Human Papillomavirus Infection: Molecular Epidemiology and Acceptability of Screening and Vaccination among Women in Eastern Kenya Counties

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Summary

BACKGROUND

Human Papillomavirus associated cervical cancer in Kenya caused 3,286 deaths where cervical screening rate was 3.2% in 2018. This study examined knowledge, attitudes, practices, and perceptions (KAPP) on HPV screening and vaccination and how these influenced HPV infections among HIV-infected and uninfected women seeking reproductive health services.

MATERIALS AND METHODS

This was a cross-sectional study where socio-demographic and KAPP data on HPV screening and vaccination data was collected by the use of a questionnaire. Cervical swabs were obtained for HPV DNA-PCR and cytology. Logistic regression and Pearson chi-square tests were used to analyze statistical relationships.

RESULTS

Among the 317 women recruited, HPV infections were significantly associated with marital status, number of sexual partners, hormonal-contraceptives use, HIV infection, presence of genital warts, recurrent UTIs, and TB infection. The number of participants with knowledge on HPV screening was significant in Embu County, among those younger than 30 years, with secondary and college level education, marital status, religion, and contraceptives use. Having a relative with a history of any cancer was significantly associated with knowledge and perceiving HPV screening as important. Participants who perceived HPV vaccination as important were significant across age, family planning, and parity. Fear of embarrassment, procedures, and results, lack of time, and cost of the test were reported as reasons for failing to screen for HPV.

CONCLUSION

Knowledge, willingness, and perceiving HPV screening as important as well as willingness to vaccinate against HPV may reduce HPV infections among women seeking reproductive health services in Eastern Kenya.

***Keywords**: HPV, Vaccination, Screening, Knowledge, Attitude, Practice, and Perception.*

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Introduction

Human Papillomavirus (HPV) is sexually transmitted and causes 99.7% of global cervical cancer [1, 2] initiating as Cervical Intraepithelial Neoplasia (CIN) and progresses to either Carcinoma *in-situ* (CIS) [1, 3, 4] or invasive Cervical Cancer (ICC) [1]. In 2018 there were 3,286 cervical cancer deaths in Kenya and the HPV incidence rate among women of reproductive age was 20.6%, projected to double by 2025 [4]. HPV infections regress in two years among women under 30 years of age [5].

Other cofactors necessary for cervical cancer progression [5,6] are grouped into three: (1) exogenous such as use of oral contraceptives (OC), tobacco-use, diets, cervical trauma, co-infection with HIV and other sexually transmitted pathogens [5,7,8]; (2) viral cofactors such as infection with specific HPV types, co-infection with other types and variants of HPV and/or other viruses, viral load, and viral integration; (3) host immunity [1, 2, 4, 6].

Several cervical screening methods are recommended in Kenya and are part of the national cancer prevention measures [2]. These include the HPV Deoxyribonucleic Acid Polymerase Chain Reaction (HPV DNA PCR) test, Papanicolaou smear (Pap smear) test, visual inspection with acetic acid, and visual inspection with Lugol's iodine (VIA/VILLI) [2,3]. Evidence from randomized controlled trials has shown increased effectiveness of HPV DNA PCR testing compared with cytology-based screening [9, 10]. Pap smear screening faces challenges in most resource-constrained countries such as cost, the requirement for cytotechnologists, and specialized staining, [10, 11, and 12]. Patients follow up is lost because of the long turnaround time between sample collection and obtaining results [2,13]. Only 3.2% of women aged 18-69 years undergo cervical screening [2]. However, most women are willing and advice their daughters and close relatives to have HPV screening and HPV vaccination [2, 14, 15].

Studies report low knowledge of HPV screening and vaccination in Sub-Saharan Africa [16, 17]. Human Papillomavirus can be prevented, controlled, and monitored through increase of knowledge, practice, and change in attitude and perception on behavior, screening, vaccination, and treatment [1, 2, 4, and 5]. However, most eligible women have either never been screened or are screened late and have low knowledge of HPV screening and vaccination [5, 11, 12]. There is a lack of data on the acceptability of the HPV vaccine among women in Kenya [2, 4, and 5] and across different populations in the world [1, 9] before and after initiation into national programs [18]. Despite high acceptability, doubts surround the safety and efficacy of the vaccine [9, 19]. Willingness to vaccinate against HPV in Kenya was reported to be high in Eldoret [4] and Kitui [18] despite the limited knowledge of cervical cancer and its cause.

We, therefore, determined KAPP on HPV screening and vaccination and how these influenced HPV infections by HIV serostatus among women seeking reproductive healthcare in Eastern Kenya. This is the first KAPP study on HPV screening and vaccination in this region with limited resources and poor accessibility to healthcare [20].

Materials and Methods

This cross-sectional study involved 317 HIV seropositive and HIV seronegative female participants aged 18 – 46 who attended reproductive health clinics in referral hospitals in five counties of Isiolo, Kirinyaga, Meru, Tharaka-Nithi, and Embu. The reproductive health clinics offer HIV voluntary counseling and testing (VCT), reproductive health services, well-baby clinics, VIA/VILLI test, and colposcopy. All

VIA/VILLI positive cases are referred to Embu and Meru referral hospitals for the Pap smear test. HPV DNA PCR test is not available in Eastern Kenya.

Sampling procedure

Sample distribution was dependent on client presentation in referral hospitals reproductive health facilities and those who were due for routine HPV screening as part of Kenya National Cervical Cancer Prevention Strategy 2017-2022 (KNCCPS) for HIV positive women from June – December 2018.

Excluded were participants with an eroded cervix, pregnant, those who had undergone abrasive procedures for cervical diseases in the preceding six months, women with hysterectomy, those outside the age bracket, and mentally incompetent participants. In each referral hospital, participants were recruited at random for six months. A face-to-face interview survey was conducted by trained interviewers using a questionnaire before HIV and HPV screening.

