

Research Article

Clinicopathological Pattern of Cervical Papanicolaou (PAP) Smears: A hospital based experience

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ABSTRACT

Background and Objectives: Cervical cancer is very common type of cancer in women globally. The objective of this study was to compare the cytopathological findings of the cervical pap smears using the revised 2001 Bethesda system and to compare the cytopathological findings with the clinical features.

Material and Methods: A total of 1016 pap smear sent to the Department of Cytopathology at Peoples Dental college general hospital (PDCH), Kathmandu over a period of three years were studied. Relevant history and clinical findings were retrieved for the study. The age, caste, location, gravida of the patient, the nature of complaint of patient to the doctor along with the per speculum findings, per vaginal examination findings of the patient and their relation to the cytopathological findings of pap smears were evaluated.

Results: No significant relationship was observed between the (30-39 years) aged women and the available outcome of pap smear ($p=0.404$). Most of the females were Brahmin and Newars. The statistical analysis showed no significant relationship ($p>0.05$) between the ethnicity and pap smear result. The number of asymptomatic women in this study was found 22.9%. This study found 20.37% of intraepithelial lesion or malignancy. *Trichomonas vaginalis* and bacterial vaginosis combinely contributed to 0.7% of the total cases in this study. Three smear cases were detected having malignant epithelial cell which were diagnosed with adenocarcinoma, squamous cell carcinoma.

Conclusion: In this study cervical pap smear was able to differentiate inflammatory, benign precursors and malignant cases. So, it is desirable to conduct routine Pap smear screening in women of all reproductive age regardless of race, ethnic background and socioeconomic status.

Keywords: Adenocarcinoma, high grade squamous intraepithelial lesion, inflammatory smear, low grade squamous intraepithelial lesion, pap smear

INTRODUCTION

Cervical cancer is the third most common cancer in women, and the seventh overall globally [2]. And more than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers. Cervical cancer ranks as the most frequent cancer among women in Nepal that occurs in women age group between 15 and 44 years [3]. According to a regional study, cancer of cervix makes up about 85% of all gynecologic malignancies in Nepal [4].

Various agents have been reported either as an association or cause of cervical cancer. Both epidemiological and molecular studies provide support for human papillomavirus (HPV), particularly HPV 16, 18, 45 and 56, as a primary aetiological factor in cervical cancer [5]. Other cofactors that play important part in cervical carcinogenesis include ethnicity, lifetime number of sexual partners, early age at first sexual intercourse, and age at first child birth. Apart from sexual behavior, factors related to health behavior such as nutrition, regular screening, parity and oral contraceptive use have been reported as major environmental risk factors for cervical cancer [6].

The long latent period of intraepithelial neoplasia and availability of easy and sensitive screening test like pap smear make the cervix a useful site to screen for cancer [7]. Cervical pap smear screening is designed to detect over 90% of cytological abnormalities [8]. Since the introduction of pap smear 50 years ago, both the incidence and the mortality from cervical cancer has dropped dramatically, especially in developed countries with well established cervical screening program [9].

MATERIAL AND METHODS

This is a hospital based retrospective study retrieved from the PDCH hospital record section for a period of almost three years i.e. from July 2013 to March 2016AD. The data were retrieved from the requisition form, outpatient department document or by taking history directly from the patient. The alcohol fixed pap smear along with relevant clinical history and examination findings that were filled up in the requisition form were received in the laboratory of Pathology Department from the Department of Gynecology and Obstetrics, PDCH. The slides were stained using the papanicolaou technique.

RESULTS

A total of 1016 pap smear cases were evaluated for the study. Out of that 15 cases were excluded since they failed to meet the adequacy criteria mentioned by the 2001 Bethesda system.

The age of the woman undergoing pap smear test ranged from 19 to 73 yrs with the mean age of 38 years. The highest number of patient belonged to 35 years with highest age range belonging to the age group of 30-39 yrs. Brahmin and Newar ethnic group made the bulk of the study cases (35%) followed by Chhetri, Gurungs and Tamangs.

