

**Research Article**

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**Cervical Cancer: The outcomes of liquid-based cytology vs conventional cytology among HPV/DNA screening test positives of ever married 35 and 45 years old women in Kalutara district and unit cost estimation of colposcopy and biopsy**Perera KCM<sup>1\*</sup>; Punchihewa R<sup>2</sup>; Silva R<sup>3</sup>; Dileep De Silva<sup>4</sup>; MRM Cooray<sup>5</sup><sup>1</sup>Acting Consultant Community Physician, Epidemiology Unit, Colombo, Sri Lanka.<sup>2</sup>Consultant Histopathologist, National Hospital for Respiratory Diseases, Welisara, Sri Lanka.<sup>3</sup>Consultant Obstetrician & Gynecologist, Teaching Hospital Ragama, Sri Lanka.<sup>4</sup>Consultant Community Dentistry, Ministry of Health, Sri Lanka<sup>5</sup>Medical Officer, Kethumathie Maternity Hospital, Panadura, Sri Lanka.**\*Corresponding Author: Perera KCM**

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**Abstract**

**Background:** One major drawback of the present National Cervical Cancer Screening programme is, the suboptimal sensitivity (53%) of the pap smear to detect Cervical Intraepithelial Neoplasia (CIN). HPV/DNA test is highly sensitive (92.9%) for CIN II viral load and the feasibility of HPV/DNA screening with conventional cytology for screen positive follow-up was successfully attempted. The sensitivity of Liquid Based Cytology (LBC) to detect CIN II+ is 79.1%.

**Objective:** To describe the results of LBC vs conventional cytology among HPV/DNA screen positives of 35 and 45 year old ever-married women in MOH areas of Kalutara district.

**Methods:** There are 15 Medical Officer of Health areas in Kalutara district and the Public Health Midwife area (n=413) is taken as a cluster. Three clusters were randomly selected in each MOH area (n=45) by the lot method. Eligible family registers were the sampling frame. Nine subjects in the 35 and 45 age cohort each from all 45 clusters were selected by consecutive sampling technique. The total number of 393 and 390 subjects from 35 and 45 age cohorts were subjected to cervical specimen collection at community Well Woman Clinics (WWC) after applying exclusion criteria at field and clinic setting. HPV/DNA screen positives were subjected to both LBC and pap smear. HPV/DNA screen positive with either conventional cytology or LBC ≥ Atypical Squamous Cells of Undetermined Significance (ASCUS) were referred for colposcopy. The incremental cost of the pap smear was calculated. The Scenario-Building technique was used to calculate the per-procedure cost of colposcopy and biopsy.

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**Results:** The response rate of 35 and 45 age cohorts women was 97.5% and 96.5% respectively. The number of 25 (6.36%) among 35 and 18 (4.61%) among 45-year-old women were positive for HPV/DNA test. The number of 7 (1.78%) among 35 year and 5 (1.28%) among 45 year old women had  $\geq$ ASCUS in conventional cytology, while the number of 10 (2.54%) among 35 years and 8 (2.05%) among 45 years old women had  $\geq$ ASCUS in LBC. Prevalence of CIN by colposcopy among 35 years and 45 years women for LBC vs conventional cytology were 1.53%, 1.28% and 1.53%, 1.03% respectively and there was no significant difference. No invalid results were reported for LBC and the treatment adherence for colposcopy was 86.7%. The incremental cost of pap smear was Rs. 626.18, while the per-procedure cost of colposcopy and biopsy was Rs.1528.15 and Rs.681.16.

**Conclusions and recommendations:** To improve the quality and coverage of the programme HPV/DNA PCR test as a primary cervical cancer screening method with LBC for only screen positive follow-up can be recommended.

**Keywords:** bile cervical cancer; screening methods; HPV/DNA test; positive follow-up; conventional cytology; LBC.

**Abbreviations:** ASCUS: Atypical Squamous Cells of Undetermined Significance; CIN: Cervical Intraepithelial Neoplasia; FHB: Family Health Bureau; HGSIL: High Grade Squamous Intraepithelial Lesion; LGSIL: Low Grade Squamous Intraepithelial Lesion; MOH: Medical Officer of Health; PHNS: Public Health Nursing Sister; PHM: Public Health Midwife.