Collection of data

A structured questionnaire with three sections was used: 1) Section A, focusing on social demographic and economic factors. 2) Section B focusing on factors responsible for HPV oncogenesis that included hormonal contraceptives use, multiple-sex partners, sex debut, smoking habits, history of infection by warts, HIV, recurrent UTI, tuberculosis (TB), and Herpes. 3) Section C had KAPP close-ended (Yes/No) questions on HPV screening, vaccination, and HPV screening techniques; HPV DNA PCR test, Pap smear test, VIA/VILLI test.

HPV screening and vaccination knowledge were reported as yes/no, attitude as willing/not willing, practice as done/not done, and perception as important/not important. Vaginal swabs were obtained for HPV DNA-PCR and cytology.

Determination of HIV status

Kenya National HIV testing algorithm was applied as baseline and confirmation of HIV serostatus of case and control groups of participants. Three milliliters of venous whole blood was taken for serological HIV testing. Alere Determine®HIV-1/2 test by Abbort Co. was used as baseline screening while the First Response® HIV 1-2-0 card test by Premier Medical Corporation® was used as a confirmatory test, in case of discrepancies. The tie-breaker test was done using the *Uni-Gold*™ Recombigen® *HIV-1/2 by* Trinity Biotech.

Cervical examination

The procedure was clarified to the participant and their identity verified. Participants were requested to lie in a lithotomic position where the external genitalia was examined by a nurse followed by a cervical examination using a speculum. Excess cervical mucus was removed with a swab from the cervix.

Cervical cytological material was collected by inserting Cervical Sampler™ brush into the endocervical and ectocervical canal targeting squamocolumnar junction. The material collected was immediately spread on a Cervical Sampler™ glass slide and fixed using the fixative provided in the kit (MOH, National Cancer Screening Guidelines, 2019; WHO, 2013). The brush bristles were then dipped into aqueous Minimum Essential Media (MEM) transport media and the brush handle snapped or cut so that the brush remained in the media when the lid on the vial was tightly closed. The firmly closed vials were stored at 1-4ºC and shipped to the KEMRI HPV laboratory in a cool box. Samples were stored at -20°C for HPV DNA PCR.

HPV DNA extraction and amplification

All samples stored for HPV DNA detection were analyzed in 20-sample batch by the following procedure:

a. Preparation of lysis mastermix.

Mastermix was prepared by mixing 240µl of VDR Lysis Buffer, 8µl of Carrier RNA, and 280µl of Isopropanol per sample volume in 96-well format HighPrep™ Viral DNA/RNA Lysis kit, MagBio Genomics, Inc. US/Canada.

b. DNA extraction

Samples stored in universal bottles at 1-4ºC were thawed then vortexed for five minutes then centrifuged at 10000r/min for 5 minutes extract cytological material from the brush into the medium. Samples were subjected to the HighPrep™Viral DNA/RNA Lysis kit, MagBio Genomics, Inc. US/Canada protocol to obtain DNA extracts by magnetic beads technique. The eluate (cleared supernatant containing the DNA) was transferred to a new microplate for storage at -20°C.

c. HPV DNA PCR

HPV detection was achieved by amplifying an L1 portion of the HPV genome that is relatively conserved through L1 consensus nested PCR in the ABI thermocycler Model 9600 supplied by Applied Biosystems™. HPV consensus primary primers PGMY09 (GCACAGGGACATAACAATGG) and PGMY11 (CGTCCCAAAGGAAACTGATC) that target 450 base pair (bp) region in the L1 ORF in the primary reaction was used. Additional primer sets targeting the same region of L1, MGP5+ (ACGTTGGATGTTTGTTACTGTGGTGGATACTAC) and MGP6+ (ACGTTGGATGGAAAAATAAACTGTAAATCATATTCCT) were used to produce shorter amplicon of ~160 bp (de Roda *et al.*, 1995; World Health Organization, 2013).

Primer sets were obtained from Iqaba Biotech™. Five microMolar PGMY09 primer working stock was prepared by adding 50µL 12 PGMY09 100 µM primers to 350µL of molecular biology-grade sterile water (1ml total volume) and PGMY11 primer 5 µM working stock by adding 50 µL each 5 biotinylated PGMY11 100 µM primers to 750µL molecular biology-grade water (1mL total volume). They were later distributed each 5µM working stock in 45–90µL aliquots and stored at -20°C.

In the primary PCR, 5µl of the extracted DNA was amplified in a reaction mix containing 1X PCR buffer 2.0 mM MgCl2, 500nM forward primer MY09, 500nM reverse primer MY11 and 100µM of each dNTPs and 0.13 *Taq* polymerase enzyme. The mixture was subjected to initial denaturation for four minutes at 95ºC, cycled 30 times at the same temparature for twenty seconds, 56ºC(fouty seconds), 72ºC (two minutes) and final extension at 72ºC for seven minutes.

Later, 5µl of the product, 2mM MgCl, 500nM of GP5+, 500nM GP6+, 400µM dNTPs and 0.13*Taq* polymerase enzyme were used in nested PCR where 95ºC was applied as initial denaturation for four minutes, then 95ºC for 20 seconds, annealing at 60ºC for 40 seconds, and extension at 72ºC for seven seconds. The final extension was at 72ºC for seven minutes. After the nested PCR, a 5µl aliquot of the PCR product was mixed with 1µl of 6X loading dye and loaded onto a 2% agarose with 2µl ethidium bromide gel alongside 100 bp ladder for electrophoresis. The presence of the expected 160bp amplicon was considered as positive for HPV DNA PCR.