The pap smears in this study were obtained from nulliparous women as well women having upto 7 gravida. Women having two and three gravida were the most common involved in this study. The mean gravida was 2.82.

Cytological study of the Pap smear showed that 794 (79.62%) women smears were negative for intraepithelial lesion or

malignancy, and 207 women had intraepithelial malignancy of some kind. Out of those 207 cases, one had adenocarcinoma, two had squamous cell carcinoma, 14 had High Grade Squamous Intraepithelial Lesion (HGSIL), 29 had Low grade squamous intraepithelial lesion (LGSIL), and 58 had atypical squamous cells of undetermined significance. Interestingly, 103 cases (10.13%) showed reactive changes.

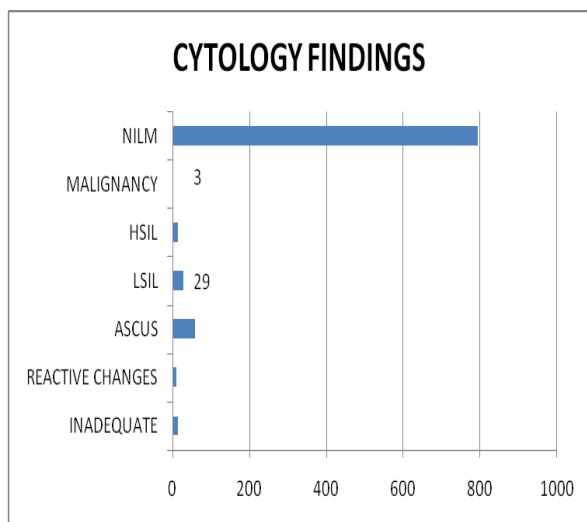


Figure 1: Distribution based on cytological findings.

The endocervical cells (transformation zone component) were present in half of the smears only. Per speculum examination of vagina showed erosion of cervix as the most common finding followed by cervix discharge, cervix hypertrophy, bulky uterus, contact bleeding and presence of polyp.

When presenting complaints and pap smear findings were seen together, frequency of abdominal pain and per vaginal discharge had the most number of inflammatory smear followed by “other “complaints that included itching of the perineal region, problems related to passing urine, uterine prolapse of various degrees etc.

DISCUSSION

The study compared the cytopathological findings of the cervical pap smears and their cytopathologic findings. The primary reasons for excluding 15 cases on the ground of inadequacy were due to the absence of sufficient numbers of cells on the smear. This could be improved by sound techniques and experience while taking Pap smear. Several reasons are identified for failure of cervical test. e.g.; Patient very tense owing to failure of reassurance at the time of procedure, cervix not visualized adequately, cervix not scraped firmly enough, material incompletely transferred to the slide, sample poorly spread (too thick or too thin or distortion due to excessive pressure), smear allowed to dry before fixation, insufficient fixative used, smear consisting mainly of blood or inflammatory cell exudates, possibly associated with menstruation. No significant relationship was observed between the age and the available outcome of pap smear from this study with p value=0.404.

Regarding the appropriate age and timing to begin the pap smear screening, The American Cancer Society, National Cancer Institute, American College of Obstetrics & Gynecologists and others recommend that all women who are sexually active above the age of 18 years should have annual pap smear for three years. If the women have three consecutive negative pap smear, the physicians may consider extending the interval of 3-5 years[10-12]. With such recommendations, the number of pap smears from younger reproductive age group is expected to increase in the coming days.

Women in this study had low gravida (less than 3) in majority which was comparable to the study by Thistle and Chirenje [13].

Whereas another study by Claeys, Gonzalez [14] found higher gravida.

There are far less study conducted in Nepal that are caste or ethnicity based pap smear.

