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Correlation of Cervical Pap Smear with Cervical Biopsy in Lesions of Cervix

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ABSTRACT

Introduction

Cervical cancer is the leading cause of mortality for women in underdeveloped nations and the 4th leading cause globally. Pap smears are non-invasive method, but are unable to pinpoint their location. However, cervical biopsies are an invasive but gold standard procedure.

Methods

This cross-sectional study was an analysis of all pap smears obtained during a one-year period, from April, 2022 to April, 2023. The comparison was made only for cases that had both a Pap smear and a cervical biopsy. A total of 64 cases with follow up biopsy were taken for study out of 337 pap smears received during the study period.

Results

Out of 64 patients, 32.81% had normal cytology, 25% had ASC-US, 4.68% had atypical glandular cells, and 9.37% had HSIL. The most pap smears were done on people between the ages of 31 and 40. In 64 biopsies, 23 (35.93%) had HSIL, 20 (31.25%) had LSIL, and 7 (10.93%) had chronic cervicitis, according to the histological diagnosis of biopsies. Four individuals had a cancer diagnosis, including two (3.12%) squamous cell carcinomas and two (3.12%) adenocarcinomas. The Pap smear showed a sensitivity of 25.92%, specificity of 94.59%, PPV of 77.77%, NPV of 63.63%, and a diagnostic accuracy of 65.62%.

Conclusion

The Pap smear test, had poor sensitivity but good specificity in detecting premalignant and malignant cervical abnormalities. Pap smear is a noninvasive method; however,though invasive, cervical biopsy remains a gold standard test.

Keywords

Carcinoma; cervical biopsy; HSIL; LSIL; pap smear

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INTRODUCTION

Cervical malignancy is the 4th most frequent malignancy in women worldwide. Globally, around 660 000 new cases and 348189 deaths are caused by cervical cancer in 2022.[1] In Nepal, 85% of all gynecologic malignancies are cervical according to a regional study. [2]

Being preceded by the prolonged preinvasive period, invasive cervical cancer is a preventable disorder.[3] Low grade squamous intraepithelial lesions (LSIL) in cytology are associated with mild dysplasia labeled as Cervical Intraepithelial Neoplasia -I (CIN I), while high grade intraepithelial lesions (HSIL) in cytology are associated with moderate and severe dysplasia (CIN II and CIN III) in histology. Invasive malignancy always follow the HSIL.[4]

A Pap smear test is the primary screening test for early diagnosis of invasive cervical cancer and precancerous cervical intraepithelial neoplasia.[3] Although the Pap test is widely recognized as the most effective cervical cancer screening tool, women still lose their lives to cervix carcinoma due to ignorance and negligence.[5]

PAP smear cytology is an assessable technique for cervical cancer screening. However, cervical biopsy is still the "gold standard" for the detection of precancerous cervical lesion, even in cases where smears are unsatisfactory due to obscuring hemorrhages and inflammation. Biopsy is also superior in localizing the lesion.[6] The objective of this study was to establish a correlation between changes determined in cervical cytology and cervical biopsy.

METHODS

This was a cross-sectional study conducted in Department of Pathology, Lumbini Medical College, Palpa over a period of one year from April 2022 to April 2023. Institutional ethical committee clearance was obtained on 29th March 2021 (IRC-LMC 01-B/021). 64 of the cases who underwent both the Pap test and a biopsy were included in the study. Smears were stained according to standard Papanicolaou's method. The cytological interpretation of the smears was made according to The Bethesda system - 2014. Cervical biopsies were formalin fixed, processed for paraffin block preparation, and sections were cut at 3-4 micronmeter. Sections were stained by Hematoxylin and Eosin and studied under light microscopy. Statistical evaluation was done using Microsoft Excel. Inclusion criteria were patients who underwent both pap smear study as well as Cervical biopsy. Exclusion criteria was cases without biopsy

RESULTS

In the present study, cervical lesion screening using the Papanicolaou method was conducted on individuals ranging in age from 21 to 84 years. The greatest number of Pap smears were performed in the 31 to 40-year age group, whereas HSILwere most frequently observed in the 61 to 70-year age group. (Figure 1)

According to the pap smear findings, out of 337 cases, maximum number of cases 240(71.21%) were Negative for intraepithelial lesion or malignancy (NILM) Most common Epithelial cell abnormalities (ECA) were ASC-US and seen in 35 (10.38%) cases followed by ASC-H 13 (3.85%) and