Positive control of known CIN II sample and negative control of distilled water were incorporated in all primary and secondary primer PCR run.

d. Gel electrophoresis and UV visualization

Tris-Borate-EDTA (TBE) 10X was prepared by dissolving 162 g Tris base, 50 g boric acid, 9.5 g EDTA in nanopure water to a volume slightly less than one liter and pH adjusted to 8.8 by adding HCl. The final volume of 1 liter was obtained by adding nanopure water. Tris-Borate-EDTA 0.5X was later prepared by diluting 10X TBE in nanopure water (100 mL of 10 X TBE to a final volume of 2 L) where 200mL was used to set an agarose gel and the other volume to fill the electrophoresis tank.

Four grams of agarose powder was added to 200ml of 0.5X TBE then microwaved to boil. It was then cooled for fifteen minutes at 60°C in a thermostated water-bath after which 10µL GelRed™ was added. The mixture was poured into a gel electrophoresis apparatus (14-well combs per gel), cooled to solidify then electrophoresis buffer (0.5 X TBE) was added in the electrophoresis chamber to cover the gel (one centimeter). Electrophoresis was allowed to run at 105watts constant power until bromophenol blue was one centimeter above the next wells. The gel was later visualized in a UV transilluminator. Visualization of a 450bp PCR product band in the MY09/MY11 lane and/or a 150 bp band in the nested PCR lane on the agarose gel provided evidence of HPV DNA in the sample.

Pap smear

Papanicolaou (Pap) smear staining protocol was adapted and reviewed by consultant cytopathologist at Embu and Meru Hospital using the Bethesda 2001 guidelines. Cervical cytological changes of the nucleus and cytoplasm following HPV infection were identified in the fixed smears. They were reported following the Bethesda System as normal or abnormal [**Error! Reference source not found.**, **Error! Reference source not found.**] for this study by an independent cytotechnologist.

VIA/VILLI test

A two-step approach was applied where Visual Inspection with Acetic Acid solution (VIA) was performed followed by Lugols iodine solution (VILLI) which are based on the colors taken up by the cervical transformation zone. The resulting acetowhitening was distinct as compared to the normal pinkish color of the surrounding normal squamous epithelium of the cervix (24). CIN+ lesions lack glycogen and appeared as well-defined, thick, mustard, or saffron yellow areas (2,3).

Ethical consideration

Ethical approval was sort from KEMRI Scientific and Ethics Review Unit (SERU) for ethical compliance. Further approvals were obtained from the respective county health management committees and facility managers. Informed consent was sought from all participants. Respondents did not identify themselves by names during the interviews to ensure anonymity and confidentiality. Individual consent was sought from all women who participated.

Statistical analysis

Statistical Package for the Social Sciences *7.0* for windows package program was used for data storage and statistical analysis. Categorical variables such as location, age, education, marital status, religion, income level, sex debut, parity, sexual partners, HPV prevalence, risky behavior, and infections were computed and presented as percentages. Pearson chi-square test was used to test the significant association between social-demographic and risk factors data with HPV and/or HIV infection. Logistic

regression analysis was used to compute any association between HPV screening and vaccination by KAPP and social-demographic factors by Odds ratios.

Results

i. Baseline socio-demographic characteristics and HPV prevalence

A total of 317 women (mean age: 34 years and 3 months, SD ±10.395) were recruited: Meru 81/317(25.6%), Tharaka-Nithi 31/317(9.8%), Kerugoya 56/317(17.6%), Embu 85/317(26.8%) and Isiolo 64/317(20.2%), aged ≤30 219/317(69.1%) and over 31 years 98/317(30.9%), respectively.

HPV prevalence was 26.5% (84/317); 10.8% (17/156) among HIV seropositive and 41.6% (67/161) among HIV seronegative women (p-value=<0.001). HPV was detected among 9.0 %(51/228) of married, 53.5%(16/30) of separated, 24.4%(10/41) of single, 16.7%(1/6) of widowed and 50%(6/120) of divorced (p-value=0.045). HPV infection was significantly associated with hormonal contraceptive use (p-value=0.037), number of sex-partners (p-value=0.039) history of recurrent warts infection (p-value=0.003), normal cytology (p-value=0.046) while 22.7%(72/77), abnormal cytology (p-value=<0.001) and VIA/VILLI test results (p-value=0.019) (Table 1).

ii. *Association of socio-demographic variables association with KAPP*

Twenty seven out of eighty five participants (OR:0.3CI:0.16-0.89) from Embu (p<0.005), 24/64 (OR:0.49,CI:0.20-1.17) from Isiolo, 25/56 (OR:0.66,CL: 0.27- 1.60) from Kirinyaga, 41/81(OR: 0.88CL: 0.36-1.93) from Meru and 17/31(OR: 1.02 CL: 0.66-1.58) from Tharaka-Nithi had knowledge on HPV screening. (OR: 1.00,CL:0.982-1.03) aged ≤30 (mean: 34.3 SD:10.4, range 1-8) p-value <0.005, 33/96(OR:3.74CI:0.11-1.10) with primary school education, 58/135(OR:0.24,CI:0.84-0.69), p-value=<0.005 with secondary school education and 30/67(OR:0.35,CI:0.12-0.97) p-value=<0.005 with college education had knowledge on HPV screening.

One hundred and ten out of two hundred and twenty five (OR:0.75,CL:0.59-0.97 Christians (p-value=<0.005) and 24/62(OR:0.83,CL:0.47-1.46) Muslims (p-value=<0.001) had knowledge on HPV screening whereas 110/225(OR:10.01,CI:6.5-15.4, Christians (p-value=<0.001) and 24/62(OR:0.53,CI:0.15-1.77 Muslims (p-value=<0.001) showed willingness towards the procedure. (OR: 1.94 CI: 1.69-2.22) participants across all parity had willingness towards HPV screening p-value<0.001, (OR 2.45, CI: 052.92) had history of ever being screened (p-value<0.001) while (OR: 0.74,CL:0.68-0.81) and perception on the importance of HPV screening (p-value=<0.001).

