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HPV Testing on Vaginal/Cervical Nurse Assisted Self-Samples Versus Clinician-Taken Specimens and EHE HPV Prevalence, in Adama Town, Ethiopia

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Abstract

This study aimed to determine the feasibility of vaginal/cervical Nurse Assisted Self-Sampling (NASS) and the agreement between Human papillomavirus (HPV) test on self-samples versus clinician-taken (CT) specimens.

Women participated voluntary for the cervical cancer screening at St. Aklesia Memorial Hospital. Eighty three (83) women provided a total of 166 coupled self and clinician taken specimens collected. Specimens were stored at room temperature for maximum 10 months and analyzed using validated the RIATOL qPCR HPV genotyping test, a quantitative Polymerase Chain Reaction (qPCR) high-throughput HPV E6, E7 assay.

The average age of the participating women was 32 years. Seventy three of the 83 women (87.9%) felt that NASS was easy to use. An overall HPV, HR (High Risk) HPV and LR (Low Risk) HPV prevalence was 22.7% (15/66), 18.2% (12/66) and 6.1% (4/66), respectively. The overall HR HPV prevalence was 17.2% (NASS) and 15.5% (CT). The most prevalent HPV type was HPV51; HPV 16 was only detected in 1 woman (CT+NASS) and HPV18 only in 1 woman (CT). The overall measurement agreement between self- and clinician-collected samples was moderate with a kappa value of 0.576 ($p < 0.001$). Life time partnered with more than two man were associated with HR HPV positivity (P value <0.001). There was strong statistical association between HR HPV positivity and visual inspection with acetic acid (VIA) positive (p value<0.001).

Nurse assisted self-sampling for HPV testing could be seen as alternative option and an acceptable to Ethiopian women. The overall HRHPV prevalence was comparable with Sub-Saharan countries in the general population.

Keywords: Cervical Cancer; Nurse; Self-Sampling; HPV; Thinprep Preservcyt Solution; Liquid Cytology; Clinician-Taken; Ethiopia

Introduction

Invasive cervical cancer (ICC) is the fourth most frequent malignancy and cause of death in women suffering from cancer worldwide [1]. In Ethiopia, ICC is even at the second place among women between 15 and 44 years of age. Ethiopia has 31.5 million women aged 15 years and older and 7.095 women were diagnosed yearly with ICC of whom 4.732 died from the disease, Currently, there is only sparse data on the Human papillomavirus (HPV) burden in the general population of Ethiopia [2].

A study in Nigeria for example, found 93% participation in the self-sampling arm, compared to only 56% in the hospital-collection arm [3]. Another study in Sub-Saharan Africa, indicated a comparable HPV prevalence for self- (14,6%) and physician (12,7%) samples, so similar accuracy of the test on both sampling methods [4]. A study in Madagascar showed absolute acceptance (100%) of self-sampling (with a flocked swab) followed by HPV testing as cervical cancer screening method [5].

Available data indicate that the HPV prevalence in Ethiopia among women with normal cervical cytology varies between 15.9 % and 17.5%, and 96.6% of the invasive cervical cancers are attributed to HPV16 (78.4%) and 18 (18.2%) [2].

Cervical cancer develops over a long period of time through precursor lesions. These lesions can be detected by (cytological or visual) screening, and progression towards cancer can then be stopped by treatment (ablation or excision) in an early phase [6]. Currently in Ethiopia, 200 health facilities are providing VIA (Visual Inspection with Acetic acid) screening followed by cryotherapy (ablative treatment technique), and more than 52,000 women were screened in 2016/17. Of the 20 million women eligible for screening only 0.3% of them screened. In addition, Loop electrosurgical excision procedure (LEEP) service was scaled up from five to fifteen hospitals and the Federal Ministry of Health (FMoH) is working to expand VIA screening and cryotherapy into 823 districts [7]. However, more efforts or other screening techniques are urgently necessary to scale up the cervical cancer screening coverage in Ethiopia.

In this study, the feasibility and acceptability of self-sampling followed by an HPV test was verified in the Ethiopian population.

Methodology

The study aimed to determine the feasibility of vaginal/cervical Nurse Assisted Self-Sampling (NASS) and the agreement between Human papillomavirus (HPV) testing on self-samples versus clinician-taken (CT) specimens.

