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A pilot study for high-risk HPV genotypes in Liberia: A post conflict country endemic for urogenital schistosomiasis

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A pilot study for high-risk HPV genotypes in Liberia: A post conflict country endemic for urogenital schistosomiasis.

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Abstract

Background

Cervical cancer remains a leading cause of female cancer mortality in Liberia and sub-Saharan Africa, with high-risk human papillomavirus (hr-HPV) infection as the primary driver. The continent has the highest incidence and mortality rate globally with Liberia ranking amongst the top 20 countries with the highest burden of cervical cancer. Urogenital schistosomiasis (UGS), including female genital schistosomiasis (FGS), is highly prevalent in many HPV-endemic settings and has been hypothesized to increase susceptibility to HPV infection through genital mucosal damage and immune modulation, however co-infection data are limited especially in west Africa. This study assessed HPV prevalence and its association with UGS/FGS in schistosomiasis endemic populations in Liberia. As most cases of cervical cancer and precancerous cervical lesions are attributable to hr-HPV (High Risk-HPV) types 16 and 18 globally, these high-risk HPV genotypes were the primary targets of the study.

Methods

A cross-sectional pilot study was conducted in four rural counties (Nimba, Maryland, Bong, and Lofa) in Liberia. Women aged 18-45 were recruited via community health centres, excluding pregnant or menstruating participants. Sociodemographic and clinical data were collected using a structured questionnaire. Urine samples were tested for S. *haematobium* via microscopy and qPCR. Cervical and vaginal swabs were collected to detect hr-HPV 16/18 DNA and participants were examined for FGS lesions. Laboratory analyses were performed at the Liverpool School of Tropical Medicine.

Results

Among 298 women, 22 tested positive for hr-HPV (7.38%; 95% CI: 4.93–10.92), including two cases of hr-HPV–UGS co-infection (0.67%; 95% CI: 0.18–2.41) detected in Nimba and Bong County. hr-HPV prevalence was highest in Nimba (13/79) (16.46%;95% CI: 9.88 - 26.15) and Bong (6/75) (8.00%;95% CI: 3.72 - 16.37),UGS prevalence was identical to hr-HPV prevalence amongst participants 22/298 7.4% (95% CI: 4.9-10.9) HPV18 infections outnumbered HPV16, largely driven by cases in Nimba (15/22) 65.2% (95% CI 44.9-81.2) .

Conclusion

High-risk HPV is present across all counties endemic for urogenital schistosomiasis in Liberia. The distribution of hr-HPV prevalence closely reflects the pattern of UGS prevalence across counties, with concentration in Nimba and Bong, while hr-HPV–UGS co-infection is rare. These findings highlight the need for targeted screening, public awareness campaigns, and expanded HPV vaccination to reduce cervical cancer burden in Liberia. Integration of cervical cancer, sexually transmitted infection, and schistosomiasis programs may improve early detection and prevention.

Introduction

Cervical cancer continues to represent a substantial and inequitable burden of cancer-related mortality among women, disproportionately affecting low- and middle-income countries. Although the disease is largely preventable, approximately 662,044 new cases and 348,709 deaths were estimated globally in 2022 (1). In Liberia, cervical cancer remains a leading cause of female cancer mortality (2). In 2023, an estimated 717 new cases were reported, corresponding to an age-standardised incidence rate of 39.6 per 100,000 women. In the same year, 478 deaths occurred, yielding an age-standardised mortality rate of 28.3 per 100,000 women, among the highest reported worldwide (3). Without effective and sustained interventions, projections indicate that 60,212 women in Liberia will die from cervical cancer between 2020 and 2070 (3). In recognition of this preventable burden, all 194 Member States of the World Health Assembly, including Liberia, adopted the global strategy in 2020 to eliminate cervical cancer as a public health problem (3). This commitment underscores the urgent need to scale up equitable access to prevention, screening, and treatment services in high-burden settings.

High-risk human papillomavirus (hr-HPV) infection is responsible for nearly all cervical cancer cases. HPV16 accounts for 40–50% of cervical cancers, while HPV18 contributes to approximately 4% of cases. Lifetime infection with HPV in general occurs in an estimated 70% of women, decreasing to 48% among women who have had only a single sexual partner (4). Although genital HPV infection is the primary driver of cervical cancer, it is not the sole mechanism underlying disease progression. Additional risk factors include long-term use of oral contraceptives, tobacco smoking, persistent HPV infection, and co-infection with other sexually transmitted infections, including HIV, all of which increase the likelihood of cervical cancer development (4).

Situation Analysis of HPV and Cervical Cancer in Liberia

A situational assessment conducted at the Oncology Unit at Liberia's referral hospital, John F. Kennedy (JFK) for the purpose of this study, indicates that HPV infection remains a significant public health concern in Liberia, with cervical cancer representing the most common malignancy among women. The disease is most frequently diagnosed in women aged 40-55 years, although the oncology unit has witnessed a rise in cases in women in their 30s. While HPV is believed to be prevalent, national epidemiological data remain limited.

Although cervical cancer screening services are available, uptake is constrained by low awareness, financial barriers, shortages of trained personnel, limited screening infrastructure, and sociocultural stigma. Rural populations are disproportionately affected due to limited decentralization of services.

