COMPARISON OF VISUAL INSPECTION WITH ACETIC ACID (VIA) WITH PAPANICOLAOU (PAP) SMEAR METHOD OF CERVICAL CANCER SCREENING AMONG WOMEN ATTENDING A TERTIARY HOSPITAL IN LAFIA, NORTH CENTRAL NIGERIA.

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Key Words: Visual Inspection with Acetic acid, Papanicolaou smear, comparison, cervical cancer.

ABSTRACT

Background: Cervical cancer is the second most common killer disease of women in the world, and the commonest killer of women in developing countries like Nigeria, with about 86% of the disease occurring in those countries. There is therefore the need to improve on the current screening measures for the disease.

Method: This hospital based descriptive cross sectional study involved women aged 21 to 65 years who attended the GOPC of Dalhatu Araf Specialist Hospital Lafia either as patients or patient relatives during the study period. A simple random sampling technique was used to recruit 239 participants. Data collected about the participants included socio-demographic background, gynaecologic and other relevant medical histories, and the presence of risk factors for cervical cancer. Physical examination included the weight, height, BMI and blood pressure of the study participants. All women enrolled in the study underwent both VIA and Pap smear tests. The chi square test was used to determine significance of associations between groups. Student's t-test was used to compare means of results as appropriate. A P-value less than 0.05 was considered significant. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for VIA using Pap smear as the reference standard.

Results: Only 28 (11.7%) of the study participants had heard about cervical cancer. None of them had ever heard about VIA while 10 (4.2%) had heard about Pap smear test as a screening test for cervical cancer. Fifty four (22.6%) of the 239 participants had VIA positive results while 33 (13.8%) of the study participants had Pap smear positive results. Eleven (4.6%) of the participants had inconclusive Pap smear results. The sensitivity of VIA was 66.7%, the specificity, positive predictive value and negative predictive value were 84.5%, 40.7% and 94.1% respectively. VIA results were available immediately whereas Pap smear results took four to eight weeks to obtain. VIA procedure was also much cheaper than Pap smear.

Conclusion: This study revealed that the level of awareness about cervical cancer among the study participants was low. No participant was aware of VIA as a screening method for cervical cancer but a small percentage of the participants were aware of Pap smear test. VIA was much cheaper to carry out than Pap smear and it took less time to obtain results. VIA is a reliable alternative to Pap smear test as a screening test for cervical cancer.

INTRODUCTION

Cancer of the uterine cervix is a malignant change that has its origin at the squamo-columnar junction of the cervix.[1] Cervical cancer is the second most common cancer in women worldwide and the leading cause of cancer deaths in developing countries.[2, 3] While incidence and mortality rates of cervical cancer have fallen significantly in developed countries, the incidence is still very high in developing countries with 85% of all deaths from the disease occurring in this region.[4] In Nigeria, 12% of women screened at the University College Hospital Ibadan between 1992 to 1995 had early cervical dysplasia,[5] while in Jos, Sagay et al reported in 1999 that cervical pre-cancer lesions were more common among HIV infected women (40%) when compared with HIV negative controls (17%).[6]

There are some known aetiological factors for the development of cervical cancer. Ninety-nine point seven percent (99.7%) of the cases are associated with prior infection with one or more oncogenic types of human papilloma virus (HPV).[3] Two strains of the virus, known as HPV 16 and 18, are estimated to be involved in the development of 70% of all cervical cancer cases. Risk factors for cervical cancer include early onset of sexual activity, multiple sexual partners, herpes simplex infection especially type II, cigarette smoking and infrequent or no cervical cancer screening.[5]

The new guidelines by the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology on Cervical Cancer Screening as at May 2012 recommended that cervical cancer screening should begin at age 21 years irrespective of age of sexual initiation or other risk factors. For this to be effective, a good preventive programme must use a screening test that is safe, accurate, affordable, accessible and practical, for "cervical cancer prevention is not about doing the best test but about doing the best test that one can do".[7]

Cervical cancer screening tests include the conventional cytology (Papanicolaou smear), HPV DNA test, Visual Inspection with Acetic acid (VIA), Visual Inspection with Acetic acid and Magnification (VIAM) and, Visual Inspection with Lugol's Iodine (VILI).[3] Pap smear involves a microscopic examination of the cells scraped from the opening of

the cervix. Pap smear has been considered to be the Gold standard in spite of its limitations such as its being a complex laboratory test which requires a trained cytotechnician for reading and a pathologist for review.[3]

Use of VIA has been advocated as an alternative screening method to Pap smear in developing countries. The attractive features of VIA include low cost, simple administration, immediate availability of results and accuracy comparable to good quality Pap smears.