The study was conducted in Adama Town, Oromia region, having a total population of 1,356,342 people of whom 659,992 are females. The St. Aklesia Memorial Hospital (SAMH), located in Adama Town, is a private hospital with a long time historyand expertise in cervical cancer screening.

To reach in an efficient way a lot of woman for recruitment in the study, radio calls and face to face interactions were organized. Through these channels, women were encouraged to schedule an appointment for cervical cancer screening approximately two weeks (10-18 days) after the first day of their last menstrual period. Also women visiting the hospital for reproductive health related issues were called for participation in the study.

Women were eligible if they were 20 years or older, had an intact uterus, had no history of cervical cancer, were mentally competent and able and willing to provide informed consent. Based on the upset of this study, a cross-sectional and probability sampling technique was used. The sample size was calculated by considering 5% margin error; 95% confidence level, 659,992 female populations of East Shewa, and according to pilot study 95% of a time women were responded self-sampling was acceptable means of screening and by adding 10% of non-respondent rate the minimum sample size was 73.

Women who were interested in participating in the study were given following instructions: no douche 48 hours prior to the test; no use of tampons, birth control foams, jellies or other vaginal creams or vaginal medications for 48 hours prior to the test and also advised to refrain from intercourse 48 hours prior to the test.

After signing an informed consent document, women were subjected to two ways of sample collection, both performed within the clinic: 1) nurse assisted self-sampling with supervision; 2) clinician-taken specimens i.e. a physician collected the samples according to the standard procedure of the clinic. Women were also asked to fill in a questionnaire.

Nurse Assisted Self-Sampling (NASS) at the Clinic

Women were invited to the private area of the clinic and were given verbal and printed diagrammatic instructions by the trained nurse for collecting the vaginal specimen. When the women confirmed that al instruction were clear, the nurse opened the collection kit and handed over the collection devices (in sequence order of spatula followed by cytobrush) to the woman.

The vaginal fornix and ectocervix was sampled before the endocervix. To start the NASS, women were instructed to take a sample of the ectocervix using a plastic spatula, without speculum. The women were asked to insert the spatula, laying on the bed, into their vagina and to rotate three times 360˚, to remove and to handover the collection device to the nurse. The nurse then rinsed the spatula into a labeled vial with ThinPrep PreservCyt solution.

In the next step, the nurse provided the cytobrush to the woman to sample the endocervix. It was inserted by the woman herself until it met with resistance, rotated 45-90°, removed and handed over to the nurse. The nurse inserted the cytobrush sample into the same ThinPrep PreservCyt labeled vial. This procedure was not involving any invasive steps rather non-invasive simple and easy collection techniques. Collected samples were kept at 22˚C (room temperature) for about 10 months, until shipment and processing.

Clinician-Taken (CT) Sample at the Clinic

The clinicians collected cervical samples according to standard protocols i.e. both ectocervix and endocervix samples were collected with a cytobrush and rinsed in a labeled vial with ThinPrep PreservCyt solution. Collected samples were kept at 22°C (room temperature) for about 10 months, untilshipment and processing.

Visual Inspection with Acetic Acid (VIA)

After the NASS and the CT sample, all women underwent VIA. A women was classified as VIA positive when acetowhite lesions were visualized by the clinician. All VIA positive women were eligible for cryotherapy and were treated.

Ethical Clearance

The ethical committee of the College of Natural Sciences, Addis Ababa University, has examined the project and approved. The SAMH Hospital also approved the project. All women signed an informed consent before enrolment in the study.

Laboratory

Both CT and NASS specimens were tested for presence of HPV with the RIOTOL qPCR HPV genotyping test (Algemeen Medisch Laboratorium (AML), Belgium).This clinically validated and ISO certified lab developed (LDT) high-throughput HPV test, detects 14 high risk HPV (HR HPV) types i.e. 16,18,31,33,35,39,45,51,52,56,57,58,59,66 and 68, 4 intermediate/low risk HPV (LR HPV) types i.e. 6, 11, 53 and 67,68 and a cell control [8,9]. Samples with less than 10 cell/µl are considered as invalid and reported as samples of poor quality.

