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Original Article

Incidence of Cervical Precancerous Lesions by Pap Smear Screening

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Abstract

Background: Cervical cancer remains a significant global health concern, with early detection of precancerous lesions being crucial for prevention. Pap smear screening is a widely used method for identifying cervical abnormalities at an early stage, allowing for timely intervention and reducing disease burden. This study aimed to assess the incidence of cervical precancerous lesions through Pap smear screening and to analyze associated risk factors among women undergoing routine cervical screening.

Patients and methods: A prospective observational cross-sectional study was conducted on 300 patients attending the outpatient clinic. All participants underwent Pap smear screening to assess the presence of cervical precancerous lesions. The distribution of these lesions across different age groups and demographic characteristics was analyzed. Colposcopic examination and biopsy were performed in selected cases with abnormal findings.

Results: Among the 300 patients, 16 [5.33%] had positive Pap smear results. Cytological analysis revealed that 281 [93.67%] were classified as negative for intraepithelial lesion [NILM], 8 [2.67%] patients had atypical squamous cells of undetermined significance [ASCUS], 5 [1.67%] patients had Low-grade squamous intraepithelial lesion [LSIL], and 3 [1%] patients had high-grade squamous intraepithelial lesion [HSIL]. Colposcopic biopsy findings confirmed CIN II and CIN III in two cases with abnormal colposcopic features.

Conclusion: This study highlights a notable prevalence of precancerous cervical lesions, reinforcing the importance of routine Pap smear screening for early detection. Larger studies are recommended to establish national screening guidelines and identify high-risk populations, integrating HPV testing for a more comprehensive cervical cancer prevention strategy.

INTRODUCTION

Cervical cancer ranks as the fourth most common cancer globally, with 80% of cases occurring in developing countries. Unlike many other cancers, it is largely preventable. Preventing HPV infection, the sexually transmitted virus responsible for cervical cancer, serves as a primary prevention strategy that can significantly reduce mortality rates associated with the disease [1].

In 2008, the Nobel Prize was awarded for the discovery of human papillomavirus [HPV] as the primary cause of cervical intraepithelial neoplasia and cervical cancer. This widespread, small, double-stranded DNA virus is transmitted through skin-to-skin or mucosal contact, with its highest prevalence occurring around the age of 20 [2].

More than 90% of human papillomavirus [HPV] infections are temporary and are eliminated by an immune response that is not yet fully understood within 6 to 18 months. However, persistent HPV infection is necessary for the development of high-grade cervical intraepithelial neoplasia and cervical cancer [3].

Cervical intraepithelial neoplasia does not present with specific clinical symptoms but can be readily detected in its premalignant stage. Diagnosis of dysplasia is typically based on cytological findings from a Pap smear test. As dysplasia represents a transitional phase in the development of cervical cancer, early identification is crucial for timely intervention and prevention [4].

The Pap smear involves collecting superficial cells from the transformation zone for microscopic examination [5]. It is a cervical screening method designed to detect precancerous and cancerous changes. Abnormal results typically require further diagnostic evaluation. When integrated into a routine screening program with proper follow-up, the Pap test can reduce cervical cancer mortality by up to 80%. [6].

The effectiveness of the Pap test in preventing cancer can be compromised by various factors, including irregular screening, inadequate follow-up of abnormal results, and errors in sample collection or interpretation [7].

In Egypt, Pap smear screening is not routinely implemented as a standard practice for cervical cancer detection. A significant study conducted in Alexandria, Egypt, in 2015 revealed a low incidence of HPV infection and cervical cancer cases in the region. This finding has led to the conclusion that the necessity for a national cervical cancer screening program is not a current priority in Egypt [8].

Given the dynamic nature of environmental and cultural factors across the country, regular screening research studies are essential to periodically assess the appropriateness and effectiveness of Pap smear screening in Egypt. This approach ensures that the status of cervical cancer screening methods, including Pap smears, is continuously evaluated to align with the evolving healthcare needs of the population.

