Cervical cancer screening: A comparative analysis of visual inspection with acetic acid (VIA), colposcopy and histopathology in a community survey in Osun State, Nigeria

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Article Info

Article type:
Original Article

Article history:
Received: December 17, 2023
Accepted: March 7, 2024
Published: June 30, 2024

Keywords:
Cervical cancer, screening, visual inspection with acetic acid (VIA)

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This article can be accessed at:
www.rjhs.org

http://dx.doi.org/10.4314/rejhs.v12i3.4

Abstract

Background: The second target for the global strategy for eliminating cervical cancer is impossible without mass screening of women at risk of cervical cancer with a high-performance screening test. VIA may need to be replaced with a low-cost high performing test that can be used for all age groups.
Objective: To determine the CCS uptake, VIA-positivity rate, and correlation between VIA results and histology reports in VIA-positive women in Osun State, Nigeria.
Methodology: We conducted a community-based study on 600 women recruited from 3 communities in Osun State, Nigeria. Participants had sensitization and then cervical screening with VIA. VIA-positive women were triaged with colposcopy ± biopsy. Participants were treated based on colposcopy findings. Data was analyzed with SPSS version 26. A p-value < 0.05 was taken as statistically significant.
Results: The CCS uptake rate was 89.5% while the VIA-positivity rate was 4.9%. 10 out of 23 (43.5%) of VIA-positive women had CIN on histology.
Conclusion: The "screen-triage-treat" approach in which colposcopy was used to triage the VIA-positive women performed better in this population.

Dépistage du cancer du col de l'utérus : une analyse comparative de l'inspection visuelle avec l'acide acétique (IVA), de la colposcopie et de l'histopathologie dans le cadre d'une enquête communautaire dans l'État d'Osun, au Nigéria

Résumé
Contexte de l'étude: Le deuxième objectif de la stratégie mondiale d'élimination du cancer du col de l'utérus est impossible sans un dépistage massif des femmes à risque de cancer du col de l'utérus au moyen d'un test de dépistage performant. IVA devra peut-être être remplacé par un test peu coûteux et très performant pouvant être utilisé pour tous les groupes d'âge.
Objectif de l'étude : Déterminer l'adoption du CCS, le taux de positivité du IVA et la corrélation entre les résultats d'IVA et les rapports histologiques chez les femmes séropositives pour l'IVA dans l'État d'Osun, au Nigéria.
Méthode de l'étude : Nous avons mené une étude communautaire sur 600 femmes recrutées dans 3 communautés de l'État d'Osun, au Nigéria. Les participantes ont subi une sensibilisation puis un dépistage cervical avec IVA. Les femmes IVA-positives ont été triées par colposcopie ± biopsie. Les participants ont été traités sur la base des résultats de la colposcopie. Les données ont été analysées avec SPSS version 26. Une valeur p <0,05 a été considérée comme statistiquement significative.
Résultat de l'étude: Le taux de recours au CCS était de 89,5 % tandis que le taux de positivité au VIA était de 4,9 %. 10 femmes sur 23 (43,5 %) séropositives pour IVA présentaient une CIN à l'histologie.
Conclusion : L'approche « dépistage-triage-traitement » dans laquelle la colposcopie a été utilisée pour trier les femmes IVA-positives a donné de meilleurs résultats dans cette population.
Mots-clés : Cancer du col de l'utérus, Dépistage, Inspection visuelle à l'acide acétique (IVA)

INTRODUCTION

Cervical cancer is the fourth most common cancer among women worldwide (1,2). It is a preventable disease, yet it remains one of the leading causes of cancer deaths among women in developing countries (3). It is a public health problem in developing countries such as Nigeria (4). The World Health Organization Director General, Tedros in 2020 estimated that one woman dies from cervical cancer every two minutes (3). Over 90% of cervical cancer cases and deaths occur in Africa and Asia (4). The cervical cancer death rate in low- and middle-income countries (LMIC) is reported as 13.0/100,000 women in 2020 (5). In Nigeria, 12,075 new cases of cervical cancer and 7,968 deaths are reported annually (4). This is largely due to the inequitable distribution of cervical cancer screening services and immunization in Nigeria and other developing countries (3,4). Despite the high burden of the disease, screening in these countries is still at best opportunistic, sporadic, poorly coordinated, and sponsored by donors or done as part of Research (5,6). The overall screening rate in LMIC is low, rates between 2.2% and 19% have been reported (1,6–9).

