RESEARCH ARTICLE

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HPV Screening in Women Living with HIV (WLHIV) in Karnataka, India: Can it be Integrated into ART Centres?

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Abstract

Background: Women living with HIV (WLHIV) face a six-to-tenfold increased risk of cervical cancer due to higher HPV prevalence and persistence. Despite an estimated 1.05 million WLHIV in India and a vast National AIDS Control Programme (NACP) network, no organized cervical screening exists within this infrastructure. **Objective:** This pilot implementation project aimed to demonstrate a feasible and efficacious model for integrating cervical cancer prevention services, including HPV screening and a 'see and treat' approach, for WLHIV within or near ART centres in hard-to-reach Indian settings. **Methods:** A total of 368 WLHIV aged >21 years on ART from three centres were invited. 314 (85.3%) were screened using the COBAS 6800 high-risk HPV test. HPV-positive women were recalled for colposcopy using a portable digital device. A 'see and treat' approach was applied, using thermal ablation or LLETZ for minor/major lesions suggestive of precancer in field clinics. **Result:** 76 of 314 screened women (24.2%) tested positive for high-risk HPV. 65 of 76 HPV positive women (85.5%) complied with colposcopy and treatment. Histology from these 65 women showed 17 high-grade squamous intraepithelial lesions (HSIL), 23 low-grade SIL (LSIL), and 2 invasive cancers. The overall prevalence of HSIL or worse lesions was 5.7% among screened WLHIV. High participation was observed despite logistical challenges. **Conclusion:** The study confirms the significant burden of cervical neoplasia in WLHIV and demonstrates the feasibility and importance of integrating HPV screening and 'see and treat' services within or near existing ART centres using portable technologies. Leveraging the extensive NACP network offers a strategic opportunity for nationwide implementation, crucial for cervical cancer elimination efforts in this high-risk population.

Keywords: Women living with HIV- Cervical cancer- HPV screening- ART centre- NACO- MobileODT device

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Introduction

Persistent infection with one of the 14 high-risk human papillomaviruses (hrHPV) is the necessary cause of cervical cancer [1, 2]. Cervical cancer is the second most common cancer in women in India. Women living with HIV (WLHIV) are at a disproportionately increased risk of acquiring HPV infection and developing cervical cancer compared to women in the general population. This is attributed to a higher prevalence and longer persistence of HPV infection among WLHIV, along with improved life expectancy thanks to antiretroviral therapy (ART), which increases the population at risk. Among the oncogenic HPV types, HPV16 alone causes around 63-81% of cervical cancers in the general population and HPV18 accounts for another 10 to 15% in India [3–5]. While cervical HPV infection is common and typically clears or becomes latent within two years, a subset of infections persists [6, 7]. Nearly all cervical cancers harbour HPV DNA, particularly oncogenic sequences such as E6 and E7, emphasizing the causal role of persistent HPV infection in cervical carcinogenesis [5, 6].

Women living with HIV (WLHIV) face an almost six-to-ten-fold increased risk of cervical cancer compared to HIV-negative women [8–10]. In India, home to an estimated 1.05 million WLHIV, we estimate this increased risk translates to approximately 1500 new cervical cancer cases annually in this population [11, 12]. This number is derived by multiplying the estimated 1.05 million WLHIV by the incidence rate, adjusted for the 6-10-fold increased risk compared to the general population's cervical cancer incidence. Despite screening and treatment of precancerous lesions being essential preventive interventions for WLHIV [8–10], there is currently no

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organised cervical screening available for them in India. This gap exists despite the vast infrastructure of India's globally acclaimed National AIDS Control Programme (NACP) [13, 14], which includes a network of over 2500 ART centres (including ART centres, link ART centres, and care support centres) providing regular care to over a million people living with HIV across the country [8, 10, 13]. This established network represents a real and strategic opportunity to integrate cervical cancer prevention services and address the significant burden in WLHIV.

This pilot implementation project was therefore planned to demonstrate a feasible and efficacious model of providing cervical cancer prevention services to WLHIV, integrated within the context of ART centres. Building on recent WHO recommendations [15, 16] favouring HPV testing due to its high sensitivity and objectivity over cytology or VIA, our model implemented HPV testing for screening. A novel feature of the approach was the use of a portable, light-weight, handheld digital point-of-care device for image magnification, coupled with a 'see-and-treat' policy using thermal ablation or Large Loop Excision of the Transformation Zone (LLETZ) for HPV positive women with colposcopic abnormalities. This 'see-and-treat' approach was adopted in this high-risk population to decrease attrition and improve adherence to treatment. The aim of this project is to demonstrate how cervical cancer screening can be implemented for WLHIV, particularly addressing the challenges in hard-to-reach settings in India, and to evaluate the feasibility of integrating these cervical cancer screening services into the existing ART centre network. The study describes the observations and discusses the potential integration of HPV screening services as a key part of HIV prevention initiatives in India.

Materials and Methods

Study Design

This study was conducted as a pilot implementation project, utilising a cross-sectional study design. This design was chosen to provide a snapshot of the prevalence of HPV infection and cervical neoplasia, and to simultaneously evaluate the feasibility and outcomes of integrated HPV screening, triaging, diagnosis, and treatment services among women living with HIV (WLHIV) from Anti-Retroviral Therapy (ART) centres in hard-to-reach settings in India. The cross-sectional approach allowed for the assessment of participation rates in screening, diagnosis, and treatment within the specified timeframe of the pilot project.

