Agreement between cervical cancer screening methods in Nepal: A cross-sectional study

Rupa Paneru[1]*, Shree Prasad Adhikari[2], Sapana Amatya Vaidya[2], Sandesh Poudel[2],
Bandana Paneru[3], Pratiksha Paudel[3], Sabin Shrestha[1], Achyut Acharya[4]

[1]Department of Obstetrics and Gynaecology, Gandaki Medical College College Teaching Hospital & Research Center, Pokhara, Nepal, [2]Paropakar Maternity and Women's Hospital, Kathmandu, Nepal, [3]Department of Public Health, Kathmandu University School of Medical Sciences, Dhulikhel, Nepal, [4]Department of Psychiatry, Gandaki Medical College Teaching Hospital & Research Center, Pokhara, Nepal

ABSTRACT

Introduction: Cervical cancer is a leading health concern in Nepal, prompting the utilization of various screening methods like visual inspection with acetic acid (VIA), human papillomavirus deoxyribonucleic acid testing (HPV DNA), and liquid-based cytology (LBC). Yet, understanding their comparative performance remains subject of research. Hence, this study aimed to assess the agreement levels among VIA, HPV DNA, and LBC. **Methods:** A cross-sectional survey was conducted involving 68 women aged 30 to 60 years visiting Paropakar Maternity and Women's Hospital. Each woman underwent LBC, VIA, and HPV DNA testing during their outpatient visits after receiving written informed consent and taking detailed history. Those with positive results from any test underwent cervical biopsy and managed. Data were analyzed using SPSS version 22.0 to calculate agreement percentages and kappa values, which range from -1 to 1, with 1 indicating perfect agreement. **Results:** The result showed 7% positivity rate for visual inspection with acetic acid, 5.9% for Human papillomavirus deoxyribonucleic acid testing, and 4.4% for liquid-based cytology. Agreement between VIA and LBC stood at 85.3%, with a low Kappa value of 0.0047, VIA and HPV DNA testing agreed at 83.8%, with a Kappa value of 0.0064. Conversely, LBC and HPV DNA testing showed higher agreement at 95.6%, with a moderate Kappa value of 0.55. **Conclusions:** While there is some agreement between LBC and HPV testing, the preliminary findings suggest a difference between agreement and Kappa values between VIA and LBC, as well as VIA and HPV testing, which requires confirmation in a larger, powered study.

Keywords: Agreement, HPV DNA, LBC, screening, VIA, women.

INTRODUCTION

Cervical cancer is an increasing health problem associated with mortality in women worldwide.[1] The persistent infection with carcinogenic human papilloma virus (HPV) types is the main cause of developing cervical cancer.[2] It is the fourth most common cancer in women, contributing 6.9% of total new cases diagnosed in 2018.[3] It is the most common gynecological cancer among women in Nepal, and estimated that 26,000-45,000 women currently have undiagnosed pre-cancerous lesions at this moment.[4]

Program for appropriate technology in health, cervical cancer prevention has stated that only 5% of women have been screened for cervical cancer in past five years in developing countries compared to 85% in developed countries.[5]

The illness can be diagnosed in a pre-carcinogenic state by proper screening method. Various screening methods like Visual Inspection with Acetic acid (VIA), Visual Inspection with Lugol's Iodine (VILI), Papanicolaou smear, Liquid-based cytology (LBC), HPV Deoxyribonucleic Acid (HPV DNA) testing/typing are available.[6]

The main objective of our study was to assess the agreement of various cervical cancer screening methods in Nepal between three available cervical cancer screening methods including VIA, HPV DNA testing, and LBC in order to determine their comparative performance in detecting cervical abnormalities among women in Nepal as these tests are used in Nepal, there is limited data on how often they agree with each other in routine practice.

METHODS

A cross-sectional study was conducted at the Department of Gynaecology at Paropakar Maternity and Women's Hospital (PMWH) from Aswin 1, 2078 to Chaitra 31, 2078. The hospital is a tertiary-level central hospital located in the capital city of Nepal, Kathmandu. The study was conducted after receiving an ethical clearance from the Institutional Review Committee (Ref. No. 62/474) of PMWH.