Radiotherapy services are currently unavailable in Liberia, limiting cervical cancer treatment primarily to chemotherapy and surgery. Access to these services is further constrained, as facilities capable of providing cancer treatment are largely centralized in Monrovia. Immunotherapy options for advanced-stage disease are not readily accessible.

In the absence of radiotherapy and other advanced treatments, patients who have the capacity may seek care abroad. Although a small proportion of patients may pursue treatment abroad, limited financial resources compel many to rely solely on palliative care. These systemic resource limitations contribute to delays in diagnosis and treatment, interruptions in care, and suboptimal clinical outcomes.

HPV vaccination has been available in Liberia since 2019. In November 2025, a national campaign vaccinated approximately 665,958 girls aged 9 -18 years. However, vaccine uptake continues to be challenged by misinformation, particularly concerns regarding infertility, as well as broader cultural barriers. Boys are not currently included in the vaccination program (Ministry of Health Liberia, 2026). Strengthening vaccination coverage and expanding screening services will be critical to reducing the future burden of cervical cancer in Liberia.

Urogenital Schistosomiasis, Cervical Pathology, FGS and Cervical Cancer

Mature haematobium worms can persist for many years within the pelvic venous plexus of the human host where hundreds of eggs can be produced each day (Fig.1a). Proteolytic enzymes are secreted by the miracidium inside the egg. This enables the egg to penetrate the vessel wall and migrate through adjacent tissues toward the mucosal surface of the urogenital tract. Although a proportion of eggs are successfully expelled in urine or genital secretions, many become lodged within urogenital tissues. Retained eggs provoke sustained inflammatory and granulomatous responses, leading to both acute and chronic tissue pathology (5). Prolonged tissue damage in women eventually results in FGS (fig.1b) characterized by mucosal damage, genital lesions, immune alterations, and epithelial barrier compromise.

Schistosoma *haematobium* infection may compromise antiviral defence mechanisms within the female genital mucosa by altering local immune responses. Through its effects on genital mucosal immunity, S. *haematobium* infection may facilitate the persistence of high-risk human papillomavirus (hr-HPV). Persistent cervical HPV infection develops in approximately 10–20% of women following initial acquisition and is implicated in nearly all cases of cervical cancer (Fig.1c) (6).

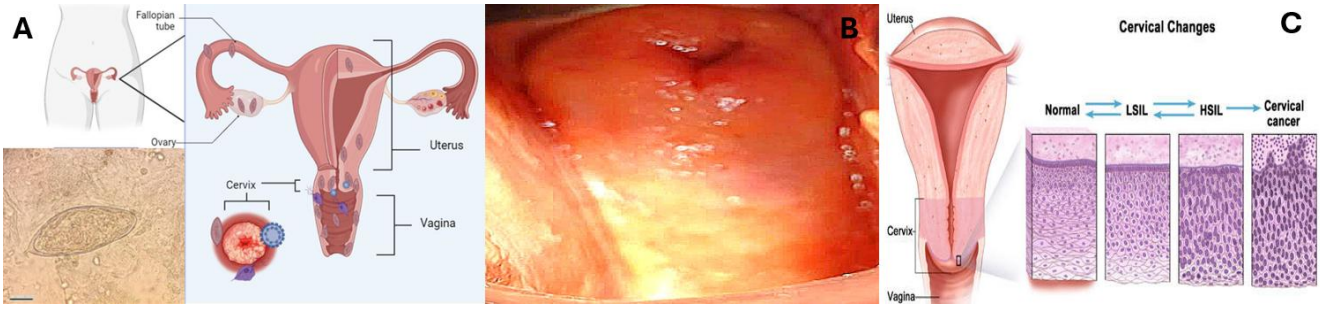


Figure 1: (A) Urogenital infection by S.*haematobium* (UGS). Adapted from Stothard *et al* (7). **(B)** A participant in Liberia positive for UGS who had also developed FGS characterized by yellow sandy patches, mucosal damage and lesions. Adapted from Bell-Gam Woto *et al* **(C)** Shows the progression of healthy cervical cells to cancer Adapted from The National Cancer Institute (8). It shows a state of hyperplasia (an increase of healthy cells to dysplasia where there is an increase in abnormal cells. LSIL (Low-grade Squamous Intraepithelial Lesion) which is equivalent to mild dysplasia or (CIN 1) may progress to HSIL (High-grade Squamous Intraepithelial Lesion) Includes moderate dysplasia (CIN 2). Severe Dysplasia/Carcinoma in situ (CIN3) can be considered a very early stage of cancer. At this stage the cancer is not invasive. It may take years for the cancerous cells of the cervix to grow into deeper surrounding tissue where the cancer is considered invasive (9).

Molecular Mechanism of Disease

Cervical cancer progression results from dysregulation of the cell cycle following infection with high-risk human papillomavirus (hr-HPV). hr-HPV promotes inappropriate entry into the S phase of the cell cycle within the upper epithelial layers. The viral E7 oncoprotein drives this process by disrupting normal cell-cycle checkpoints, allowing proliferation to proceed independently of external growth signals. Under physiological conditions, p14^ARF regulates the activity of MDM2 (mouse double minute 2), an E3 ubiquitin ligase responsible for controlling p53 protein levels. MDM2 maintains p53 at concentrations below the threshold required to trigger cell-cycle arrest or apoptosis. In hr-HPV infection, disruption of the p16-mediated feedback pathway leads to altered p14^ARF expression, interfering with MDM2 function and destabilizing normal p53 regulation. Collectively, these molecular alterations impair apoptosis and promote uncontrolled cellular proliferation, contributing to cervical carcinogenesis (10).