Sixty out of eighty five (OR:0.46,CL:0.16-1.33) from Embu, 48/64(OR:0.57,CL:0.190-1.75) from Isiolo, 40/56(OR:0.48,CL0.157-1.47) from Kirinyaga 62/81(OR:0.62,CL:0.12-1.86) from Meru and 26/31 (OR:0.62,CL:0.12-1.86) from Tharaka-Nithi had knowledge on HPV vaccination (p-value<0.005) (Table 2).

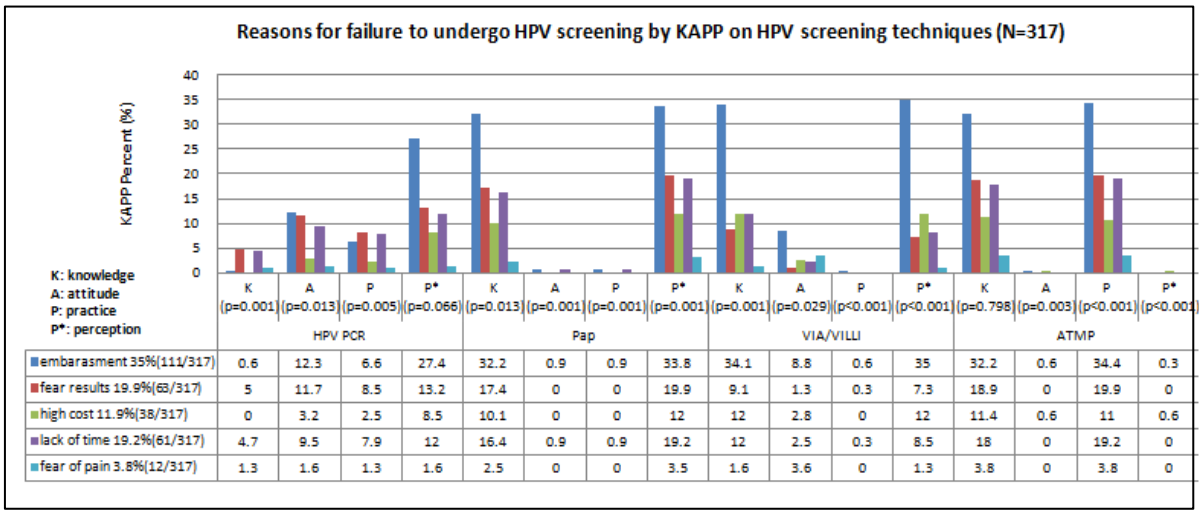
iii. *Association between socio-demographic factors with KAPP*

Knowledge on HPV screening was significantly associated with low (p<0.001), middle (p<0.001) and high (p<0.001) income status among HIV negative participants and residence (p<0.05), <30 years (p<0.05) and >30years (p<0.05) among HIV positive participants. History of HPV screening was significantly associated with primary (p<0.05), secondary school (p<0.05), college

(p<0.05), and university (p<0.05) level of education among HIV negative participants. Positive perception of HPV screening was significantly associated with hormonal contraceptives use p<0.05) and non-hormonal contraceptives use (p<0.05) among HIV positive participants. Participants; regardless of their HIV status who reported having a relative with a history of cervical disease were significantly associated with knowing (p<0.05) and perception on the importance (p<0.05) of HPV screening (Table 3).

iv. Reasons for failure to undertake HPV screening

Reasons for not screening for HPV included fear of embarrassment 111/317(35.0%), fear of results 63/317(19.9%), lack of time 61/317(19.2%), cost of the test 38/317(12.0%), and fear of pain 12/317(3.8%). There was a significant association between reasons expressed and knowledge (p=0.001), willingness (p=0.013), history of screening (p=0.005) and perception on the importance (p=0.066) of HPV DNA PCR; knowledge (p=0.013), attitude (p=0.001), history of screening (p=0.001) and perception on the importance (p=0.001) of Pap smear test (Figure 1).



	K (p=0.001)	A (p=0.013)	P (p=0.005)	P* (p=0.066)	K (p=0.013)	A (p=0.001)	P (p=0.001)	P* (p=0.001)	K (p=0.001)	A (p=0.029)	P (p<0.001)	P* (p<0.001)	K (p=0.798)	A (p=0.003)	P (p<0.001)	P* (p<0.001)
embarasment 35%(111/317)	0.6	12.3	6.6	27.4	32.2	0.9	0.9	33.8	34.1	8.8	0.6	35	32.2	0.6	34.4	0.3
fear results 19.9%(63/317)	5	11.7	8.5	13.2	17.4	0	0	19.9	9.1	1.3	0.3	7.3	18.9	0	19.9	0
high cost 11.9%(38/317)	0	3.2	2.5	8.5	10.1	0	0	12	12	2.8	0	12	11.4	0.6	11	0.6
lack of time 19.2%(61/317)	4.7	9.5	7.9	12	16.4	0.9	0.9	19.2	12	2.5	0.3	8.5	18	0	19.2	0
fear of pain 3.8%(12/317)	1.3	1.6	1.3	1.6	2.5	0	0	3.5	1.6	3.6	0	1.3	3.8	0	3.8	0