Setting and Participants

The study was implemented in the Koppal district of Karnataka, India, described as a hard-to-reach setting. Participants were WLHIV aged 21 years and above who were receiving ART. Participants were identified by field-level health workers from a grassroot-level NGO (Samraksha). These women were invited from three specific ART centres located in Gangavathi, Koppal, and Gadag towns within north Karnataka. These three centres are part of a larger network of approximately 2500 ART centres under the National AIDS Control Programme (NACP) in India. The invited women were part of a larger cohort of about 4000 WLHIV in Koppal district, known to the collaborating NGO.

Recruitment and Invitation Process

A total of 368 WLHIV were invited from this larger cohort of approximately 4000 WLHIV registered with the NGO and attending the three ART centres. The selection of these 368 women for invitation was based on their active engagement with the NGO's community outreach programs and their attendance at the specified ART centres during the study period. Invitations were delivered individually by field workers of the NGO through telephone or direct person-to-person contact, detailing the date, time, and venue of the screening clinic.

Screening Procedure

Participants were offered HPV screening and treatment services in field screening clinics located closer to their homes. The field screening clinics were organised around ART centres within the district. Participating women travelled distances ranging from approximately 10 to 90 kilometres to reach the field screening clinic locations on pre-fixed dates. After providing informed consent for screening and investigations/treatment, screening was performed in makeshift field screening clinics. The screening method used was the WHO recommended HPV DNA test on COBAS 6800, which tested for 14 types of high-risk HPV infection (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). Cervical samples for HPV testing were collected by trained healthcare providers. The HPV test results were sent to field workers of the NGO. Women who tested negative for HPV were counselled and advised re-screening after 3 years, in line with WHO recommendations.

Colposcopy and Treatment ('See-and-Treat' Approach)

Women who screened positive for HPV were recalled and advised to report to a treatment clinic on specific days. The treatment clinic was set up in a local hospital in Koppal. This clinic was equipped with point-of-care devices including a clinically validated, portable, light weight, handheld and digital MobileODT, a thermal ablation device, and electrosurgical equipment with a smoke evacuator for LLETZ. HPV positive women underwent colposcopy examination. Colposcopy findings were reported according to IFCCP criteria [17]. Based on colposcopic findings, directed biopsies were taken from abnormal areas suggestive of precancerous lesions.

A 'see-and-treat' approach was employed. All HPV positive women with colposcopic abnormalities suggestive of precancerous lesions (minor or major) were treated immediately. Treatment involved either thermal ablation or LLETZ, depending upon the lesion characteristics. HPV positive women without any visible colposcopic lesion were counselled about their HPV positive status and advised for follow-up within 12 months with repeat HPV testing. This 'see-and-treat' algorithm ensured that eligible HPV positive women with colposcopic

abnormalities received immediate intervention. Directed punch biopsies were taken before thermal ablation for women with suspected precancer. This was done to obtain histological confirmation prior to any treatment, especially if there was any ambiguity. Importantly, women who presented with definitive clinical features of invasive cervical cancer based on visual inspection and colposcopy were not treated with thermal ablation or LLETZ in the field clinics. Instead, after initial biopsies were taken to confirm the diagnosis, these women were immediately referred for comprehensive cancer management at the anchor centre, as explicitly stated. This protocol ensured that thermal ablation was only performed on precancerous lesions and never on confirmed or clinically overt invasive cancers. The LLETZ specimen itself provided histological confirmation in those who underwent LLETZ. Thus, all 65 women who proceeded to treatment and underwent a procedure had tissue specimens for histology.

LLETZ procedures were performed by qualified gynaecologists who were part of the study team, ensuring appropriate clinical expertise. Consistent with the 'see-and-treat' approach, LLETZ was performed on the same day as colposcopy and diagnosis for eligible women, immediately following the colposcopic assessment and biopsy (where indicated for suspected cancer).

The thermal ablation procedures were performed by trained gynecological oncologists who were part of the study team. While the study ensured that the procedures were performed by qualified personnel, the specific temperature of the probe used and the precise duration of each application were not explicitly recorded as outcome measures in this pilot implementation project and are therefore not detailed in the manuscript. However, standard thermal ablation protocols, typically involving heating the probe tip with a temperature of 100°C for 45 seconds per application, were followed according to manufacturer (Liger) guidelines.

The choice between thermal ablation and LLETZ was made depending upon the lesion characteristics, as determined by colposcopic findings and the clinical judgment of the treating gynaecological oncologist. The decision to proceed with a particular treatment modality via LLETZ / thermal ablation was on the basis of initial screening result, type of transformation zone and colposcopy findings. If the screening result is other high-risk HPV, type 1 TZ and low-grade colposcopy findings, thermal ablation was done for those cases. Similarly, for type 3 TZ and high-grade colposcopy findings, LEEP/ LLETZ was carried out. As part of the 'see-and-treat' strategy aimed at reducing loss-to-follow-up, LLETZ was performed on the same day as colposcopy and diagnosis, immediately after the lesion assessment.