The aim of this study was to detect the incidence of cervical precancerous lesions in Pap smears taken from women attending the obstetrics and gynecology outpatient clinic, Damietta Faculty of Medicine, Al-Azhar University Hospital.

PATIENTS AND METHODS

This is a prospective observational cross-sectional study conducted at the obstetrics and gynecology outpatient clinic of Damietta Faculty of Medicine, Al-Azhar University Hospital, over the duration from August 2022 to March 2024, with a cohort comprising 300 patients actively seeking care at the outpatient clinic.

The inclusion criteria encompassed all married women attending the obstetrics and gynecology outpatient clinic, while the exclusion criteria involved menstruating females, pregnant women, and patients presenting with clinically suspicious cervix conditions.

Sample Size: This study is based on a study carried out by **Sachan et al. [6]**. Epi Info 7 STATCALC was used to calculate the sample size by considering the following assumptions: -95% two-sided confidence level, with a power of 80%. An error of 5% odds ratiod = 1.115. The final maximum sample size taken from the Epi-Info output was 291. Thus, the sample size was increased to 300 subjects to account for any dropout cases during follow-up.

After an explanation of the nature of the study, written informed consent was obtained from all participants, and approval from the local ethical committee was also obtained.

Data collection: All patients underwent a comprehensive assessment that included personal history, any complaints, obstetric history, menstrual history, family history, and past medical and surgical history, with specific attention given to ascertaining the date of the last menstrual period, current pregnancy status, exogenous hormone use, menopausal status, presence of abnormal bleeding, previous abnormal Pap test results, and the presence of an intrauterine device [IUD], as this could cause reactive cellular changes that might have impacted the accurate interpretation of the Pap test.

Pap smear: Precautions before Pap smear testing included patients abstaining from intercourse, vaginal tampons, and intravaginal medication for up to 24 to 48 hours before the test, along with the treatment of vaginitis and cervicitis prior to Pap testing. The optimal timing for the test was considered to be 5 days after menstruation.

During the procedure of Pap smear testing, patients were positioned in the lithotomy stance, with a sterile dry Cusco speculum carefully inserted into the vagina, potentially using saline, and expanded to allow a thorough view of the cervix to identify any visible lesions or the SCJ [squamocolumnar junction]. The protocol involved avoiding contact with the cervix prior to the Pap testing to prevent the inadvertent removal of dysplastic epithelium due to minimal trauma. Discharge around the cervix was delicately absorbed using a large cotton swab without touching the cervix directly, as excessive blotting or rubbing might potentially lead to reduced cellularity or yield false-negative Pap test outcomes. For the collection of samples, an ectocervical sample was acquired using a wooden Ayers spatula contoured to fit the ectocervix best, and an endocervical sample was obtained with an endocervical brush. Both samples were gently spread onto a glass slide and promptly fixed with 95% ethyl alcohol using the conventional method. The labeled sample was then forwarded to the lab for assessment, and the patient was instructed to schedule a follow-up appointment in two weeks. Subsequent to staining, the slides were examined, and the results were reported based on the Bethesda System [9].

Pap test samples that have no abnormalities are reported as negative for intraepithelial lesion or malignancy.

Epithelial cell abnormalities in samples are categorized into squamous cell variations like atypical squamous cells, low-grade squamous intraepithelial lesions [LSIL], and high-grade squamous intraepithelial lesions [HSIL], with an additional category for suspicious invasion features and squamous cell carcinoma. Glandular cell anomalies include atypical findings such as endocervical cells, endometrial cells, glandular cells, endocervical cells favoring neoplastic conditions, glandular cells favoring neoplastic conditions, endocervical adenocarcinoma in situ, adenocarcinomas like endocervical, endometrial, extrauterine, and those not otherwise specified [NOS]. Furthermore, there are considerations for other malignant neoplasms with specified characteristics.

Patients with positive smears underwent colposcopic-guided biopsies for further evaluation.