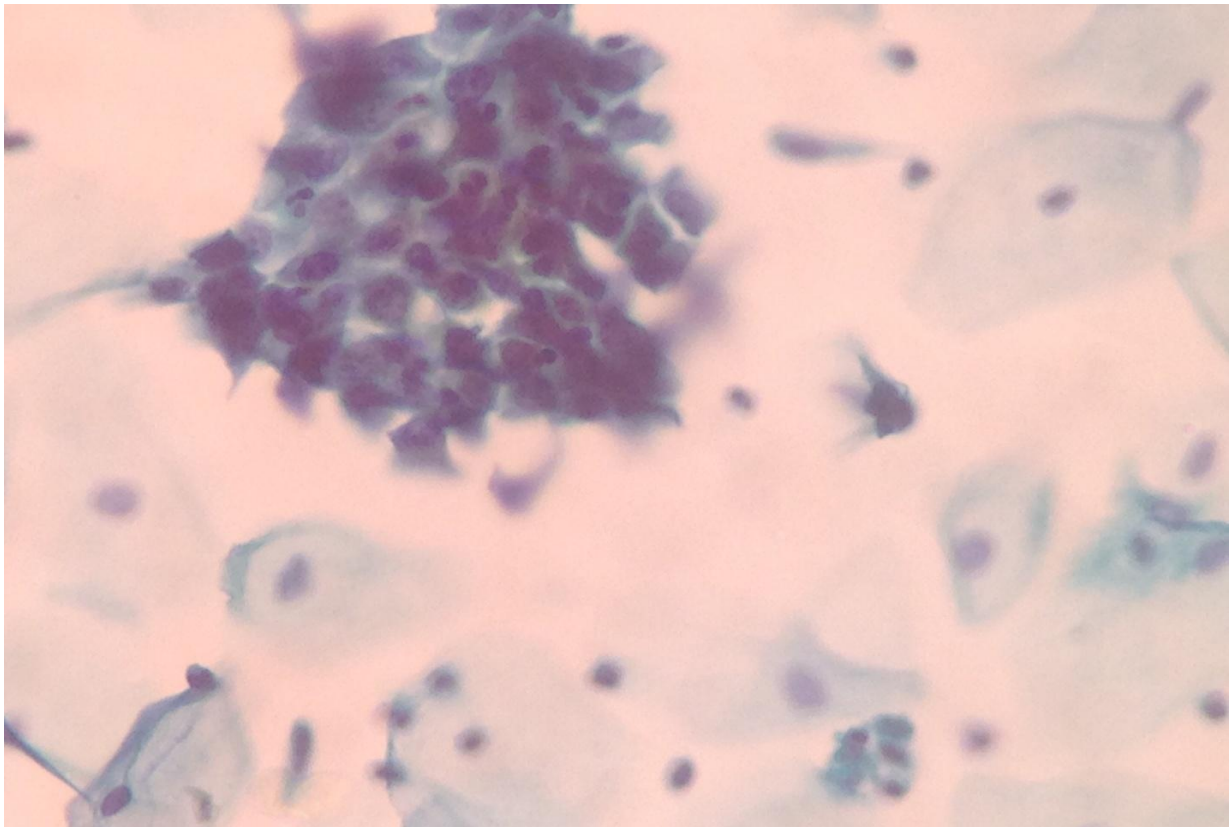


Figure 4: pap smear microscopic view under 40 x SCC

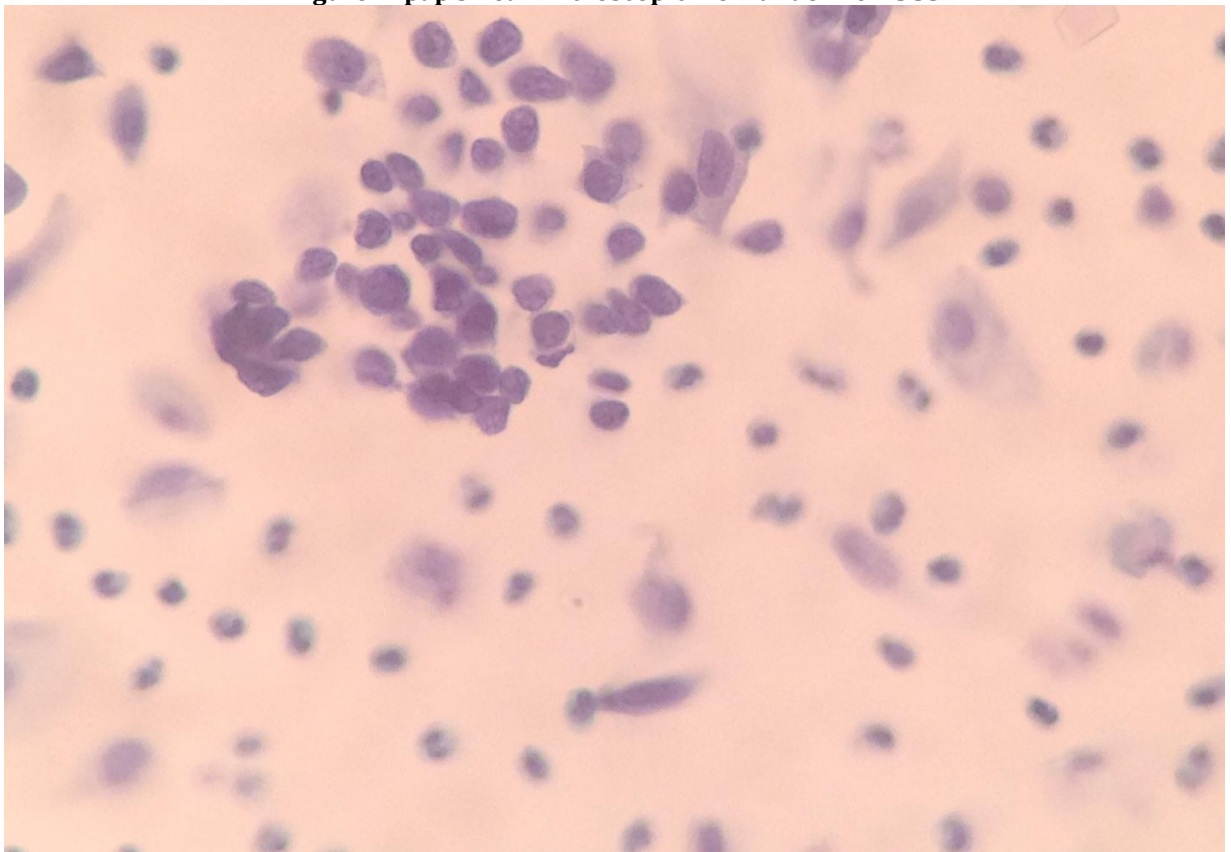


Figure 5: pap smear showing high grade squamous epithelial lesion. (viewed under X400 objective)