Thermal ablation was generally offered for smaller, less extensive lesions that were fully visualised on colposcopy and confined to the ectocervix, especially those with minor colposcopic findings or suspected LSIL/HSIL without suspicion of invasive cancer. LLETZ was reserved for larger or more extensive lesions, those extending into the endocervix beyond full visualisation with thermal ablation, or for cases where there was a higher suspicion of HSIL (CIN2/3) or early invasive cancer. In all cases, the primary goal of LLETZ was to both excise the abnormal tissue and provide a definitive histological specimen for diagnosis and confirmation of treatment adequacy. Women with definitive clinical features of invasive cervical cancer were referred for comprehensive cancer management, after initial biopsies for diagnosis, rather than undergoing ablative or excisional treatment in the field clinics.

After treatment, women were observed for 30 minutes and counselled for follow-up care. Appropriate precautions, including advice to abstain from sexual intercourse for a month, were given. Women with clinical features of invasive cervical cancer were referred for cancer management after taking biopsies.

A critical component of this strategy involved the management of women living with HIV, a population with a 6 to 10-fold increased risk of cervical neoplasia and disproportionately high rates of loss to follow-up. In recognition of their elevated risk and the challenges associated with longitudinal monitoring, all colposcopically visible lesions minor or otherwise and without any visible lesions were equally treated during the initial encounter. While this approach leads to potential overtreatment, it was deemed a clinically and ethically appropriate measure within a high-risk context. The strategy prioritized immediate intervention to prevent disease progression, addressing structural vulnerabilities that often preclude reliable follow-up, and reflects the necessity of pragmatic, equity-oriented models of cervical cancer prevention.

Outcome Measures

The study evaluated the following outcome measures

- Compliance to invitation for screening: Calculated as a proportion of invited women who underwent screening.
- HPV positivity frequency: The proportion of screened women who tested positive for high-risk HPV.
- Frequency of HPV 16 positivity: The proportion of all HPV positive women who were positive for HPV 16.
- Compliance of screen positive women for treatment: The proportion of screen positive women who attended the treatment clinic.
- Complications: Any complications experienced during or after treatment were recorded.

Data Management and Analysis

Data regarding socioeconomic factors, personal characteristics, reproductive factors, interventions, and outcomes were collected using a case report form. This data was then entered into an electronic database (Karkinos Web Application). The data were analysed using SPSS Statistics 28 software. The analysis primarily involved reporting frequencies of different variables and outcome measures.

Results

368 women from 3 ART centres were invited for cervical cancer screening. Among 314 (85.3%) participating women in screening, 76 (24.2%) were screened positive. The details of age distribution,

occupation, ART centre from where the women were recruited, and distance travelled from their home to reach the screening clinic are given in Table 1. Half of the screened women were between 31-40 years old and around three fourths worked as agricultural labourers or as daily wagers engaged in other manual work such as construction; almost half of the women travelled more than 40 kms to reach the screening clinic.

Figure 1, provides a comprehensive overview of the study's participant recruitment demographics and the key virological findings. Specifically, Figure 1a. illustrates the geographical origins of participant recruitment, offering insights into the diverse areas from which individuals were enrolled. Figure 1b. details the logistical aspect of participation by displaying the distances travelled by individuals to access the screening clinic. Furthermore, Figure 1c. presents the critical epidemiological data on the distribution of specific human papillomavirus (HPV) types identified among women who screened positive. This figure collectively highlights both the practical reach of the study and the prevalent HPV genotypes within the screened population.

This figure presents key geographical and clinical aspects of the study participants. Figure 1a. illustrates the locations where participants were recruited for the study. Figure 1b. depicts the distance travelled by participants to reach the screening clinic. Figure 1c. details the distribution of different human papillomavirus (HPV) types found in women who screened positive.

