Integrating cervical cancer screening with HIV care in a district hospital in Abuja, Nigeria

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ABSTRACT

Background: Human immunodeficiency virus positive (HIV+) women have a higher risk of developing invasive cervical cancer compared with uninfected women. This study aims to document programmatic experience of integrating cervical cancer screening using Visual Inspection and Acetic Acid (VIA) into HIV care as well as to describe patients' characteristics associated with positive VIA findings amongst HIV+ women. **Materials and Methods:** A cross-sectional study analysed routine service data collected at the antiretroviral therapy (ART) and cervical cancer screening services. Our program integrated screening for cervical cancer using VIA technique to HIV care and treatment services through a combination of stakeholder engagement, capacity building for health workers, creating a bi-directional referral between HIV and reproductive health (RH) services and provider initiated counselling and screening for cervical cancer. Information on patients' baseline and clinical characteristics were captured using an electronic medical records system and then exported to Statistical Package for the Social Sciences (SPSS). Logistic regression model was used to estimate factors that influence VIA results. **Results:** A total of 834 HIV+ women were offered VIA screening between April 2010 and April 2011, and 805 (96.5%) accepted it. Complete data was available for 802 (96.2%) women. The mean age at screening and first sexual contact were 32.0 (SD 6.6) and 18.8 (SD 3.5) years, respectively. VIA was positive in 52 (6.5%) women while 199 (24.8%) had a sexually transmitted infection (STI). Of the 199 who had a STI, eight (4.0%) had genital ulcer syndrome, 30 (15.1%) had lower abdominal pain syndrome and 161 (80.9%) had vaginal discharge syndrome. Presence of lower abdominal pain syndrome was found to be a significant predictor of a positive VIA result ($P = 0.001$). Women with lower abdominal pain syndrome appeared to be more likely (OR 47.9, 95% CI: 4.8-480.4, $P = 0.001$) to have a positive VIA result. **Conclusion:** The high burden of both HIV and cervical cancer in developing countries makes it a necessity for integrating services that offer early detection and treatment for both diseases. The findings from our study suggest that integrating VIA screening into the package of care offered to HIV+ women is feasible and acceptable.

Key words: Cervical cancer screening, human immunodeficiency virus, integration, Nigeria, visual inspection with acetic acid

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INTRODUCTION

In sub-Saharan Africa, women account for about 60% of people living with human immunodeficiency virus (HIV)[1], and young women aged 15-24 years are as much as eight times more likely than men to be HIV positive (HIV+).[2] Cervical cancer is the second most common type of cancer amongst women worldwide.[3] Human papilloma virus (HPV) is the primary etiologic agent of cervical cancer.[4,5] Globally, HPV types 16 and 18, both of which are vaccine-preventable types, contribute to more than 70% of all cervical cancer cases.[6] HPV-16 and 18, also contribute between 41% and 67% of high-grade and 16-32% of low-grade cervical lesions.[6] Transmission of HPV occurs primarily by sexual contact.[4,7,8] Known predisposing factors for HPV infection and later cervical cancer include early age at first sexual intercourse, multiple sexual partners, a male spouse who has had intercourse with multiple women, smoking and women who are immunosuppressed.[7-10]

About 83% of new cases of cervical cancer and 85% of associated mortality occur in developing countries.[3] Low perception of risks and lack of awareness about cervical cancer screening amongst women and challenges of access to cervical cancer screening for early detection of disease have been reported amongst factors responsible for increasing incidence and mortality due to cervical cancer in developing countries.[11-15] A four- to six-fold increased risk for squamous intraepithelial lesions (SIL) or cervical intraepithelial neoplasia (CIN) is estimated in HIV+ women compared with negative women.[16-20] HIV+ women are also more likely to have cervical abnormalities that can progressively lead to invasive cervical cancer.[21-24] Cervical cancer incidence and related mortality have decreased in developed countries due mainly to regular screening and prompt treatment for sexually active women.[25] HIV treatment recommendations advise that a woman who is diagnosed with HIV should also be screened for cervical cancer.[26]