## Background

Malignant, autonomous and uncontrolled growth of cells & tissues which occur in the cervix of the female uterus is called cervical cancer. Ninety percent of cervical cancers are squamous cell cancers and occurs in the transformation zone of the ectocervix and the rest of the 10% are adenocarcinomas, which arise in the glandular columnar layer of the endocervix [1]. Cervical cancers may invade surrounding tissues and produce new growths similar to original cancer in distant parts of the body which are called metastases [2].

As in some other cancers, cervical cancer is also preceded by a precursor stage called cervical precancer. According to the histology used for the diagnosis, there are 3 types of precancer stages before the invasive cervical carcinoma; Cervical Intraepithelial Neoplasia (CIN) stages 1, II, & III. According to the Cytology classification used for screening, there are two types of precancer stages before an invasive cervical carcinoma such as; Low-Grade Squamous Intraepithelial Lesion (LGSIL) and High-Grade Squamous Intraepithelial Lesion (HGSIL). Low-Grade Squamous Intraepithelial Lesion is compatible with CIN I, while the HGSIL is compatible with either CIN II or CIN III [3].

According to the incidence rate cervical cancer is the 2nd leading cause of female cancer in Sri Lanka and women at risk for cervical cancer is more than 8.4 million [3]. In Sri Lanka, annually thousand seven hundred and twenty-one new cases of cervical cancers are diagnosed and 690 women have died from

the disease [3]. There was no marked reduction in age-specific incidence rates of cervical cancer in Sri Lanka from 2006 to 2010 (eg; age-specific incidence rate for the 50-54 age group in 2006 was 23, while in 2010 it was 22.5 per 100,000 women population) [4]. Comparison of age-specific incidence rates between 55 and 75 age group females in Sri Lanka, across the other areas within the Southeast-Asian region and the rest of the world, had shown an increasing trend according to the 2012 estimates [3]. Moreover, deaths due to cervical cancer in Sri Lanka from 2000 to 2012 almost remained unchanged [1].

Cervical cancer is almost always associated with Human Papillomavirus Infection (HPV) but HPV infection does not always cause cervical cancer [1]. The overall HPV prevalence rate was 3.3% among 20-59 age ever-married women in Sri Lanka [5]. Most women even infected with high-risk HPV types never develop cervical cancer, as most of these infections regardless of HPV type are short-lived and the body eliminates them spontaneously in  $\leq 2$  years. A small percentage of women with high-risk HPV infection can have persistent infection and progress into pre-cancer and even fewer women will progress to have invasive cancer [1]. Compared to other carcinogenic genotypes of HPV infection, genotypes 16 and 18 have 190.3 times increased risk of developing cervical cancer [5].

There are some popular screening methods now used in the world for cervical cancer screening; Visual Inspection with Lugol's Iodine (VILI), Visual Inspection with Acetic acid (VIA) or Visual Inspection with A Magnifying device (VIAM), conventional

pap cytology, liquid-based cytology and HPV/DNA screening test [6].

Visual Inspection with Lugol's Iodine is a suitable screening modality in low resource settings. Iodine uptake was noted as brown (positive uptake), yellow-brown (partial uptake) and mustard yellow (no uptake). Areas where there no uptake were considered as VILI positive, while areas of either partial or positive uptake were considered as VILI negative [6]. Visual Inspection with Acetic Acid (VIA) is a suitable screening method that can be used in women whose Squamocolumnar Junction (SCJ) is visible, typically in those  $\leq 50$  years, as SCJ gradually precedes into the endocervical canal with menopause, which can lead to the missing of lesions on visual inspection.

Pap smear screening is an important method of cervical cancer screening and it is acytological test to detect abnormal cervical cells. A fixed sample of cells from the entire SCJ of the cervix taken by using the long tip of a spatula is called a pap smear. It would take only  $<5$  minutes to perform a pap smear. This procedure is not painful and could be performed in an outpatient set-up or at a community clinic.

The sensitivity of VILI and pap smear for CIN2+ was 100% and 52.6% respectively, while the specificity of VILI and pap smear was 59.3% and 99.1% respectively [6]. The sensitivity of VIA and pap smear for CIN 2+ was 88.8% and 58% respectively, while the specificity of VIA and pap smear was 43.8% and 85.2% respectively [7].

Liquid Based Cytology (LBC) is used as a cervical cancer screening method in some developed countries, where more resources are available. In LBC a sample is taken by using a brush or a spatula and placed in a transport medium and then sent to the laboratory for microscopic examination [1]. Supplies and laboratory facilities are more expensive in LBC than for conventional pap smear cytology [8].