In 2020, the WHO launched Cervical Cancer Elimination Initiative (CCEI) and unveiled a triple strategy recommendation that 90% of girls should be vaccinated for Human papillomavirus, while 70% of women should be screened and 90% of screened-positive women and women with cervical cancer should be treated by 2030 (4,10). To achieve this, there is a need for developing countries to harken and hasten activities towards adopting a sustainable screening method that is adaptable to the environment and reduces loss to follow-up. Low or moderate cost also contributes to the potential of screening tests for stage shifting (3,4).

Visual inspection with acetic acid (VIA) meets these criteria. It is feasible and acceptable as patients know the results of their tests almost immediately. It has been found to reduce the prevalence of cervical cancer by 25% and mortality by 35% over 7 years (11). Good training and sustained quality assurance are however necessary for effective VIA screening (3,11,12). Its main drawback lack of standardization, intra and inter-observer variations is that it may not be appropriate in older women due to the repositioning of the transformation zone (3,13). VIA may be a test of choice in resource-constrained settings.

Community-based health screening programs are important in reaching a wider population at high risk of cervical cancer than the current opportunistic screening that targets low-risk women. It increases screening coverage (15–18). This has gained popularity in recent times as it has been found to increase the screening uptake rate with some cost savings (9,19). Community-based screening for cervical cancer has been found to yield a better response rate compared to hospital–based screening (8,9,20). In addition, effective mass screening programs must make provision for follow-up and treatment (9,21). Another population-specific strategy proven to improve the uptake of cervical screening is the provision of incentives like transportation for follow-up and treatment (8).

We therefore carried out a community-based study on screening of cervical cancer with VIA in Osun State, Nigeria. VIA-positive participants were transported for treatment in a tertiary hospital within the State.

Objectives:

We aimed to

I) Determine the uptake rate of cervical screening in this community,

II) Determine the prevalence of screen-positive women in this group and

III) Assess the degree of concordance between VIA results and histology reports for biopsied specimens among individuals identified as VIA-positive.

MATERIALS AND METHODS

This was a descriptive cross-sectional community-based study carried out within three communities in Osun State, Nigeria between September 2021, and April 2022. Osun State is in the Southwestern part of Nigeria with a land mass area of 8,699,836m^2 (22). The total population of the residents is 3,416.959 with a population of women aged 21 to 65 years being 775,794 (22). The residents are mainly traders, farmers, and civil servants.

The sample size was calculated using Leslie Fisher's formula with a confidence interval set at 95%, a normal deviation of 1.96, and d=0.025 (24). Using 8% cervical cancer screening uptake from a previous community-based study in Nigeria and 20% attrition because the study involved transportation to another town for cervical biopsy, a minimum sample size of 548 was obtained (6). The sample size was rounded up to 600 and 200 participants were recruited from each of the three communities. The three communities were selected randomly. The selected communities were the Oke-Baale and Atelewo communities in Osogbo and the

Eleyele community in Ile-Ife. Each of these communities has a Primary Health Care Centre domiciled therein.

A purposive sampling method was used for this study. The inclusion criteria were women between 21 and 49 years, who were not menstruating and were at least six weeks postpartum while the exclusion criterion was refusal to give consent. Ethical clearance was obtained from the Ethics and Research Committee of Ladoke Akintola University Teaching Hospital (UTH/EC/2021/04/513), Osogbo, and Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State. Osun State Primary Health Care Board (OSPHCB) gave written approval for the conduct of the study.

Two Community mobilizers (CM) were recruited in each of the three communities. These CMs mobilized women for sensitization and cervical cancer screening. Community sensitization visits were held in each community and women were recruited from these meetings. Women mobilized were directed to the PHCs located within the communities. During these sensitization meetings, women had 10 minutes of health education on cervical cancer prevention and treatment. Those who consented were then enrolled in the study. The health education and cervical cancer screening were held at the Primary Health Centre, Oke-Baale, Atelewo Model Primary Health Centre, and Comprehensive Health Centre, Eleyele located within the communities respectively.