Figure 1: Reasons for Failure to Undertake HPV Screening and Associated KAPP

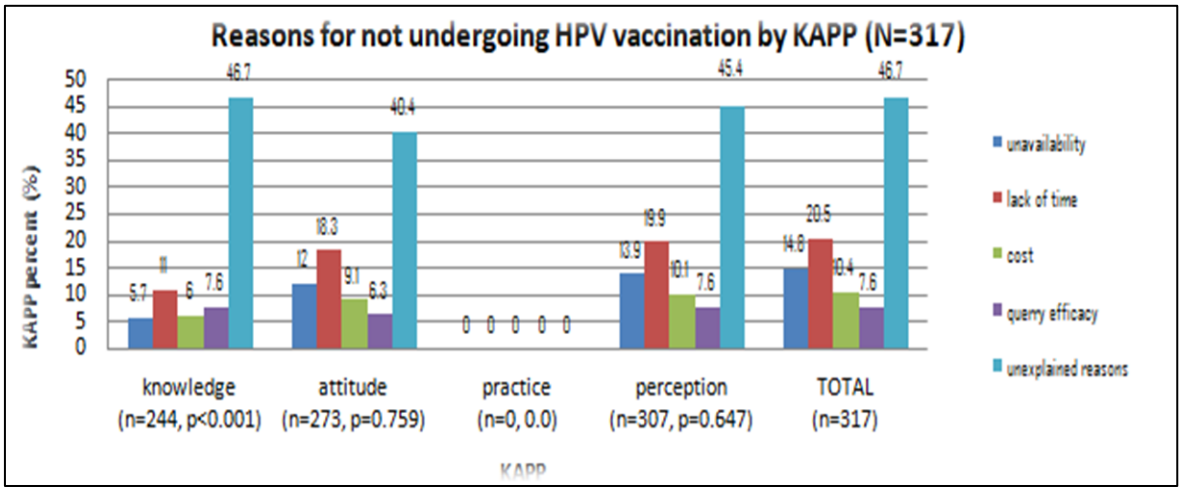


Figure 2: Reasons for not Undergoing HPV Vaccination by KAPP

Reasons for not undergoing HPV vaccination

Participants with knowledge on HPV vaccination 244/317(76.9%) expressed unavailability of the vaccine 18/317(5.7%), lack of time 35/317(11.0%), cost 19/317(6.0%) efficacy of the vaccine 24/317(7.6%), and unexplained reasons 148/317(46.7%) as reasons for not undergoing HPV vaccination ($p<0.001$). Those with the willingness to vaccinate against HPV 273/317(86.1%) expressed unavailability of the vaccine 38% (12.0%), lack of time 58/317(18.3%), cost 29/317(9.1%), vaccine efficacy 20/317(6.3%), and unexplained reasons 128/317(40.4%).

Participants with perception on the importance of HPV vaccination 307/317(96.8%) expressed unavailability of the vaccine (44/317(13.9%), lack of time 63/317(19.9%), cost (32/317(10.1%), the efficacy of the vaccine 24/317(7.6%) and unexplained reasons 144/317(45.4%) (Figure 2).

Discussion

This study established an HPV prevalence of 26.5% (84/317) among women aged between 15 to 46 years in Eastern Kenya; a high prevalence of41.6% (67/161) among HIV positive women and 10.8% (17/156) among HIV seronegative women. Our data, according to data of literature [21, 22, 23] showed a higher prevalence of HPV infection in HIV-seropositive (>70%)women compared to HIV-seronegative women (30.0%) across the residence, age, education level, religion, family planning methods, and sex partners. Kirinyaga County residents had the highest HPV prevalence (37.5%) despite the statistically significant perception of the importance, safety, and effectiveness of HPV screening.

The county of residence was a predicting factor for knowledge on HPV screening. Women in Tharaka Nithi County were highly likely to know about HPV screening and had lower HPV prevalence 16% (5/31) than other counties. The proportion of women in counties that were less likely to know the procedure (<0.50 Odds) and had higher HPV prevalence were Isiolo 26.6% (17/64) and Embu 23.5% (20/85).

Though women aged $\leq$30 years were highly probable to know about HPV screening, they reported low screening rate, low willingness to undergo screening, and low perception of the importance and effectiveness of the procedure. They, in turn, had a high HPV-HIV co-infection prevalence rate (80.4%). HPV penetration into the target cell, replication, and escape from host immune defenses are favored by HIV infection [21, 24].

This study established high proportions of women in Eastern Kenya had a secondary school and college education but did not have knowledge on HPV screening. Despite high educational attainment, they also did not undergo HPV screening and lacked the perception of the importance of the procedure. This can be attributed to the highest HPV (52.6%) and HPV-HIV (90.0%) co-infection rate by a university education. Women with low education levels were more likely to undergo HPV screening than those with higher educational attainment.

Most participants were Christians. Religion influenced KAPP on HPV screening. Muslim women had less knowledge, lower willingness, less likely to be screened and lower perception on the benefit of HPV screening than Christians. They had higher HPV prevalence (30.6% vs. 25.5%) and higher HPV prevalence among HIV negative women (26.3% vs. 18.5%) than Christians.

Many women who reported to be using non-hormonal contraceptives had knowledge of HPV screening, showed more

willingness, and were highly likely to undertake the procedure than those who used hormonal contraceptives. HPV infection and the choice of family planning method were significantly associated (p=0.037) as well as HIV serostatus (p=0.009). Hormonal contraceptives have been postulated to be one mechanism by which HPV exerts its tumorigenic effect on cervical tissue. Steroids bind to specific DNA sequences within transcriptional regulatory regions on the HPV DNA, either to increase or suppress the transcription of various genes [24].

Having multiple sex-partners was significantly associated with HPV infection (p=0.039) but did not influence KAPP on HPV screening. Women with more than one sex partner had higher HPV prevalence (32%) than those with one (22%). Both groups were equally likely to undergo HPV screening and equally had a perception of the importance of the procedure.