OBJECTIVE

To determine the reliability of Visual Inspection with Acetic acid (VIA) as a screening test for cervical cancer with a view to recommending it as an alternative to Papanicolaou smear method of cervical cancer screening.

MATERIALS AND METHOD

The study was conducted in the Family Medicine Department of the Dalhatu Araf Specialist Hospital, Lafia, between 1st August 2013 and 30th September 2013. It was a descriptive cross sectional study. The participants were women between 21 and 65 years of age who presented at the General Out Patients Clinic either as patients or as caregivers, within the period of the study, irrespective of their complaints. The sample size of this study was determined using the Kish Leslie formula.[8] The confidence level was taken at 95%, prevalence of pre-cancerous (CIN) cervical lesions in a previous study in Jos was 17 % (0.17),[7] sampling error was taken to be 5% (0.05) and the determined minimum sample size (n) was 217. An attrition rate of 10% of the participants was assumed for the study, therefore, total number of participants recruited for the study was 239.

At recruitment, the study was explained to the participants and consent obtained. Participants were instructed not to douche, use tampons, birth control foams or jellies, other vaginal creams or medications and to refrain from sexual intercourse 48 hours prior to the test. Their next appointment was scheduled approximately 10 to 18 days after the first day of the last menstrual period. A questionnaire was completed for each eligible participant including demographic data such as age and occupation of participants. Features of cervical cancer, other gynaecological conditions such as pelvic inflammatory disease and cervicitis were sought for. Questions related to awareness and risk factors for the disease were also asked.

Only the investigator carried out all the tests. Each participant was assessed in lithotomy position on a standard examination couch. Under good fluorescent light source, the perineal area was inspected and finding(s) were recorded. Under aseptic condition, sterilised Cusco's speculum was lubricated with warm water then inserted into the vagina. The light source was adjusted until a clear view of the cervix was achieved. For the VIA, cotton wool swab soaked in 5% acetic acid and held with a sponge holding forcep was used to flood the cervix. The cotton wool was withdrawn after one minute and the cervix was inspected in each case. The VIA test outcome was reported according to the WHO and International Agency on Research against Cancer format.[1] Where VIA was positive but associated with cervicitis, a swab was taken for culture. The participant was treated and was advised to come for re-examination in six weeks. The tests were then repeated at that visit.

For Pap smear, the participant was placed in lithotomy position and good cervical visualisation was ensured as for VIA above. Two slides were prepared for each patient. Ayre's spatula was used to scrape the transformation zone. It was rotated through 360°. The spatula was then withdrawn and the sample quickly smeared unto the proximal halves of already labelled pair of clean, dry glass slides. The sample collection was repeated immediately using a cytobrush but this time smeared unto the distal halves of the partly used slides for the same patient. The Cusco's speculum was withdrawn immediately and the participant was cleaned up. The slides were immediately fixed while still wet in 95% ethanol in a coupling jar for a minimum of 30 minutes. Each participant was also informed of the preliminary findings.

The samples were organised in batches and sent to the laboratory for Papanicolaou staining. The Bethesda classification was used for reporting.[3] Those with positive smear (LSIL and HSIL) were referred appropriately to Gynaecologists for further review. Those participants with normal results were given three years follow-up appointment.[9]

Approval for the study was obtained from the Health Research Ethics Committee of Dalhatu Araf Specialist Hospital Lafia. Participation was voluntary, with provision for opt out. Access to the results of the study was restricted to the investigator, research assistant and the individual participants only. All the participants completed the study.