The comprehensive flow of participants through the

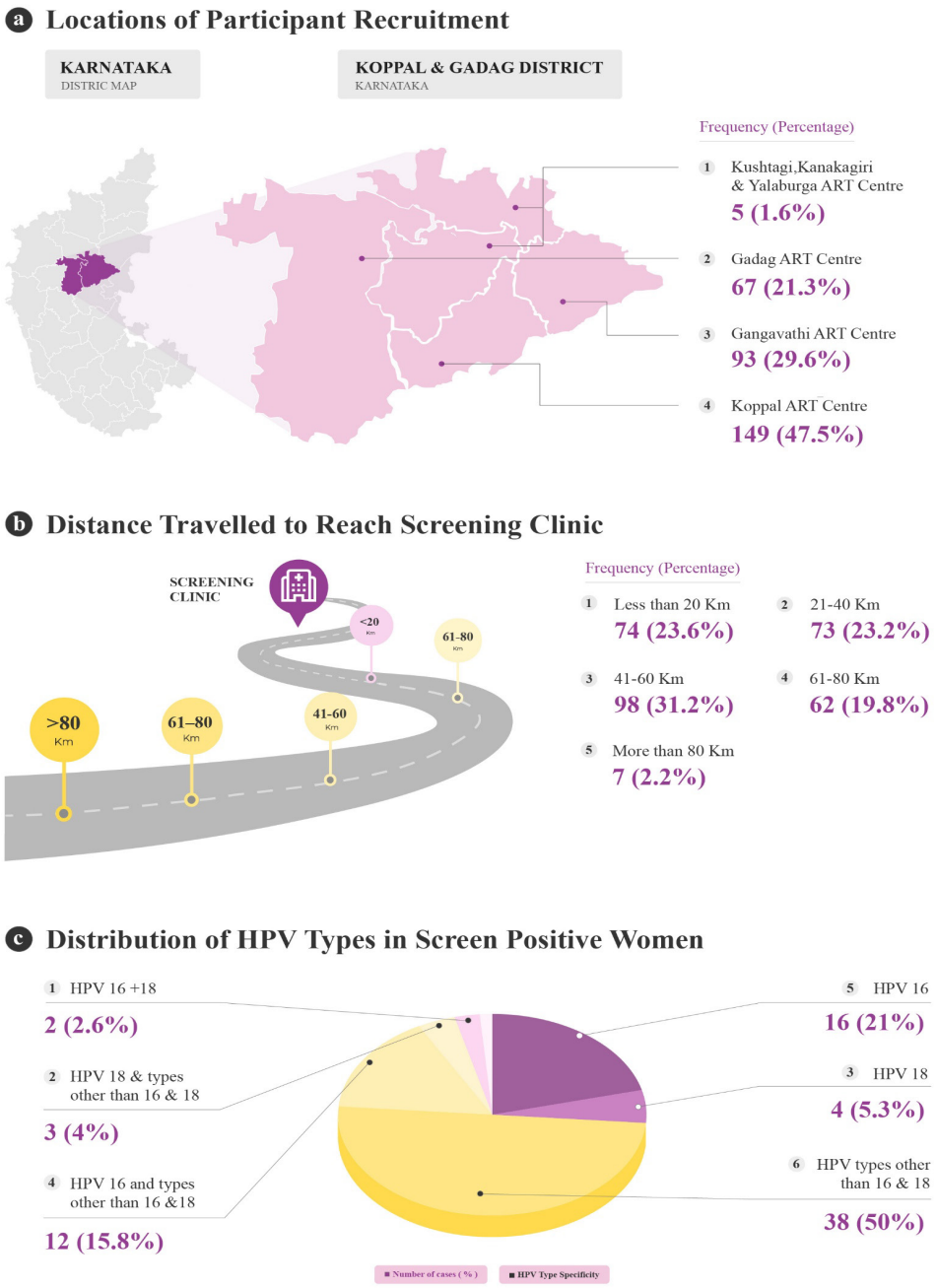

Figure 1. Study Demographics and Distribution of Human Papillomavirus Types among Women Living with HIV in Karnataka, India.

screening and treatment pathway, detailing recruitment, screening uptake, and compliance with subsequent diagnostic and treatment steps, is precisely illustrated in Figure 2. This visual representation emphasizes the notably high participation from invitation to screening (85.3%) and the strong adherence to diagnostic and treatment interventions (85.5% among HPV-positive women), thereby affirming the feasibility of this integrated approach.

This Figure (Figure 2) delineates the progression of women living with HIV (WLHIV) from initial invitation through the high-risk human papillomavirus (HPV) screening, diagnosis, and 'see-and-treat' cervical cancer prevention pathway, as implemented in this study at Antiretroviral Therapy (ART) centres in Karnataka, India. Invited WLHIV (N=368): Total number of women living with HIV who received an invitation to participate in the study. Screened WLHIV (N=314, 85.3%): Participants who underwent HPV DNA testing. HPV Positive WLHIV (N=76, 24.2%): Screened women who tested positive for high-risk HPV. Complied with Colposcopy/Treatment (N=65, 85.5%): HPV-positive women who attended the treatment clinic for colposcopy and subsequent treatment or referral. Treated with Thermal Ablation (N=45): Women who received thermal ablation based on colposcopic findings. Treated with LLETZ (N=19): Women who received Large Loop Excision of the Transformation Zone (LLETZ) based on colposcopic findings. Referred for Cancer Management (N=1): A single woman with definitive clinical features of invasive cervical cancer, or whose LLETZ specimen showed cancer, referred to an anchor centre for comprehensive management.

The distribution of HPV types among the 76 HPV screen positive women is detailed in Table 2. HPV 16 was the most prevalent type, detected in 31 women (40.8% of HPV positive cases). Among these, 16 women (21.0%) had HPV 16 as a sole infection, while the remaining 15 women (19.8%) had HPV 16 in combination with HPV 18 or other high-risk HPV types. HPV 18 was identified in 8 women (10.5%), with 4 cases (5.3%) being a mono-infection and 4 cases (5.3%) occurring in combination with HPV 16 or other types. Types other than HPV 16 and 18 were found in 54 women (71.0%), among whom 38 women (50.0%) were infected with only non-16/18 HPV types (i.e., without co-infection of HPV 16 or HPV 18). The details of CD 4 count on registration at ART centres were not available for 99 (31.5%) of WLHIV in the study. Among 215 women whose CD4 counts were known, 67 (31.2%) had counts less than 500. All the screened women were on ART of whom, 294 (93.6%) were known to be on ART for a period varying from 1 to 20 years duration and for the remaining 20 women, the duration was not known (Table 3). Among women receiving ART, two thirds received it for more than 5 years.

65 of the 76 HPV positive women (85.5%) complied with further triaging/diagnostic investigations such as colposcopy using mobileODT point of care device and directed biopsies from abnormal areas on the cervix. On colposcopy, 19 women had major lesions, 45 had minor lesions and 1 had clinical features of invasive cervical cancer (Table 4). 43 women treated with thermal ablation and 1 woman with suspected cancer had directed punch biopsies before treatment; the LLETZ specimen provided histological confirmation in those who had LLETZ excision. Thus, all the 65 women had tissue specimens for histology.