Statistical analysis

Statistical analysis was done by SPSS v26 [IBM Inc., Armonk, NY, USA]. Data analysis was conducted using appropriate statistical methods. Descriptive statistics, including means and standard deviations, were used for continuous variables, while categorical variables were expressed as frequencies and percentages. The chi-square test was employed to compare categorical variables, while an independent *t*-test was used to assess differences in continuous variables between groups. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

In terms of Pap test samples, 16 patients [5.33%] exhibited positive Pap smear results. Concerning cervical cytology status, 281 patients [93.67%] were reported as having NILM, 8 patients [2.67%] showed ASCUS, 5 patients [1.67%] presented with LSIL, 3 patients [1%] were diagnosed with HSIL, 3 patients [1%] had unsatisfactory samples, and none were found to have squamous cell carcinoma [SCC]. Regarding the types of infections observed, the majority of cases with negative Pap smears [53.3%] were attributed to non-specific cervicitis, followed by candida infections at 17.7%, instances where no abnormality was detected at 16.3%, and bacterial vaginosis and Trichomonas vaginalis detected in 7.1% and 5.3% of cases, respectively [figure 1].

The results indicate that individuals with positive Pap results had a younger mean age [35 ± 9.1 years] compared to those with negative results [46 ± 11.67 years, p < 0.001]. BMI did not show a significant difference between the two groups [p = 0.47]. The percentage of smokers was higher among positive cases [37.5%] compared to negative cases [7.33%], with a statistically significant difference [p = 0.001]. Family history of cervical disease was more prevalent among positive Pap cases [12.5%] compared to negative cases [1%], with a statistically significant association [p < 0.001], as shown in Table 1.

Regarding reproductive factors, the percentage of individuals who had their first sexual intercourse before the age of 20 was higher among positive cases [50%] than negative cases [26.67%], though the difference was not statistically significant [p = 0.07]. The proportion of individuals who had their first menstruation at or before the age of 15 was higher in positive cases [87.5%] compared to negative cases

[66.7%], but the difference was not statistically significant [p = 0.1] [Table 1].

Parity did not show a significant difference between groups [p = 0.61]. The percentage of individuals using contraception was slightly lower among positive cases [37.5%] compared to negative cases [49.67%], but the difference was not statistically significant [p = 0.34]. Koilocytic changes, suggestive of HPV infection, were present in 50% of positive Pap cases compared to 2.7% of negative cases, with a statistically significant difference [p < 0.001] [Table 1].

The three cases with HSIL underwent further colposcopic examination. The first case had a normal colposcopic finding, so a biopsy was not indicated, and follow-up was recommended. The second case exhibited acetowhite epithelium on colposcopy, and a biopsy confirmed CIN II. The third case showed a mosaic appearance on colposcopy, with a biopsy revealing CIN III [Table 2].

DISCUSSION

Cervical cancer is a significant global health concern, particularly in low- and middle-income countries, where it accounts for 86% of related deaths. It is a leading cause of illness and death among women in resource-limited settings, especially in Africa, highlighting health inequities worldwide [10, 11].

Cervical cancer is largely preventable through effective screening, early detection, and treatment of pre-invasive lesions [12, 13]. Due to its long preinvasive stage, timely screening can identify early cervical epithelial changes, enabling appropriate intervention. The widespread use of Pap testing has significantly reduced cervical cancer mortality in developed countries, emphasizing the importance of robust screening programs [13, 14].

In this study, we found that 16 patients [5.33%] had positive PAP test results. Regarding cervical cytology status, 281 patients [93.67%] were classified as NILM, while 8 [2.67%] had ASCUS, 5 [1.67%] had LSIL, and 3 [1%] had HSIL. Additionally, 3 patients [1%] had unsatisfactory samples, and no cases of SCC were detected.