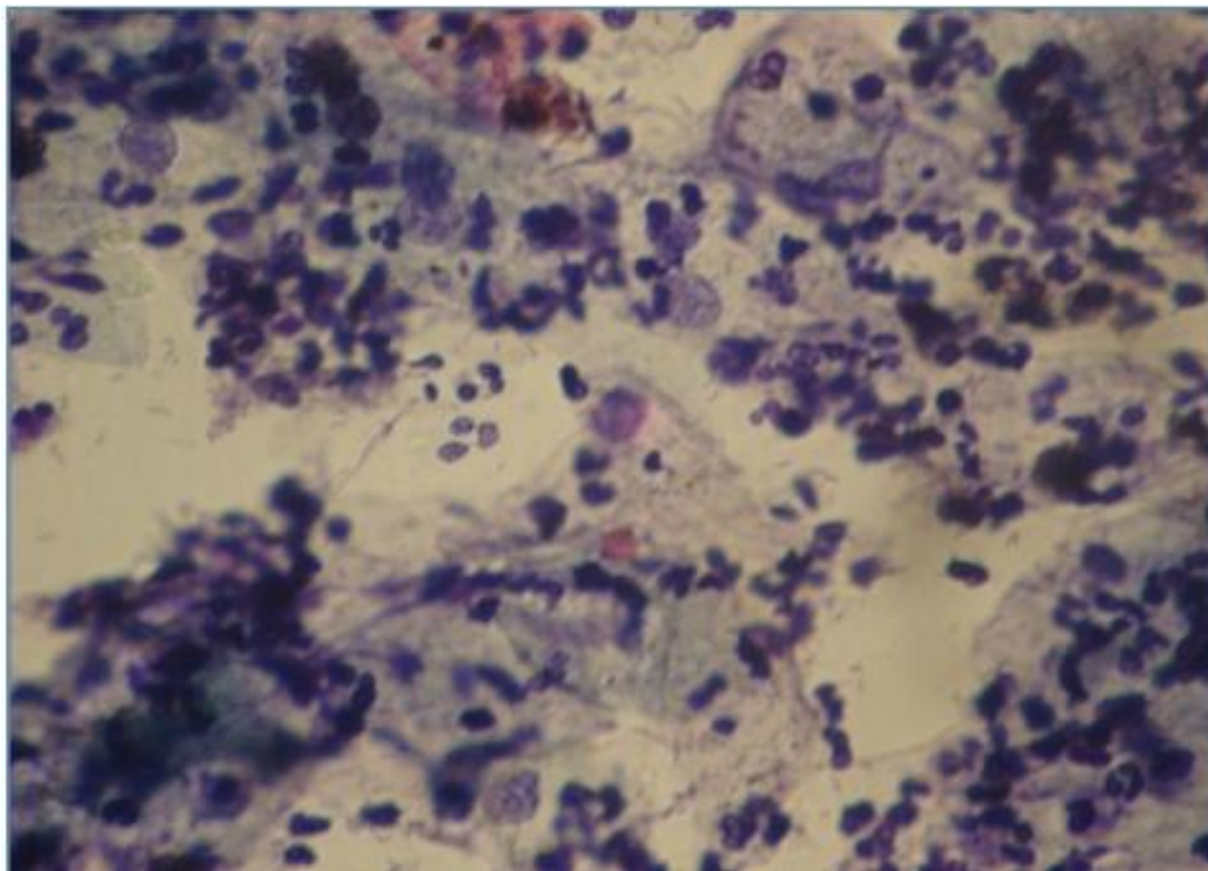


Figure 6: Pap smear showing inflammatory smears. (x400)

There are far less study conducted in Nepal that are caste or ethnicity based pap smear. The pap result showed the Brahmin, Newar caste women having highest number of abnormal smears. However, this bias could also be due to the fact that the women belonging to Brahmin, and Newar ethnic group were highest in number participating in the test. On statistical analysis relationship between caste and pap smear result had no significance (P value >0.05). This finding is similar to the finding by Pradhan [15]. They found higher rate of an abnormal smear as well in Brahmin ethnic group.

The number of asymptomatic women in this study was 22.9% whereas Shrivastava, Shrivastava [16] study found to be lower (13.38%). In this study, pelvic pain (lower backache, pain in lower abdomen)

were the most common presenting complaint which was similar to other study [15, 17, 18].

Regarding the most common presentation (chief complaint), Pradhan, Pradhan [19] found irregular vaginal bleeding as chief complaint while discharge per vagina as number one complaint was found in several studies [14, 16, 20]. In contrast to previous studies, this study found “discharge per vagina” as the second most common mode of presentation. Contrary to all this post-menopausal bleeding was the most common presentation in another study [21].