Data Source and Analysis

Quantitative data was collected and for some of demographic variables were decode accordingly. Any missed variables identified during collection of data, the supervisor was responsible to follow up the patients and correct it accordingly. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20 software. The overall measurement agreement between self- and clinician-collected samples was calculated with a kappa value. The dependent variable was HPV outcome and independent variables are socio-demographic. Pearson's chi-squared test and 95% confidence interval (CI) were used and statistically significant if the p-value was less than or equal to 0.05.

Results

A total of 83 eligible women were enrolled between October 2015 and July 2016 at SAMH hospital, Adama, Oromia region, Ethiopia. The study had no missed data or variables.

Patient Demographics

The average age of the participating and eligible women was 32 years, with the youngest being 20 and the oldest 65 years. Fourty-seven women (56.6%) had an education level below grade 10 (high school); 33.7% (28/83) and 27.7% (23/83) of the study population were laborers and housewives, respectively. Seventy one

women (85.5%) were married at the time of the study and 69.9% had one life time partner. A total of 80.7% (67/83) had gravidity equal to or above one and 7.5% (5/67) of these women had a spontaneous abortion before. Women who used birth control and smoking cigarettes were 39.8% (33/83) and 18.1% (15/83), respectively. Four (4.8%) women reported to be infected with HIV at the time of study (Table 1).

Categories	Variables	Count	%
Age Group	20-30	39	46.9
	31-40	34	40.9
	41-50	8	9.6
	51-60	1	1.2
	>=61	1	1.2
Education	Under grade 8	23	27.7
	Under grade 10	24	28.9
	Preparatory (University)	3	3.6
	Diploma	19	22.9
	Degree	13	15.7
	PhD	1	1.2
Occupation	Student	3	3.6
	House wife	23	27.7
	Laborer	28	33.7
	Government Employee	7	8.4
	Private employee	15	18.1
	Self-employee	7	8.4
Marital Status	Married	71	85.5
	Single	7	8.4
	Separated	4	4.8
	Living with partners	1	1.2
Life time partners	1	58	69.9
	2	21	25.3
	3	4	4.8
Gravidity	0	16	19.3
	1	21	25.3
	2	32	38.6
	3	6	7.2
	4	6	7.2
	5	1	1.2
	6	1	1.2
Abortion	Induced	5	7.5
	Spontaneous	5	7.5
	No abortion	57	85.1
Current use of any birth control	Yes	33	39.8
	No	50	60.2
Current Smoking	Yes	15	18.1
	No	68	81.9
HIV Status	Reactive	4	4.8
	Non-Reactive	70	84.3
	Unknown	9	10.8
Chief presenting symptoms	Dyspareunia	4	4.8
	Intermestral	6	7.2
	Urinary Symptom	34	41
	Backache	14	16.9

	Vaginal discharge	25	30.1
VIA results	No acetowhite lesion	57	68.7
	Acetowhite lesion	9	10.8

Table 1: Characteristics of women enrolled in our cervical cancer screening study (N=83), between October 2015 and July 2016, at SAMH hospital, Adama, Oromia region, Ethiopia.

Acceptance and Feasibility of Self-Samples

In the feasibility questionnaire (Table 2), a high number of the women indicated that self-sampling was easy to use (87.9%); easy to insert and collect (79.5%) and user-friendly (91.6%). Especially the privacy of a self-sample compared to a clinician-taken specimen scored very high (92.8%). More than 80.0% of the women had confidence in the results of their self-taken sample. Furthermore, over 85.0% of the women were willing to perform self-sampling at the clinic or home, would go to a clinic that would provide the self-sampling and were even willing to pay for a NASS followed by an HPV test if it would be available over the counter.

Categories	Variables	Count	%
Practicability	Easy	73	87.9
	Moderate	7	8.4
	Difficult	3	3.6
Is easy to insert and collect the device?	Yes	66	79.5
	No	17	20.5
Is collection device user friendly?	Yes	76	91.6
	No	7	8.4
Is self-sampling more private compared to sampling by clinician?	Yes	77	92.8
	No	6	7.2
Do you believe on the results that were taken by yourself?	Yes	69	83.1
	No	14	16.9
Do you have plans to visit the clinic that provides self-sampling thereafter?	Yes	71	85.5
	No	12	14.5
Preference of self-sampling over clinician?	Yes	79	95.1
	No	4	4.9
Willing to pay for HPV self-test if available over the counter?	Yes	71	85.5
	No	12	14.5
Willing to perform self-sampling at clinic or home	Yes	73	88
	No	10	12

Table 2: Acceptability and feasibility of vaginal self-sampling by women enrolled in our cervical cancer screening study (N=83).

