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Pre-Malignant Lesions of Cervix in Female Attending a Tertiary Hospital of Nepal

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ABSTRACT

Introduction

Cervical cancer is killing Nepali women in gross even though cervical cancer is preventable with time-tested screening strategies in Nepal. Detection of premalignant lesions of cervix is preliminary step for early treatment and to minimise the tragedy of death. The aim of this research is to co-relate the Pap smear, colposcopy and guided biopsy findings with histopathology to detect pre-malignant lesion of cervix.

Methods

A prospective observational study conducted among 145 women attending gynaecology OPD with symptoms during reproductive age 21-65 years. Collection of Pap smear was conducted by conventional method, colposcopy and guided biopsy in selected women were performed and the sample was sent to pathology department for histopathological confirmation.

Results

The pre-malignant lesions in cytology were ASCUS (Atypical Squamous Cells of Undetermined Significance) 11%, ASC-H (Atypical Squamous cell- cannot exclude High Grade)1.3 %, LSIL (Low Grade Intraepithelial Lesion)28.2 %, and HSIL (High Grade Intraepithelial Lesion) 7.5 %. The colposcopy detected 54.4% atypical transformation zone. The histopathology detected Cervical Intra-epithelial Neoplasia I (CIN I) 26.1%, CIN II 11.7%, and CIN III 7.5%. The sensitivity of Pap smear and colposcopy was 83%, the specificity of Pap smear was 88%, and colposcopy was 98%. The positive predictive value(PPV)were 89% and 98 %, negative predictive value(NPV)were 81% and 83%.and accuracy was 88 % and 98% in Cytology and Colposcopy.

Conclusions

Pap smear and colposcopy were effective tools to detect premalignant lesions of cervix in comparison to histopathological findings.

Keywords: Colposcopy; Colposcopy guided biopsy; Histopathology; Pap smear; Pre-malignant lesions of cervix.

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INTRODUCTION

Nepal is aiming for majority of women to be screened with high performance test by 35 years age and repeated by 45 years of age to meet the WHO cervical cancer elimination strategy target for 2030.[1] Cervical cytological screening, a secondary prevention, has been proven to minimize the cervical cancer incidence of morbidity and mortality in developed countries[2]. Scenario of Nepal, a low and middle income country, differs with developed one regarding lower screening coverage (5%) and higher incidence of disease mortality.[3]

In a tertiary care hospital, cervical premalignant lesion detection with conventional Pap test along with colposcopy & its guided biopsy and expert pathologist for histopathological confirmation will increase the sensitivity of test so will the treatment for cure. [4]Pap smear is simple, safe, non-invasive and effective tool to detect premalignant cervical lesion under microscopic study whereas Colposcopy is a unique, modern magnification system with lens to increase visual detection of abnormal transformation zone with filter when 5% acetic acid or lugol's iodine is applied to cervix to decide biopsy area[5]. None of the screening test has cent percent sensitivity for detecting premalignant cervical lesion which favours combine evaluation for accuracy; pap test & colposcopy in combination gained WHO recommendation.[6] So, we aimed to detect premalignant cervical lesions with pap smear and colposcopy and guided biopsy in abnormal findings along with the accuracy of test compared with histopathology in our hospital.

METHODS

A hospital based cross sectional study was conducted from 2019 June 15-2020 June 15 in the department of Obstetrics and Gynecology, College of Medical Sciences, Bharatpur-10, Chitan, Nepal. Ethical clearance was taken from Institutional review committee of, College of Medical Sciences (Ref No.2019-022.1). A research conducted by Narasimhamurthy showed the prevalence of cancer cervix as 17%.[7] By taking this as a prevalence with 5% margin of error and 95% confidence interval sample size was calculated by the following formula. (n= =110). But this research was conducted among 150 women. Informed and written consent was obtained from all the women under study after brief explanation of the procedure. A detailed and careful history including age, socioeconomic status, education, parity, age of marriage and contact number was noted. General and systemic examination was conducted. The information was documented in preformed proforma and later PAP and histo-pathological results were also noted on patient's follow up. One hundred and fifty women of age 21-65 were enrolled who had symptoms i.e. Abnormal vaginal discharge, persistent vaginal discharge, post coital bleeding, lower abdominal pain, recurrent lower genital tract infection attending gynaecological outpatient department of college of medical sciences, Bharatpur, Nepal. Women of age >65 years and ≤20 years, women with frank cervical cancer, pregnant women, and post total hysterectomy patients; Unsatisfactory smears for evaluation were excluded from this research. Detailed and required history, general and gynaecological examination performed along with collecting Pap smear. All the symptomatic women were subjected to Pap smear; and colposcopy (B'ORZE) & directed biopsy if abnormal colposcopy on the same setting. Colposcopic findings were noted in preformed proforma. Pap smear (slides in 95% ethyl alcohol) and Colposcopy guided biopsy specimen (tissue in 10% neutral buffer formalin) were sent to pathology department and report was collected tracing identification number of Pap (in 3 days) and Tissue biopsy (in 21 days).

