota as being 3.5% LSIL, 1.5% ASCUS, 0.7% atypical glandular cells of undetermined significance (AGUS), 0.4% HSIL, and 1.3% inadequate pap smear, but in our study the results were different as we found ASCUS in 5(2.4%), LSIL in 8(3.8%) and HSIL in 4(1.9%) patients.

Few very important activities yielding a great impact can be proposed.^{18,19} These include increasing programme coverage using motivation and active user search; establishing an ongoing information and educational network; educating the community in aspects related to cervical cancer risk factors; establishing an ongoing surveillance programme regarding this pathology; getting women's partners actively involved in these strategies; establishing a support strategy at secretary of Education or Health level; and increasing the scope of being able to enroll in a social and health security system.

In one study, 20,603 women participated and 80% had never had a pap smear before and just over 91% had not had a pap smear in the preceding 5 years.²⁰ Of the women screened, 468 had LSIL and the average age of these women was 33.1 years; 366 had HSIL and these women were statistically significantly older at 37.97 years of age; and 92 women had cytologically-diagnosed invasive cancer.²⁰

We also found the risk for cervical pre-cancer and cancer to be associated with age (≥40 years) which supports the natural history of cervical carcinogenesis from HPV infection through cervical dysplasia, pre-cancer and cancer; having five or more abortions and the presence of vaginal wall abnormalities suggesting a generalised increased risk of sexually-

transmitted diseases (STDs) in women who had cervical pre-cancer and cancer and mean age was also >40 years.²¹

The point prevalence of post-coital bleeding in the community ranged from 0.7% to 9% among women. One study reported an annual cumulative incidence of 6% of menstruating women. The prevalence of post-coital bleeding in women with cervical cancer ranged from 0.7% to 39% but in our study the frequency was different.²²

As this was a cross-sectional study it was not possible to explore cause-and-effect relationships. We did not perform HPV deoxyribonucleic acid (DNA) testing, or biopsies to confirm the result of cytological smears. However, the study does demonstrate the risk factors of positive cervical cancer screening test in our population.

Regardless of the challenges of executing and scaling up cervical malignancy screening programmes, clinical studies of test performance suggest that one- and two-visit screen-and-treat approaches using visual inspection with acetic acid (VIA) or HPV DNA testing could be feasible, beneficial and cost-effective in resource-poor settings.²³

Conclusion

The frequency of premalignant cervical lesions in symptomatic patients was 8.1%, which was high enough to highlight the importance of the early detection of cervical cancers, thus saving lives. This fact also emphasises the need for inclusion of Papanicolaou smear as a screening tool on a mass level.

Disclaimer: The text is based on a research paper, and represents the opinions of the authors.

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