HPV/DNA screening methods are based on the detection of high-risk HPV/DNA in vaginal or cervical smears [8]. The specimen is collected from the SCJ of the cervix or upper vagina using a brush and placed in a small container with a preservative solution. Detection of high-risk HPV does not always mean that there is cancer or its precursor; it simply shows that there is an HPV infection. In a woman aged 35 years or older, HPV/DNA test performs better than in younger women, as a positive HPV/DNA test is more likely due to a persistent HPV infection. The average sensitivity & specificity in this age cohort are 89% and 90% respectively [8].

In primary screening, all HPV/DNA screen positives are referred for cytology (ASC-US triage) according to the positive follow-up algorithm of Asia Oceania guidelines for the implementation of programs for cervical cancer prevention and control [9]. HPV/DNA screen positive with cytology (either conventional or Liquid Based)  $\geq$ ASCUS women are referred for colposcopy procedure, while the HPV/DNA screen positive but cytology negative women are re-screened for HPV/DNA after one year.

A diagnostic or confirmatory test is a medical test, which is performed in the diagnosis or detection of disease [1]. Colposcopy and biopsy is the gold standard, confirmatory test to diagnose CIN. The objective of the study was to describe the results of LBC vs. conventional cytology among HPV/DNA screen positives of 35 and 45-year-old ever-married women in the Kalutara district and to estimate the incremental cost and per-proce-

dure cost of the colposcopy and biopsy.

## Methodology

A community-based cross-sectional study was conducted from 1st of September 2019 to 28th February 2021. The study population comprised of ever-married women of 35 and 45 year age cohort in Kalutara district. Women with diagnosed invasive cervical cancer, per vaginal bleeding, active infection at the time of examination evidenced by medical records or by visual inspection, who were currently on treatment for HPV infection were excluded from the study.

There were 15 Medical Officer of Health (MOH) areas in the Kalutara district and 413 Public Health Midwife (PHM) areas. Public Health Midwife (PHM) area was taken as a cluster. Usually, a PHM area was defined with an estimated population  $\geq 3000$ . Assuming 1% of the estimated population, each PHM area consists of  $\geq 30$ , thirty-five years and 45 year age cohort women population. In each MOH area, three clusters were randomly selected by the Principal Investigator (PI) by using a lot method.

For the calculation of the sample size, we assumed that the expected prevalence of HPV was 6.2% [10] and the degree of accuracy desired specified as 0.031 (6.2/100x2). Therefore we needed 233 women from each 35 and 45 age cohort. To account for the cluster effect, it was necessary to adjust the required sample size having it multiplied by the design effect, which was taken as 1.5. Further adjustment to the sample size was made for the WWC non-response rate (10%) in the Kalutara district and the final required sample size was 389 from each 35 and 45 age cohorts.

Eligible family register/registers were the sampling frame. Nine subjects in 35 and 45 age cohort each from all 45 clusters after applying possible exclusion criteria were selected for the study by consecutive sampling technique from the list of 35 years and 45 year age cohort ever-married women population prepared from relevant area eligible family register/s according to the ascending order of register number/s. The Principal Investigator selected the first subject from the list by using a lot method and then eight more subjects were selected forward and consecutively from each of 35 and 45 year age cohort women. Selected subjects were recruited for the study.

The main objective and the nature of the study, the purpose and the importance of educating and motivating eligible women regarding participation in the study were explained. Field guides were given a self-administered questionnaire (Supplementary file 1) to the selected eligible participants in the field after taking informed written consent. Once completed, the questionnaire was collected back and the respondent participant was given a clinic appointment and invited to attend the clinic.

Specimens were collected at community WWC. At WWCs pelvic examination of selected subjects were carried out and visual inspection of the cervix done following Cusco's speculum insertion. Speculum examination and cervical specimen collection were carried out only by the Medical Officer of Health (MOH) or Public Health Nursing Sister (PHNS) of each MOH area. HPV/DNA specimen was obtained from the cervix using a special broom-like device and placed into an HPV/DNA specimen collection container with cell collection media (specimen collection instrument). This collected specimen can be used for both LBC and HPV/DNA screening. Collected specimens were

then sent along with separate referral forms to the Family Health Bureau, Colombo laboratory for screening by the cobas 4800 HPV/DNA screening machine.

All HPV/DNA positive subjects were subjected to LBC and referred for a pap smear at community WWC. Liquid-based cytoscreening was done by one of the co-researchers, who is a Consultant Histopathologist. Pap smear was collected by MOH or PHNS using a spatula, under the Cusco's speculum. Before taking the specimen the MOH or PHNS was explained to participants regarding the procedure. Collected specimens were then sent with separate referral forms to the DGH Kalutara laboratory for cyto-screening.