On histopathological examination of tissue specimens, 17 (26%) women were found to have high-grade

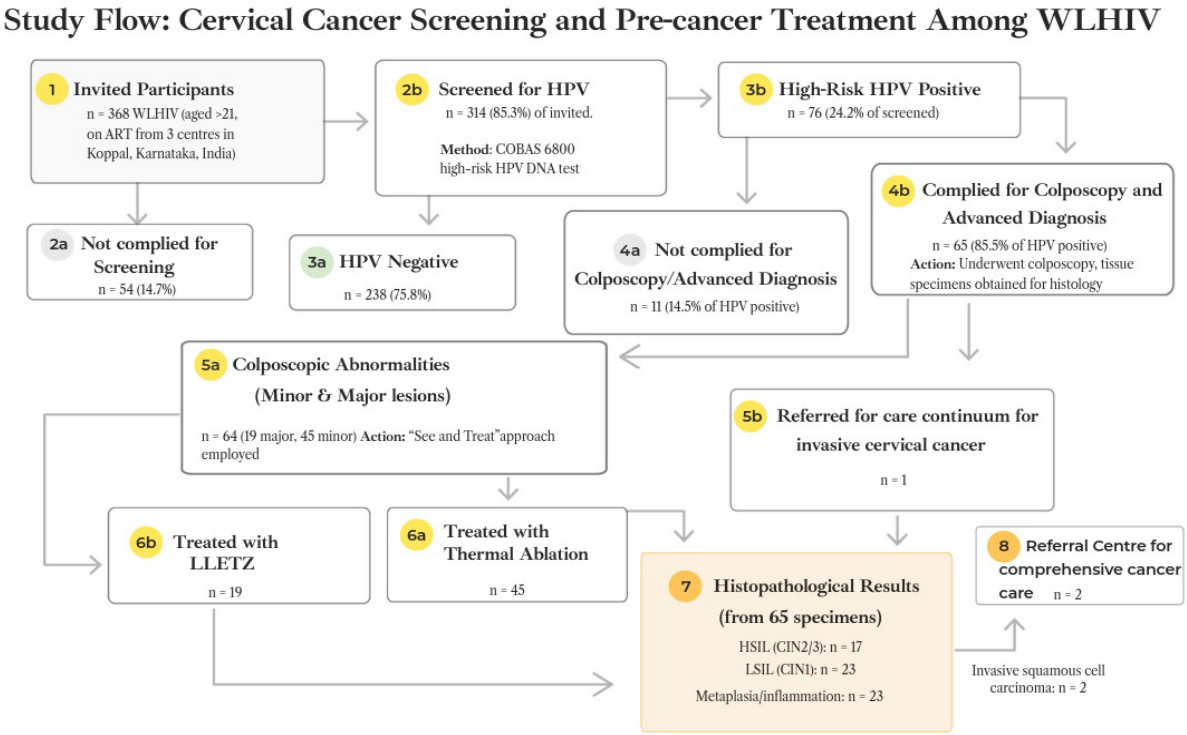

Figure 2. Participant Flow through the Cervical Cancer Screening and Treatment Pathway for Women Living with HIV (WLHIV)

Table 1. Demographic Characteristics of Women Living with HIV (WLHIV) Screened for Human Papillomavirus (HPV) Infection in Karnataka, India.

Demographic Variable	Categories	Frequency (Percentage)
Age	21-30	29 (9.2)
	31-40	156 (49.7)
	41-50	105 (33.5)
	51-60	19 (6)
	61-70	5 (1.6)
Occupation	Daily wagers	191 (60.8)
	Agriculture sector	35 (11.2)
	Employed (small business, self-employed & others)	43 (13.7)
	Unemployed	45 (14.3)
Anti-retroviral therapy (ART) Centre	Gangavathi	93 (29.6)
	Koppal	149 (47.5)
	Gadag	67 (21.3)
	Other sites (Kanakagiri, Kushtagi & Yalaburga)	5 (1.6)
Distance travelled to reach screening clinic	Less than 20 Km	74 (23.6)
	21-40 Km	73 (23.2)
	41-60 Km	98 (31.2)
	61-80 Km	62 (19.8)
	More than 80 Km	7 (2.2)

This table presents the demographic profile, including age distribution, occupation, Anti-Retroviral Therapy (ART) centre of recruitment, and distance travelled to screening clinics, for the 314 WLHIV who participated in the cervical cancer screening in this pilot implementation project.

Table 2. Distribution of High-Risk Human Papillomavirus (hrHPV) Types Identified among Screen-Positive Women.

HPV type	Number (%)
HPV 16	16 (21)
HPV 18	4 (5.3)
HPV types other than 16 & 18	38 (50)
HPV 16 and types other than 16 &18	12 (15.8)
HPV 18 and types other than 16 &18	3 (4)
HPV 16 +18	2 (2.6)
HPV 16, 18 and types other than 16 &18	1 (1.3)
Total	76

This table details the prevalence of specific hrHPV types, including mono-infections and co-infections involving HPV 16, HPV 18, and other hrHPV types, among the 76 women who tested positive for hrHPV in this study.

Table 3. Duration of Anti-Retroviral Therapy (ART) among Screened Women Living with HIV (WLHIV).