Studies have reported that the leading signs in the women undergoing pap smear test on touch were cervix erosion, cervical discharge, cervical hypertrophied and cervical bleeding [15, 16, 19]. The overwhelming number of these presenting signs and symptoms are

consistent with chronic pelvic inflammatory disease findings which suggest the possibility of high prevalence of this disease in women involved in this test. When presence or absence of chief complaints were compared with smears having normal result and other than normal smears in this study, there were absence of any significant association between them (p value >0.05). But when presence or absence of positive per speculum of vagina examination was compared with smears having normal result and rest of the smear, existence of significant relationship was observed with p value <0.05 .

This study showed 20.37% of epithelial cell abnormalities suggestive of intraepithelial lesion or malignancy. However, higher number of smears with abnormal epithelial cells compared to this study was found in other studies [3, 13, 22, 23]. Adenocarcinoma and squamous cell carcinoma were detected on single and two women respectively in the current study. Al-Maghrabi [23] found slightly higher (1.9%) number of Adenocarcinoma compared to 0.19% in this study. However, Altaf [22] found just 0.16 % of Adenocarcinoma which was similar to this study findings.

With reference to the detection of epithelial abnormalities, which is the main reason for advocating routine cervical smear examinations, the prevalence of intraepithelial abnormalities in studies around the world has shown a wide range from as low as 0.98% [13] to as high as 15.5% [24]. The sensitivity and specificity of pap test accuracy ranges from 11 to 99% and 14 to 97% respectively [25-28]. Whereas reports of cytology sensitivity in detecting cervical neoplasia ranged from 50%-98% [28]. It should be borne in mind that the wide range

of variation in the performance of pap smear screening regarding sensitivity and specificity as mentioned by the above studies may have some bearing in the outcome from it based on different setup.

In order to improve effectiveness of cervical screening several factors were identified as necessary. For e.g. spread screening evenly across a wide age range, ensure a high participation rate of the target population by making the service acceptable to women, repeat the tests at a suitable interval, ensure adequate facilities and quality control for taking and interpreting smears in the cytopathology lab, ensure adequate facilities for appropriate treatment, ensure systematic evaluation and monitoring [29].

CONCLUSION

Cervical smear was able to differentiate inflammatory, benign precursors and malignant cases in this study. As cervical cancer is one of the most common malignancies among the women of Nepal, it is recommended to conduct routine pap smear screening in all women regardless of age, race, ethnic background and socioeconomic status.

LIMITATIONS

Limited number of cases and limited to one general hospital and therefore cannot be generalized to the whole country or global population.

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AUTHOR'S CONTRIBUTION

SS- main author, contributed on data collection, analysis, interpretation and manuscript preparation; **RS-** statistical tool application on data and editing the article; **SNG-** references search and editing the article.

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CONFLICT OF INTEREST: None declared.