Cervical cancer screening using visual VIA was conducted for all participants between 21 and 49 years old after signing the informed consent. Those above 49 were referred for Pap smear in the neighbouring teaching hospitals. The screenings were done on specific days of the week by two of the authors, who are Gynaecologic Oncologists. The screening procedure used is elucidated as follows. A pelvic examination was done by exposing the cervix with a bivalve speculum under direct vision with a good light source. Excess discharge or mucus was cleaned with a swab stick soaked with Normal Saline. The transformation zone was identified following which their cervix was painted with 5% acetic acid. The presence or absence of aceto-whitening was noted after 60 seconds of painting with 5% acetic acid. Participants with aceto-whitening were tagged VIA positive while participants without aceto-whitening were tagged VIA negative. VIA-positive women were referred for colposcopy with biopsy at the Gynae-Oncology unit of Obafemi Awolowo Teaching Hospital Complex, Ile-Ife, Osun State. Transportation arrangements were made for the referrals at no cost to the participants. Colposcopy and biopsies were done by SBB and CAA. All VIA-positive participants had cervical biopsies done and tissue sent for histology. Pre-cancerous lesions were treated with thermal ablation while participants with cervical cancer had surgical management. The outcome measures were the prevalence of VIA-positive subjects among the study population, the percentage of VIA-positive women who had abnormal findings on histopathologic examination, and the percentage of VIA-positive women who had treatment.

Statistical analysis was done with Statistical Package for Social Sciences (SPSS) 26.0 by IBM. The frequency table was constructed for the variables. Categorical variables were analyzed by Chi-square while numerical variables were analyzed by Student T-test. The Fisher Exact Test was used to determine the association between demographic factors and the need for thermal ablation treatment among VIA-positive participants. A p-value less than 0.05 was taken as statistically significant.

RESULTS

Out of the 600 women who presented at the PHCs after sensitization, 537 (89.5%) consented to cervical cancer screening after health education and were enrolled in the study. 71 could not be screened with VIA as they were above 49 years old. Therefore, 466 were screened with VIA. Figure 1 shows the study flow chart. The mean age of these participants was 35.10±7.35 years, while the mean parity was 2.38±1.57. About half (53.6%) of the subjects had tertiary education while (366) 63.5 % were employed as unskilled workers. (Table 1).

The squamocolumnar junction (SCJ) was visualized in 452 (97.0%) (Table 2). Twenty-three participants were VIA-positive, this gave a VIA-positive rate of 4.9%.

Although 23 women were VIA positive, Triaging was done with colposcopy and five participants had normal findings and were neither treated nor biopsied. Eighteen had lesions on colposcopy and therefore had colposcopically directed biopsy. Six participants had treatment with thermal ablation on account of colposcopically diagnosed CIN 2 and CIN3 lesions (table 2).

Cervical biopsy tissue was subjected to histology. Histology report was normal in

3(0.6%) while cervicitis was seen in 5(1.1%). Low-grade CIN (CIN 1) was reported in 6 (1.3%) while 4 (0.9%) had high-grade CIN (CIN 2). 10 out of 23 (43.47%) had CIN out of the VIA-positive women on histology.

Amongst the participants that were treated only 4 out of 6 (66.0%) had CIN 2 which merited treatment. Therefore 14 out of 23 participants (60.9%) would have had treatment despite not having high-grade CIN if the 'see and treat' approach had been used as against the 'see, triage and treat' approach utilized.

Analysis for association between treatment and sociodemographic factors did not attain statistical significance Table 3.

Out of the 6 subjects who had treatment, 3 were confirmed to have CIN 2 by histology (table 4). Table 4 shows an analysis of the association between histology and the need for treatment and did not attain statistical significance (p value=0.233).

DISCUSSION

The prevalence of VIA positivity in this studied population is 4.9%. This is lower than findings from previous works with the range of 5.8-27.4 % (2,23–26). This wide range may be attributed to variations in the age of the women, training, and skill of the provider, community/hospital-based, and characteristics of the screened population (23). The low VIA positivity rate in our study may be due to this being a community-based survey. Our study was community-based screening as compared to David et al who reported a higher VIA-positive rate in a hospital-based screening conducted in a Gynaecology clinic (24). Also, the proportion of pre-malignant lesions was lower than reports from David et al (24). This may be attributable to the fact that we screened women without symptoms within the community. This may contribute to the generalizability of this study result.