All HPV/DNA positive with positive cytology (LBC or conventional) were referred for colposcopy at colposcopy clinic, Family Health Bureau. All categories of staff including colposcopist were given uniform training to ensure the quality of performance. Training of Trainers (MOH, Colposcopist, PHNS and Cytoscreener) was done by relevant area specialists (e.g.-Consultant Obstetrician and Gynecologists, Consultant Histopathologists). Follow-up of all positive clients was done by each relevant area MOH. A positive follow-up register at the MOH office was used for that. This register was available at each relevant MOH office. Relevant area MOH was responsible for all referrals.

Incremental cost calculation of the pap smear was done according to the Scenario-Building Technique. To estimate the unit cost of colposcopy & biopsy screening procedure Scenario-Building Technique will be used.

Data entry by using statistical package SPSS version 20. Descriptive statistics were used in data analysis. All HPV/DNA screened positives were subjected to conventional cytology and LBC. Technical and operational feasibility of screen positive follow-up with LBC was assessed. All HPV/DNA positive with either LBC or conventional cytology  $\geq$  ASCUS were referred to colposcopy. Prevalence of CIN by HPV/DNA screened positive with LBC vs conventional cytology  $\geq$ ASCUS was calculated.

## Results

The response rate among 35 and 45 year age cohorts participants was 99.5% and 99.8% respectively. The majority of women who participated in the study were Sinhala (97.2%) and Buddhist (97.1%), Out of the total subjects 8.9% had not completed years of school education beyond the 5th grade level of education and another 12.3% of the subjects remained at the 6-11th grade level of education. The majority (59%) were educated up to O/L passed the level of education (Table 1). One recruit was excluded at the clinic setting from the study due to vaginal discharge (50%), while another one was due to cervicitis (50%) (Table 2).

The majority of 45-year-old women who participated in the study were Sinhala (96.8%) and Buddhist (96.7%). Out of the total subjects, 8.9% had not completed years of school education beyond the 5th grade level of education and another 14.2% of the subjects remained at the 6-11th grade level of education. The majority (62.9%) were educated up to O/L passed the level of education (Table 3). One recruit was excluded due to cervicitis (50%), while the other was due to cervical erosion (50%) (Table 4).

**Table 1:** Distribution of 35 year old participants according to socio-demographic and economic characteristics.

Characteristics	Number of women (n)	Percentage (%)
<b>Nationality</b>		
Sinhala	382	97.2
Tamil	07	1.6
Muslim	04	1.2
<b>Total</b>	<b>393</b>	<b>100.0</b>
<b>Religion</b>		
Buddhism	381	97.1
Catholic	05	1.1
Hindu	03	0.6
Islam	04	1.2
<b>Total</b>	<b>393</b>	<b>100.0</b>
<b>Educational level</b>		
No schooling	1	0.2
Grade 1-5	35	8.7
Grade 6-11	48	12.3
O/L* passed	148	37.8
A/L** passed	116	29.5
Degree & above	45	11.5
<b>Total</b>	<b>393</b>	<b>100.0</b>
<b>Occupational status</b>		
Working women	99	25.3
Non-Working women	294	74.7
<b>Total</b>	<b>393</b>	<b>100.0</b>
<b>Average Monthly Income (Rs)</b>		
$\leq$ 15,000	30	7.5
>15,000	363	92.5
<b>Total</b>	<b>393</b>	<b>100.0</b>

**Table 2:** Reasons to exclude 35 year old recruits from the study at clinic setting.

Reason	Number of women (n)	Percentage (%)
PV discharge	01	50
Cervicitis	01	50
<b>Total</b>	<b>02</b>	<b>100</b>

**Table 3:** Distribution of 45- year- old participants according to socio-demographic and economic characteristics.

Characteristics	Number of women (n)	Percentage %
<b>Nationality</b>		
Sinhala	378	96.8
Tamil	07	1.8
Muslim	05	1.4
<b>Total</b>	<b>390</b>	<b>100.0</b>
<b>Religion</b>		
Buddhism	377	96.7
Catholic	05	1.2
Hindu	03	0.8
Islam	05	1.4
<b>Total</b>	<b>390</b>	<b>100.0</b>
<b>Educational level</b>		
No schooling	1	0.2
Grade 1-5	34	8.7
Grade 6-11	55	14.2
O/L* passed	155	39.8
A/L** passed	108	27.7
Degree & above	37	9.4
<b>Total</b>	<b>390</b>	<b>100.0</b>
<b>Occupational status</b>		
Working women	79	20.0
Non-Working women	311	80.0
<b>Total</b>	<b>390</b>	<b>100.0</b>
<b>Average Monthly Income (Rs)</b>		
≤15,000	38	9.6
>15,000	352	90.4
<b>Total</b>	<b>390</b>	<b>100.0</b>

\*General Certificate Examination Ordinary Level. \*\*General Certificate Examination Advance Level.