REFERENCES

1. Solomon D, Davey D, Kurman R et al. The 2001 Bethesda system: terminology for reporting results of cervical cytology. *J Nepal Med Assoc* 2002; 287(16):2114-9.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008. *Int J Cancer* 2010; 127(12):2893-917.
3. Ranabhat S, Tiwari M, Dhungana G et al. Association of knowledge, attitude and demographic variables with cervical Pap smear practice in Nepal. *Asian Pac J Cancer Prev* 2014; 15(20):8905-10.
4. Pradhan M, Dhakal HP, Pun CB et al. Gynecological malignancy BPKMCH, Bharatpur: a retrospective analysis of 321 cases. *J Nepal Med Assoc* 2001; 40:108-111.
5. Reeves WC, Brinton LA, Mariana García M et al. Human papillomavirus infection and cervical cancer in Latin America. *N Engl J Med* 1989; 320(22):1437-41.
6. Juneja A, Sehgal A, Mitra AB et al. A survey on risk factors associated with cervical cancer. *Indian J Cancer* 2003; 40(1):15-22.
7. Schiffman M, Castle PE. The promise of global cancer prevention. *N Engl J Med* 2005; 353(20):2101-4.
8. Schiffman M, Herrero R, Hildesheim A et al. HPV DNA testing in cervical cancer screening: results from women in a high risk province of Costa Rica. *J Nepal Med Assoc* 2000; 283(1):87-93.
9. Walton RJ. The task force on cervical cancer screening programs. *Can Med Assoc J* 1976; 114(11):981
10. Austoker J. Cancer prevention in primary care: screening for cervical cancer. *BMJ* 1994; 309(6949):241-8.
11. Mettlin C, Dodd GD. The American cancer society guidelines for the cancer-related checkup: An update. *CA Cancer J Clin* 1991; 41(5):279-82.
12. Sigurdsson K, Sigvaldason H. Effectiveness of cervical cancer screening in Iceland, 1964-2002: a study on trends in incidence and mortality and the effect of risk factors. *Acta Obstet Gynecol Scand*. 2006; 85(3):343-9.
13. Thistle PJ, Chirenje ZM. Cervical cancer screening in a rural population of Zimbabwe. *Cent Afr J Med*. 1997; 43(9):246-51.
14. Claeys P, Gonzalez C, Gonzalez M et al. Prevalence and risk factors of sexually transmitted infections and cervical neoplasia in women's health clinics in Nicaragua. *Sex Transm Infect* 2002; 78(3):204-7.
15. Pradhan P. Prevention of carcinoma cervix: role of Pap smear screening. *Nepal Med Coll J* 2003; 5(2):82-6.
16. Shrivastava M, Shrivastava O P, Jaiswal S S. Pattern of cervical smear cytology in rural medical college. *Pravara Med Rev* 2011; 3(1):4-8.
17. Jayant DD, Deepak BP, Vaishali DP. Profile of cervical smear cytology in women attending health center in rural area of Western Maharashtra. *Int J Biomed Adv Re* 2012; 3:205-8.
18. Dhaubhadel P, Vaidya A, Choudhary P. Early detection of precursors of cervical cancer with cervical cytology and visual inspection of cervix with acetic Acid. *J Nepal Med Assoc* 2008; 47(170):71-6.
19. Pradhan B, Pradhan SB, Mital VP. Correlation of PAP smear findings with clinical findings and cervical biopsy. *Kathmandu Univ Med J* 2007; 5(4):461-7.
20. Khattak ST, Khattak I, Naheed T et al. Detection of abnormal cervical cytology by pap smears. *Gomal J Med Sci*. 2006; 4:74-7.
21. Konje JC, Ogunniyi JO, Otolorin EO et al. Cervical cancer screening at Ibadan. *Eur J Gynaecol Oncol* 1991; 12(1):55-61.
22. Altaf FJ. Cervical cancer screening with pattern of pap smear. Review of multicenter studies. *Saudi Med J* 2006; 27(10):1498-502.

23. Jamal A, Al-Maghrabi JA. Profile of Pap smear cytology in the Western region of Saudi Arabia. Saudi Med J 2003; 24(11):1225-9.
24. Sadan O, Schejter E, Ginath S et al. Premalignant lesions of the uterine cervix in a large cohort of Israeli Jewish women. Arch Gynecol Obstet 2004; 269(3):188-91.
25. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. Am J Epidemiol 1995 ;141(7):680-89.
26. Visual inspection with acetic acid for cervical-cancer screening: test qualities in a primary-care setting. University of Zimbabwe/JHPIEGO Cervical Cancer Project. Lancet. 1999; 353(9156):869-73.
27. Cronjé HS, Cooreman BF, Beyer E, Bam RH, Middlecote BD and Divall PDJ. Screening for cervical neoplasia in a developing country utilizing cytology, cervicography and the acetic acid test. Int Journal of Gynecology & Obstetrics 2001; 72: 151-157.
28. Boyes DA, Nichols TM, Millner AM, Worth AJ. Recent results from the British Columbia screening program for cervical cancer. Am J Obstet Gynecol 1977; 128(6):692-3.
29. Mettlin C, Dodd G. The American cancer society guidelines for the cancer related check-up. Cancer journal for clinicians 2008; 41(5):279-82.

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