Original Article

Pap Smear as a Screening Tool for Cervical Cancer in a Tertiary Care Centre in Nepal: A Retrospective Cross-sectional Analysis

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ABSTRACT

Introduction: Pap smear is a time-tested screening test to diagnose cervical carcinoma at an early stage. It allows clinicians to take intervention measures, prevent the progression of the disease to invasive forms and decrease the burden of carcinoma as a whole. The objective of this study is to determine the values regarding the diagnostic accuracy of Pap smear and establish its role in the health care setting of Nepal.

Materials and Methods: This is a retrospective cross-sectional analysis of the records from April 14, 2018, to April 12, 2020, of the Department of Pathology in a tertiary care hospital in the capital city of Nepal. Ethical approval for the study was taken from the Institutional Review Board and the demographic and clinical data of patients were analyzed anonymously. The consecutive sampling technique as used for data collection and analysis was done in Microsoft Excel 2019 and Statistical Packages for Social Sciences Version 25. The diagnostic accuracy parameters were calculated from a contingency table prepared from the collected data.

Results: Out of 3095 Pap smears, 72 had a positive finding of some sort. 74 cases had a positive finding in the form of a biopsy out of 573. The sensitivity, specificity, positive predictive value, and negative predictive value of Pap smear at the institution were found to be 0.70, 0.94, 0.78, and 0.91 respectively with an overall accuracy of 88.36%.

Conclusions: Pap smear can still play a pivotal role in the diagnosis of cervical neoplastic lesions.

Keywords: Carcinoma; Cervix; Pap smear;

INTRODUCTION

Cervical cancer is the fourth most commonly diagnosed cancer with about 604,000 new cases and the fourth most common cause of cancer mortality in women with 342,000 deaths worldwide in 2020.[1] In Nepal, it is the leading cause of cancer in women with a predicted 2,942 cases annually.[2] The age-standardized incidence rate for cervical cancer in Nepal is 21.5 per 100,000 women per year while it is 13.0 in Southern Asia and 13.1 in the rest of the world.[2] It was believed that India, Bangladesh, Nepal, and Sri Lanka had the burden of one-third of the world's cervical cancer burden.[3] The difference in Human Development Index (HDI) and poverty rate accounts for more than 52% of the global variance in mortality due to cervical cancer with HDI, poverty rate, health expenditure per capita, urbanization, and literacy rate strongly related to cervical cancer incidence and mortality.[4] A research based on data collected from National Cancer Registry Program in Nepal demonstrated a rising trend of cervical carcinoma in the country, thus emphasizing the need for programs to facilitate prevention, early detection, and treatment of the same.[5]

Papanicolaou (Pap) smear is an important screening tool to detect cervical carcinoma.[6] It has been estimated that when a Pap smear is combined with a regular screening and follow-up program, mortality due to cervical carcinoma can be reduced by up to 80%.[7] There has been a decline in the incidence of cervical carcinoma in developed countries in recent decades which has been attributed to improvement in genital hygiene and decreasing trend of sexually transmitted diseases.[8] Implementation of robust screening programs has reduced the mortality due to cervical cancer in developed countries.[9]

Although population-based programs offering Papanicolaou testing every 3 to 5 years have reduced cervical cancer incidence and mortality in high-income countries, such programs have been less successful in reducing the cervical cancer burden in low and middle-income countries due to poor organization, lack of coverage, and lack of quality assurance.[10] A similar study at a tertiary care center in Nepal demonstrated the effectiveness of a Pap smear in the early diagnosis of cervical carcinoma.[11] By calculating the diagnostic accuracy of Pap smear, we aim to firmly establish its role in a setting like ours where usually cancer screening lags behind the recommendations.

MATERIALS AND METHODS

This is a retrospective cross-sectional analysis of secondary data obtained from the records from April 14, 2018, to April 12, 2020, of the Department of Pathology in a tertiary care hospital in the capital city of Nepal. Ethical approval for the study was taken from the Institutional Review Board. All female patients who visited Shree Birendra Hospital and underwent Pap smear and/or cervical biopsy for any reason were included in the study. Shree Birendra Hospital is a tertiary referral center in Kathmandu that caters primarily to military persons and their families.

Retrospectively data collection was done from the electronic database from the pathology department of the hospital. Collected data included demographic details of the patients, indications for the procedure, gross and microscopic findings in the specimen, and the pathologist's impression/diagnosis. Data from April 14, 2018, to April 12, 2020, were taken for analysis. Separate entries were collected regarding Pap smear and cervical biopsy. The demographic variables and date of collection of samples were cross-matched across those two entries to determine the subsequent cervical biopsy after the Pap smear. The entries with inadequate samples and doubtful diagnoses were removed during analysis. For calculation of diagnostic accuracy of Pap smear, cervical biopsy results were taken as the gold standard for diagnosis. The positive malignancy reports in the biopsy were either Cervical Intraepithelial Neoplasia (CIN) or invasive carcinoma. The Pap smear results of Atypical Squamous Cells of Undetermined Significance (ASCUS), Low-grade Squamous Intraepithelial Lesion(LSIL), High-grade Squamous Intraepithelial Lesion(HSIL), and Squamous Cell carcinoma were taken as positive results in the calculation of diagnostic accuracy. The positive diagnosis from the cervical biopsy was the finding of any form of carcinoma in the report.

Initial data from the electronic database from the Pathology department was imported into Microsoft Excel 2019. The data were subsequently streamlined and imported into IBM SPSS 25.0 for further analysis. The positive diagnosis from both Pap smear and cervical biopsy were initially separated into different age groups. Besides the differentiation according to age group, a contingency table comparing positive and negative results from Pap smear and cervical carcinoma was created from which, the diagnostic values were calculated.