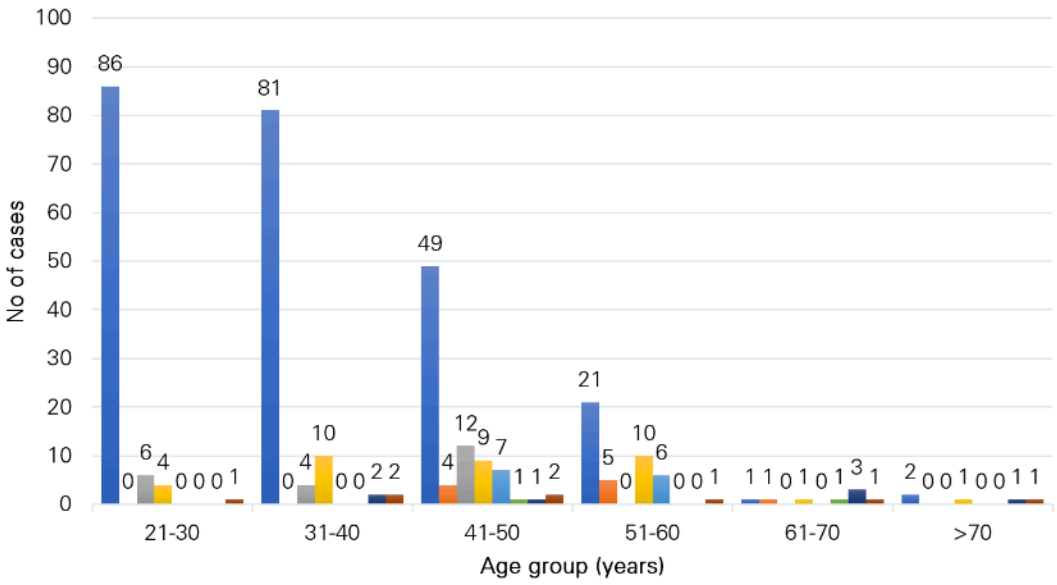

Figure 1. Distributions of the patients according to age with pap smear interpretations

Table 1. Findings of pap smear cytology

Diagnosis	Number (%)
NILM	240 (71.21)
Atrophic smear	10 (2.96)
Unsatisfactory	22 (6.52)
ASC-US	35 (10.38)
ASC-H	13 (3.85)
LSIL	2 (0.59)
HSIL	7 (2.07)
AGC	8 (2.37)
Total	337 (100)

Table 2. Findings of pap smear cytology

Pap findings	Number (%)
NILM	21 (32.81)
Unsatisfactory	7 (10.93)
AGC	3 (4.68)
ASC-US	16 (25)
ASC-H	9 (14.06)
LSIL	2 (3.12)
HSIL	6 (9.37)
Total	64 (100)

Table 3. Histomorphology of cervical biopsies

Histomorphology	Number (%)
Chronic cervicitis	7 (10.93)
Squamous metaplasia associated with Chronic cervicitis	4 (6.25)
Endocervical polyp	6 (9.37)
LSIL	20 (31.25)
HSIL	23 (35.93)
Squamous cell carcinoma	2 (3.12)
Adenocarcinoma	2 (3.12)
Total	64 (100)

Atypical glandular cells 8 (2.37%). (Table 1) and (Table 2)

According to histopathological diagnosis of biopsies, out of 64 cases 23 (35.93%) cases were HSIL followed by LSIL 20 (31.25%) and chronic cervicitis 7 (10.93%). Malignancy was diagnosed in 4 patients which comprises of 2 (3.12%) squamous cell carcinoma and 2 (3.12%) adenocarcinoma. (Table 3) Out of the 21 cases with normal cytology, six were diagnosed with chronic cervicitis, and two had HSIL. Additionally, among the cases identified with atypical glandular cells on the Pap smear, three were noted, two of which were later diagnosed as adenocarcinoma upon further investigation. Six HSIL cases on smear constituted three HSIL and 2 had squamous cell carcinoma (Table 4)

The "disease state" that distinguishes a test as "positive" or "negative" determines a test's sensitivity, specificity, positive predictive value, and negative predictive value. For statistical analysis, the interpretation of HSIL, adenocarcinoma and squamous cell carcinoma on pap smear are regarded as positive. The overall sensitivity was 25.92 %, specificity (94.59%), positive predictive value (77.77%) and negative predictive value was 63.63%. (Table 5)

Table 5. Comparison between cytology and histology findings for detecting malignancy

Observation on pap smear	Histopathological diagnosis		Total
	Positive	Negative	
Positive	7	2	9
Negative	20	35	55
Total	27	37	64

Table 4. Correlation between pap smear and biopsies

Pap findings	No. of cases on pap smear (%)	Chronic cervicitis	Chronic cervicitis with squamous metaplasia	Endocervical polyp	LSIL	HSIL	Squamous cell carcinoma	Adeno carcinoma
NILM	21 (32.81)	6	1	5	7	2	0	0
Unsatisfactory	7 (10.93)	0	0	1	3	3	0	0
AGC	3 (4.68)	0	0	0	1	0	0	2
ASC-US	16 (25)	1	2	0	4	9	0	0
ASC-H	9 (14.06)	0	1	0	3	5	0	0
LSIL	2 (3.12)	0	0	0	1	1	0	0
HSIL	6 (9.37)	0	0	0	1	3	2	0
Total	64 (100)	7	4	6	20	23	2	2

