

# STUDY OF CERVICAL BIOPSY OVER A DECADE AT A TERTIARY LEVEL HOSPITAL, NEPAL

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## ABSTRACT

Cervical carcinoma is the most common gynecological malignancy and almost curable cancer, if identified at an early stage. Cervical biopsy remains the 'gold standard' for the diagnosis of precancerous cervical lesion. The objective of this study was to review the histopathological findings of cervical biopsy including cervical polypectomy and hysterectomy specimens at Dhulikhel Hospital from January 2008 to December 2018. Out of 2098 cases, almost half of the cases (49.3%) were of Brahmin/Chhetri castes. There were significant differences in mean ages among hysterectomy cases (47.55±9.26), cervical biopsy cases (43.08±11.50) and polypectomy cases (33.59±12.47) (p value < 0.005). Out of 925 cervical specimens (cervical biopsy and polypectomy), colposcopy and hysteroscopy were performed in 18.2% and 12.7%, respectively. Out of 1173 hysterectomies, there were 110 cases (9.4%) of malignancies and cervical cancer was the most common (67, 60.9%). The mean age of cervical cancer patients was 52.87±11.94 years. Cervical cancer detected in age group of 40 – 59 years was significantly high (p value < 0.005). Incidence of cervical cancer was lowest in Brahmin/Chhetris (2.4%) compared to Newars (3.4%) and other Janajatis (12.8%) and the difference was statistically significant (p value < 0.005). The findings of this study is useful in updating the histopathological pattern of cervical biopsies.

## KEYWORDS

Biopsy, cervical cancer, colposcopy, hysterectomy, polypectomy

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## INTRODUCTION

Cervical carcinoma is one of the most common gynecological carcinoma and leading cause of mortality in females.<sup>1</sup> Cervical cancer is almost curable if identified at an early stage.<sup>2</sup> Five screening methods, namely naked eye visual inspection of the cervix after application of diluted acetic acid (VIA), Lugol's iodine (VILI) or with a magnifying device (VIAM), the pap smear and human papilloma virus (HPV) testing with high-risk probe of the Hybrid Capture-2 assay (HC2) are being used to screen and detect the cervical cancer in precancerous stage.<sup>3</sup> But these tests may fail to localize the lesion and, cervical biopsy remains the 'gold standard' for the diagnosis of precancerous cervical lesion.<sup>4</sup>

Cervical cancer screening tests along with the confirmatory tests and appropriate treatment for premalignant cervical conditions and cervical cancers were regularly done in Dhulikhel Hospital (DH) since its establishment (1996). Though, there are ample of studies done in the field of cervical cancer globally, only limited publications related to cervical screening tests were available from Nepal, and the available publications were not focused on cervical biopsies.<sup>5-8</sup> Only two articles related to cervical cancer screening and cervical biopsy were published from DH.<sup>9,10</sup> Twenty two low grade squamous intraepithelial lesions (LSIL) and four frank malignant cases were detected in 1062 pap smear examination.<sup>9</sup> In a study of 1922 pap smear, there was 0.4% high grade squamous intraepithelial lesions (HSIL). In another study done in Dhulikhel hospital, 1.3% moderate SIL, 6.7% SIL and 5.3% frank malignancy were detected in 75 cervical biopsy.<sup>10</sup>

Therefore, this study was carried out to investigate and analyze the histopathological findings in targeted cervical biopsy, polypectomy specimens and hysterectomy specimens evaluated and/or treated in Dhulikhel Hospital, a University Hospital of Kathmandu University.

## MATERIALS AND METHODS

This was a study of the histopathological findings in targeted cervical biopsy, polypectomy specimens and hysterectomy specimens evaluated and/or treated cases in DH from January 2008 to December 2018. This study was carried out in the Department of Obstetrics and Gynecology. The medical records from OPD patients, inpatients and histopathology records including electronic records were reviewed. Socio-demographic information (caste, age) and diagnostic procedures were also analyzed.

Ethical clearance was taken from the hospital research committee (IRC-KUSMS). All data were analyzed by SPSS 16 packages using appropriate statistical tools.