Several African countries have used cytologic screening to screen for cervical cancer among HIV+ women; studies on these programs reported that 55-76% of HIV+ women had an abnormal Pap smear.[27-29] Early detection of potentially cancerous cervical cell changes provides the best opportunity for effective treatment. However, access to screening and treatment for cervical cancer in Sub-Sahara Africa[30] and Nigeria in particular is limited.[13] A recent review estimated that rates of cervical screening coverage in sub-Saharan Africa in general range from 2% to 20.2% in urban areas and 0.4% to 14% in rural areas.[31] Challenges to the provision of cervical cancer screening include poor infrastructural facilities, lack of skilled human resources, lack of commodities needed to carry out screening, and low levels of awareness amongst patients and health workers.[11,14,32-34] Cervical cancer screening messages are also not part of routine HIV counselling in many Nigerian clinics.[12]

Various attempts at improving cervical cancer screening in developing countries have been made.[35] Different screening methods have also been evaluated.[35] The cost of deploying cytology-based screening, followed by colposcopy, is not suitable for widespread scale up of cervical cancer screening in many developing countries. However, techniques such as visual inspection with acetic acid (VIA) and visual inspection with Lugol's Iodine (VILI) are less expensive and require minimal supplies and infrastructure.[36] The U.S. Centre for Disease Control and Prevention (CDC) has funded programs that recorded demonstrable success in using VIA for cervical cancer screening, through advocacy and capacity building in Kenya, Bolivia, and India.[37] In Peru, VIA was found to be useful for detection of precursor lesions of cervical cancer not only in low-resource settings but also in well-equipped health centres and cancer centres.[38] Its positive predictive value was comparable to the conventional Pap smear.[38] VIA was found to be more likely to achieve earlier diagnosis, follow-up, and treatment than cytology based screening.[38] VIA in screening for cervical cancer has also been successfully used in Nigeria and Zambia and other developing countries and has been found to compare favourably with cytology.[39-44]

There is an increasing focus on ensuring that the gains of antiretroviral therapy (ART) are sustained through prevention of other causes of morbidity and mortality in those living with HIV. Nonetheless screening for cervical cancer in Nigeria remains poor.[13] In an effort to address this gap, Family Health International (FHI) 360 launched a pilot program to integrate cervical cancer screening services using VIA for HIV+ women attending the ART clinic in a public health facility in Abuja, Nigeria. This paper aims to document programmatic experience of integrating VIA screening into HIV care as well as to describe patients' characteristics associated with positive VIA findings among the HIV+ women who participated in the pilot.

MATERIALS AND METHODS

This was a cross-sectional study using linked routine service data collected at the ART and cervical cancer screening service delivery points between April 2010 and April 2011.

The study was conducted in Maitama District Hospital (MDH), a government-owned 93 bed secondary healthcare public hospital that provides comprehensive HIV/AIDS prevention, care and treatment services in the Abuja metropolis in Nigeria. The hospital was one of the sites supported by Global HIV/AIDS Initiative Nigeria (GHAIN) project through funding from the United States Agency for International Development (USAID) under the United States President's Emergency Plan for AIDS Relief (PEPFAR). FHI 360 piloted the integration of cervical cancer screening using VIA technique in this hospital over a 1-year-period from April 2010 and April 2011.

Considerations for choosing a site for this pilot were: 1) Presence of a comprehensive HIV treatment program; 2) presence of a reproductive health unit that can be supported to provide VIA; 3) presence of an Electronic Medical Records (EMR) system and 4) a high patient load (average general outpatient attendance of over 1,000/month). The Maitama District Hospital (MDH) was chosen for this pilot because it met all the above criteria.

This study focussed on adult female patients in the reproductive age group (20-49 years). Women with a total hysterectomy, history of cervical cancer, or current pregnancy were excluded from the study. All other women aged 20-49 years either newly diagnosed of HIV or with known HIV+ on ART who accepted VIA screening for cervical cancer between April 2010 and April 2011 at MDH constitute the study population.

The integration process was preceded by advocacy meetings and enlisting of support of various stakeholders followed by a site assessment. Data from an EMR system developed by FHI 360, the Lafiya Management Information System (LAMIS®) were reviewed to ascertain the number of HIV+ women meeting selection criteria enrolled in the ART program. The reproductive health (RH) and ART units were assessed to determine infrastructure, basic equipment and supplies, and training needs for the pilot program. Nurses/midwives at the reproductive health unit were trained during a 2-day intensive course on-site on use of the VIA technique, using the practical manual on visual screening for cervical neoplasia published by World Health Organization (WHO)-International Agency for Research on Cancer (IARC).[45] Trainings were conducted by a gynaecologist and FHI technical staff experienced on use of the VIA technique. Additional training included practical sessions at clinics and review of pictures of normal and abnormal cervix. Additionally, refresher trainings were provided during the pilot. The implementation process was supervised daily by an experienced gynaecologist and FHI technical staff to ensure quality of screening process.