Over 75% of the participants reported having suffered herpes, warts, and recurrent UTI which are predictor diseases to risk developing persistent HPV infection that progress to cervical cancer. These diseases were more common among HIV positive (>80%) than HIV negative (<19%) participants. Complex interactions between pathogens have been described in many studies [10, 24]. HPV screening results by HPV DNA PCR was significantly associated (p<0.001) with other HPV screening methods results; pap smear and VIA/VILLI confirming the specificity of the procedures.

Willingness to screen for HPV was high among HIV positive women as compared to HIV negative. This study further established that HIV positive women had less perception of the benefit of HPV screening and did not screen by either technique during routine HIV check-up clinics. The Kenyan government aims to integrate infectious agents screening into HIV, Maternal, Neonatal and Child Health (MNCH), Reproductive Health (RH), and family planning programs in the 2017-2022 National Cancer Control Strategy that would, in turn, benefit them [3].

Embarrassment, fear of results, and lack of time were significant reasons for failure to undergo HPV screening despite KAPP on the procedures. The majority of participants had knowledge and perception on the importance of Pap smear test but poor attitude and less screening practices. Age and sex differences between the screening personnel and women who may require HPV screening could have been the cause of embarrassment. In a study conducted in western Kenya, 94%of women had never done HPV screening and cited barriers such as fear of results, lack of time, and knowledge. The main reason was given for failure to do HPV screening in a Zimbabwean study [28] and Cambodia [27] was low knowledge about the test. Other barriers have been documented for failure to screen [22, 23, 24, 24, 25, and 26].

This study established that no participant had ever been vaccinated against HPV despite knowledge and acceptability. This study concurs with Vermandere *et al.*, 2003, that HPV vaccine acceptability was not a strong predictor of vaccine uptake. HPV vaccination may not be affordable and also available to most women in developing countries (8, 9). In eastern Kenya, the HPV vaccine costs $25 in private health facilities.

Most participants were unable to give a specific reason for failure to undergo HPV vaccination though some cited lack of time, cost of the vaccine, and unavailability of the vaccine in their respective health facilities upon visit.

Conclusions

Knowledge, willingness, and perceiving HPV screening as important as well as willingness to vaccinate against HPV

may reduce HPV infections among women seeking reproductive health services in Eastern Kenya.

Acknowledgment

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Access to data

The datasets and questionnaires used in the study can be provided by the corresponding author upon request.

Authors' contributions

NJK, MWM, LK, JM, and RL designed the study. NJK conducted the survey, analyzed and interpreted the data, and wrote the main manuscript text. All authors reviewed the final manuscript.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflicting interests.

Abbreviations

CI: Confidence Interval;
HPV: KAP: Knowledge, Attitudes, Practices, And Perception;
KEMRI: Kenya Medical Research Institute;
NACOSTI: National Council For Science, Technology, And Innovations;
NRF: National Research Fund;
OR: Odds Ratio;
Pap: Papanicolaou

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Appendix

Table 1: Baseline Information, HPV Prevalence among HIV Serostatus

Variables	**category**	**N (%)**	**HPV Positive (n=84)**	***p-value***	**HIV negative N = 156 (n) %**	**HIV positive, N = 161 (n)%**	***p-value***
Location (county)	Meru	81(25.6)	21(25.9)		3(14.3)	18(85.7)	
	T. Nithi	31(9.8)	5(16.1)		0(0)	5(100)	
	Kirinyaga	56(17.6)	21(37.5)		4(19.0)	17(81.0)	
	Embu	85(26.8)	20(23.5)		5(25.0)	15(75.0)	
	Isiolo	64(20.2)	17(26.6)	*0.232*	5(29.4)	12(70.6)	*0.572*
Age	≤30	219(69.1)	56(25.6)		11(19.6)	45(80.4)	
	>30	98(30.8)	28(28.6)	*0.584*	6(21.4)	22(78.6)	*0.848*
Education level	Primary	96(30.3)	23(24.0)		6 (26.1)	17 (73.9)	
	Secondary	135(42.6)	34(25.2)		6 (17.6)	28 (82.4)	
	College	67(21.1)	17(25.4)		4 (23.5)	13 (76.5)	
	university	19(6)	10(52.6)	*0.067*	1 (10.0)	9 (90.0)	*0.707*
Marital status	Married	228(71.9)	51(39.0)		13 (25.5)	38 (74.5)	
	separated	30(9.5)	16(53.5)		2 (12.5)	14(87.5)	
	Single	41(12.9)	10(24.4)		2(20.0)	8(80.0)	
	Divorced	12(3.8)	6(50.0)	*0.045*	0 (0.0)	6 (1.67)	*0.518*
Religion	Christian	255(80.4)	65(25.5)		12 (18.5)	53 (81.5)	
	Muslim	62(19.6)	19(30.6)	*0.409*	5 (26.3)	14 (73.7)	*0.454*
Income level	Low	208(65.6)	53(25.5)		10(18.9)	43(81.1)	
	Medium	95(30.0)	28(29.5)		5(17.9)	23(82.1)	
	High	14(4.4)	3(21.4)	*0.695*	2(66.7)	3(33.3)	*0.077*