All the cases were initially categorized into cervical tissue and hysterectomy specimen groups for analysis purpose. The cervical tissue group was further divided into targeted cervical biopsy group and cervical polypectomy group as per need. Though histopathological findings and other information were analyzed in all these three groups (targeted cervical biopsy, polypectomy specimens and hysterectomy specimens), meticulous analysis was carried out primarily in targeted cervical biopsy group.

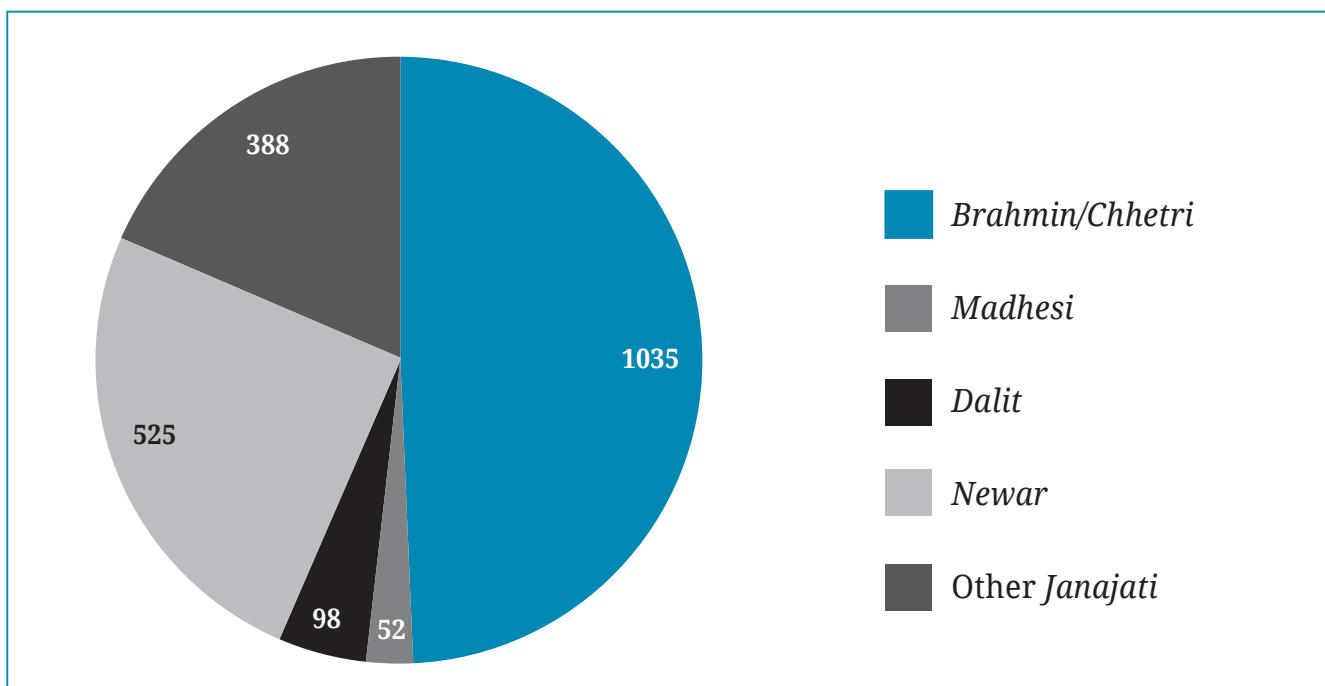


Fig. 1: Caste distribution of the cases

## RESULTS

Out of the 2098 cases, almost half of the cases were of Brahmin/Chhetri (49.3%) followed by a quarter of Newar caste (25%) and rests were of other castes (Fig. 1). Mean age of the cases was shown in Table-1. There was significant difference in mean age of hysterectomy cases with cervical biopsy cases, p value <0.0001 (95% CI 3.5244 to 5.4156) and that with polypectomy cases, p value <0.0001 (95% CI 1.9884 to 4.8116) but there was no significant difference between mean age of cases with cervical biopsy and that of polypectomy, p value =0.2332 (95% CI -2.8322 to 0.6922).