Furthermore, relevant supplies required for VIA screening were provided. Nurses/midwives at both the ART and RH units were also trained on counselling, appointment setting and a bi-directional referral and patient tracking system were established. Messages on cervical cancer prevention and importance of screening were introduced as part of health talks delivered to patients in the ART clinic. During implementation, women attending the ART clinic were counselled on cervical cancer screening, and patients accepting to test were subsequently referred to the RH unit for a same-day screening using the VIA technique.

At the RH unit, women participated in a group education session. Subsequently, women were individually counselled and provided their consent. The trained nurses/midwifes then completed patients' information on the cervical cancer screening form. To begin the screening, a midwife performed abdominal and external genitalia examinations, a Graves' speculum was inserted, and the cervix was brought into view. The midwife then examined the cervix using an examination light and identified the squamocolumnar junction (SCJ). The cervix was then assessed for the presence of gross lesions consistent with possible cancer. After cleaning out excess mucus using a cotton swab, a dilute (5%) acetic acid solution was applied liberally to the cervix. After waiting for 1 min, the cervix was re-examined for lesions. Midwifes were trained to ensure that the entire SCJ was visualised. Assessment findings were recorded with three standardised VIA categories.[45] The VIA test outcome were classified as negative, positive or indicative using the classifications described in the

IARC training manual[45] and appropriately recorded on a cervical cancer screening data collection form after each screening procedure. VIA positive test outcome includes the presence of distinct, well-defined, dense acetowhite areas with regular or irregular margins, close to or bordering the SCJ in the transformation zone or close to the external os, if the SCJ is not visible.[45] Women with suspicious lesions were referred to a tertiary centre for colposcopy and treatment. The VIA service at MDH was offered free of charge, however, patients referred to the tertiary center for confirmatory testing and possible treatment were required to pay for services rendered.

Routine service data from the VIA screening process and ART services were collected at the program monitoring unit, ART clinic and cervical cancer screening unit. A cervical screening data collection form capturing patients ART unique identification number and outcome of screening, was specifically developed for collecting data at the VIA screening point. LAMIS was used to capture linked patients' information on demographic, including age, age at first sexual contact, marital status, and level of education. Information on baseline clinical characteristics obtained included weight, CD4 count and WHO staging.

Data analysis
The data were exported from LAMIS to SPSS for statistical analysis. Patients' personal identifiers were removed at the point of data export. Automated and manual consistency checks were performed on the data. In instances where inconsistencies were found in the EMR, data inconsistencies were corrected using source documents. A logistic regression model was used for univariate and multivariate analyses of the association between the outcome of the VIA test (i.e., positive and negative) and patients' characteristics. All statistical tests were two-sided at $\alpha = 0.05$.

Ethical considerations
Ethical approval was obtained from the Nigerian National Health and Research Ethics Committee (NHREC) and FHI's Protection of Human Subjects Committee (PHSC). In addition, data entry clerks were trained on confidentiality. Secure data entry, transmission and storage were ensured. Patients who accepted to be screened for cervical cancer were further required to give verbal consent before the screening was performed, as part of the ethical requirements.

RESULTS

Eight hundred and thirty-four HIV+ women on ART were offered VIA screening between April 2010 and April 2011. Eight hundred and five (96.5%) of these women accepted screening and complete records were available for 802 (96.2%) of them. The mean age of those women with complete records was 32.0 (SD 6.6) years. Nearly half of the

study population (47.4%, *n* = 380) had secondary education, about one third (29.5%, *n* = 237) had tertiary education, 15.1% (*n* = 121) had primary education, 5.7% (*n* = 46) had no formal education, and the level of education was not stated for 2.2% (*n* = 18) women. Married women accounted for 56.1% (*n* = 451) of the study population, while 29.4% (*n* = 237) were single, 13.4% (*n* = 106) were either divorced or widowed, and 1.0% (*n* = 8) did not have a marital status recorded. The mean age at first sexual contact was 18.8 (SD 3.5) years. Table 1 summarizes baseline characteristics of study population.