The mean age and parity of the participants were comparable with previous reports (2). More than half of the screened population had tertiary education (53.6%). Their educational status might have influenced their willingness to be screened. It is however of concern that despite this high level of education, most of the screened population were either unemployed or employed in semi-skilled positions. This low earning power may underscore poor health-seeking behaviours reported in low-resource settings where healthcare financing remains largely out of pocket.

After histology reports, only 4 (22.2%) of the VIA-positive women had high-grade CIN which is an indication for treatment (27). Furthermore, only 10 (43.5%) of the VIA-positive women had CIN on histology. If a screen-and-treat approach had been used for this study population, (14 out of 23) 60.8% would have been overtreated while 5 out of 23 (21.7%) would have received inappropriate treatment for cervicitis. This underscores the reported overtreatment rate of the see-and-treat approach to cervical screening using VIA (28). Although WHO screening guidelines recommended HPV testing as the primary screening method for premalignant lesions of the cervix, it was concluded that VIA can be used in resource-constrained settings until HPV tests become available (3,9,11,14). HPV tests are important in cervical cancer risk stratification. In addition, HPV screening often requires a triage test to determine who is truly at risk of developing cervical cancer as HPV infections could later spontaneously disappear (29). The main reason VIA is still being employed for primary cervical cancer screening in LIMCs is due to inadequate financial and human resources.

As cervical cancer screening with VIA is still indispensable in resource-constrained settings, there is a need to mitigate its shortcomings. A proposed approach to this is the use of the “Screen, triage and treat” approach instead of the “Screen and treat” approach. The introduction of a second test like an HPV test or colposcopy to triage VIA-positive women will reduce overtreatment in the screened population. Screening of 70% of women using high-performance tests by ages 35, and 45 is one of the three targets of WHO to reduce the scourge of cervical cancer by 2030 (4). The inclusion of a triage test such as a low-cost HPV DNA test will increase the performance of VIA in screening for premalignant lesions of the cervix. A good example can be found in India which operates a stratified screening based on resources available which is categorized as good or limited by the Federation of Obstetricians and Gynaecologists Societies of India (FOGSI) (14). VIA along with colposcopy triage is recommended for limited resource settings in India (14). Nigeria and other low-resourced settings can also add a triage test to VIA to improve its performance. WHO may consider this option for LMIC as there have been calls to adjust its global strategy for cervical cancer elimination (30). The current WHO global strategy for the elimination of cervical cancer did

not include specific guidelines for LMIC where 90% of cervical cancer deaths occur and the recommended HPV screening is out of reach because of limited resources (4,29).

A component of the third target of the global strategy for eliminating cervical cancer; the treatment of 90% of women with pre-cancerous lesions can be achieved by a single-visit approach (4,29). This can be achieved by including HPV point-of-care screening along with VIA. Many women are often lost to follow-up with a multiple-visit approach (30). This study adopted a multiple-visit approach but none of the participants was lost to follow-up due to the provision of transportation logistics for further visits.

Furthermore, age was found to be significantly associated with lesions that required thermal ablation (high-grade CIN), although the sample affected was small compared to the population screened. High-grade CIN (confirmed by histology) was significantly higher in women aged 30 years and above. This might be due to the higher incidence of regression of CIN lesions in younger women (31). Although the mechanism remains unclear, an association between high-grade CIN lesions and elevated vaginal pH in the presence of HPV infection has been suggested by recent pieces of literature (32,33). Postmenopausal women are known to have elevated vaginal pH due to reduced estrogen levels (34,35).

The strength of this study is the inclusion of biopsy and histology to confirm the true diagnosis of precancer in VIA-positive participants and this afforded them appropriate treatment and follow-up. This study also attempted to verify the effectiveness of the "screen and treat" approach with VIA as the primary screening test. The findings from this study also emphasize the over-treatment and missed opportunity for appropriate treatment associated with the "screen and treat" approach with VIA in resource-constrained settings. The limitation of this study is the sample size. Further studies with a larger sample size are recommended.

CONCLUSION

Cervical screening uptake was high in this population, but the VIA positivity rate was low. The "screen and treat" approach is associated with significant inappropriate treatment. The "screen, triage and treat" approach in which a second test to triage the VIA-positive women may be better in this population in a bid to meet the second target of global strategy for CCE; screening 70% of women with a high-performance test. The inclusion of low-cost HPV tests which can be interpreted immediately has the potential to improve the yield of cervical cancer screening in LIMCs.