Table-2: Indications of the procedures

Diagnosis	Frequency	Percent
Polyp	312	14.9
Unhealthy cervix or cervical lesions	429	20.4
Premalignant condition	151	7.2
Abnormal uterine bleeding	364	17.3
Prolapse	279	13.3
Fibroid or uterine cause	411	19.6
Ovarian tumours	113	5.4
Other pathology	39	1.9
Total	2098	100.0

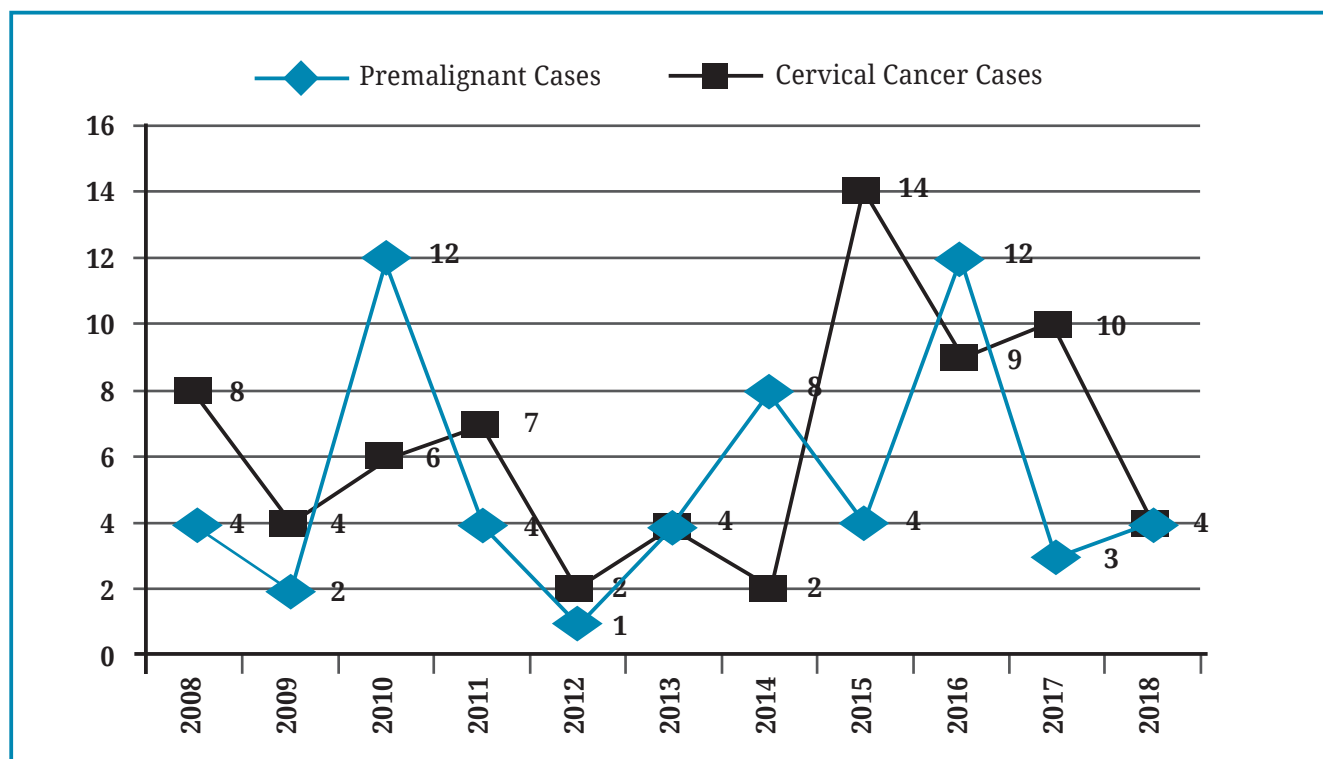


Fig. 2: Year-wise trend of premalignant and cervical cancer cases

Table-1: Distribution of mean age of the cases

Cases	Mean age (years)	Range (years)
Overall cases (n=2098)	45.68±10.43	20-86
Cervical biopsy cases (n=721)	43.08±11.50	20-86
Cervical polypectomy cases (n=204)	33.59±12.47	20-81
Hysterectomy cases (n=1173)	47.55±9.26	26-79