Pap was reported with Bethesda system (2014) and biopsy reported with WHO classification. The reports were noted in the prior detailed proforma of the same patient.

The data was entered in Microsoft excel and converted to SPSS 22. Frequencies with percentages were used for descriptive statistics. The calculation of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Pap smear and colposcopy was completed in SPSS with chi-square test in comparison to histopathological findings. P-value<0.05 was considered as statistically significant.

RESULTS

Out of 150 women enrolled in our study, 5 cases were excluded when biopsy proved malignancy of cervix. Total 145 women's Pap smear, colposcopy and guided biopsy was conducted and were enrolled only with histopathology determined premalignant lesion of cervix. In our study, women subjected to Pap smear were also taken for colposcopy and guided biopsy in abnormal Colposcopic results. The mean age of women under study was 39 years (Std Dev 9.79), 60% reproductive age group and 11.03% were postmenopausal women, 93.7% were literate, 40% were from Janajati ethnicity and 89% had middle socioeconomic status. Among the reproductive age group, multiparous women were higher in number (73%). Forty percent of women were married before 20 years of age, 40% were from Janajati ethnicity and only 11.2% had previous Pap smear examination (Table 1).

Table 1. Socio-demographic profile of women (n=145).

Socio- Demographic variables	Frequency (%)
Age Group (years)	
21-40	87(60)
41-65	58(40)
Parity	
Nulliparous	2(1.37)
Prim parous	36(24.82)
Multiparous	107(73.79)
Ethnicity:	
Chhetri	20(13.79)
Brahmins	48(33.1)
Janajati	59(40.68)
Madhesi	6(4.13)
Dalit	12(8.27)
Age of Marriage (years)	
<20	58(40)
>20	87(60)
Socio- economic Status	
Low	15(10.34)
Middle	130(89.65)
Education:	
Literate	136(93.79)
Illiterate	9(6.2)
Previous Pap smear study:	
Yes	17(11.72)
No	128(88.27)

The common cause of visiting to hospital was per vaginal discharge in 66.6% women (Figure 1).

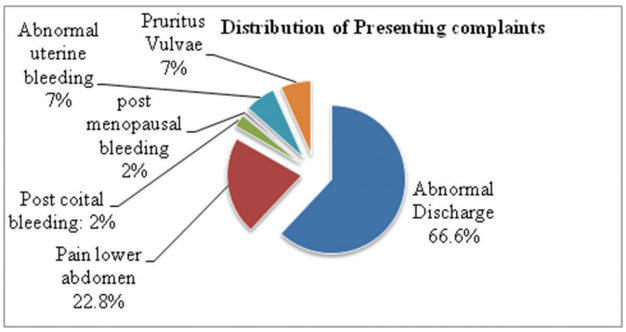

Figure 1. Distribution of women according to presenting complaints.

The higher number of women had negative for intraepithelial lesion or malignancy in Pap

report (50.3%). The pre-malignant lesions in cytology were ASCUS (Atypical Squamous Cells of Undetermined Significance) 11%, ASC-H (Atypical Squamous cell- cannot exclude High Grade) 1.3 %, LSIL (Low Grade Intraepithelial Lesion) 28.2 %, and HSIL (High Grade Intraepithelial Lesion) 7.5 % (Table 2).

2%, punctuation+mosaic + atypical vessels 2% (Table 3). The histo-pathology had detected Cervical Intra-epithelial Neoplasia I (CIN I) 26.1%, CIN II 11.7%, and CIN III 7.5% (Table 3).

The sensitivity of Pap smear and colposcopy was 83%, the specificity of Pap smear was 88%, and colposcopy was 98%. The positive predictive value(PPV)were 89% and 98 %, negative predictive value(NPV)were 81% and 83%.and accuracy was 88 % and 98% in Cytology and Colposcopy(Table 4).

Table 2. Co-relation of Pap smear with histopathological findings.

Pap	HPE Finding					
	Acute Cervicitis	Chronic Cervicitis	CIN I	CIN II	CIN III	Total
NILM	6	59	7	1	0	73
ASCUS	0	10	4	2	0	16
ASC-H	0	0	0	2	2	4
LSIL	0	3	28	9	1	41
HSIL	0	0	0	3	8	11
Total	6	72	39	17	11	145

The colposcopy detected 54.4% atypical transformation zone. Among them, aceto-white epithelium was 35.8%, mosaic pattern 4.8%, Punctation 9.6%, Punctation and mosaic pattern

Colposcopy	HPE Finding					
	Acute Cervicitis	Chronic Cervicitis	CIN I	CIN II	CIN III	Total
Normal	5	60	1	0	0	66
ACW	1	12	35	4	0	52
Mosaic pattern	0	0	0	4	3	7
Punctation	0	0	3	8	3	14
Punctation+Mosaic pattern	0	0	0	1	2	3
Punctation+Mosaic pattern+Atypical Vessels	0	0	0	0	3	3
Total	6	72	39	17	11	145

Table 4. Sensitivity, specificity, PPV and NPV of Pap smear and colposcopy.