Table 1: Socio-demographic characteristics of the study participants. N = 239

Variable	No	Percentage	X^2	P-value
Age (years)			16.750	
21 - 30	70	29.3		0.001*
31 - 40	66	27.6		
41 - 50	61	25.5		
≥ 51	42	17.6		
Ethnicity			-	
Eggo n	61	25.5		0.234[F]
Hausa	35	14.6		
Alago	33	13.6		
Kanuri	22	9.2		
Igbo	12	5.0		
Mada	8	3.3		
Others	68	28.5		
Marital Status			-	
Single	10	4.2		0.043*[F]
Married	206	86.2		
Divorced	7	2.9		
Widowed	16	6.7		
Religion			0.472	
Christianity	111	46.4		0.492
Islam	128	53.6		
Education			3.177	
No formal	82	34.3		0.365
Primary	47	19.7		
Secondary	57	23.8		
Tertiary	53	22.2		
Occupation			-	
Trading	86	36.0		0.471[F]
Civil Servant	67	28.0		
Housewife	27	11.3		
Artisan	16	6.7		
Farming	11	4.6		
Unemployed	32	13.4		

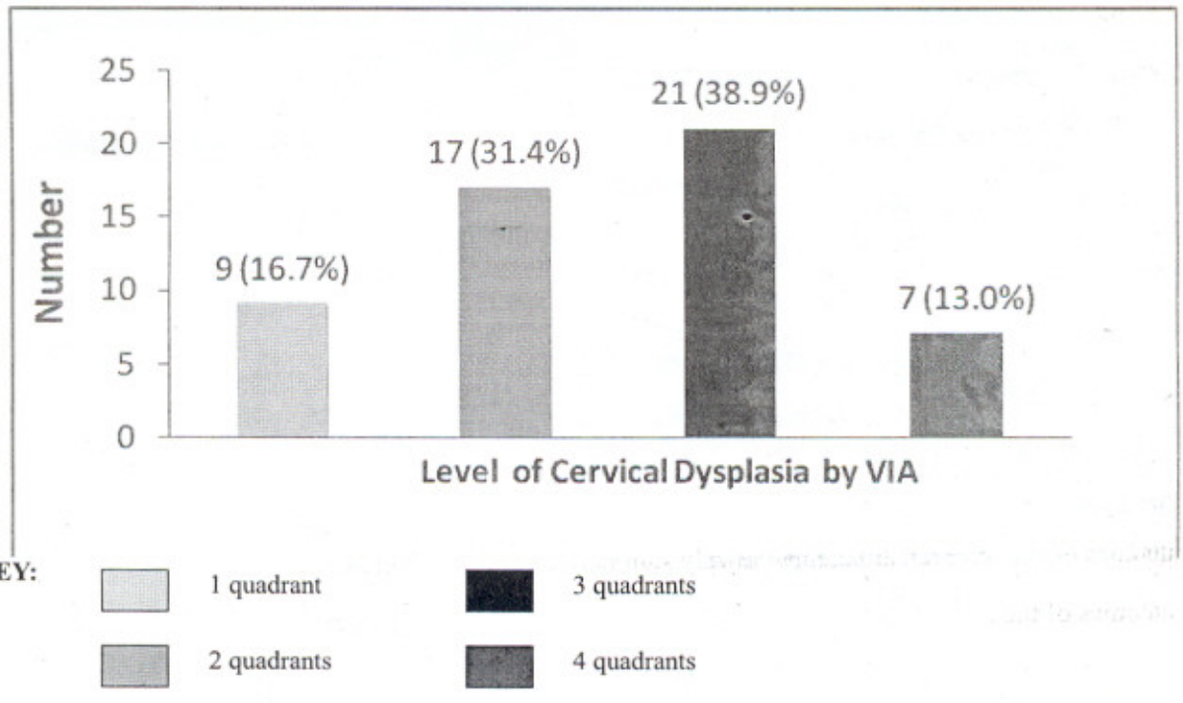
KEY : * = Statistically significant, F = Fisher's exact test

Level of cervical dysplasia among the study participants.

Level of cervical dysplasia by VIA.