Gap and Rationale

A five-year follow-up study was conducted among women previously enrolled in a genital schistosomiasis cohort in rural Zimbabwe. Women who tested positive for high-risk HPV at baseline were re-invited after five years for assessment of cervical cell atypia, genital schistosomiasis, and high-risk HPV status. The study aimed to evaluate whether longstanding Schistosoma haematobium infection influenced HPV persistence and progression to cervical epithelial abnormalities. Among the 37 women re-examined, genital schistosomiasis of at least five years' duration was associated with the development of high-grade squamous intraepithelial neoplasia, but not with persistent high-risk HPV infection (11). A cross-sectional study community-based study in Zambia recruited sexually active women aged 15–50 years who were not menstruating or pregnant and collected two cervicovaginal self-swabs and a urine sample during home visits by community health workers. Samples were tested for 14 high-risk HPV genotypes using GeneXpert and for Schistosoma DNA using ITS-2 qPCR. This study identified a weak association between molecularly defined FGS and high-risk HPV (12), further supporting a potential link between schistosomiasis and hr-HPV infection in sub-Saharan Africa. Overall studies on hr-HPV and UGS association with links to cervical cancer has been limited and produced mixed conclusions making it difficult to confirm an association (13).

Previously methodologies used to estimate the burden of HPV infection in Liberia were largely derived from systematic reviews and meta-analyses of published literature. However, given the inherent limitations of HPV DNA detection techniques and variations in study design, these estimates should be interpreted with caution and considered indicative rather than definitive measures of population level burden. To date, there are no published data on crude age-specific HPV prevalence and corresponding 95% confidence intervals among women with normal cervical cytology in Liberia. Similarly, HPV prevalence stratified by study among women with normal cytology has not been reported in this setting (14). This pilot study represents the first effort to generate such baseline epidemiological data for Liberia.

In a setting of high schistosomiasis endemicity such as Liberia (15), chronic schistosome infection may alter genital mucosal immunity and thereby modify the risk of HPV persistence and progression which

is a major cause of cervical cancer. Epidemiological data on HPV prevalence and genotype along with associations with urogenital schistosomiasis provides vital data for this post conflict nation.

Study Objectives

The primary objective of this plot study is to estimate prevalence and distribution of high-risk HPV genotypes HPV 16 and HPV 18. within counties endemic for Schistosoma *haematobium* in Liberia. In addition, to assess possible associations between urogenital schistosomiasis and high-risk HPV infection.

Methods

This was a cross-sectional pilot study conducted to determine the prevalence of high-risk HPV 16 and 18 in Liberia targeting counties endemic for S. *haematobium*. The counties and location of study sites were as follow; Nimba (Duo district), Bong (Panta Kpaii district), Lofa (Foya district) and Maryland (Barrobo Farjah district) all located in rural parts of Liberia (15). Community health care centres were allocated for women from nearby villages to participate in the study. Women aged 18 – 45 were the target group. Due to the invasive nature of the clinical examination pregnant women and menstruating women were excluded from the study. 289 women participated in the study. The CHAs (County Health Assistants) played a key role in ensuring that all participants understood the nature of the study and what was required from the participant before they signed a consent form. CHAs explained the study in local vernacular where appropriate and where a participant was illiterate a thumb print was required on their consent form prior to enrolment. Informed consent was obtained from all participants prior to their participation in the study. All participants had the right to withdraw from the study at any point in time.

Data Collection

Each participant was given a questionnaire (an FGS symptom and risk factor check) (16). This questionnaire which had public health and environment risk factors for FGS as well as questions on clinical symptoms and indicators was used to assess women who may be at risk of FGS but also used to help identify women who may be presenting with other gynaecological conditions such as cervical cancer. Clinical symptoms such as unusual vaginal bleeding (after sex, between periods,), changes in discharge, pain during sex or in the pelvis are symptoms indicative of both FGS and cervical cancer. STI's (sexually transmitted Infections) may also cause these same clinical symptoms in women. Sociodemographic aspects such as age, occupation, sexual history, contraceptive use, prior screening history, and schistosomiasis exposure was noted for each participant. Sample Collection

Urine was collected from each participant and initially assessed for the presence of S.*haematobium* via microscopy, sediments from urine was later analysed using qPCR for the presence of S.*haematobium* DNA. Each participant received a gynaecological examination with a speculum conducted by a midwife. The midwife examined the cervix of each participant noting the presence of any typical FGS lesions or cervical dysplasia. A cervical/vaginal swab was obtained from each participant to be

examined for high-risk HPV 16 and 18 DNA. The swabs were stored in Copan Universal Transport Medium (UTM) and shipped to The Liverpool School of Tropical Medicine for molecular analysis.