Table 1: Baseline Information, HPV Prevalence among HIV Serostatus Continued

Variables	**category**	**N (%)**	**HPV Positive (n=84)**	***p-value***	**HIV negative N = 156 (n) %**	**HIV positive, N = 161 (n)%**	***p-value***
Sexual debut	15-20	32(10.1)	8(2.5)		1 (12.5)	7 (87.5)	
	21-25	237(74.8)	63(19.9)		13(20.6)	50 (79.4)	
	26-30	38(12)	9(2.8)		3(33.3)	6 (66.7)	
	31-35	10(3.2)	4(1.3)	*0.770*	0(0.0)	4 (100.0)	*0.518*
Parity	1	26(8.2)	8(30.8)		1(12.5)	7(39.5)	
	≥2	291(91.8)	76(26.1)	*0.607*	16(21.1)	60(78.9)	*0.252*
Contraceptive use	hormonal	222(70.1)	51(22.9)		8(24.2)	25(75.8)	
	other	95(29.9)	33(34.7)	*0.037*	9(17.6)	42(82.4)	*0.009*
Sex partners	1	186(59.3)	41(22.0)		10(24.4)	31(75.6)	
	≥2	131(40.7)	43(32.0)	*0.039*	7(16.3)	36(83.7)	*0.680*
Risky behaviors and infections	smoking	5(1.6)	2(40.0)	*0.490*	1 (50.0)	1 (50.0)	*0.289*
	herpes	309(97.5)	82(25.5)	*0.923*	15(18.3)	67(81.7)	*0.004*
	warts	250(78.9)	56(22.4)	*0.003*	10(17.9)	46(82.1)	*0.442*
	UTI	243(76.7)	53(21.8)	*<0.001*	7(13.2)	46(86.8)	*0.036*
	TB	*6(1.8)*	5(83.3)	*<0.001*	4(80.0)	1(20.0)	*0.046*
HIV	negative	156(49.2)	17(10.8)		139(43.8)	17(5.4)	
	positive	161(50.8)	67(41.6)	*<0.001*	94(29.7)	67(21.1)	*<0.001*
Pap smear test	normal	240(75.7)	12(5.0)		5(41.7)	7(58.3)	
	abnormal	77(24.3)	72(22.7)	*<0.001*	12(16.7)	60(83.3)	*0.046*
VIA/VILLI test	normal	236(74.4)	57(24.1)		10(17.5)	*47(82.5)*	
	abnormal	81(25.6)	27(33.3)	*<0.001*	7(25.9)	*20(74.1)*	*0.019*
Total		317(100.0)	84(26.5)		233(73.5)	84(26.5)	*<0.001*

Table 2: Association of Social-Demographic Variables with KAPP on HPV Screening and HPV Vaccination

Characteristics	Category	N (%)	KAPP on HPV screening OR (95% CI) p-value			
			Knowledge	Attitude	Practice	Perception
Facility	Embu	85	0.38(0.12-0.9) *	0.37(0.44-3.15)	0.59 (0.15-2.24)	1.60(0.54-4.71)
	Isiolo	64	0.49(0.20-1.17)	0.68(0.68-6.79)	0.87(0.21-3.63)	1.88(0.62-5.68)
	Kirinyaga	56	0.66(0.27-1.60)	0.20(0.24-1.68)	1.39(0.29-6.66)	3.12(1.03-9.36) *
	Meru	81	0.88(0.36-1.93)	0.35(0.42-2.98)	1.13(0.27-4.68)	1.82(0.61-5.35)
	Tharaka Nithi	31	1.02(0.66-1.58)	2.7(0.32-22.81)	1.68(0.45-6.36)	0.55(0.22-1.36)
Age M:34.3 SD:10.4	≤30	219	1.57(0.9-2.54)**	0.810(0.3-1.99)	0.92(0.42-2.01)	0.78(0.46-1.30)
	>30	98	0.63(0.39-1.02)	1.23(0.50-3.04)	1.08(0.49-2.36)	1.28(0.77-2.15)
Education	primary	96	3.74(0.11-1.10)	0.1(0.0-0.0)	2.51(0.38-16.24)	0.31(0.11-0.9)**
	secondary	135	0.24(0.84-0.69)*	0.1(0.0-0.0)	0.58(0.12-2.80)	0.28(0.10-0.8)**
	college	67	0.35(0.12-0.97)*	0.1(0.0-0.0)	1.10(0.29-5.32)	0.303(0.1-0.8)**
Marital status	Married	226	0.05(0.01-0.43)*	1.05(0.12-8.6)	0.80(0.09-6.50)	0.43(0.15-1.16)
	Separated	32	0.08(0.09-0.69)*	0.87(0.82-9.4)	0.63(0.64-6.34)	1.34(0.67-2.69)
	single	41	0.09(0.01-0.73)*	1.15(0.1-12.20)	0.06(0.7-6.21)	1.16(0.21-6.49)
	divorced	6	0.09(0.007-1.2)*	0.45(0.23-8.8)	0.45(0.2-8.82)	0.46(0.99-2.18)
	widowed	12	0.91(0.01-1.22)*	0.95(0.15-7.79)	0.45(0.23-8.82)	2.50(0.25-24-37)
Religion	Christians	225	0.75(0.59-0.97)*	10(6.5-15.4)**	7.5(5.12-10.9)**	8.1(5.47-12.0)**
	Islam	62	0.83(0.5-1.46)**	0.53(0.2-1.8)**	0.52(0.17-1.5)**	0.41(0.2-0.72)**
F.P	hormonal	222	0.57(0.35-0.95)*	0.94(0.39-2.25)	0.71(0.40--1.86)	1.13(0.67-1.91)
	other	95	1.74(1.05-2.88)*	1.05(0.44-2.52)	1.15(0.53-2.47)	0.88(0.52-1.49)
sex partners	1	186	1.27(0.55-2.77)	1.23(0.73-5.04)	0.75(0.35-1.57)	0.94(0.57-1.53)
	≥2	131	0.56(0.49-1.22)	2.32(0.55-2.77)	0.75(0.35-1.58)	0.94(0.57-1.53)

Table 2: Association of Social-Demographic Variables with KAPP on HPV Screening and HPV Vaccination Continued