The indications for cervical biopsy, polypectomy or hysterectomy were shown in Table-2. Out of 925 cervical specimens (that of biopsy and polypectomy), 168 biopsies were taken under colposcopy guidance. Fifteen premalignant lesions and three cervical cancer cases were

detected among 168 biopsies. One hundred seventeen cervical biopsies were taken under hysteroscopy guidance. Out of them, five cases of cervical cancer were detected. Three hundred twenty eight cases had unhealthy cervix and 75 cases had suspicious cervix on clinical evaluation, those cases were scheduled for cervical biopsy. Eighteen premalignant lesions (5.5%) and three malignant lesions (0.9%) were detected among 328 unhealthy cervixes. Likewise three premalignant lesions (4%) and twenty three (30.7%) malignant lesions were detected among 75 suspicious cervixes.

Out of 2098 biopsies, 70.2% were benign lesions, 2.8% were CIN (cervical intraepithelial neoplasia)/pre-malignant lesions, 3.3% were frank malignant lesions and 23.7% were normal (Table-3). Likewise, 71.0% were benign lesions, 5.4% were

**Table-3: Histopathological results (n=2098)**

HPE	n	%
Chronic cervicitis	728	34.7
Nabothian cyst	25	1.2
Benign lesions	292	13.9
Benign ecto/endocervical polyp	292	13.9
Squamous metaplasia	311	14.8
Other benign lesions	104	5.0
Leiomyoma	13	0.6
CIN/premalignant	58	2.8
Malignancy (cervical)	67	3.2
Unremarkable	497	23.7
<b>Total</b>	<b>2098</b>	<b>100.0</b>

**Table – 4: Histopathological results among targeted cervical biopsy cases (n=721)**

HPE	n	%
Chronic cervicitis	278	38.6
Nabothian cyst	8	1.1
Benign lesions	121	16.8
Benign ecto/endocervical polyp	121	16.8
Squamous metaplasia	93	12.9
Other benign lesions	7	0.9
Leiomyoma	5	0.7
CIN/premalignant	39	5.4
Malignancy	56	7.8
Unremarkable	114	15.8
<b>Total</b>	<b>721</b>	<b>100.0</b>

CIN/premalignant lesions, 7.8% were frank malignant lesions and 15.8% were normal among targeted cervical biopsy cases (n=720) (Table-4). On caste-wise distribution of premalignant and malignant results among targeted cervical biopsies, Newar and Janajati castes had more premalignant and malignant lesions (Table-5). Year-wise trend of premalignant and cervical cancer cases of DH was shown in Fig. 2.

We had altogether 110 cases of gynaecological malignancy, cervical cancer was the most common cancer (67,60.9%) followed by ovarian cancer (21,19.09%) and endometrial cancer (10, 9.09%). Cervical cancer cases detected in Newar and other Janajati caste were high which is statistically significant (p value <0.005 in both cases) (Table-6). The age group of cervical cancer cases detected among 2098 cases were also analyzed (Table-7).

**Table-5: Castewise distribution of premalignant and malignant results among targeted cervical biopsy (n=721)**

Result	Brahmin/Chhetri (n=349)	Madhesi (n=16)	Dalit (n=37)	Newar (n=178)	Other Janajati (n=141)	Total (n=721)
Cervical biopsy						
CIN	19 (5.44%)	0	2 (5.41%)	11 (6.18%)	7 (5.97%)	39(5.41%)
Ca Cervix	25 (7.16%)	2 (12,5%)	5 (12,51%)	6 (3.37%)	18(12.77%)	56(7.77%)

**Table-6: Comparison of cervical cancer in Newar and other Janajati castes**

Caste	Cancer	No cancer	P value	Caste	Cancer	No cancer	P value
Newar	6	172	0.0116	Janajati	18	123	0.0134
Other castes	50	493		Other castes	38	542	
<b>Total</b>	<b>56</b>	<b>665</b>		<b>Total</b>	<b>56</b>	<b>665</b>	