Sample Quality

Out of 166 samples (two specimen per women) and 26.6% (44/166) had not enough cells (>10 cells/µl) and were considered as samples with poor quality. According to Fisher`s exact test, there was no statistically significant difference in number of samples with poor quality between the two sample groups (NASS: 19/83 and CT: 25/83) (p=0.3794). (Table 3).For 17 women (20.5%), both the CT and the NASS sample were of poor sample quality (Table 4). These 17 women were excluded from further analysis.

Sample types	Human DNA detected	No Human DNA detected	Total
SS	64	19	83
CT	58	25	83
Total	122	44	166

Table 3: Sample quality comparison between self-samples (SS) and clinician-taken samples (CT) (N=166).

Clinician taken (CT) sample	Self-sample (SS)			
	HPV (+)	HPV (-)	No DNA	Total
HPV (+)	5	3	1	9
HPV (-)	6	42	1	49
No DNA	0	8	17	25
Total	11	53	19	83

Table 4: HPV test results of the self-samples (SS) and clinician-taken (CT) samples (N=83).Type specific qPCR (Riatol HPV test).

HPV Test Results from the NASS and CT Specimens

On all collected NASS and CT specimens the RIATOL qPCR HPV genotyping test was performed. The HPV results of the remaining 66 women are presented in detail in table 5. The overall prevalence of HPV was 22.7% (15/66). The prevalence of HR HPV was 18.2% (12/66) and LR HPV types 6.1% (4/66). The CT samples had an HPV prevalence of 15.5% (9/58) (all types), with a prevalence of 12.1% (7/58) for the high risk types and 3.4% (2/58) for the low risk types. The results from the NASS samples showed a somewhat higher prevalence of 17.2% (11/64), and 14.1% (9/64) and 4.7% (3/64) for all HPV types, HR and LR types respectively (Tables 4 and 5).

# of HPV positive women	Type of samples	High risk HPV typing									Low risk HPV typing			Total		
		16	18	31	45	51	56	58	59	68	6	53	67	Overall	SS	CT
1	CT	-	1	-	-	-	-	-	-	-	-	-	-	1		1
2	CT	-	-	1	-	-	-	-	-	-	-	-	-	1		1
3	SS	-	-	-	1	-	-	-	-	-	-	-	-	1	1	1
	CT	-	-	-	1	-	-	-	-	-	-	-	-			
4	SS	-	-	-	-	-	-	-	1	-	-	-	-	1	1	
5	CT	-	-	1	-	-	-	-	-	-	-	-	-	1	1	1
	SS	-	-	1	-	-	-	-	-	-	-	-	-			
6	CT	-	-	-	-	-	-	-	-	-	-	1		1	1	1
	SS	-	-	-	-	-	-	-	-	-	-	1				
7	SS	-	-	-	-	-	1	-	-	-	-	-	-	1	1	
8	CT	-	-	-	-	-	-	-	-	-		-	1	1		1
9	CT	-	-	-	-	-	-	-	-	1	-	-	-	1		1
10	SS	-	-	-	-	-	-	1	-	-	-	-	-	1	1	
11	SS	-	-	-	-	-	-	-	-	-	1		-	1	1	
12	SS	-	-	-	-	1	-	-	-	-	-	-	-	1	1	
13	CT	-	-	-	-	1	-	1	-	-	-	-	-	1	1	1
	SS	-	-	-	-	1	-	-	-	-	-	-	-			
14	SS	-	-	-	-	1	-	-	-	-	-	-	-	1	1	
15	CT	1	-	-	-	1	-	-	-	1	-	-	-	1	1	1
	SS	1	-	-	-	1	-	-	-	1	1	-	1			
Total														15	11	9

Table 5: HPV distribution by type, of the self-samples (SS) and clinician-taken (CT) samples. Type specific qPCR (Riatol HPV test) (N=66).

The overall agreement of HPV test results between NASS- and CT samples was moderate, with a kappa value of 0.58 (95%CI: 0.41-0.76). A total of 47/66 (71.2%) CT and NASS samples were in agreement in terms of HPV test results. From the 15 positive HPV samples, only 33.3% (5/15) were positive in both the NASS and CT sample, while for the HPV negative results there was 82.4% agreement (42/51).