Laboratory Procedures

HPV DNA Extraction

DNA was extracted using the QIAamp DNA Mini Blood and Tissue Kit (Qiagen, Manchester UK) according to the manufacturer's instructions, with the inclusion of an additional bead-beating step to step for the mechanical disruption of co-infected *Schistosom* sp. eggs. Briefly, prior to incubation with ATL buffer and Proteinase K, each sample was subjected to mechanical disruption using a Magnalyser (Roche) for 30 s at 3000 rpm in the presence of 0.5 g of 1.4-mm ceramic beads. Phocine herpesvirus (PhHV) was included as an internal DNA-extraction control. A blank sample tube was included to act as a negative extraction control alongside samples during each extraction batch to assess potential contamination.

HPV Genotype and Schistosome sp. analysis.

Real time PCR (rt-PCR) assays were performed using Type-it HRM PCR Kit (Qiagen, Manchester, UK). Briefly reaction conditions were as follows: initial denaturation at 95 ºC for five minutes followed by 40 cycles of 95 ºC for 10 seconds, 60 ºC for 30 seconds and 72 ºC for 30 seconds followed by a melt step from 70 ºC to 95 ºC at 0.1 ºC/second. The 12 µL reaction consisted of 6µL of Type-it HRM mix, 2 µL of template and a concentration of 200 nM for both pairs of primers targeting HPV 16 and HPV 18 (Table 1), with the remaining volume made up with nuclease free water. Samples were analysed using the MIC real-time PCR cycler in combination with the Myra liquid handling system from Bio Molecular Systems (BMS). The PCR products produced by the type-specific primers (HPV 16 and HPV 18) specific melt-peaks with the HPV 16 product producing a peak at ~80.5 ºC and HPV 18 producing a peak at ~77.7 ºC

Schistosomiasis testing and microscopy was conducted as per the protocol outlined by (Cunningham et al., 2024) and (Ayesha Bell-Gam Woto *et al* 2025)

Table 1. Primers used for (HR-HPV) qPCR

Target sp.	Primer name	Primer sequence	Primer Tm (°C)	Product size (bp)	molecular target
HPV 16	Primer E7 F	5'-TCA GAG GAG GAG GAT GAA ATAGA-3'	80.1	111 bp	E7 gene
	Primer E7 R	5'-GCA CAA CCG AAG CGT AGA -3'	80.6		
HPV 18	Primer E6 F	5'-ACC CTA CAA GCT ACC TGA TCT-3'	77.3	100 pb	E6 gene
	Primer E6 R	5'-ACC TCT GTA AGT TCC AAT ACT GTC -3'	77.9		

Statistical Analysis

Analyses were conducted at the county level and designed to estimate prevalence rather than model individual-level risk. For each outcome, proportions (x/n) were calculated and uncertainty quantified using binomial 95% confidence intervals. The Wilson score interval was used as the primary method because it performs well with small sample sizes and proportions near zero. Clopper-Pearson (exact) intervals were additionally calculated as a sensitivity analysis, particularly for the co-infection outcome.

To explore whether counties with higher HPV burden also exhibited higher UGS burden, Spearman's rank correlation was applied to county-level HPV-positive counts and UGS counts. This nonparametric approach was selected due to the small number of counties and its lack of reliance on normality assumptions. Odds ratios and inferential tests such as chi-square or Fisher's exact tests were not performed, as the analysis was not intended to assess individual-level associations between HPV and UGS. Analyses were performed in R (v4.4.3) (2025-02-28).

Results

Among 298 women recruited from four counties Nimba (n=79), Maryland (n=72), Bong (n=75), and Lofa (n=72) a total of 22 tested positive for hr-HPV, including 2 cases of hr-HPV and urogenital schistosomiasis (UGS) co-infection. The overall HPV prevalence was 7.38% (95% CI: 4.93-10.92,) (Table 2), while the prevalence of HPV–UGS co-infection was 0.67% (95% CI: 0.18-2.41) (Table 3). County-level

analysis showed the highest HPV prevalence in Nimba (13/79) 16.46% (95% CI: 9.88 - 26.15), followed by Bong (6/75) 8.00% (95% CI: 3.72 - 16.37). Co-infections were rare and detected only in Nimba (1 case) and Bong (1 case), with none identified in Maryland or Lofa. Overall, HPV18 accounted for more infections than HPV16.Total HPV 16 infection was 7/22 30.4% (95% CI:15.6-50.9), while Total HPV18 infection was (15/22) 65.2% (95% CI 44.9-81.2). largely driven by cases identified in Nimba. A total of 22/298 women) 7.4% (95% CI: 4.9-10.9) tested positive for generic Schistosoma species by high-resolution melt (HRM) real-time PCR analysis, indicating urogenital schistosomiasis (UGS) infection. Nimba County recorded the highest UGS prevalence at 11/79 13.9 % (95% CI:13.9% (8–23.2%), followed by Maryland 6/72 8.3% (95% CI: 3.9–17%). Bong County had a prevalence of 5.3% (95% CI: 2.1–12.9%) 4/75, while Lofa reported the lowest prevalence at 1.4% (95% CI: 0.2–7.5%) 1/72.