	No (%)
Duration in years	
<2 years	20 (6.4)
2-5 years	39 (12.4)
6-10 years	116 (36.9)
>10 years	119 (37.9)
On ART but duration not known	20 (6.4)
Total	314 (100.0)

This table shows the distribution of the duration of ART received by the 314 screened WLHIV. The duration of ART was known for 294 women (93.6%), while it was unknown for 20 women.

cervical intraepithelial neoplasia (HSIL), 23 (35.4%) had low-grade intraepithelial neoplasia (LSIL), 2 (3.1%) had invasive squamous cell carcinoma and 23 (35.4%) had either metaplasia or inflammation (Table 4 & 5). The overall prevalence of LSIL or worse lesions was 13.3% and that of HSIL or worse was 5.7% in WLHIV.

All 64 HPV positive women with colposcopic abnormalities suggestive of minor or major lesions were offered treatment in the field clinics: 43 had thermal ablation and 21 women had LLETZ (Table 5). Of the 43 women who had thermal ablation, 27 (62.8%) had either HSIL or LSIL on histology. Of the 21 women treated with LLETZ, 13 (61.9%) had HSIL or LSIL; one woman who had no clinical features of cancer had LLETZ which on histopathology proved to be invasive cancer. She was recalled and referred for further investigations and treatment. One woman who had clinical features of cancer was referred for cancer management after taking biopsies. All the women accepted the treatment and had no side effects except two: one woman had bleeding after LLETZ which was managed conservatively by vaginal packs; another woman had a fainting attack after thermal ablation which was essentially due to hypoglycemia which was managed conservatively.

Discussion

The present study reveals critical insights into HPV prevalence and cervical cancer screening outcomes among women living with HIV (WLHIV) in India. Our findings

Table 4. Histopathological Findings Stratified by Colposcopic assessment in Women Living with HIV (WLHIV) with Human Papillomavirus (HPV) Infection.

Colposcopy findings	HSIL	LSIL	Carcinoma	Inflammation/metaplasia	Total
Major lesions	6	5	1	7	19
Minor lesions	11	18	0	16	45
Carcinoma	0	0	1	0	1
Total	17	23	2	23	65

This table presents the histological diagnoses, including high-grade squamous intraepithelial lesions (HSIL), low-grade squamous intraepithelial lesions (LSIL), carcinoma, and inflammation/metaplasia, corresponding to colposcopic findings (major lesions, minor lesions, or clinical features suggestive of carcinoma) for the 65 HPV-positive WLHIV who underwent colposcopy and had tissue specimens for histology. HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

Table 5. Distribution of Treatment Modalities by Histopathological Diagnosis in Women Living with HIV (WLHIV) with Human Papillomavirus (HPV) Infection

Treatment	HSIL	LSIL	Inflammation/metaplasia	Carcinoma	Total
Thermal Ablation	11	16	16	0	43
LLETZ	6	7	7	1#	21
Total	17	23	23	1*	64

This table details the chosen treatment methods, thermal ablation and Large Loop Excision of the Transformation Zone (LLETZ), in relation to the histopathological diagnoses (high-grade squamous intraepithelial lesion [HSIL], low-grade squamous intraepithelial lesion [LSIL], inflammation/metaplasia, or carcinoma). The data pertains to the 64 HPV-positive WLHIV who received treatment in the field clinics. *This patient, who presented with definitive clinical features of invasive cervical cancer, was referred for comprehensive cancer management at the anchor centre after initial biopsies confirmed the diagnosis. #This patient had a major lesion with no clinical suspicion of cancer on colposcopy, but the LLETZ specimen revealed invasive cancer, necessitating recall and referral for further investigation and treatment. HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion; LLETZ = Large Loop Excision of the Transformation Zone.

demonstrate a 24.2% HPV positivity rate among screened women, with 85.5% compliance to colposcopy referral, a remarkably high rate that emphasizes the feasibility of implementing effective screening-to-treatment cascades in resource-limited settings. These results have significant implications for cervical cancer prevention strategies in high-risk populations across low- and middle-income countries (LMICs).

Cervical cancer remains a significant global health challenge, particularly for women living with HIV (WLHIV), who face a six-to-ten-fold increased risk compared to HIV-negative women. This elevated risk is due to the higher prevalence and longer persistence of high-risk human papillomavirus (hrHPV) infection in this population. While antiretroviral therapy (ART) has dramatically improved life expectancy for WLHIV, it has not eliminated the need for cervical cancer screening. ART has been shown to lower progression from normal cytology to LSIL but not to HSIL, and critically, cervical cancer incidence has not been lowered by ART. Therefore, cervical cancer screening is an essential and independent preventive intervention for WLHIV [18].

In India, an estimated 1.05 million women are living with HIV, with approximately 25,000 new infections annually. Despite this substantial burden and the existence of a globally acclaimed national AIDS control programme (NACP) with a vast network of ART centres, no organised cervical screening is currently available for WLHIV within this system. This gap is critical, as we estimate approximately 1500 new cervical cancer cases annually in Indian WLHIV based on the estimated population and increased risk. Without concerted efforts to integrate cervical cancer prevention services into the existing ART centre network, achieving the WHO's elimination targets will be exceptionally difficult for this vulnerable population [11].

Among the screened women, 76 (24.2%) tested positive for hrHPV. Our findings regarding the high prevalence of hrHPV infection (above 20%) and a substantial frequency of high-grade squamous intraepithelial lesions (HSIL) or worse lesions (exceeding 5%) among screened WLHIV are consistent with observations from other studies in India and elsewhere. Specifically, the overall prevalence of HSIL or worse lesions in our screened cohort was 5.7% (Table 4, Table 5). This prevalence emphasizes the urgent need for effective screening strategies in this population.