The most prevalent HPV type was HR HPV51 (4/66, 6.1%), followed by HR HPV31, 58 and 68 and LR HPV6 and 67 which were all found twice (2/66, 3.0%). HPV16

was detected in 1 woman, in both the CT and the NASS sample (overall prevalence: 1/66=1.5%) and HPV18 also in 1 woman, but only in the CT sample (overall/CT: 1/66=1.5%, NASS: 0%). Two women were co-infected with at least two HPV types (multiple infections: 2/66=3.0%).One woman out of these two was co-infected with 5 HPV subtypes: HPV6, 16, 51, 67, and 68 (according to the NASS HPV DNA result). A total of 12 different HPV types were identified in this study, out of the 18 HPV types that were tested for (Table 5).

Results from NASS and CT HPV Test Versus (VIA)

A total of 66 women underwent VIA. In 9/66 (13.6%) women, acetowhite lesions were visualized. When excluding the CT samples with poor sample quality, five of the 9 women with a positive VIA result, were HPV positive (sensitivity of 55.5% (Cl: 26.6% to 81.1%)) and 84.5% (49/58). On the other hand, 45 of the49 women with no acetowhite lesions were HPV negative (specificity of 91.8% (Cl: 80.8% to 96.8%). The overall agreement between HPV and VIA result from CT sample was 86.2% (Table 6).

HPV result	CT VIA test		
	Acetowhite lesion	No acetowhite lesion	Total
HPV (+)	5	4	9
HPV (-)	4	45	49
Total	9	49	58
HPV result	**SS VIA test**		
	Acetowhite lesion	**No acetowhite lesion**	**Total**
HPV (+)	7	4	11
HPV (-)	1	52	53
Total	8	56	64

Table 6: HPV test results versus VIA CT & SS HPV test results (N=58, N=64).

When excluding NASS samples with poor sample quality, 7 of the 8 women with acetowhite lesions, were HPV positive (sensitivity of 87.5% (95% Cl: 52.9%-97.8%)) and 52women of the 56 with no visual lesions, were HPV negativity of 92.8% (Cl: 83.0% to 97.2%). The overall agreement between HPV and VIA result from NASS sample was 92.2% (Table 6).

Pearson's Chi-Squared Test

Table 7 shows the result of the Pearson's Chi-square test using the HR HPV test result (combined NASS and CT results) and all collected variables, with HR HPV-negative status as the reference group. Having more than two life time sexual partners (p=0.000447) and being VIA positive was causally associated with a HR HPV positive test result, and not a difference by chance. Spontaneous abortion (p-value=0.021) and being a housewife (p-value=0.016) was also associated with HR HPV positive results. Younger age groups (<40 years) showed a trend towards a correlation with a positive HPV test result (p-value=0.058); there were about 19.6% (11/56) HR HPV positive women in the age groups under 40, while only 10% (1/10) in the combined age groups above 40. House wife and laborer were statistically associated with HR HPV (Chi-square = 13.880 and p=0.0016). No statistical association was found between HR HPV positivity and all other collected variables.

Variables		HRHPV Result		Pearson Chi-Square (value)	p-value
		Pos	Neg		
Age Group	20-30	3	24	9.132	0.058
	31-40	8	21		
	41-50	0	8		
	51-60	1	0		
	>=61	0	1		
Education	Under grade 8	3	11	1.115	0.953
	Under grade 10	4	15		

	Preparatory (University)	0	3		
	Diploma	3	14		
	Degree	2	10		
	PhD	0	1		
Occupation	Student	1	1	13.88	0.016
	House wife	8	11		
	Laborer	2	15		
	Government Employee	0	6		
	Private employee	0	15		
	Self-employee	1	6		
Marital Status	Married	11	46	0.724	0.868
	Single	1	5		
	Separated	0	2		
	Living with partners	0	1		
Life time partners	1	2	41	15.424	0.000447
	2	9	11		
	3	1	2		
Gravidity	0	6	9	7.643	0.265
	1	2	17		
	2	3	21		
	3	0	3		
	4	1	2		
	5	0	1		
	6	0	1		
Abortion	Induced	1	1	7..694	0.021
	Spontaneous	2	3		
	No abortion	3	41		
Current use of any birth control	Yes	7	22	1.234	0.267
	No	5	32		
Current smoking	Yes	3	7	1.107	0.293
	No	9	47		
HIV Status	Reactive	0	3	2.933	0.231
	Non-Reactive	12	43		
	Unknown	0	8		
Chief presenting symptoms	Dyspareunia	0	3	0.816	0.936
	Intermestral	1	3		
	Urinary Symptom	5	22		
	Backache	2	8		
	Vaginal discharge	4	18		
VIA results	No acetowhite lesion	4	53	35.236	0 2.23E-8
	Acetowhite lesion	8	1		