Complete baseline CD4 count records were available for 495 (61.7%) of women screened. Clinical records showed that 287 (35.8%) of the women screened had baseline CD4 counts <200 cells/µl, 186 (23.2%) had counts between 200-350 cells/µl, and 22 (2.7%) had CD4 count >350 cells/µl. HIV clinical staging at baseline was recorded for only 535 (66.7%) of women screened, of which 235 were in WHO stage I, 144 women were at stage II, 150 women stage III, and six of them had stage IV disease.

Unaided visual inspection revealed a healthy cervix in 543 (67.7%) of women, redness in 51 (6.4%), Nabothian follicles in 49 (6.1%), while the results for unaided visual inspection were not documented for 159 (19.8%). Visual inspection with acetic acid was positive in 52 (6.5%) women. All the women were also screened for STI using symptom checklist and 199 (24.8%) had a STI syndrome. Of the 199 women, who had an STI syndrome, eight (4.0%) had genital ulcer syndrome, 30 (15.1%) had lower abdominal pain syndrome and 161 (80.9%) had vaginal discharge syndrome. Table 2 summarizes the findings from clinical consultation and VIA screening. Figure 1 summarizes cervical cancer screening patient flow.

The mean patients' age and age at first sexual contact were not associated with a positive VIA result (*P* = 0.669 and *P* = 0.876 respectively). A statistically significant association was observed for positive VIA results and having STI syndrome (*P* = 0.001). However, no statistically significant associations were observed for: Positive VIA results and HIV clinical staging at baseline (*P* = 0.999); level of education (*P* = 0.157); marital status (*P* = 0.546) and CD4 count values (*P* = 0.279). Table 3 summarizes factors associated with a positive VIA result. The results from the regression model showed that after controlling for the effect of other factors, having lower abdominal pain syndrome was found to significantly predict a positive VIA result (*P* = 0.001). Women with lower abdominal pain syndrome in this study were more likely to have a positive VIA result (OR 47.9, 95% CI: 4.8-480.4, *P* = 0.001).

DISCUSSION

The results obtained in this study appear to indicate that

Table 1: Baseline characteristics of respondents

Characteristic	*n* (802)	%
Level of education		
No formal education	46	5.7
Primary	121	15.1
Secondary	380	47.4
Tertiary	237	29.6
Not stated	18	2.2
Marital status		
Ever married		
Married	451	56.23
Divorced	55	6.86
Widowed	51	6.36
Never married		
Single	237	29.55
Not stated	8	1.00
	Mean	**SD**
Age	32.0	6.6
Age at first sexual contact	18.8	3.5

Table 2: Findings from clinical consultations and screening

Finding	*n*	%
Unaided visual inspection		
Healthy cervix	543	67.71
Redness	51	6.36
Nabothian follicles	49	6.11
Not recorded	159	19.83
Total	802	100.00
VIA result		
Negative	750	93.52
Positive	52	6.48
suspicious of Cancer	0	0
Total	802	100.00
STI syndrome		
No STI syndrome	545	68.0
Has STI		
Genital ulcer syndrome	8	1.0
Lower abdominal pain syndrome	30	3.7
Vaginal discharge syndrome	161	20.1
Not recorded	58	7.2
Total	802	100.00
CD4 counts		
<200	287	35.8
200–350	186	23.2
>350	22	2.7
Not recorded	307	38.3
Total	802	100.00
WHO clinical stage (HIV)		
Stage I	235	29.3
Stage II	144	18.0
Stage III	150	18.7
Stage IV	6	0.8
Not recorded	267	33.3
Total	802	100.00

VIA – Visual inspection with acetic acid; WHO – World health organization

demographic and baseline clinical characteristics such as age, weight, CD4 count, and WHO staging were not significantly associated with positive VIA results amongst

Table 3: Factors influencing a positive VIA result (logistic regression)

Dependent variable=VIA result	Odds ratio	95% C.I. for OR		Sig.
		Lower	Upper	
Marital status				
Single	1.000			
Married	1.713	0.245	11.949	0.587
Divorce	2.258	0.405	12.574	0.353
Widowed	1.235	0.134	11.372	0.852
STI syndrome				
None	1.000			
Genital ulcer syndrome	2.073	0.635	6.763	0.227
Lower abdominal pain syndrome	47.921	4.781	480.350	0.001
Vaginal discharge syndrome	0.000	0.000	.	0.999
CD4 counts				
<200	1.000			
200-350	1.681	0.195	14.457	0.636
>350	0.673	0.071	6.408	0.731
HIV Clinical staging at baseline				
I	1.000			
II	9.5447	0.000	-	0.999
III	3.6228	0.000	-	0.999
IV	7.9247	0.000	-	0.999
Age (yrs)	1.002	0.938	1.070	0.958
Age at first sexual contact (yrs)	1.053	0.934	1.188	0.395
Weight at baseline	1.011	0.978	1.045	0.527
Model Chi-square				0.006
Constant	0.000			0.999