We chose to screen WLHIV in our study using HPV testing, which is the most preferred test according to recent WHO recommendations, superior to cytology or VIA [16]. The rationale for this choice lies in HPV testing's high sensitivity for detecting precancerous lesions in WLHIV and its inherent advantages of objectivity and reproducibility compared to visual inspection methods like VIA or subjective assessments like cytology [19–23]. The increased sensitivity of HPV testing for cervical precancerous lesions has been shown to be due to earlier detection rather than overdiagnosis [22–25]. A negative HPV test offers greater reassurance of a low long-term risk of CIN 3 and invasive cancer compared to negative cytology or VIA, reducing the chance of missed lesions and delayed treatment. Furthermore, practical advantages such as limited training requirements and the potential for self-sampling ease the burden on healthcare resources, making it suitable for resource-limited settings [22, 24–26].

HPV testing demonstrates superior sensitivity in detecting high-grade cervical lesions among women living with HIV (WLHIV). In a cohort of 1128 WLHIV, HPV testing achieved a sensitivity of 94.5% for detecting LSIL or worse, outperforming VIA (83.6%) and Pap smear (63.3%). Although Pap smear showed the highest specificity (94.5%), it missed a substantial proportion of HSIL+ lesions, emphasizing the clinical advantage of HPV testing in this population [21, 22, 24, 25, 27]. Our findings align with prior studies in India, reporting hrHPV prevalence exceeding 20% and HSIL+ lesions in over 5% of screened WLHIV [21, 24, 26]. These data support the need for earlier screening initiation in WLHIV, ideally at the time of HIV diagnosis; given their elevated risk profile compared with the general population.

A key feature of our study was the adoption of a 'see-and-treat' approach for all HPV-positive women with colposcopic (magnified cervical visualization at 16X) abnormalities suggestive of lesions. This strategy was implemented using a portable digital colposcope for triaging and guiding biopsies, followed immediately by treatment with thermal ablation or LLETZ where appropriate [27]. The 'see-and-treat' model was chosen specifically because of the high risk of cervical neoplasia in screen-positive WLHIV and, crucially, to mitigate the significant challenge of potential drop-outs for subsequent diagnostic and treatment visits. For this socio-economically disadvantaged population, travelling long distances involves lost wages and travel expenditures,

making repeat visits a considerable barrier to completing the care pathway. Studies have shown a substantial risk of incident HSIL among HPV-positive WLHIV who did not have histological evidence of CIN at baseline, further supporting the rationale for immediate treatment to prevent future disease [28, 29]. Implementing a 'see-and-treat' policy using HPV DNA testing has been shown to be highly effective, reducing the risk of CIN2+ by 80% in HIV-positive women within 36 months [30].

We were able to document the extent of overtreatment in our study because tissue specimens were obtained from all treated women [24, 31, 32]. The 'see-and-treat' approach resulted in overtreatment for approximately a third of the treated women who had no histological evidence of precancer, primarily showing inflammation or metaplasia (Table 5). This rate is comparable to previously documented rates with ablative treatments like cryotherapy in 'see-and-treat' settings. While acknowledging this, it is important to consider the trade-off between potential overtreatment and preventing loss-to-follow-up for women who may have high-grade lesions requiring treatment. Previous studies have indicated that such overtreatment has not been associated with adverse events during follow-up. Concerns about increased genital HIV shedding post-treatment are mitigated by advising abstinence and the known effect of ART in rapidly decreasing genital HIV shedding. The risk of HIV transmission after treatment is considered not significant in women on ART [24, 25, 27, 33–35].

However, there are concerns that in treated WLHIV there may be increased shedding of the virus in women following treatment and increased infectivity [31]. To minimise this risk, as is standard practice for all women undergoing these procedures, women were advised to abstain from sexual intercourse for 4 weeks [32]. Women in our study were advised appropriate precautions of abstinence for a month. It has been reported no increase in detectable cervical HIV-1 RNA after ablative treatment among HIV-positive women already on ART. ART has been demonstrated to rapidly decrease genital shedding of HIV [34]. The risk of HIV transmission after treatment may not be significant in these women [35]. 'See- and-treat' may be safely done in WLHIV without significant risk of HIV transmission following ablative and excisional treatment.

Our experience strongly supports the feasibility and critical importance of integrating cervical cancer screening and treatment into India's ART centres. The National AIDS Control Programme (NACP) offers an obvious and powerful platform for launching such services, leveraging its existing network of over 2500 ART centres providing care to approximately 1.4 million PLHIV across the country [13]. The massive scale-up and decentralisation of ART services by the Government of India since 2004 has created a globally acclaimed infrastructure that can effectively deliver integrated services [14]. Integration with ART services has seen successful sustenance and expansion of cervical screening programmes (often VIA-based) in several sub-Saharan African countries, demonstrating the potential of this model [10, 36].