Fifty four (22.6%) of the 239 participants had VIA positive results. Of the 54 VIA - positive results, 9 (16.7%) had 1 quadrant of the cervix involved, indicating dysplasia. Seventeen (31.4%) had 2 quadrants of the cervix involved, 21 (38.9%) had three quadrants involved while 7 (13.0%) of these participants had 4 quadrants of the cervix involved. These findings are presented in Figure 1 below:

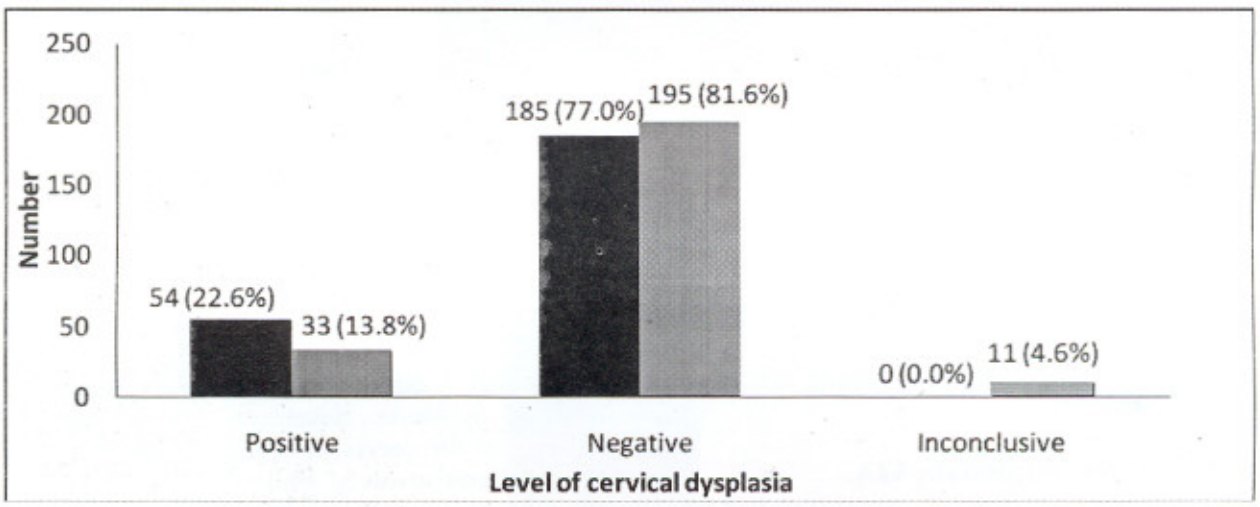
Figure 1: Level of cervical dysplasia as determined by VIA.



Level of cervical dysplasia by Pap smear test.
Low grade Squamous Intraepithelial Lesion was the test threshold. Thirty three (13.8%) of the 239 study participants had Pap smear positive results, 195 (81.6%) had Pap smear negative results while 11 (4.6%) had inconclusive results (inadequate smear, hypo cellular results and missing results). Further breakdown of the 33 Pap smear positive result showed that Low-grade Squamous Intraepithelial Lesion (LSIL) was reported in 30 (12.6%) of the participants while 3 (1.2%) had High Grade Squamous Intraepithelial Lesion (HSIL).

Comparison of cervical cancer screening by VIA, with Pap smear test.
The study revealed that 54 (22.6%) of the 239 study participants had a positive VIA result while 184 of the participants had negative VIA results. The Pap smear results revealed 33 (13.8%) had Pap smear positive results while 195 (81.6%) of the participants had Pap smear negative results. While the results of VIA was 100% conclusive, that of Pap smear was conclusive in 95.4% of the participants. Eleven (4.6%) of the 239 participants that had inconclusive Pap smear results included 5 (2.0%) with inadequate smear, 3 (1.0%) with hypo cellular results and 3 (1.0%) with missing results.
These findings are presented in Figure 4 below:

Figure 3: Bar chart comparing cervical cancer screening by VIA, with Pap smear test.



Sensitivity and Specificity of VIA
Table 2 summarizes the outcomes of VIA result against the standard (Pap smear) results. The true positive outcome of VIA was 22 (a), while the false negative outcome was 32 (b). The false positive outcome of VIA was 11 (c) and the true negative outcome was 174 (d).

Table 2: Standard two by two table of Sensitivity and Specificity of VIA against the standard (Pap smear)

VIA	Pap smear	
	Positive	Negative
Positive	(a) 22 (66.7%) ^{Sn}	(b) 32
Negative	(c) 11	(d) 174 (84.5%) ^{Sp}
Total	33	206

Sensitivity = a/a + c x 100%
= 22/(22 + 11) x 100% = 22/33 x 100% = 66.7%
Specificity = d/b + d x 100%.
= 174/(32 + 174) x 100% = 22/206 x 100% = 84.5%.
McNemar χ^2 = 9.302, p-value = 0.001
NB: Sn = Sensitivity
Sp = Specificity

The outcomes of the research are comparatively summarized in Table 3 below.