Table 2. Total hr-HPV positives per county

County	n	Count	Percentage	(95% CI)
	Participants			
Nimba	79	13	16.46%	(9.88 - 26.15)
Maryland	72	2	2.78%	(0.77 - 9.57)
Bong	75	6	8.00%	(3.72 - 16.37)
Lofa	72	1	1.39%	(0.25 - 7.46)
Total	**298**	**22**	**7.38%**	**(4.93 - 10.92)**

Table 3. hr - HPV & UGS co-infection per county

County	n	Count	Percentage	(95% CI)
	Participants			
Nimba	79	1	1.27%	(0.22 - 6.83)
Maryland	72	0	0.0%	(0.00 - 5.07)
Bong	75	1	1.33%	(0.24 - 7.17)
Lofa	72	0	0.0%	(0.00 - 5.07)
Total	**289**	**2**	**0.67%**	**(0.18 - 2.41)**

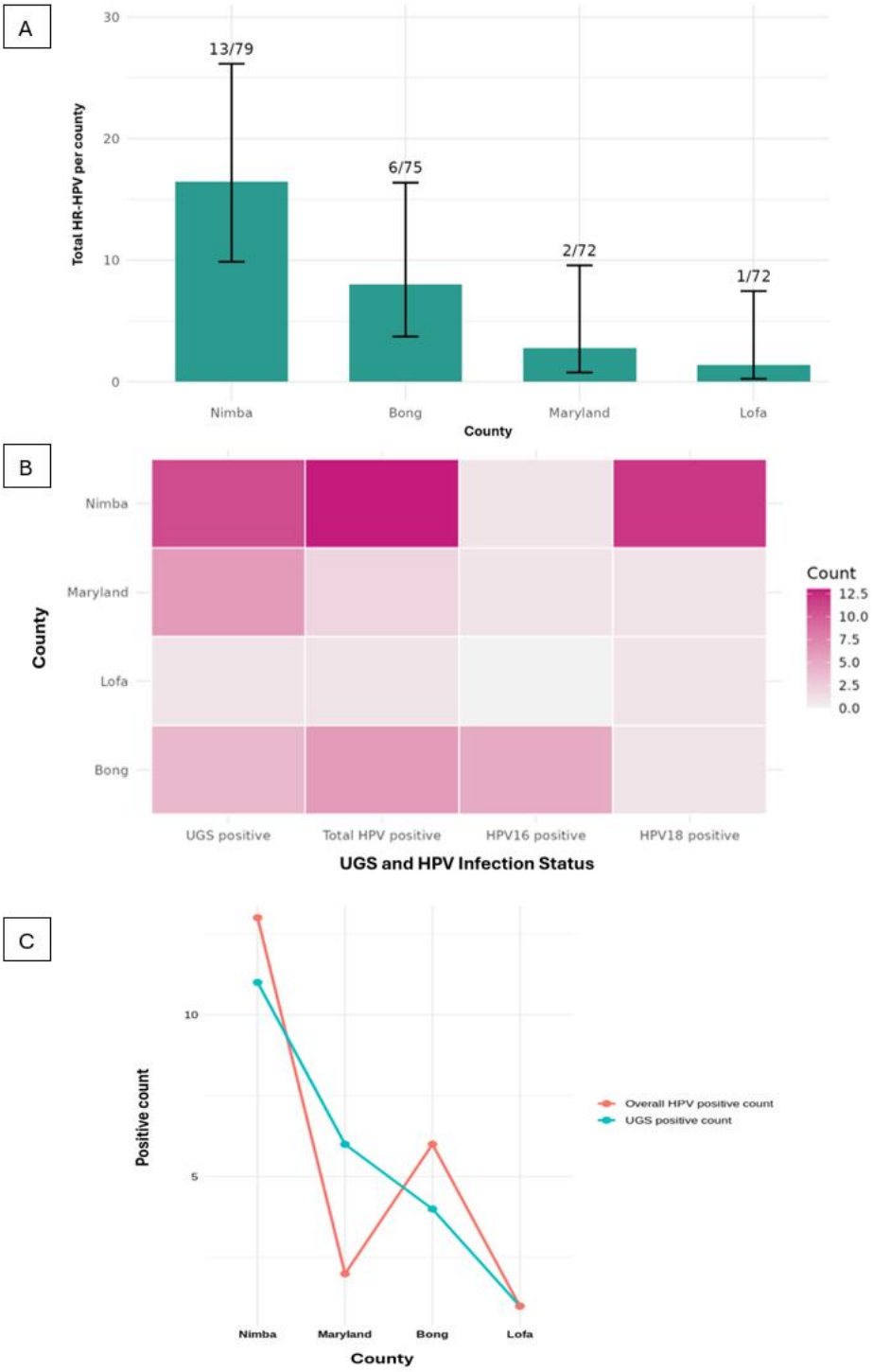


Fig.3 (A) Total hr-HPV per county. **(B)** Heatmap showing the distribution of urogenital schistosomiasis (UGS) and high-risk HPV (HPV16 and HPV18) positive cases by county. **(C)** Trends in total urogenital schistosomiasis (UGS) and hr-HPV-positive cases by county.

Distribution of HPV and UGS by county

Overall, positive cases were disproportionately concentrated in Nimba County (Fig.3a), with Bong representing a secondary cluster. Maryland demonstrated lower counts across most indicators, and Lofa consistently recorded the fewest positive cases.

When aggregated across all measures, Nimba had the highest overall burden (total count = 24), with elevated counts for both UGS and HPV outcomes. The largest individual measures in Nimba were total HPV-positive cases (n = 13), and UGS cases (n = 11). Bong ranked second (total = 10), driven mainly by HPV16-positive cases (n = 5), total HPV-positive cases (n = 6), and UGS (n = 4). Maryland had a total of 8 cases, UGS (n = 6) and HPV (n=2). Lofa had the lowest burden (total = 2), with values of 1 UGS and 1 HPV infection.