While policy recommendations for HPV DNA testing exist in some African nations, widespread implementation is still pending [10, 36]. This pilot study highlights the feasibility and urgency of integrating cervical cancer screening and treatment into existing ART centres in India. Using ART clinics as points of entry, our model provided HPV screening, colposcopy, biopsy, and treatment in field settings. Given their reach and infrastructure, India's 2500 ART centres represent a strategic platform for delivering see-and-treat cervical services to women living with HIV (WLHIV). Similar integration in sub-Saharan Africa has yielded sustainable screening programmes [10, 36]. Despite WHO recommendations and national policies endorsing HPV testing, implementation remains limited. India's ART programme, second largest globally, has led to a decline in adult HIV prevalence and AIDS-related mortality [14]. Embedding cervical screening within this system aligns with global best practices and would advance national and global goals for cervical cancer elimination. Regular follow-up in ART clinics presents a missed opportunity for comprehensive care that must now be addressed.

Our findings confirm the high risk of HPV infection and cervical neoplasia in WLHIV and demonstrate the feasibility of providing the entire continuum of care via. screening, triaging, diagnosis, and treatment using portable point-of-care devices within or near the ART centre structure. Despite travel burdens and economic constraints, high screening compliance among women living with HIV (WLHIV) in our study highlights the impact of pre-screening counselling and community-based interventions. Engagement of local NGOs (e.g., Samraksha), targeted education, and navigation support were key enablers. These findings emphasize the role of decentralized, multi-stakeholder strategies in improving HPV screening uptake in WLHIV. The high compliance despite logistical challenges further validates this approach. Therefore, we strongly advocate for the urgent integration of cervical cancer prevention services by NACO into its extensive network of ART centres [13]. Leveraging this existing, accessible infrastructure presents a real opportunity to prevent cervical cancer in a million WLHIV in India. Urgent introduction of HPV screening and treatment using a 'see-and-treat' approach, integrated into the existing NACO network, aligns with global evidence, WHO recommendations, and is crucial to mitigate the disproportionately high risk faced by WLHIV.

To facilitate crucial integration of cervical cancer prevention within ART programmes, further work should prioritize

- Developing detailed national guidelines for integrating HPV screening and 'see-and-treat' into ART workflows
- Estimating resource needs for national scale-up, including equipment, reagents, and supply chains
- Creating comprehensive training for ART centre healthcare providers on integrated cervical cancer services
- Conducting a cost-effectiveness analysis comparing the integrated model to existing approaches
- Establishing a robust system for long-term follow-up and monitoring the impact on cervical cancer outcomes

in women living with HIV nationally.

Integrating cervical cancer prevention services into India's highly successful NACP is a critical and actionable step towards achieving cervical cancer elimination targets for WLHIV in the country and contributing significantly to global efforts.

Potential limitations

Several limitations warrant consideration when interpreting the findings of this pilot implementation project and cross-sectional study, conducted within a specific hard-to-reach setting in the Koppal district of Karnataka, India. The study's cross-sectional design offers a single time-point assessment and was implemented on a smaller scale than a full roll-out. Notably, the 'see-and-treat' strategy led to the overtreatment of approximately one-third of treated women, who presented without histological evidence of precancer, primarily showing inflammation or metaplasia. While potential concerns regarding increased post-treatment HIV shedding exist, particularly for women not on ART, this is likely less significant for those on ART with the recommendation of abstinence. Furthermore, CD4 count data at ART registration was unavailable for a notable proportion (31.5%) of the screened women. Finally, the study's focus on a specific geographical setting may limit the direct generalisability of the findings to other diverse regions within India, rather than the broader Asia-Pacific region

In conclusions, this pilot study in north Karnataka, India, provides critical evidence of a high burden of hrHPV infection (24.2%) and cervical neoplasia (HSIL+ prevalence of 5.7%) among Women Living with HIV (WLHIV). The research demonstrates the feasibility and high compliance (85.5% for diagnosis/treatment among HPV+) of integrating WHO-recommended HPV DNA testing and a 'see-and-treat' approach using mobile colposcopy and ablative therapies within or near existing ART centres. The findings strongly advocate for leveraging India's extensive National AIDS Control Programme (NACP) network to implement cervical cancer prevention services for WLHIV, aligning with global best practices and offering a realistic pathway to address their disproportionately high risk and contribute to cervical cancer elimination goals. Future efforts should focus on developing national guidelines, resource estimation, training, cost-effectiveness analysis, and long-term follow-up systems for national scale-up. Integrating HPV screening and treatment into ART centres is presented as an effective and feasible strategy to reduce cervical cancer risk in WLHIV in India.

Author Contribution Statement

Sripriya Rao: project administration, methodology, resources, supervision, validation; Divya Sarma: conceptualisation, data curation, formal analysis, methodology, project administration, resources; Ashwathy G Nath: project administration, resources; Anuradha R: project administration, resources, supervision; Latha Jagannathan: conceptualisation, methodology, supervision, validation; Anjali Rao: conceptualisation, methodology, supervision, validation; Guru Suhas: conceptualisation, methodology; Sanghamitra Iyengar: conceptualisation, project administration, supervision, validation; Rajalakshmi V: data curation, formal analysis, software; Mayank Chhabra: formal analysis, software, visualisation, writing – original draft; R. Sankaranarayanan: conceptualisation, investigation, methodology, supervision, validation, visualisation, writing – original draft; Venkataramanan Ramachandran: investigation, supervision.

All authors had contributed in review/editing and had full access to all the data in the study & approved the final manuscript. Sripriya Rao & Mayank Chhabra had full access to all the data in the study..

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Data sharing statement

Raw data collected and generated in Web-application. Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of Interest

Authors declare no conflict of interest

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