Recommendation: Cervical screening with screen, triage, and treat is more likely to be associated with less risk of over-treatment.

Limitations: This study did not include tests that can be used in women over 50 years such as Pap smear and VIA. Thus, this category of women could not be analyzed. A study encompassing these other tests may be more generalizable in the community.
A larger sample size may be needed to further explore the prevalence of wrong treatment in women treated following cervical screening with only VIA.

Authors' contribution: All authors contributed to the conceptualization of the study and manuscript preparation. SBB (Sekinah B. Bola-Oyebamiji) and CAA (Clement A. Adepiti) performed VIA, Colposcopy, and treatment.

Declaration: We declare that the abstract of this study was accepted and presented at the 64th Annual Scientific Conference and Annual General Meeting of the West African College of Surgeons which was held in Freetown on the 3rd to the 8th of March 2024.

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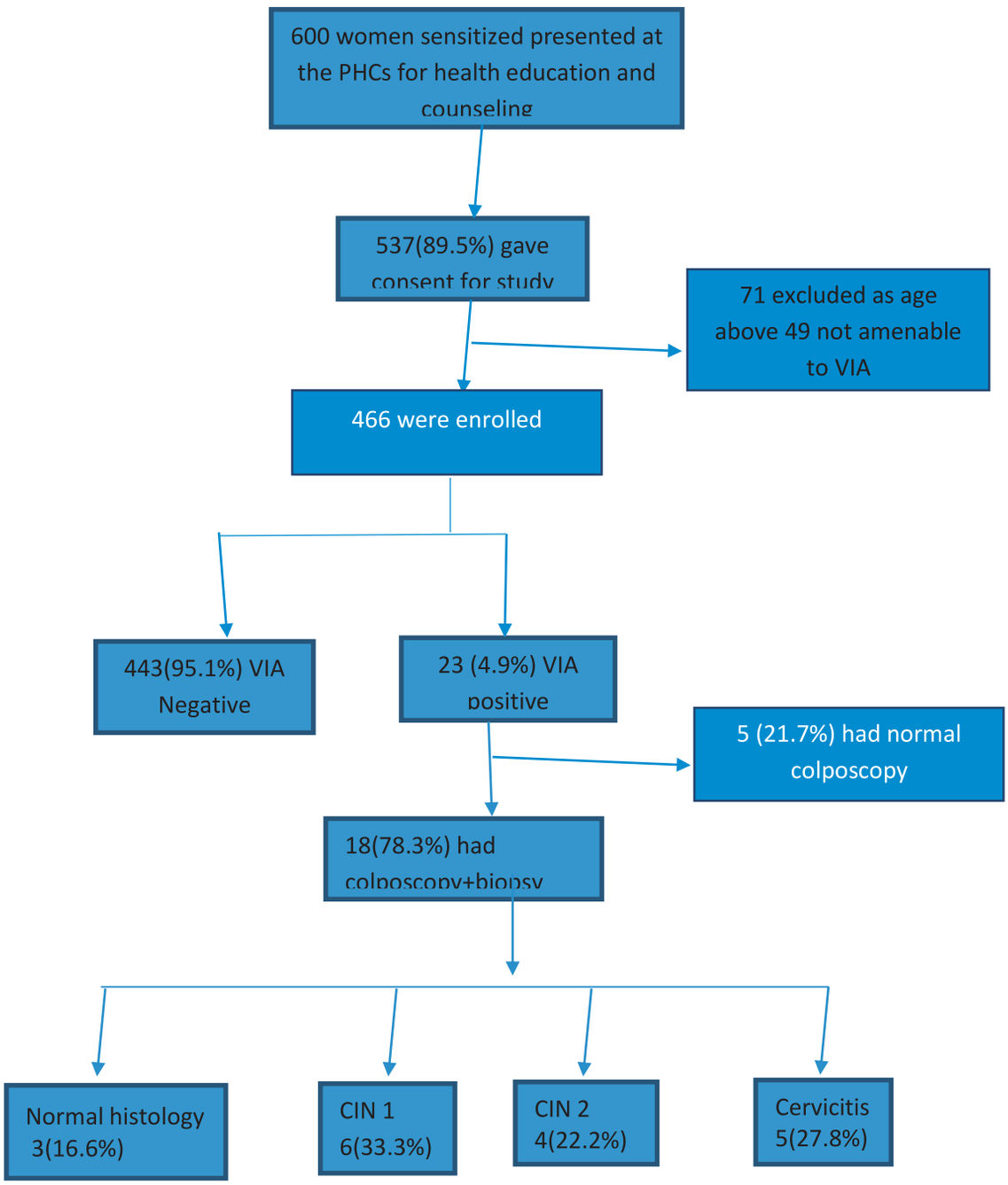