Characteristics	Category		N (%)	KAPP on HPV screening OR (95% CI) p-value		
			Knowledge	Attitude	Practice	Perception
Parity	M: 2 SD: 1		0.93(0.86-1.00)	1.94(1.7-2.2)**	2.45(2.052.92)**	0.74(0.68-0.8)**
KAPP on HPV vaccination						
Facility	Embu	85	0.46(0.16-1.33)	0.76(0.27-2.29)	-	0.67(0.73-6.28)
	Isiolo	64	0.57(0.190-1.75)	2.88(0.7-11.61)	-	2.10(0.13-34.73)
	Kirinyaga	56	0.48(0.157-1.47)	1.34(0.39-4.66)	-	1.83(0.11-30.37)
	Meru	81	0.62(0.12-1.7)**	1.22(0.39-3.86)	-	0.867(0.87-8.66)
	(Parity)		1.09(0.818-1.47)	0.54(0.2-0.9)**		0.68(0.42-0.88)*
Age	18-47	49	1.00(0.98-1.1)**	0.99(0.97-1.03)	-	0.94(0.89-1.01)*
Education	primary	96	0.41(0.11-1.56)	0.47(0.55-4.13)	-	0.36(0.22-61.54)
	secondary	135	0.67(0.18-2.52)	0.30(0.04-2.42)	-	1.27(0.13-12.11)
	college	67	0.51 (0.14-1.87)	0.030(0.4-2.38)	-	1.82(0.19-17.19)
F.P.	hormonal	236	0.64(0.37-1.08)	0.98(0.50-2.02)	-	0.045(0.07-0.9)*
	Non-hormonal	81	0.93(0.93-2.69)	0.99(0.49-1.99)		0.26(0.74-0.97)*
Parity	M: 2 SD: 1.		1.41(1.28-1.5)**	1.72(1.5-1.9)**	-	3.27(2.6-4.17)**

FP- family planning, *p=<0.05, **p=<0.0001, M: Mean, SD: Standard deviation, - no data available; not vaccinated.

Table 3: Association between Social-Demographic Factors, KAPP on HPV Screening and HIV-Serostatus.

	KAPP on HPV Screening							
	HIV Negative				HIV Positive			
Description	K	A	P	Pr	K	A	P	Pr
Location								
Embu	11(15.7)	37(25.9)	5(29.4)	32(23.7)	16(25.0)*	41(27.7)	36(25.0)	37(26.8)
Isiolo	14(20.0)	36(25.2)	34(24.5)	35(25.9)	10(15.6)*	25(16.9)	23(16.0)	22(15.9)
Kirinyaga	10(14.3)	20(14.0)	20(14.4)	19(14.1)	15(23.4)*	28(18.9)	32(22.2)	27(19.6)
Meru	25(35.7)	36(25.2)	36(25.9)	35(25.9)	16(25.0)*	38(25.7)	38(26.4)	37(26.8)
T. Nithi	10(14.3)	14(9.8)	13(9.4)	14(10.4)	7(10.9)*	16(10.8)	15(10.4)	15(10.9)
Age								
≤30	44(62.9)	94(65.7)	13(76.5)	87(64.4)	41(64.1)*	106(71.6)	105(72.9)	99(71.7)
>30	26(73.1)	49(34.5)	4(23.5)	48(35.6)	23(35.9)*	42(28.4)	39(27.1)	39(28.3)
Education								
Primary	15(21.4)	41(28.7)	10(58.8)*	40(29.6)	18(28.1)	46(31.1)	6(11.3)	42(30.4)
Secondary	36(51.4)	64(44.8)	6(35.3)*	59(43.7)	22(34.4)	61(41.2)	7(41.2)	57(41.3)
College	14(20.0)	32(22.4)	0(0)*	30(22.2)	16(25.0)	28(18.9)	3(17.6)	27(19.6)
University	5(7.1)	6(4.2)	1(5.9)*	6(4.4)	8(12.5)	13(8.8)	1(5.9)	12(8.7)

Table 3: Association between Social-Demographic Factors, KAPP on HPV Screening and HIV-Serostatus **Continued**

	KAPP on HPV Screening							
	HIV Negative				HIV Positive			
Description	**K**	**A**	**P**	**Pr**	**K**	**A**	**P**	**Pr**
Religion								
Christian	57(81.4)	106(74.1)	15(88.2)	99(73.3)	53(82.8)	126(92.0)	122(84.7)	20(87.0)
Islam	13(18.6)	37(25.9)	2(11.8)	36(26.7)	11(17.2)	22(14.9)	22(15.3)	3(13.0)
Income level								
Low	40(57.1)*	96(67.1)	9(52.9)	91(67.4)	36(56.2)	95(64.2)	91(63.2)	87(63.0)
Middle	28(40.0)*	42(29.4)	8(47.1)	40(29.6)	24(37.5)	45(30.5)	44(30.6)	43(31.2)
high	2(2.9)*	5(3.5)	0(0)	4(3.0)	4(6.2)	8(5.4)	9(6.2)	8(5.8)
Family planning methods								
contraceptive	17(24.3)	95(66.4)	7(41.2)	42(31.1)	50(41.7)	110(91.7)	13(76.5)	34(24.6)*
other	53(75.7)	48(90.6)	10(58.8)	93(68.9)	14(21.9)	38(25.7)	4(9.8)	104(75.4)*
Relative history of tumor/cancer								
No	0(0)*	9(69.2)**	8(47.1)	50(37)**	5(7.8)**	68(45.9)	10(58.8)	60(43.5)*
Yes	70(100.)*	4(30.8)*	9(9.9)	85(63.)*	59(92.2)*	80(45.9)	7(41.2)	78(56.5)*

FP- family planning, *p=<0.05, **p=<0.001, M: Mean, SD: Standard deviation, - no data available; not vaccinated