**Table-7: Age group of cervical cancer cases detected among 2098 cases**

Age group	n	%
20-29	1	1.5
30-39	3	4.5
40-49	27	40.3
50-59	17	25.4
60 or above	19	28.4
<b>Total</b>	<b>67</b>	<b>100.0</b>

## DISCUSSION

Cervical carcinoma is one of the commonest gynecological carcinoma.<sup>1</sup> One of the regional studies showed that cervical cancer was seen in 85% of all gynecologic malignancies in Nepal.<sup>11</sup> The cancer incidence per 100,000 females was 15.1 in 2003 and 26.7 per 100,000 in 2012. Cancer incidence was low at early age but it was increased with age in both sexes in Nepal. Cervix uteri were the most common site of cancer in females.<sup>12</sup> The prevalence of cervical cancer was second to breast cancer in females.<sup>13</sup>

Khan *et al*<sup>13</sup> showed that cancer prevalence among the *Newars* was highest. The majority of local inhabitants in his study site were *Newars*, *Chhetris* and *Brahmins*. Hence the caste-wise cancer prevalence was expected.<sup>13</sup> The ethnic distribution of the cases of old study was different from our study. The ethnic distribution of State 3 is *Tamang* 20.42%, *Brahmin* 18.28%, *Chhetri* 17.28%, *Newar* 16.92% and *Magar* 4.89%.<sup>14</sup>

The mean age of cervical cancer patients was 52.75 years in an earlier study of DH.<sup>10</sup> This finding was comparable to our study. In a study done by Bodal *et al*,<sup>15</sup> the mean age of cervical cancer patient was 51.94 years in Indian population.

The cancer incidence in Nepalese female is increased sharply from the age group of 30-34 years. The highest incidence (140.61 per 100,000) was found in age group of 65-69 years.<sup>16</sup> In a study by Jha *et al* 29% cases were of cervical carcinoma and about 71% of them were of age group 40-59 years.<sup>17</sup> These findings were similar to our study. In our study, cervical cancer was detected in age group of 40-59 years and was significantly high (p value <0.005) followed by age group above 60 years.

Crude incidence rates and age standardized incidence rates for cervical cancer increased in China from 2000 to 2014. And, the highest incidence risk was seen in age group of 40-69 years.<sup>18</sup> The peak age of occurrence of cervical cancer in India is between 55 and 59 years.<sup>19</sup>

The accuracy of colposcopy guided biopsy appears to increase when three biopsy specimens were

taken and was particularly high for younger patients.<sup>20</sup> In this study, only fifteen premalignant cases and three cervical cases were detected out of 168 colposcopy guided procedures. Colposcopy, the single and irreplaceable second-level procedure for triage of cervical abnormalities, is challenged to match the today's screening tests, especially in view of the extended intervals that increase the risks for patients with missed disease.<sup>21</sup> Bifulco *et al*<sup>22</sup> concluded that the ability of a colposcopist in grading cervical lesion depends on his experience.

Unhealthy cervix with discharge was found to be common even in chronic cervicitis however bleeding and tenderness along with unhealthy cervixes were associated with more advanced lesions.<sup>6</sup> In a study of unhealthy cervixes (n=100), 18% had a positive pap smear. Among 18 positive cases, there were thirteen LSIL and five HSIL but no case of malignancy. On colposcopy, 30% cases were found to have premalignant lesions.<sup>23</sup> In a study of 100 pap smear by Pradhan N *et al*, six had dysplasia in healthy cervix group and eight had dysplasia in unhealthy cervix group. Though, the difference was not statistically significant (p=0.78), dysplasia was slightly higher among the women with unhealthy cervix.<sup>24</sup> These findings were similar to our study findings. In our study, premalignant lesions (including LSIL and HSIL) were detected in 5.5% and cervical cancer cases in 0.9% of 328 unhealthy cervixes.

We conclude that cervical biopsy should be performed whenever there is doubt. In cases of unhealthy and suspicious cervixes, colposcopy guided cervical biopsy can be the gold standard, and experienced colposcopist should do the procedure. Finally, every hysterectomy specimen must be sent for histopathological evaluation to rule any abnormal lesions in cervix, even if cervical screening was done earlier.

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