The study participants consisted of women aged 30 to 60 years who attended the Outpatient Department of Gynaecology at PMWH. Those who attended the department on Tuesday and gave informed consent were included in this study. Exclusion criteria included individuals with a known history of cervical carcinoma, those who were pregnant at the time of evaluation, and patients experiencing active per vaginal bleeding during the evaluation. Sixty-eight women visiting PMWH hospital during our study period were enrolled. The data was collected by researcher herself after explaining all the procedures to be performed and taking informed consent. A detailed history and general physical and systemic examination were done by the attending doctor. Per speculum examination followed by VIA and LBC was performed as described below.

After asking the patient to empty her bladder she was kept in a dorsal position on the examination table and Cusco's self-retaining bivalve vaginal speculum was inserted and fixed to view the cervix. Any visible abnormal discharge was noted and cleaned with a cotton swab. The squamocolumnar junction was visualized and LBC and HPV DNA sample was taken using a sure path vial. After this, a solution of 5% acetic acid was applied to the cervix using a cotton swab. The cervix was visualized after one minute using an adequate light source and the appearance of any distinct acetowhite opaque areas at the transformation zone touching the squamo-columnar junction was considered to be a positive result. LBC and HPV DNA samples were sent for interpretation.

Cytology was considered positive if it revealed squamous cell abnormalities like Atypical squamous cells for undetermined significance (ASCUS), Low grade squamous intraepithelial lesion (LSIL), High Grade squamous intraepithelial lesion (HSIL) or squamous cell carcinoma and glandular cell abnormalities like Atypical glandular cells (AGC), Atypical glandular cells, favors neoplastic, Endocervical adenocarcinoma in situ (AIS), and Adenocarcinoma. Women who had severe cervicitis were first treated and VIA and LBC were done in subsequent visits. The women with abnormal reports were counseled about the nature of the disease, the need for follow-up, possible interventions at PMWH, and referral to other centers.

Cases were enrolled once a week on Tuesday from 9:00 am to 3:00 pm, except on public holidays when the Outpatient Department (OPD) was closed. Data collection was carried out by filling out a designed proforma, and the obtained data were entered into a master chart daily. The continuous variables data were presented in mean and standard deviation, whereas for the categorical variables data were presented in frequency, percentage including the graphical representations using bar charts. Statistical analysis was performed using Statistical package for the social sciences (SPSS) version 22.0, with the chi-square test applied. A p-value of <0.05 was considered statistically significant. Kappa values were calculated to assess the agreement between VIA Vs LBC, LBC Vs HPV and HPV Vs VIA. The values of kappa range from -1 to 1, where 0.81-1 indicates almost, 0.61-0.80 indicates substantial agreement, 0.41-0.60 indicates moderate agreement, 0.21-0.40 indicates fair agreement, 0.00-0.20 indicates slight agreement and less than 0 indicates no agreement.[7]

RESULTS

This study was done among 68 women attending the outpatient department of gynaecology at PMWH. The women ranged from 30 years to 56 years, and their mean age was 41.9±9.0 years.
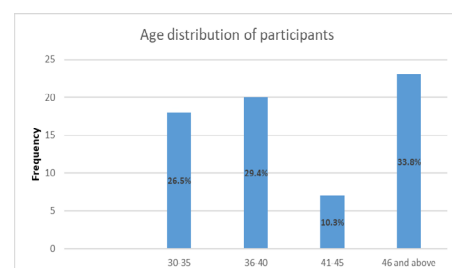

Figure 1: Bar graph showing the age distribution of the participants

Table 1 depicts the information regarding the percentage of positive and negative results for VIA, LBC, and HPV testing. VIA had the lowest rates of negative result (89.71%) when compared to LBC (95.59%), and HPV (94.12%).