Table 7: Pearson's chi-squared test of HRHPV test result (SS+CT results) with all studied variables (N=66).

Discussion

Feasibility/Acceptability of Self Sampling

Self-sampling devices are not commercially available in Ethiopia and not used for routine basis for cervical cancer screening. Moreover this study can be considered as first in kind where no other similar studies currently found in Ethiopia. The acceptability of a self-sampling (SS) device was very high in this study and women felt self-sampling device was easy to use, to insert and to collect and user-friendly. Women were willing to perform the self-sampling because of its privacy nature. Ghanaian women reported that 76.3% self-collected (SC) were very easy/easy to obtain, 57.7% preferred SS over clinician sample (CS) and felt SC would increase their likelihood to

access cervical cancer screening which were comparable percentage of women felt same in our study too [10,11].

Our study was further supported by data from Bolivia where SS was generally preferred over CS for a screening program based on HPV detection [12]. Furthermore, a number of studies report that HPV self-sampling was found to be highly acceptable and feasible among hard-to-reach women.

A study in El Salvador that reported Self-sampling revealed an acceptability of 68%, although lower than reported in our study [13]. Others studies from American Indian and Hopi women were also supported our findings where self-sampling HPV testing was feasible and acceptable that may contribute to an increase of uptake [14].

Most women showed a willingness to pay for self-sampling services and believed their results which could be seen as a driving force for screening among hard-to-reach women [15].

Almost the same percentage of women between our study and Japanese were reported they would use self-sampling again and found instructions easy to follow and reported no issues with the usability of the self-sampling device. However, women in our study reported that they had confidence in the results of self-taken sampling unlike of women who lacked confidence on the test [16].

Similar studies supported our findings from Latinas and Haitian populations where women agreed HPV self-sampling was faster, more private, easy to use, and would prefer to use it again [17]. Furthermore, in German, self-sampling is considered to be easy by 89.0 % as well as user-friendly by 96.0% of the women [18]. Therefore, Ethiopian women might use nurse assisted self-sampling service as alternative options for fighting cervical cancer prevention.

HPV Prevalence in General Population

We reported an overall HPV prevalence in this study of22.7% and a prevalence of HR HPV 18.2% and LR HPV of6.1%. HPV prevalence in Africa varied within a range of 12% to 46% [19]. Studies elsewhere in Ethiopia reported an HPV prevalence of 17.3% and 15.8% for HR HPV [20,21]. Thus, our study revealed an HR HPV prevalence that is consistent with sub-Saharan Africa report with slightly higher. The overall HPV prevalence from SS and CT sample was 10.8% and 13.2% respectively. The author concluded that no report found on HR HPV prevalence among self-sampling and doctor sampling was 14.1% and 12.1% respectively in general population in Ethiopia.

In Rwanda HR HPV prevalence was 19.0% that was slightly higher than our result [22]. The prevalence of HR HPV in Dakar was 17.4% as comparable to our 18.2% where geographical and population difference could be a reason [23]. HPV prevalence in Cameroon was 18.5% that was comparable to our findings [24].

A study from Northern Africa, a Muslim community, HPV infection was 6.3% (4.0% of high-risk types), with no significant variation by age [25]. However, a study done by Traore IMA, et al. [26] in Burkina Faso showed that HR HPV prevalence was 38.3% which was twice of our result. Therefore, HPV prevalence in different countries and segment of population is varies as indicated in all previous studies.