Across counties, the total was UGS (n = 22), closely mirrored the total hr-HPV positive cases (n = 22) (Fig 3b). hr-HPV18 positive cases (n = 15) were more common than hr-HPV16 positive cases (n = 7) with Nimba having the largest burden of hr-HPV18 (n = 12). HPV-UGS co-infection was rare (n = 2) across all counties. The highest individual counts were observed in Nimba for total HPV-positive cases, HPV18-positive cases, and UGS. Outside Nimba, the largest single counts were UGS in Maryland (n = 6) and total HPV-positive cases in Bong (n = 6).

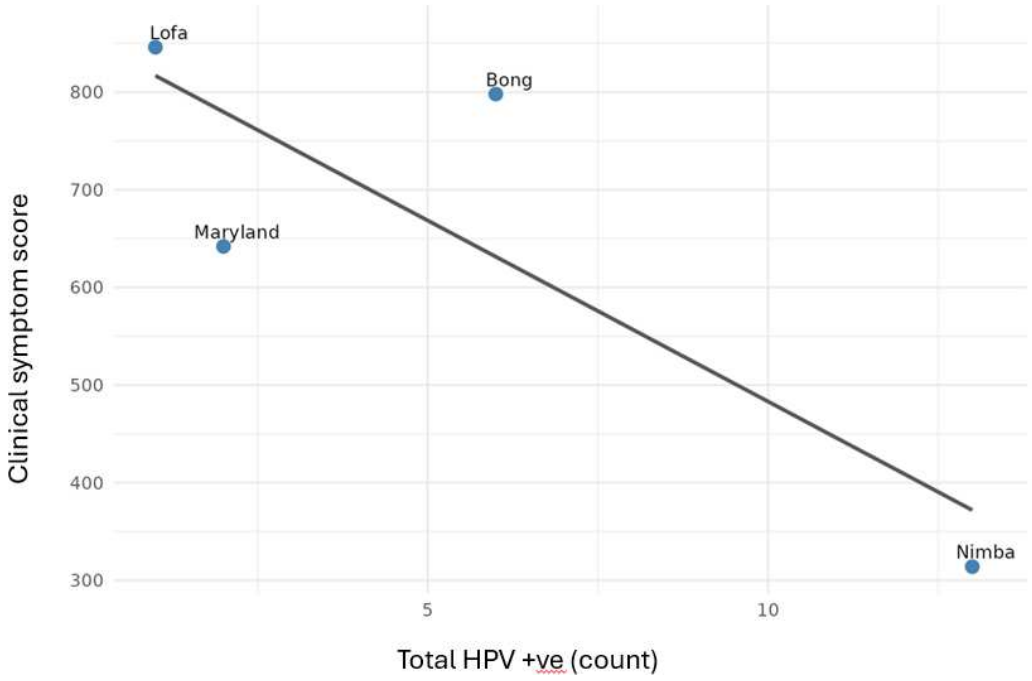


Fig 4. County -level association: Total HPV positives vs clinical symptom score from FGS score card

Clinical symptom scoring and comparison with HPV positivity

Section 2 of the FGS scorecard/questionnaire assessed seven clinical symptoms or indicators: intermittent genital bleeding, post-coital bleeding, pelvic pain, genital lesions, irregular menstruation, abnormal genital discharge, and urinary symptoms. Each reported symptom was assigned 2 points, yielding a maximum individual score of 14 points. Given that the largest county sample size was 79 participants, the maximum possible aggregate clinical symptom score per county was 1106 (79 × 14) (Nimba) which had the most participants, assuming all participants reported all seven symptoms. Figure 4 presents the total aggregated clinical symptom scores for each county alongside corresponding HPV-positive counts, allowing visual comparison of symptom burden relative to HPV positivity across study sites. The clinical symptom score for each county was the following. Lofa (845), Maryland (646), Bong (796), Nimba (326).

Table 4. Clinical symptoms and hr-HPV type distribution (HPV16 vs HPV18)

Clinical symptom	Total (n) hr-HPV+ve participants with symptom	Total HPV+ve symptom (95% CI)	(n) HPV 16 +ve with symptom	HPV16 % symptom (95% CI)	(n) HPV 18 +ve with symptom	HPV18 % symptom (95% CI)
Genital lesions/ulcerations	6	27.3% (13.2-48.2)	5	83.3% (43.6-97.0)	1	16.7% (3.0-56.4)
Pelvic pain	22	100.0% (85.1-100)	7	31.8% (16.4-52.7)	15	68.2% (47.3-83.6)
Post coital bleeding	4	18.2% (7.3-38.5)	2	50.0% (15.0-85.0)	2	50.0% (15.0-85.0)
Abnormal genital discharge	16	72.7% (51.8-86.8)	5	31.2% (14.2 - 55.6)	11	68.8% (44.4-85.8)
Irregular menstruation	9	40.9% (23.3-61.3)	6	66.7% (35.4 - 87.9)	3	33.3% (12.1- 64.6)
Urinary symptoms (hematuria, pain during urination, urine leaking)	7	31.8% (16.4-52.7)	4	57.1% (25.0 - 84.2)	3	42.9% (15.8-75.0)
Genital bleeding	2	9.1% (2.5-27.8)	1	50.0% (9.5-90.5)	1	50.0% (9.5-90.5)