**Table 4:** Reasons to exclude 45 year old recruits from the study at clinic setting.

Reason	Number of women (n)	Percentage (%)
Cervicitis	01	50.0
Cervical erosion	01	50.0
<b>Total</b>	<b>02</b>	<b>100</b>

**Table 5:** Percentage of cervical cancer precursors in HPV/DNA screen positive follow-up.

Age of women (Years)	% of Cervical cancer precursors in HPV/DNA screen positive follow-up		
	Conventional Cytology	LBC	HPV/DNA
35	1.78% (n=7)	2.54% (n=10)	6.36% (n=25)
45	1.28% (n=5)	2.05% (n=8)	4.61% (n=18)

**Table 6:** Distribution of 35 year old participants according to cervical HPV/DNA specimen results for high risk genotypes.

Cervical HPV/DNA specimen results for HR-HPV genotypes	Number of women	Percentage (%)
Negative	368	93.7
12 pooled positive	18	4.6
16 positive	06	1.5
18 positive	01	0.2
<b>Total</b>	<b>393</b>	<b>100.0</b>

**Table 7:** Distribution of 45 year old participants according to cervical HPV/DNA specimen results for high risk genotypes.

Cervical HPV/DNA specimen results for HR-HPV genotypes	Number of women	Percentage (%)
Negative	372	95.4
12 pooled positive	17	3.4
16 positive	04	1
18 positive	01	0.3
<b>Total</b>	<b>390</b>	<b>100.0</b>

**Table 8:** Percentage of women with confirmed CIN by colposcopy (gold standard for CIN) from LBC vs conventional cytology in HPV/DNA screen positive follow-up among 35 and 45 year age cohorts.

Age of women (Years)	Prevalence of CIN by colposcopy in HPV/DNA screen positive follow-up by LBC vs Conventional cytology	
	Conventional Cytology	LBC
35	1.53% (n=6)	1.53% (n=6)
45	1.03% (n=4)	1.28% (n=5)



The total number of 25 women (6.36%) among the 35 age cohort were positive for HPV/DNA test. On screen positive follow-up number of 7 women (1.78%) were  $\geq$ ASCUS in conventional cytology, while the number of 10 (2.58%) in LBC. The total number of 18 women (4.61%) among 45 age cohort were positive for HPV/DNA test. On- screen, a positive follow-up number of 5 women (1.28%) were  $\geq$ ASCUS in conventional cytology, while the number of 8 (2.05%) in LBC (Table 5).

The overall prevalence of the high-risk HPV genotype infection among 35- year- age cohort ever- married women in Kalutara district was 6.36%, while the prevalence of high- risk HPV genotype 16 among 35- year-age cohort ever- married women in Kalutara district was 1.53%. Prevalence of high-risk HPV genotype 18 among 35- year- age cohort ever-married women in Kalutara district was 0.25%, while the prevalence of the high-risk HPV12 pooled risk among 35- year- age cohort ever married women in Kalutara district was 4.58% (Table 6).

The overall prevalence of the high-risk HPV genotype infection among 45- year- age cohort ever- married women in Kalutara district was 4.61%, while the prevalence of high- risk HPV genotype 16 among 45- year- age cohort ever- married women in Kalutara district was 1%. Prevalence of high- risk HPV genotype 18 among 45- year- age cohort ever married women in Kalutara district was 0.25%, while the prevalence of the high-risk HPV 12 pooled among 45- year- age cohort ever- married women in Kalutara district was 4.4% (Table 7).