Table 1: Positive and negative results for VIA, LBC, and HPV testing

Result	VIA	LBC	HPV testing
	n(%)	n(%)	n(%)
Positive	7(10.29%)	3(4.41%)	4(5.88%)
Negative	61(89.71%)	65(95.59%)	64(94.12%)

Agreement between VIA and LBC stood at 85.29%, with a low Kappa value of 0.0047, this could mean that there is essentially no agreement between VIA or LBC being compared. Similarly, the Kappa score for HPV and VIA was also very low (0.0064). However, the Kappa value for LBC Vs HPV was moderate at 0.55. (Table 2)

Table 2: Agreement between VIA, LBC and HPV testing

VIA Vs LBC % (Kappa)	LBC Vs HPV testing	HPV testing Vs VIA
85.29% (0.0047)	95.59% (0.55)	83.82% (0.0064)

DISCUSSION

In South-East Asia Region, cervical cancer ranks as the second most common cancer in women and is becoming a major cause of cancer deaths in low and middle-income countries like Nepal.[8] In the year 2022, the age standardized incidence of cervical cancer was 16.4 cases per 100,000.[9] However, the screening coverage in Nepal is very low at 8% according to the steps survey 2019.[10] This study is a comparative hospital based study conducted in Paropakar Maternity and Women's Hospital, Thapathali. Sixty-eight women attending the Outpatient Department of Gynaecology were enrolled in the study.

In our study, the mean age of the participants was 41±9.0 years while one-third (33.82%) of the participants were above the age of 46 years. In our study, we found a higher percentage (95.59%) of women showing negative results in LBC as compared to HPV (94.12%) and VIA (89.71%), which is similar to a study conducted in India.[11] The agreement between VIA and LBC was very low which means that there is no agreement between the two variables being compared, which is similar to the study conducted in Ethiopia.[12]

The agreement between LBC and HPV was moderate, indicating that it is certainly better than chance. LBC and HPV are the two most used methods of screening. While one could be better than another in various settings, the American Society for Colposcopy and Cervical Pathology suggests using both methods together for better accuracy.[13]

A meta-analysis conducted in China showed 88% accuracy of LBC while magnified VIA had 91% accuracy which is in contrast to our findings.[14] This can be because of the use of the magnified VIA rather than the usual VIA.

While VIA has been advocated as an alternative screening method to PAP smears and liquid-based cytology in developing countries as it is cost-effective, requires simple administration, high sensitivity, and real-time screening of results,[15,16] our study also showed 10.3% positive results. However, the agreement of VIA with HPV and LBC was very low thus we cannot make any conclusions about choosing one alternative. In a developing nation like Nepal, VIA would be a possible alternative screening tool for early detection of cervical cancer. But still, there needs to be more research specifically focusing on the sensitivity and specificity of various methods. Also, we will focus on a combination of methods for the screening specifically for cervical screening.

This study had various limitations, as the study only assessed the agreement between various screening methods, further research for assessing the sensitivity and specificity of each method is necessary. Moreover, the critically low number of positive cases (n=3 to 7) makes the kappa statistics unstable and unreliable. Additionally, screening is affected by various factors; thus, assessing the relationship of cervical cancer screening with various socio-demographic and reproductive factors will provide more understanding for designing cervical cancer screening programs.

CONCLUSIONS

The findings are preliminary and suggest a trend indicating moderate agreement between LBC and HPV, while agreement between LBC and VIA, and HPV and VIA being nearly zero. Further research is imperative to justify the above shown trend and improve the reliability of cervical cancer screening methods. The findings of this pilot study will be crucial for designing a subsequent, larger study which should incorporate a full gold standard evaluation like colposcopy or biopsy for all participants or a randomly selected sub-group to definitively assess the sensitivity and specificity of each screening method.

CONFLICTS OF INTEREST: None declared

AUTHOR'S CONTRIBUTIONS

RP designed the research, reviewed literature, collected data, and prepared manuscript. SPA did data entry. PP did data entry and analysis. SAV and SP did literature review and data collection. SS did data collection and literature review. BP and AA did data analysis.

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