Among the 22 hr-HPV positive participants, pelvic pain was reported by all individuals (22/22), corresponding to a prevalence of 100.0% (95% CI: 85.1–100.0%). Abnormal genital discharge was reported by 16/22 women (72.7%; 95% CI: 51.8–86.8%), irregular menstruation by 9/22 (40.9%; 95% CI: 23.3–61.3%), and urinary symptoms by 7/22 (31.8%; 95% CI: 16.4–52.7%). Less commonly reported symptoms included genital lesions or ulcerations (6/22; 27.3%; 95% CI: 13.2–48.2%), post-coital bleeding (4/22; 18.2%; 95% CI: 7.3–38.5%), and genital bleeding (2/22; 9.1%; 95% CI: 2.5–27.8%).Pelvic pain and abnormal genital discharge were the most frequently reported symptoms among women who tested positive for high-risk HPV16 and HPV18. (Table 4).

When stratified by genotype, pelvic pain was reported among 15/22 (68.2%; 95% CI: 47.3–83.6%) participants with HPV18 and 7/22 (31.8%; 95% CI: 16.4–52.7%) with HPV16.

Because participants could report more than one symptom, the total number of symptom reports exceeded the number of HPV positive individuals. Therefore, proportions represent the percentage of HPV positive participants reporting each symptom and should not be interpreted as mutually exclusive categories.

Sociodemographic background, Occupation and age of participants

The average age of participants varied by county: Nimba 23 years, Bong 25 years, Maryland 30 years, and Lofa 35 years. Participants' occupations included fishing, farming, and running local food businesses. Educational attainment also differed by county: Maryland had the lowest, with only 5% completing elementary school, followed by Bong and Lofa, while Nimba had the highest, with all participants having attended elementary school and 40% having completed secondary education.

Discussion

Sociodemographic background, Occupation and age of participants.

Given recent evidence of rising cervical cancer incidence among women aged 20-24, (17) the combination of Nimba's younger age profile and its highest hr-HPV burden in Liberia is particularly concerning. There was no correlation found between hr-HPV 16 and HPV 18 infection and occupation or level of education amongst the participants.

UGS-HPV co-infection

UGS-HPV co-infection was rare in this study population. Across all four counties combined, only two participants were positive for both HPV and UGS. At the county level, co-infection was observed exclusively in Nimba and Bong with a single case observed in each county, while no co-infections were detected in Maryland or Lofa. Importantly, even in counties with relatively high counts of hr-HPV or UGS individually such as Nimba the overlap between the two infections remained minimal. These findings indicate that, within this dataset, UGS-HPV co-infection contributes only marginally to the overall burden of HPV or UGS. Although co-infection is present, the absolute numbers are very small.

Relationship between HPV positivity and clinical symptom burden

County-level analyses indicate that HPV positivity and aggregate clinical symptom scores do not follow the same pattern. The heatmap demonstrates that Nimba has the highest counts for both UGS and total HPV-positive cases, whereas Lofa consistently records the lowest counts across most infection measures.

However, the scatter plot (Fig.4) reveals an overall negative association between total HPV16/18-and clinical symptom scores at the county level. This pattern is primarily driven by Nimba, which shows relatively high HPV16/18 counts but comparatively lower symptom scores, and Lofa, which shows low HPV counts despite higher symptom scores.

Collectively, these findings suggest that reported clinical symptoms alone may not serve as a reliable proxy for HPV burden at the population level. Possibly differences in health-seeking behaviour, and the presence of other gynaecological conditions may likely contribute to the observed discordance between symptom burden and HPV16/18 positivity across counties.

Comparison to Regional and Global Data

For many years Liberia lacked both a nationwide and county pilot programs for HPV screening or infection prevention, unlike its (ECOWAS) Economic Community of West African States neighbours, Ghana and Nigeria. As a result, while in West Africa the estimated prevalence of HR-HPV 16 and 18 is around 4.3% in women (18), provisional findings from this pilot study shows that at 7.38% (95% CI 4.93 - 10.92), high risk HPV 16 and 18 prevalence in women in Liberia is almost double that of other countries in the region. Compared to the global north, where the UK has a HR-HPV 16 and 18 prevalence of just 3.2% (19) and the U.S.A 3.9% (20), the disparity between the global north and south in terms of HR-HPV prevalence and cervical cancer remains. HPV vaccination strategies and routine screening have resulted in a major reduction in HR-HPV 16 and 18 infection and in turn cervical cancer.

Especially for the UK which offers universal health care through the NHS (National Health Service), despite a decline of cervical screening uptake during the Covid 19 pandemic (21), (22).

Although (HPV) vaccination has been incorporated into Liberia's national immunization program, coverage remains suboptimal, with 42% of eligible girls receiving the first dose and only 18% completing the second. The program, supported by Gavi, the Vaccine Alliance, had previously targeted only nine-year-old girls. The lack of national cervical cancer screening programs has resulted in delayed diagnoses and missed cases. Treatment and supportive care are further limited by shortages of radiotherapy facilities, essential medical supplies, and trained healthcare personnel, including surgeons. In 2018, an International Atomic Energy Agency (IAEA) mission emphasized the urgent need to rebuild and strengthen Liberia's health workforce, which was severely depleted following the Ebola epidemic and prior to that the country's 14 year long civil war (23).