Figure 1: Study flow chart of participants

Table 1: socio-demographic data of Participants (n=466)

Variable		Percentage
Age	Mean age ±SD	35.10±7.35
Parity	Mean parity ±SD	2.38±1.57
	Frequency	**Percentage**
Educational Status		
No/Primary education	49	10.5
Secondary School	167	35.9
Tertiary education	250	53.6
Occupation Status		
Skilled	143	30.7
Unskilled	296	63.5
Unemployed	27	5.8
Marital Status		
Single	25	5.4
Married	438	94.0
Widow	3	0.6
Parity		
Nulliparous	73	15.6
Multiparous	354	76.0
Grand multiparous	39	8.4

Table 2: Findings during the Screening of Participants

Variable	Frequency	Percentage (%)
SCJ		
Visualized	452	97.0
Not visualized	13	2.8
Partial	1	0.2
VIA Findings		
Negative	443	95.1
Positive	23	4.9
Colposcopy		
Colposcopy Not done	446	95.7
Normal colposcopy	5	0.01
Colposcopy+ Histology	18	0.04
Histology		
Normal Histology	3	0.64
CIN1	6	1.29
CIN 2	4	0.86
Cervicitis	5	1.07
VIA Positive (n=23)		
Yes (Had Treatment)	6	26.0
No (Did not have treatment)	17	73.9.

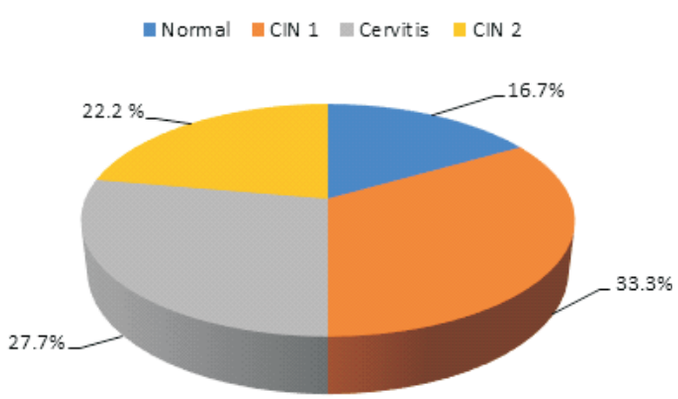

Figure 2: Histology Result of VIA Positive Participants

TABLE 3: Association between Demographic Factors and Participants' who were VIA positive and had treatment.

Sociodemographic factor	Participants who had treatment N=6 (%)	Participants who did not have treatment N=17 (%)	Fisher Exact test	P value
Age 21-29 years	0(0)	1(7.1)	1.164	0.559
30-39 years	4(66.7)	6(42.9)		
40-49 years	2(33.3)	7 (50.0)		
Marital Status: Single	0	0	0.952	0.329
Married	6(100.0)	12(85.7)		
Widowed	0	2(14.3)		
Educational Status				
Primary education	1(16.7)	0		
Junior Education	0	1(7.1)		
Secondary education	2(33.3)	4(28.6)	2.937	0.402
Tertiary Education	3(50.0)	9 (64.3)		
Occupation Skilled	3(50.0)	5(35.7)	0.357	0.550
Unskilled	3(50.0)	9(64.3)		
Unemployed	0	0		
Parity				
Nulliparous	0	0		
Multiparous	6(100.0)	12(85.7)	0.952	0.329
Grand Multiparous	0	2(14.3)		

*Statistically significant

Table 4 Association between Histology and Treatment (n=18)

Variable		Yes (%) (had treatment)	No (%) (Did not have treatment)	X^2 value	p-value
Histology:	Normal	1(16.7%)	2 (16.7%)		
	CIN 1	1(16.7%)	5 (41.7%)	4.275	0.233
	CIN 2	3 (50%)	1 (8.3%)		
	Cervicitis	1(16.7%)	4 (33.3%)		
Total		6	12		