Accordingly to study done by Laia Bruni, et al. [19] the estimated prevalence of HPV in Sub-Saharan Africa is 24.4% and global prevalence was 11.7% where almost comparable in our study [19]. Further studies from 11 countries (Nigeria, India, Vietnam, Thailand, Korea, Colombia, Argentina, Chile, the Netherlands, Italy, and Spain) without cytological abnormalities were included and age-standardized HPV prevalence varied from nearly 20 times between populations, from 1.4% in Spain to 25.6% in Nigeria where 22.5% HPV prevalence were presented in our study [27].

HPV Type Distribution

From our study the most prevalent HPV type was HPV51 and followed by HPV31, 58 and 68 (HR types) and HPV6 and 67 (LR types). Women were co-infected with at least two HPV types and the higher were co-infected with five HPV subtypes: HPV6, 16, 51, 67, and 68. A total of 12 HPV types were identified in this study, out of the 19 HPV types that were tested. HPV 16 was the most frequent genotype identified in samples from previous Ethiopia studies and HPV 52, 58, and 18 were the second, third and fourth common genotypes identified respectively, whereas in our study HPV 51 and 31 were the common genotypes identified [28]. Thus, even within the same country, it observed that there are genotypes differences among population segments.

Study from South Africa, HPV 16, 35, and 58 were the most common high-risk HPV types with no major differences in the type distribution by HIV status [29]. In Mozambique, most frequently were HPV51, HPV35, HPV18, HPV31 and HPV52. Likewise multiple infections

were detected in HPV51 of HPVs 16/18 normal cytology. While HPVs 51 and 35 were the two most common types [30].

HPV positive women in Europe were significantly more likely to be infected with HPV16 than those in sub-Saharan Africa. Heterogeneity between areas of Asia was significant where that supported by previous Ethiopian studies [27,31]. Study from Burkna Faso HPV 52, HPV 33, and HPV 59 were most identified genotypes where HPV 51, 31, and58 were most prevalent in our study.

HPV 52 (3.2%) was the most prevalent HPV type, followed by HPV 31 (3.0%) and HPV 16, 45, and 53 (all 2.8% [23]. In a study from Nigeria, the prevalence of HPV35 and HPV16 were equally frequent [32]. HPV16 was the most common type among the general population of Guinea (7.3%) [33].

HPV Tests Versus VIA

In this study, the overall agreement between SS HPV and VIA result was higher than CT results. Sensitivity between HPV and VIA test results was relatively higher on self- sampling over clinician- taken samples. There was an almost equal specificity value found between SS and CT samples. Study from Cameroon, indicated that the sensitivity and specificity of VIA/VILI among HPV positive women 80.0% and 44.0%, respectively that was less compared with this study [24].

A combination of HPV-based and VIA screen-and-treat approach may be feasible in a low-resource context and may contribute to improving the effectiveness of CC prevention programs. The combination of HPV-testing and VIA/VILI for CC screening might reduce overtreatment [24].

Agreement between NASS and CT HPV Test

The overall agreement of HPV test results between NASS and CT samples was moderate, with a kappa value of 0.58.A study from Bolivia showed good agreement between self- and physician collected samples for HR HPV detection (κ = 0.71) was higher as compared to this study [12]. A study from Sub-Saharan Africa revealed that the overall HPV positivity agreement between Self- and doctor was κ value of 0.52, respectively which had similar agreement with our study [34].

Conclusion

There was a moderate agreement between a NASS and a CT sample for HPV detection. NASS could replace CT samples for HPV testing as an alternative ways in Ethiopia; however, the sample quality may need improvement. NASS-HPV is a valuable tool for the follow-up of HPV-positive women in low-resource settings. NASS HPV testing using Thin Prep Preserv Cyt solution could be considered an alternative for cervical cancer screening modality in low-resource setting countries where the coverage is low. This strategy may increase cervical cancer screening coverage in Ethiopia and other countries.

Individuals living in different geographical localities should receive vaccines based on the specific genotypes circulating in the area and according to our findings a vaccine targeting HPV 51, 31, 16, 45, 52, and 58 may be optimal for the prevention of cervical cancer in Ethiopia. Genotyping information could be important to guide vaccine policy. Our study was the first report on self-sampling using Thin Prep Preserv Cyt solution or liquid based cytology in Ethiopia and may be used as a platform for similar studies in the future.

Limitation

Although this research was carefully prepared, we concluded that the sample size was small and not able to generalize.

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