VIA – Visual inspection and acetic acid

HIV positive women on ART. However, lower abdominal pain syndrome was a significant predictor of positive VIA result. This finding is consistent with findings reported in another study in Nigeria that found higher incidence of cervical dysplasia amongst patients with chronic pelvic inflammatory disease.[46] Findings from another study in the United States suggested that coexistent of pelvic infection in HIV+ women may contribute to development and spread of cervical cancer.[47]

In our study, 96.5% of women offered screening for cervical cancer accepted testing. This finding was comparable with findings from studies in Kenya and Mozambique that reported acceptance rates of 87% and 86%, respectively, of cervical cancer screening using VIA technique.[48,49] Though level of patients' satisfaction with the VIA screening provided was not specifically assessed in this study, in a similar study in Thailand, over 95% of women expressed satisfaction with their experience with visual inspection test.[50] This finding indicated that majority of women will accept screening for cervical cancer, if offered the opportunity to test.

There appear to be conflicting evidence, based on previously published data, regarding the influence of clinical characteristics and ART on Human Papilloma Virus (HPV) infection, and the development of intraepithelial neoplasia.[16,27,51-54] For example, an analysis of 1639 HIV+ and 452 HIV negative women in a study in the United States showed that abnormal cytology progression was significantly increased only among the most immunosuppressed
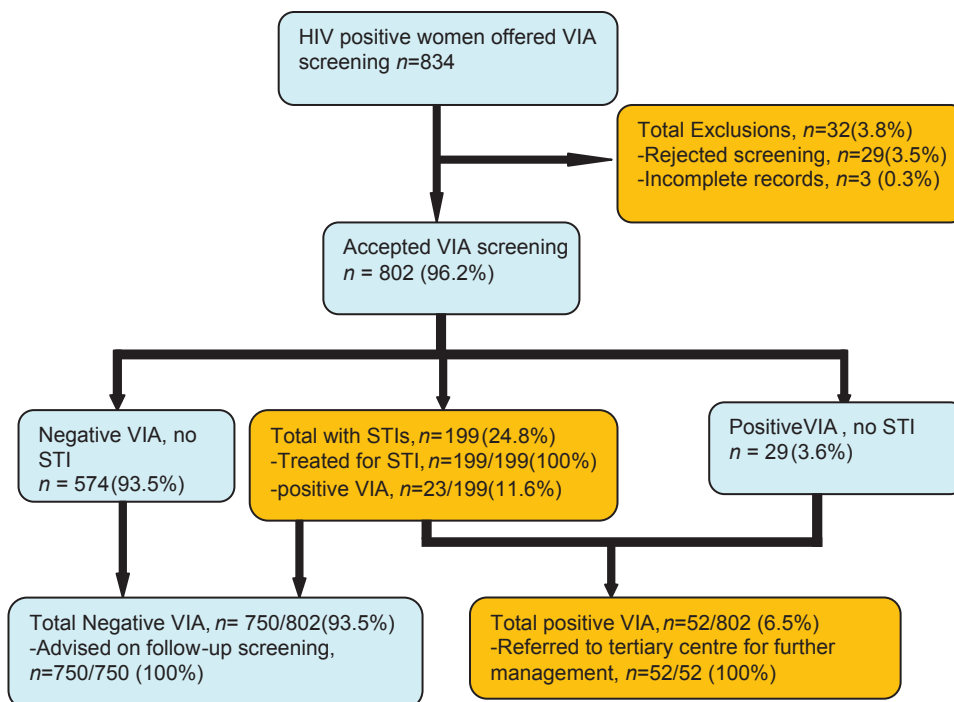
Figure 1: Cervical cancer (VIA) screening flow chart

women, while regression was significantly reduced in all HIV seropositive women except those with the best controlled HIV disease.[16] In this study, however, there was no statistically significant association observed between CD4 count values and the occurrence of cervical neoplasia, which was consistent with findings reported by some studies.[55,56]