Comparatively, **Abdel-Hadi et al.** [8]'s larger study of 6173 Pap smears found a lower incidence of abnormal results, with only 1.63% of cases classified as abnormal. Their study reported 61 cases of ASC-US [0.99%], 7 cases of atypical squamous cells that cannot exclude HSIL [ASC-H] [0.11%], 6 cases of LSIL [0.09%], and 1 case of HSIL [0.016%], which are lower than the rates observed in our study. Additionally, their findings emphasized the role of follow-up and colposcopic biopsy in confirming diagnoses, with some cases of atypia of repair and CIN detected upon further evaluation. Unlike our study, which did not detect any cases of SCC, Abdel-Hadi et al. identified one case of cervical adenocarcinoma in situ [AIS], managed by cold knife conization. The discrepancy in prevalence rates between the two studies may be attributed to differences in sample size, population characteristics, and screening protocols. Our findings suggest a relatively higher prevalence of precancerous cervical lesions, emphasizing the importance of routine Pap smear screening in early detection and prevention of cervical cancer.
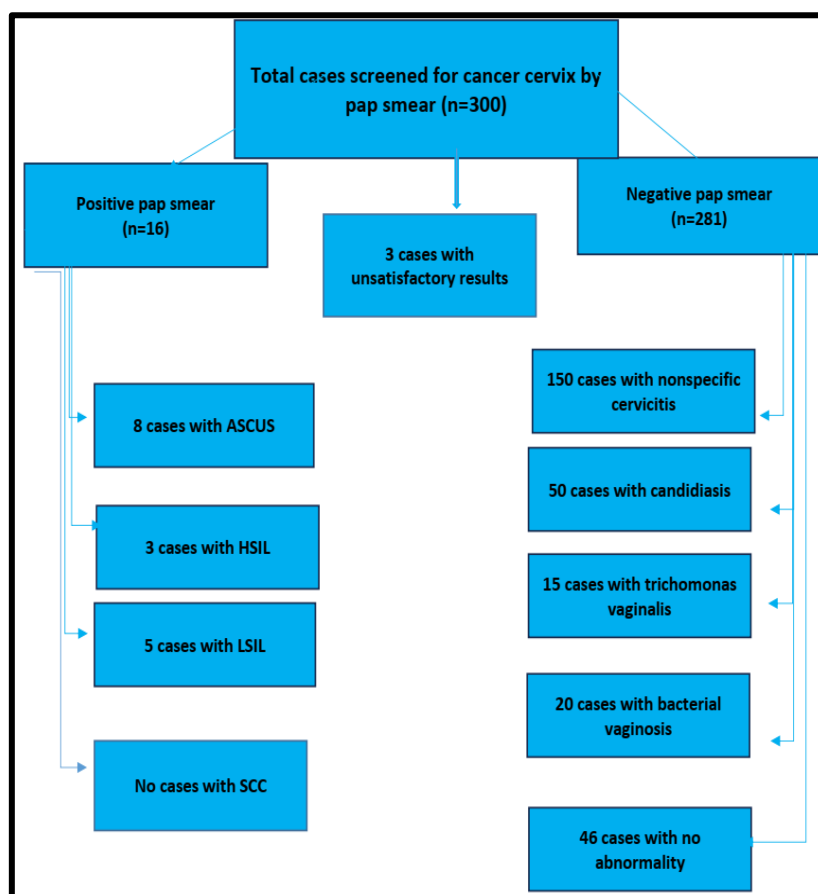
NILM: Negative for Intraepithelial Lesion, ASCUS: Atypical Squamous Cells of Undetermined Significance, LSIL: Low-Grade Squamous Intraepithelial Lesion, HSIL: High-Grade Squamous Intraepithelial Lesion, SCC: Squamous Cell Carcinoma.

Figure [1]: Distribution of Pap Smear Screening Results Among the Studied Population [n=300]

Table [1]: Comparison of Socio-Demographic Factors Between Negative and Positive Pap Smear Cases