RESULTS

A total of 3095 cases qualified for analysis of Pap smear. The age of patients ranged from 20 years to 90 years. The mean age of women who underwent Pap smear for any reason was 43.40+/-12.4 years. The age group 56 and above accounted for 37.5% (27/72) of the total positive burden of Pap smear, followed by the age group 46 to 55 with 25% (18/72), 36 to 45 with 19.4% (14/72), 26 to 35 with 13.9% (10/72) and 25 and below with 4.2% (3/72).

The highest burden of LSIL was among the age group 36 to 45 with 41.67% (5/12) of the burden. HSIL was commonest among the age group 56 and above comprising 72.2% (3/18) of the total burden. AUS and AUS-H were respectively 34.2% (13/38) and 75% (3/4) accounting for the highest share among the age group 46 to 55. (Table 1)

Table 1: Distribution of different categories of Pap smear based on age group

Diagnosis	Age groups (years)				
	≤ 25	26 - 35	36 - 45	46 - 55	≥56
Normal	349	791	812	659	412
LSIL	1	2	5	2	2
HSIL	2	2	1	0	13
AUS	0	6	8	13	11
AUS-H	0	0	0	3	1

573 patients who underwent cervical biopsy were included in the study. The age range was from 19 years to 70 years with a mean of 48.13 +/- 12.2 years.

There were a total of 74 cases detected positive by cervical biopsy, out of which 50% (37/ 74) belonged to the age group 55 and above. It was followed by the age group 46 to 55 with 19% (14/74), 36 to 45 with 12.2% (9/74), and age groups 26 to 35 and 25 and below with 9.5% (7/74) each.

The highest burden of CIN I was among the age group 46 to 55 comprising 26.9% (7/26) of the total disease burden followed by the age group 55 and above comprising 23% (6/26) of the total burden. CIN II, CIN III, and Invasive carcinoma were all found to be highest among the age group 55 and above with respective burdens of 57.1% (4/7), 58.3% (7/12), and 69% (20/29) of the corresponding category. (Table 2)

Table 2: Distribution of different categories of cervical biopsy based on age group

Diagnosis	Age groups (years)				
	≤ 25	26 - 35	36 - 45	46 - 55	≥56
Normal	26	65	134	176	98
CIN I	4	4	5	7	6
CIN II	1	0	1	1	4
CIN III	1	1	0	3	7
Invasive Carcinoma	1	2	3	3	20

Out of all collected data entries, only 189 cases with matching entries of both Pap smear and cervical biopsy could be determined. Detection of any form of malignancy in either Pap smear or cervical biopsy was taken as a positive result in the respective study. The absence of malignancy was taken as a negative result.

Table 3: Diagnostic performance of Pap smear as compared to Cervical biopsy

		Cervical Biopsy	
		Positive	Negative
Pap Smear	Positive	31	9
	Negative	13	136

The sensitivity and specificity were found to be 0.70 and 0.94 respectively. Similarly, the positive and negative predictive values were 0.78 and 0.91 respectively. The overall accuracy was 88.36%.

DISCUSSION

Out of 3095 patients who underwent Pap smear, 3023 (97.67%) had a non-malignant report with 72 (2.33%) of patients being detected positive for some sort of malignancy. A population-based study in Nepal reported a result of 95.6% for normal and inflammatory results in Pap smear which is similar to our findings.[12] The highest burden among Pap smear positive findings were among AUS with 38 (1.22%) entries. It is similar to 2.8% in a study in Nepal.[12]

The rate of cytology positivity increased with age, with the highest rate (8.76%) in women ages 50–65, but the rate of positivity of Visual Inspection with acetic acid and Lugol's iodine decreased with increasing age of women.[13]

The age of the patients undergoing Pap smear ranged from age 20 to 90 years. Though it might not be within the range as determined by the guidelines, oftentimes in a health care system like ours it is necessary to perform procedures either because it is the patient's first contact with the health care provider or due to fear of loss of patient follow-up. Among the data selected from patients undergoing a cervical biopsy, the age range was from 19 years to 70 years. The need for an early biopsy may be due to an early suspicious lesion. One study showed that the maximum frequency of cervical cancer cases in Nepal was found in the age group 40 to 49 years. our study found maximum cervical carcinoma in the age group 55 and above.[14]

The highest burden of HSIL was among the age group 56 and above comprising 13/27 (48.1%) of all HSIL cases. The population-based study had the highest HSIL burden among the age group 30 to 44.[12]

Compared to similar studies, the sensitivity of Pap Smear in our study was significantly higher, which could be attributed to the level of expertise in the tertiary level center as well as increased true positive as most of the cervical biopsies would be done if Pap smear came positive. (Table 4)

Table 4: Comparison of Diagnostic Values of Pap Smear with published articles

	Current Study	Macharia HC et al[15]	Barut MU et al[16]	Nkwabong et al[17]	Bhattacharyya et al[18]
Sensitivity	0.7	50	0.57	55.5	52%
Specificity	0.94	57	0.76	75	95%
Positive Predictive Value	0.78	13	0.26	88.2	
Negative Predictive Value	0.91	90	0.92	33.3	

The data was collected from a single tertiary center, thereby the elements of selection bias were introduced with smaller sample sizes and relatively advanced diseases. Data were collected for two years to try to increase the number of cases. To eliminate the bias introduced by diagnosed malignant cases, they were excluded from the calculation of diagnostic accuracy.

CONCLUSIONS

The diagnostic accuracy of the Pap smear at our tertiary care center was found to be relatively high which cements the role of Pap smear in the screening of cervical carcinoma.

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