DISCUSSION

Cervical cancer is the 4th most frequent malignancy in women worldwide.[1] Cervical cancer screening programs can identify pre-cancerous lesions, and low-cost surgeries can treat them.[7] 70% of cervical cancer cases are caused by oncogenic genotypes (types 16 and 18). The Cervarix vaccination protects against these genotypes.[8]The Pap smear has been the primary screening method for cervical abnormalities since 1941.[9]A large-scale cervical cytology screening program has led to a more than 50% reduction in the incidence of cervical cancer over the past 30 years.[10] All sexually active women over the age of 18 are advised to obtain yearly Pap smears for a period of three years by the American Cancer Society, National Cancer Institute, and American College of Obstetrics and Gynecologists. The test can be prolonged for three to five years in the event that three consecutive negative pap smears occur.[11]

This was a prospective study carried out in a Department of Pathology, Lumbini Medical College from a period of one year from 14th April 2022 to 12th April 2023. The study included a total of 337 patients, with ages ranging from 21 to 86 years. PAP smear study was followed by corresponding 64 cervical biopsies. Cytological and histomorphological findings were correlated.

As in our study, Dhakal et al and Pradhan et al, also compared 75 and 40 biopsies with cytology respectively.[4,12]

In this current study, most common age group was 31 to 40 year which constitutes of 29.3% followed by 21 to 30 years (28.7%) which was similar to the study done by Dhakal et al, and the maximum number of patients were in between 31 to 40 years (35.4%).[4]

In our current study, NILM (71.21%) was most common followed by ASC-US (10.38%), which was similar to Farooq et al (56.9% NILM followed by 19.2% ASC-US).[13]

In the study conducted by Sinchana et al and Meghana et al., 18 cases (9%) and 53 (9%) respectively were reported as ECA (Epithelial cell abnormalities), which were in line with this study, where 53 cases (19.26%) were also reported as ECA.[14,15]

In study out of all epithelial cell abnormalities, ASC-US was found to be most common followed by ASC-H and then HSIL. However, in a study by Ranabhat et al HSIL was the most common lesion.[10]

In a study by Bansal et al.[16] (2021), 15 cases (3.3%) were diagnosed as ASC-US, which is consistent with the findings of this study, where 35 cases (10.38%) were reported. Number/percentage of ASCUS are more in present study due to presence of atypical cells overlapping with inflammatory background, reactive, regenerative and reparative changes. In this study, histopathological findings were analyzed in 64 patients who underwent both Pap smear and biopsy. The results showed that 23 patients (35.93%) had HSIL, 20 (31.25%) had LSIL, 7 (10.93%) had chronic cervicitis, and 4 (6.24%) had malignancy.

A similar study by Mainali et al. involving 118 patients found that 13 (11.01%) had HSIL, 12 (10.17%) had LSIL, 78 (66.10%) had chronic cervicitis, and 7 (5.94%) had malignancy.[6]

The mean age ± SD for carcinoma in our study was 47.85 ± 13.27 years, which is comparable to the study by Bodal et al., where the mean age for carcinoma was 51.94 years in the Indian population.[17]

The sensitivity of pap smear in current study was 25.92% while specificity was 94.59%, PPV and NPV was 77.77 %, 63.63% respectively while diagnostic accuracy was 65.62%. Our study showed comparable sensitivity and specificity to the findings of Vidyadhar et al (29.7% and 94.4%) and Ashmita et al (19.51% and 83.33%).[18,19] The diagnostic accuracy in our study was in accordance to Jain et al (73.2%) and Naiket al (74.5%).[20,21] However, Ashmita et al and Mallur et al showed lower accuracy.[19,22] (Table 5) The sensitivity of pap smear of 25.92% is possibly due to lost to follow up of patients who could undergo histopathological evaluation due to patient's preference of Medical Centres. The sensitivity of pap test in present study appears to be lower, possibly due to limited cases undergoing histopathological evaluation after interpretation of HSIL on cytology. Small sample size could also be one of the possibility of this finding.

Limitation of this study is the less number of cases had undergone both cervical pap and cervical biopsy. Greater number of cases would give better idea of comparison. In addition, because the study was conducted in hospitals, there was bias in the referrals to higher centers.

CONCLUSION

The Pap smear test, highlighting its poor sensitivity but good specificity in detecting premalignant and malignant cervical abnormalities. It notes a strong correlation between histopathology and cytological findings. To improve the sensitivity of cervical cancer screening, it is crucial to ensure adequate sampling and minimize technical errors, such as air-drying and fixation artifacts, which can compromise the accuracy of cytological results. Proper specimen handling is key to preventing these issues. Furthermore, the correlation between cytology and histopathology is essential for quality improvement. This correlation not only aids in confirming diagnoses but also enhances overall

evaluation, resulting in better patient outcomes and more accurate detection of abnormalities. Therefore, screening programs should be initiated at a young age for sexually active women to facilitate early detection and effective management of cervical lesions.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Study concept and design, Data collection, Analysis and interpretation of the data, manuscript preparation: Archana Tiwari; Data collection and manuscript preparation: Anupa Khanal; Analysis and interpretation of the data: Asmita Karki; Data analysis and manuscript preparation: Pratima Sapkota. All authors read and approved the final manuscript.

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