Table 3: Comparison of VIA with Pap smear: N = 239

Parameter	Test	
	VIA	Pap smear (Gold standard)
Positive results	54 (22.6%)	33 (13.8%)
True Positive	22 (9.0%)	22 (9.0%)
True Negative	174 (72.0%)	174 (72.0%)
False Positive	29 (12.0%)	-
False Negative	-	11 (4.0%)
Cost of investigation	N311/ participant	N1108/ participant
Availability of results	Immediate	4 – 8 weeks later

DISCUSSION

The VIA positive rate was 22.6%. This is much higher than the prevalence of 1.4% reported by Albert et al in Zaria[10]. The prevalence noted in previous studies by Ahmed et al in Zaria[11] and Swende et al in Makurdi[12] were 4.8% and 14% respectively. On the other hand, a slightly higher VIA positive rate of 37.1% was reported by Mahmud et al in Islamabad[13] and 38.1% reported by Ekalaksananan et al in Thailand.[14]

One of the major reasons for the wide variation in results of VIA in many studies is the lack of standardized criteria for a positive result. VIA is also provider dependent (due to the difference in interpretation by the investigators). The VIA findings also depend on the study participants since few studies were done on a symptomatic hospital-based population[15] while others were done as a mass screening test as reported by Ibrahim et al in Sudan[16] and in this study.

In this study, although the level of cervical dysplasia by VIA was also determined by the number of quadrants involved in the acetowhitening based on the WHO reporting format[1] and was found to be statistically significant, most of the studies reviewed reported the outcome of VIA results without recourse to the issue of the level of cervical dysplasia.

Thirteen point eight percent of the participants in this study had a positive Pap smear test. This is slightly higher than the 11.7% reported by Hegde et al in India[15] but markedly higher than the 0.9% positive rate reported by Albert et al in Zaria.[10] The likely explanation for the variation in the rates obtained could be because Hedge excluded women aged above 50 years, since the fifth decade manifests the peak incidence of the disease.[17] The much lower Pap positive rate in Zaria is likely because as high as 41.6% of the study participants were between 14 to19 years of age, this age range is expected to be the least likely to have cervical dysplasia. Although all the study participants in Zaria were married, and parity is a known risk factor for cervical dysplasia,[18] it did not make any significant impact.

The VIA sensitivity in this study was 66.7%. This is slightly higher than the 60.2% reported by Ibrahim et al in Sudan[16] but lower than the 80.0% reported by Sahasrabuddhe et al in India.[19]

The positive results for VIA was 22.6% compared to 13.8% for Pap smear test. This implied that VIA had good sensitivity.[10] Pap smear on the other hand had good specificity.[20] VIA is a good screening test that can be used before a more specific test like the Pap smear which can then be used to confirm or exclude the disease. Such approaches help save resources of already resource constrained countries and reduce the excessive work load of the scarce healthcare providers in developing countries.[20] On the other hand, the low false negatives of 11 (4.0%) reported with Pap smear test implies that very few participants that actually had the disease were labelled as not having the disease. There is a risk that people who received false negative results may experience delays in diagnosis and treatment.[21]

The cost of investigation of three hundred and eleven naira (N311. 00k) only per participant for VIA is also shown to be much cheaper and more affordable compared to Pap smear test which cost N1,108: 00k . This finding agrees with previous reports.[1, 5] The results for VIA was available immediately after the procedure but took four to eight weeks for the Pap smear test results to be available.[22]

CONCLUSION

This study showed that VIA is a reliable screening test for cervical cancer in the study area. It was able to detect pre-invasive cervical lesions with good sensitivity, specificity, positive predictive and negative predictive values comparable to results of other studies. Overall, VIA is comparable to Pap smear in performance yet much cheaper to organise and carry out. This study also found out that the level of awareness about cervical cancer among the study participants was low. No participant was aware of VIA as a screening method for cervical cancer but a very small percentage of participants were aware of Pap smear test. A higher number of participants were detected to have cervical dysplasia by VIA method

(22.6%) than by Pap smear method (13.8%).

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