		Benign	Premalignant	PPV	NPV	Sensitivity	Specificity
Pap	Benign	65	8	89.04%	81.94%	83.33%	88.05%
	Premalignant	13	59				
Colposcopy	Normal	65	1	98.48%	83.54%	83.33%	98.50%
	Abnormal	13	66				

DISCUSSION

Nepal has higher number of cancer cervix primarily due to limited screening. The PAP smear screening should be carried out in all women of reproductive and menopausal age group at least once in a lifetime.[7] Screening and early treatment in low income country like Nepal will decrease the disease mortality due to detection in late stage as well cure is possible if diagnosed in time to reduce financial burden.[8] In our study, 60% women were of age 21-40 years among the study population, which was similar to the study by Subedi et al at Paropakar hospital.[8] Early age of marriage is a risk factor for precancerous lesion and cancer cervix[9]. In our study, 40% women were married before the age of 20, which was similar to the study by Nair R et al.[10] Our area falls under Terai region, and the residence are Janajati in highest frequency to visit hospital and so for the testing contrast to finding of Shrestha A et al[11] in a study of women at hilly region where Brahmins were major ethnic variants of Nepal. The majority of women were multiparous (73%) in our study and literate (93%), 89% middle socioeconomic status similar to study by Sah R et al,[11] Subedi K[8] and Shrestha A[12] Abormal vaginal discharge (66%) and pain abdomen (22%) were the major presenting symptom in our study population (Figure 1) which is a common presentation and risk factor for cancer cervix, and similar to other studies.[12,13] Our study reported NILM in 50% women similar to Sahen et al (48%)[14] but the premalignant lesions were 28.2% LSIL (31%[8], 10%[12]) , 11% ASCUS (10%[12]), 7.5% HSIL(15%[8] ,11%[12]), and 1.3 % ASC-H (6.6%[8],6%[12]) in cytology excluding cervicitis contrary to Sahen et. Al (LSIL: 5% and HSIL 0.48%) but similar to Shrestha A and Subedi K.[8,12,14] The colposcopy detected 54% abnormal finding i.e. aceto-white epithelium 35.8%, mosaic pattern4.8%, punctation 9.6%, combined 2% in our study which is higher compared to Shrestha A(40%)[12], and lower compared to Bhattacharjee S et al (88%)[15].

The histopathological diagnosis of CIN I was 26.1%, CIN II was 11.7% and CIN III was 7.5% in our study which was comparable with study by Shrestha (CIN I 28%, CIN II and III 39%)[12], Bhattacharjee (CIN I 45%, CIN II 30%, CIN III 8%)[15] and higher CIN I(26 % vs 18%) and CIN II (11.7% vs 8.3% and lower CIN III (7.5% vs 15%) compared to Subedi.[8] Various studies had wide range of Pap smear sensitivity (11-99%) and specificity (14-97%).[16]The sensitivity and specificity of Pap smear were 83% and 88%. The sensitivity and specificity of colposcopy were 83% and 98%. Our study outcome was similar to the findings of Shrestha et al[12] in regards to Pap test (sensitivity 63-19%, specificity 66-86%) and Bhattacharjee et al[15] in colposcopic evaluation (sensitivity 83.6%, accuracy 98.3%) and Asmita et al (sensitivity 90.2%, specificity 72.7%)[17] The PPV and NPV were 89% and 81% in Cytology in our study which was similar to the study by Bhattacharjee et al (PPV 94%, NPV 71%)[15] and Ashmita et al(PPV 66.6%, NPV 86%) .[17] The PPV and NPV were 98% and 83% in Colposcopy comparable with studies by chaudhary et al [13] and Ashmita et al[16]. The accuracy was 88 % similar to study by Ashmita et al [17] in Cytology and 98% in Colposcopy matching the value with the study by Bhattacharjee et al (98.3%)[15] Due to lack of HPV DNA testing and high cost on referral testing; though recommended by WHO, we are combining the available facilities of our hospital for increasing the sensitivity and specificity of the Pap and colposcopy with histopathological correlation.

Limitation of Study

The study could have been undertaken in higher number of population for higher accuracy. We have excluded the unsatisfactory samples and

malignancy reported cases, so inclusion of those cases could have covered the malignancy of cervix during our study period.

CONCLUSIONS

Pap smear and colposcopy were effective tools with high sensitivity and accuracy to detect premalignant lesions of cervix in comparison to histopathological findings.

Conflict of interest: None

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