The incidence rates of cervical cancer have been reported to vary with geographical region.[57,58] The Eastern African region followed by the western region, then South African region have been reported to have the highest age-standardised incidence of cervical cancer in the African continent.[6,59] These regional differences might be explained by genetic variations, differences in lifestyles, environmental factors and medical practices such as screening which are important determinants of cancer risk.[60] This assumption is reinforced by migration patterns that show that incidence of cancer among migrant's changes to more closely reflect the rates in the adoptive country.[60,61] Hence, reported positivity rates with VIA also vary by country and region. A study in Côte d'Ivoire reported a rate VIA positivity rate of 9.0% amongst HIV+ women and 3.9% amongst HIV negative women.[36] A similar study in Kenya amongst women in HIV care reported a positivity rate of 7.1%.[48] Studies have also reported comparatively lower VIA positivity rates amongst HIV negative women.[36,62] Our pilot program indicated a positive VIA result of 6.4% amongst HIV+ women on ART. Our finding was comparable with the 7.7% and 7.1% VIA positivity rate observed in studies in Kenya and Bangladesh.[48,63] The lower positivity observed in our study could be ascribed to the fact that all HIV+ women screened in our program were already on ART. Studies have suggested that ART may decrease the risk of cervical cancer in HIV+ women.[64-66]

Our study could not compare positive VIA result with colposcopy and histology findings because the majority of patients did not receive colposcopy and histology. While we cannot determine the true performance of VIA screening in our context, there is evidence in the literature on the positive predictive value, sensitivity and specificity of VIA. A study in Bangladesh that compared Pap smear and VIA outcomes with histology results of tissues obtained from colposcopy directed biopsy revealed that VIA had a 94.4% sensitivity rate compared with 55.5% observed with pap smear.[63] Another study reported specificity and sensitivity rates of 82.5% and 66.9%, respectively, with VIA compared with 77.5% and 86.8%, respectively, with Pap smear in low resource settings.[67] Additional evidence on the positive predictive value (PPV), reported a PPV of 26.7% for Pap smear and 7.1% for VIA.[68]

Our pilot program integrated screening for cervical cancer using VIA technique into HIV care and treatment program in MDH through a combination of stakeholder engagement, capacity building for health workers, creating a bi-directional referral between HIV and RH services, and provision of the required commodities and equipment.

The program highlighted several lessons and identified an important challenge. First, integration of cervical cancer screening and ART services in resource-limited settings is possible, and second, the majority of HIV+ women would agree to screening for cervical cancer if offered and provided free of cost. However, the inability of the majority of patients to afford the required confirmation investigations was a considerable challenge.

We observed that out of a total of 52 VIA positive women, 35 (67.3%) could not access further care at the tertiary site due to cost. Patients' inability to pay for follow up investigations also accounted for significant losses in a similar study in Côte d'Ivoire.[36] Other programs that used a test and treat approach recorded better uptake of confirmatory test and treatment.[48,63,69] The significant losses observed in our study with an approach that refers patient for confirmation and treatment suggest that a "test and treat" approach that combines colposcopy, biopsy and immediate cryotherapy for positively screened cervical lesions in one site may provide better outcomes. However, considering the fact the majority of women in Nigeria access care in primary health centres were 'screen and refer' services maybe the only feasible option, providing free or subsidized treatment services at referral centres after screening is likely to significantly increase uptake.

Lastly, our study results should be interpreted with caution, as information on patients' clinical characteristics such as CD4 count and WHO staging were obtained from patient records entered into the LAMIS and were therefore subject to availability of data. Complete patient record for CD4 count and WHO staging were available for 61.7% and 66.7% of patients, respectively. Additionally, in our study, because the majority of women with positive VIA did not access colposcopy and histology sampling, we could not evaluate the performance of the visual inspection test in our study population.

CONCLUSION

The high burden of both HIV and cervical cancer in developing countries makes it a necessity for integrating services that offer early detection and treatment for both diseases. Our study findings suggest that integrating VIA screening into the package of care offered to HIV+ women is feasible and acceptable. Positive VIA test was associated with presence of a lower abdominal pain syndrome. Cervical cancer screening should be included as a standard package of care in HIV treatment programs. However, an approach that combines confirmation of lesions and treatment may reduce losses and improve outcomes.

ACKNOWLEDGMENTS

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