Socio-demographic factors		Negative Pap [n=281]	Cases with positive pap [n=16]	P value
Age [years]	Mean ± SD	46 ± 11.67	35 ±9.1	<0.001*
	Range	25 – 65	25-60	
BMI	Mean ± SD	26.4 ± 3.81	27.1 ± 3.4	0.47
	Range	19.26 - 34.52	19.9 - 33.5	
Smoking	Yes	16 [7.33%]	6 [37.5%]	0.001*
	No	265 [92.67%]	10 [62.5%]	
Family history	Positive	1 [1%]	2[12.5%]	<0.001*
	Negative	280 [99%]	14[87.5%]	
Age at first sexual intercourse	<20	72 [26.67%]	8 [50%]	
	20-30	147 [52%]	7 [43.7%]	0.07
	>30	62 [21.33%]	1 [6,3%]	
Age of first menses	≤15	185 [66.7%]	14 [87.5%]	0.1
	>15	96 [33.3%]	2 [12.5%]	
Parity	≤2	120 [40%]	5 [31.2%]	0.61
	>2	150 [50%]	10 [62.5%]	
	Never pregnant	30 [10%]	1 [6.3%]	
Contraception	Yes	149 [49.67%]	6 [37.5%]	0.34
	No	151 [50.33%]	10 [62.5%]	
Koilocytic changes suggest HPV		0 [2.7%]	8 [50%]	<0.001*

Table [2]: Results of colposcopic findings and biopsy for cases with HSIL on Pap smear

Colposcopic finding	Biopsy result	n =3
Normal finding	NO biopsy	1
Acetowhite epithelia	CIN II	1
Mosaic appearance	CIN III	1

Our findings align with those of **Nkwabong** *et al.* [5], who reported 14.7% abnormal Pap smear results, including 32.3% HSIL, 38.2% LSIL, and 29.4% ASCUS cases. They also observed chronic cervicitis in 22 individuals, with 46.3% having previously negative Pap smears and 53.7% never having been screened. Similarly, **Sachan** *et al.* [6] found that 48.84% of participants were negative for malignancy, while 42.66% had inflammation. Epithelial abnormalities were identified in 2.90% [ASCUS], 5.09% [LSIL], and 0.48% [HSIL] of women. Additionally, 6.42% had unsatisfactory sample reports, while the remaining cases had adequate samples. Furthermore, **Bal** *et al.* [15] identified 15 malignancies, 273 negative cases, and 12 inadequate smears. Among the negative cases, 16.7% were normal, while 74.3% showed inflammatory changes. The prevalence of ASCUS, LSIL, and HSIL was 0.3%, 2.7%, and 0.3%, respectively. Additionally, four cases had invasive cancer, including 1% squamous cell carcinoma and 0.3% adenocarcinoma, while 4.1% of the samples were inadequate. AP smear. Approximately 99.7% of cervical cancer cases are caused by human papillomavirus [HPV], with types 16 and 18 accounting for over two-thirds of all precancerous cervical lesions and cervical cancers [16]. The prevalence of cervical cancer remains uncertain among women in developing nations, unlike in developed countries where early detection efforts have significantly reduced its incidence and mortality [17].

There is a need to spread cervical cancer screening awareness programs, educate women regarding the symptoms of cancer, and motivate them to visit the hospital for a cancer screening [18]. Women and all family members should be counseled about the need for cancer screening. Pap smear-positive women need adequate treatment and regular follow-up [19].

Our study identified younger age, smoking, a family history of cervical disease, and the presence of koilocytic changes suggestive of HPV infection as significant risk factors for a positive Pap smear. These findings align with well-established risk factors for cervical cancer, which include not only younger age but also early pregnancy, prolonged use of oral contraceptives, early initiation of sexual activity, and higher parity. These factors contribute to prolonged cervical exposure to high-risk HPV infections, increasing the likelihood of developing precancerous and cancerous lesions. Recognizing these risks reinforces the importance of targeted cervical cancer screening and prevention strategies, particularly among high-risk groups, to enhance early detection and reduce disease burden [20, 21].

Our findings showed that among patients with positive Pap smear results, 14 women [73.68%] had non-specific cervicitis, 2 [10.52%] had candidiasis alone, 2 [10.52%] had bacterial vaginosis alone, and 1 [5.26%] was infected with *Trichomonas vaginalis*. Similarly, **Najib** *et al.* [22] reported that 16.9% of patients had a history of genital warts, 28.8% had vaginosis, while 58.8% showed no vaginal infection.