Overall prevalence of colposcopy confirmed CIN among 35 and 45 year old women in Kalutara district from LBC vs conventional cytology in HPV/DNA screen positive follow-up were 1.53% (n=6), 1.53% (n=6) and 1.28% (n=5), 1.03% (n=4) respectively (Table 8). There were no invalid or unsatisfactory reports of LBC. Cell collection media (thinprep) in HPV/DNA specimen collection instrument was used for LBC too and screened by a machine. Management adherence of the colposcopy after one month of the initial referral following LBC screen positive results was 90% (n=9) in 35 years age cohort and 87.5% (n=7) in 45 years age cohort. There was no significant difference ( $p \geq 0.5$ ) between the detection of CIN by colposcopy in HPV/DNA screen positive follow-up between LBC vs conventional cytology and the difference is only marginally.

The incremental cost of the conventional pap smear was Rs. 626.18 including 10% administrative cost. Building, land and transportation cost were not considered in the incremental cost calculation. Per procedure cost of colposcopy and biopsy including 10% administrative cost were Rs. 1528.15 and Rs.681.16. Building, land and transportation cost were not considered in the cost calculation procedure.

## Discussion

There was a marked elevation of the prevalence of the cervicovaginal HPV infection from 2009 (3.3%) to 2020 (6.36%) among the ever-married women population in Sri Lanka. Moreover, high-risk genotypes 16 and 18 prevalence were elevated from 1.2% to 1.78% within the same duration. HPV 16 and 18 are associated with approximately 70% of all cervical cancers. It was obvious that the prevalence of other high-risk HPV genotypes (except genotype 16 and 18) were too markedly elevated from 2.1% [5] to 4.58% in 2020. According to Gamage et al. (2012), the age group screened for HPV/DNA was 20-59 year ever- married women in the Gampaha district.

Usually, the transient HPV infection rate was high among sexually active women  $\leq 30$  years of age [1], so the absolute prevalence rates of HPV infection at 35 year age cohort in 2009 may be even smaller than the mentioned data. The overall prevalence of HPV infection genotypes 16 and 18 and genotypes 12 pooled high risk among 45 age cohort ever-married women were 4.61%, 1.28% and 3.33% in the present study, which gives similar results to the study carried out in 2019 [11].

There is a difference between LBC vs conventional cytology in the detection of CIN by colposcopy in HPV/DNA screen positive follow-up but it was not significant ( $p \leq 0.05$ ). The feasibility of LBC for HPV/DNA screen positive follow-up has well explored as the same cervical specimen can be used for both HPV/DNA and LBC.

Per procedure cost of HPV/DNA was Rs. 2881.95 [10]. Per procedure cost of conventional pap smear in 2009 excluding building, land and transportation cost was Rs. 269.57, while the similar cost in 2020 was Rs. 626.18, which gives a 232% increase. Per procedure cost of colposcopy and biopsy at government sector is affordable to the Sri Lankan setting.

This study was restricted to one district out of 25 districts in Sri Lanka due to logistic constraints. The population characteristics and the public health infrastructure of the district favoured the generalizability of the research findings to the whole country.

## Conclusions and recommendations

Procedure cost of conventional pap smear was markedly elevated from 2009 to 2020. To improve the quality and coverage of the programme HPV/DNA PCR test as a primary cervical cancer screening method with LBC for only screen positive follow-up can be recommended.

## Declarations

**Acknowledgement:** We are grateful to the study participants and the staff of the Family Health Bureau, colposcopy clinic and the staff of the National Hospital of Respiratory Diseases, laboratory.

**Funding:** There was no influence from the above-mentioned institute during the process of conducting the study or report writing.

**Availability of data and materials:** We hereby declare that the cost for specimen collection instruments and reagents (test kits) was funded by the Family Health Bureau, Colombo, Sri Lanka. The datasets used to analyze in this study is available at the corresponding author on reasonable request.

**Authors contribution:** WKCM has participated in the design of the study, coordinated data collection performed the statistical analysis and drafted the version of the manuscript. RS and RP have participated in the design of the study. KCMP has performed the statistical analysis and interpreted data. Both RS and RP were helped to draft the manuscript. All five authors were read and approved the final manuscript.

**Ethical approval and consent to participate:** Ethical clearance was obtained from the Ethics Review Committee (ERC), Faculty of Medicine, University of Colombo, Sri Lanka (ref number NIHS/ECR/20/08R). Informed written consent was obtained from each of the selected participants in the field during the initial study. Confidentiality was highly maintained while handling

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over individual colposcopy and biopsy result reports. Administrative clearance was obtained from the Director, Family Health Bureau, Colombo and Director, National Hospital for Respiratory Diseases, Welisara

**Consent for publication:** Not applicable.

**Competing interests:** The authors were declared that they have no competing interests.

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