Strengths and Limitations

Study strengths

This study provides *community-based* evidence on hr-HPV and HPV-UGS overlap from four Liberian counties using a recruitment approach that reduces the usual facility-attendance bias. Participants were randomly recruited from nearby villages by County Health Assistants, with relatively balanced county sample sizes, which supports meaningful county-level comparisons within the study catchment areas. A further strength is the quality and standardisation of cervical sampling, since midwives performed speculum examinations and collected genital swabs, which typically improves specimen adequacy and reduces outcome misclassification compared with non-speculum or self-collected approaches. The analysis reports prevalence estimates with 95% confidence intervals for overall hr-HPV and for HPV–UGS co-infection, improving interpretability and transparency around precision. Finally, reporting type-specific patterns shows clear program relevance, as the observed distribution indicates HPV18 contributed more infections than HPV16, largely driven by Nimba.

Study limitations

A major limitation was that we only screen for two hr-HPV genotypes, other hr-HPV types may have been present. Despite random recruitment, representativeness is still bounded to the sampling frame of nearby villages reached by the county teams, so generalisation to the entire county population, including more remote communities, should be made cautiously. The study is also limited by the very small number of co-infections detected n=2, which yields wide uncertainty and makes county-level inference about co-infection patterns inherently unstable; "no co-infections detected" in Maryland and Lofa should therefore be interpreted as *absence in the sample*, not absence in the population. In addition, the design is cross-sectional, so it cannot determine whether UGS predisposes to hr-HPV acquisition, whether hr-HPV influences genital tract morbidity, or whether shared underlying factors explain both infections. County-to-county differences may also reflect unmeasured confounding such as age distribution, sexual behaviour, HIV status, prior screening or treatment history, and water-contact patterns, none of which can be fully addressed without multivariable adjustment and consistent measurement across sites.

Conclusion

In a sample of 298 women across four counties, high-risk HPV (hr-HPV) prevalence was 7.38% (95% CI 4.93–10.92), while hr-HPV–UGS co-infection was rare at 0.67% (95% CI 0.18–2.41). hr-HPV was detected in all counties but concentrated in Nimba (13/79) and Bong (6/75). Co-infections occurred only in Nimba and Bong (one case each). HPV18 was more common than HPV16, largely driven by Nimba cases, highlighting HPV18 as a key contributor to hr-HPV burden. Overall, UGS does not appear to be a major co-occurring condition, suggesting that targeted interventions in higher-burden counties may be most effective. Given that Liberia has one of the highest cervical cancer mortality rates globally, the implementation of effective screening and diagnostic measures is imperative to prevent disease progression and initial HPV infection. Such interventions can be supported through public sensitization and educational awareness campaigns aimed at increasing knowledge and uptake of preventive services. Maximizing high-risk HPV vaccination coverage nationwide will be critical for cervical cancer prevention in Liberia. Integrating health and screening programs for urogenital schistosomiasis, sexually transmitted infections, and cervical cancer particularly in schistosomiasis-endemic areas could enhance early detection and reduce overall disease burden.

Future Research

Future research should include a larger, county-powered study to generate precise estimates of HPV-UGS co-infection, given that only two co-infected cases were observed in this study. Longitudinal cohort designs are needed to assess whether UGS contributes to hr-HPV persistence rather than merely infection prevalence. Expanding HPV genotyping beyond types 16 and 18, and incorporating clinically relevant outcomes such as VIA, cytology, or HPV persistence, would strengthen the connection between infection patterns and cervical precancer risk.

Declarations

Abbreviations

UGS = Urogenital Schistosomiasis

FGS = Female Genital Schistosomiasis

HrHPV = High Risk Human Papilloma Virus

LSIL = Low-grade Squamous Intraepithelial Lesion

HSIL = High-grade Squamous Intraepithelial Lesion

CIN = Carcinoma In Situ

STI's = Sexually Transmitted Infections

Rt-PCR = Real Time Polymerase Chain Reaction

PhHV = Phocine herpesvirus -

HRM = High Resolution Melting

CHA = County Health Assistant

ECOWAS = Economic Community of West African States

NHS = National Health Service

IAEA = International Atomic Energy Agency

VIA = Visual Inspection with Acetic Acid

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The study received ethical approval from the Atlantic Centre for Research and Evaluation Institutional Review Board in Liberia. In accordance with 45 CFR 46, Humans Subject Protocol by Atlantic Centre for Research and Evaluation Institutional Review Board (ACRE IRB) Liberia. Protocol Number: 22-12-354, Date: 17/11/2022 – 2/16/2027 (Renewal).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the study are available from the corresponding author on reasonable request. Corresponding author: Ayesha E.R Bell-Gam Woto, e-mail: ayesha.bell-gamwoto@lstmed.ac.uk

Competing Interest

The authors declare that they have no competing interests.

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Author Contributions

Ayesha E.R. Bell-Gam Woto: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Lucas J. Cunningham:** Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing**. Deddeh E.P Supuwood:** situational analysis, interpretation of findings, and manuscript drafting. **Bernice Dahn:** Data curation, Formal analysis, Methodology, Supervision, Writing – review & editing. **J. Russell Stothard:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

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