In the present study, we found a case who had normal colposcopic findings, no biopsy, and the recommended management was to be followed up. Case number two had acetowhite epithelia in colposcopic findings and CIN II in biopsy. Case number 3 had mosaic in colposcopic findings and CIN III in biopsy. In agreement with our results, **Şahin** *et al.* [23] examined colposcopy and cervical histopathology results in women with abnormal PAP smears and HPV. They found various colposcopic findings like leukoplakia [28%], punctuation [18.7%], mosaic appearance [12.1%], and atypical vascularization [11.2%]. Biopsies showed LGSIL in 21%, HGSIL in 7%, and carcinoma in 0.5% of cases, with cervicitis in 46.7% and metaplasia in 5.6%.

In our study, the 5.33% positivity rate for Pap smear results is notably higher than the 1.63% abnormal rate reported by an earlier study, indicating potential variations in population characteristics, sample size, or screening methods. This relatively high prevalence of precancerous cervical lesions underscores the need for larger-scale studies to accurately estimate the burden of the disease in Egypt.

Expanding research across diverse populations and regions would provide a clearer understanding of the necessity and feasibility of implementing routine Pap smear screening as a national preventive measure. Additionally, further investigations should assess contributing factors such as HPV prevalence, socioeconomic influences, and healthcare accessibility to develop an effective cervical cancer prevention strategy.

Study Limitations

1. **Cross-sectional Design**: This was a cross-sectional study, meaning that data was collected at a single point in time. As a result, it does not allow for the assessment of the incidence or progression of cervical precancerous lesions over time. Longitudinal studies would be beneficial to understand the natural progression of these lesions and the long-term outcomes of Pap smear screening.

2. **Potential Selection Bias**: The participants in this study were individuals attending an outpatient clinic, which may not represent the broader population of women who may not seek regular screening. The study could introduce a selection bias, as those attending clinics may be more health-conscious or have other factors that predispose them to seek screening. A more representative sample of women from various community settings would improve the external validity of the findings.

3. **Dependence on Pap Smear Alone**: The study primarily relied on Pap smear screening for the detection of cervical abnormalities, which, while effective, may have limitations in detecting certain types of lesions or early-stage changes. The inclusion of adjunctive tests such as HPV testing or molecular biomarkers could offer a more comprehensive understanding of the risk of cervical cancer and its precursors.

4. **Limited Follow-up**: While colposcopic examination and biopsy were performed in cases with abnormal Pap smear results, there was no long-term follow-up to assess whether the precancerous lesions progressed to cancer or were resolved. Further monitoring of patients would help in understanding the clinical outcomes and the efficacy of early detection through Pap smears.

5. **Lack of HPV Testing**: The study did not incorporate HPV testing, which is a known high-risk factor for cervical cancer. HPV testing, in combination with Pap smear screening, could have provided a clearer picture of the risk profile of the study population. Future studies could integrate HPV testing to enhance the sensitivity of cervical cancer screening.

6. **Potential Observer Bias**: The colposcopic examination and biopsy were performed based on the presence of abnormal findings from Pap smears. There is a possibility of observer bias in interpreting the colposcopic images and making clinical decisions. Standardized protocols and training for examiners could minimize this potential limitation.

7. **Lack of Socio-Demographic Data Analysis**: Although demographic factors were mentioned, there was limited in-

depth analysis of how socioeconomic status, lifestyle factors, or sexual behavior might influence the prevalence of cervical precancerous lesions. Understanding these factors could provide more context and help identify at-risk populations for more targeted interventions.

Conclusion: Our study highlights a notable prevalence of positive Pap smear results, underscoring the need for enhanced cervical cancer screening efforts. Early detection remains crucial in reducing cervical cancer incidence and mortality. We recommend larger, multi-center studies to accurately assess the prevalence of cervical precancerous lesions in Egypt. Implementing routine Pap smear screening, particularly for high-risk groups, alongside public awareness campaigns and improved accessibility to screening services, is essential for effective cervical cancer prevention. Integrating HPV testing into screening protocols should also be considered to enhance early detection and intervention strategies.

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