Journal of Health, Medicine and Nursing
ISSN 2422-8419 An International Peer-reviewed Journal
Vol.27, 2016

Prevalence of and Factors Associated with Vulva Intraepithelial Neoplasia (VIN) among HIV Positive Women at Mbarara Regional Referral Hospital, Uganda

Andrew Oryono MD[1*], Joseph Ngonzi; MD[1], Prof. Damaris Latiffa[2], Prof. YarineFajardo.PhD[1], Dr. Wasswa SsalongoMD[1], Mayanja Ronald; MD[1,]

1. Department of Obstetrics and Gynecology, Mbarara University of Science and Technology, Uganda
2. Department of Pathology, Mbarara University of Science and Technology, Uganda

Abstract

Background: Vulva intraepithelial neoplasia (VIN) is a noninvasive potential precursor of squamous cell carcinoma of the vulva. VIN is more prevalent in HIV-positive than HIV-negative women and if not identified and treated early, there is a high risk of progression to invasive cancer. Despite a large number of HIV-positive women getting care from Immunesuppression (ISS) clinic at Mbarara Regional Referral Hospital (MRRH), the local burden of VIN remains unknown in this group. **Objective:** To determine the prevalence and factors associated with vulva intraepithelial neoplasia (VIN) among HIV-positive women attending HIV care clinic at Mbarara Regional Referral Hospital (MRRH). **Methods:** This cross sectional study consisted of 225 HIV-positive women who attended the HIV care clinic at MRRH in a period of three months. Simple random sampling was used in the recruitment of study participants until the sample size was achieved. All participants underwent vulvoscopy. Any lesion detected was biopsied. Demographic and medical data were collected. The dependent variable was histologically confirmed VIN. Logistic regression analysis to assess association of factors with VIN was done. Results were presented in charts, graphs and tables. **Results:** Two hundred and twenty five HIV-positive women were enrolled. Their median age was 33 years. 14 (6.22%) had VIN; of these, 9 had VIN-1, 4 had VIN-2 and 1 had VIN-3. All the study participants with VIN had Human papilloma virus (HPV) infection and were on antiretroviral therapy (ART). The symptoms of VIN included vulvar itching (43%), vulvar burning sensation (29%), and superficial dyspareunia (14%). Age, multiple sexual partners, age of sexual debut, menarche and genital warts were not significantly associated with VIN **Conclusion:** The prevalence of VIN among HIV-positive women attending HIV care clinic at MRRH is low. All participants with VIN had the following in common, HPV infection; vulva itching, vulva burning sensation and superficial dyspareunia. **Recommendations:** Since all cases of VIN had HPV infection we recommend that HPV vaccination should be included in HIV care to prevent VIN and consequently vulva cancer. We also recommend that all women with vulva itching, vulva burning and superficial dyspareunia should be screened for VIN.

Key words: Vulva Intraepithelial Neoplasia (VIN), Human Immunodeficiency Virus (HIV)

1. Introduction

Vulva intraepithelial neoplasia is a noninvasive potential precursor of squamous cell carcinoma of the vulva (Hart WR et al., 2001). It has been found to be more frequent in patients with a younger age group (20-40 years) compared to vulva cancer; the average age being as low as 33 years (Dutta D.C. et al.,2012). The incidence of vulva intraepithelial neoplasia (VIN) is increasing, with 60–75% occurring in young women (Joura EA et al., 2000, Judson PL et al., 2006, Jones RW et al., 2005). The risk of progression from VIN to invasive cancer is 3 to 9 percent (Jones RW et al., 2005, van Seters M et al., 2005). The factors that contribute to the etiology of vulva carcinoma include vulva dystrophy (lichen sclerosus), a history of genital HPV-infection, and history of cervical neoplasia, advanced age, smoking and a compromised immunity (e.g. HIV). For the development of a vulvar carcinoma, more than one of the above mentioned factors has to be present (Ansink AC et al., 1993). High-risk human papillomavirus (HRHPV) is an established cause of a significant proportion of vulva intraepithelial neoplasia (VIN) (Koutsky L et al., 1997; van der Avoort IA et al., 2006; Skapa P et al., 2007) and this has been found to be more frequent in immune-compromised women.

Women with human immunodeficiency virus (HIV) infection are at an increased risk of vulvar neoplasia (Maiman M et al., 1990; Clark RA et al., 1993; Korn AP et al., 1996). The incidence and severity of vulvar premalignant and malignant disease appeared to correlate with worsening immunosuppression (Spitzer M et al., 1999; Robinson WR et al., 1997). Cervical intraepithelial neoplasia (CIN) has also been found to be high among

HIV-positive women (Ellerbrock TV et al., 2000). Despite standard therapy, HIV-infected women with vulva neoplasia have higher rates of persistence and recurrence than the general population (Maiman M et al., 1997; Dedes KJ et al., 2008).

HIV-positive women are five times more likely than HIV-negative women to develop lower genital tract neoplasia (Ferenczy A et al., 2003) and they have a 16-fold increase in lower genital tract lesions (excluding the cervix) than HIV-negative women (Conley LJ et al., 2002).The prevalence of VIN among HIV-seropositive women ranges from 5.6 to 57% (Kappler et al., 2011; Byrne MA et al., 1989; Chiasson MA et al., 1997; Korn AP et al., 1998; and OlamideDosekun et al., 2013). With the advent of HAART, the life expectancy of these women is increasing with an increased risk of developing high risk lesion which may progress to cancer (Francheschi S and Jaffe H, 2007).

2. Materials and Methods

2.1 Participants

This cross-sectional study consisted of 225HIV-positive women aged 18 years and above registered and attending the Immune Suppression Syndrome (ISS) clinic at Mbarara Regional Referral Hospital (MRRH) between January and March 2015. Ethics approval was obtained from both the faculty review ethical committee (FREC) and institutional research ethics committee (REC) of Mbarara University of Science and Technology.

2.2 Recruitment

Eight (8) out of every first 20 HIV-positive womenwho registered each day in ISS clinic were selected by simple random sampling and recruited in the study.
HIV-positive women were included in the study if they were aged 18 years and above, registered and attending ISS clinic at MRRH, and consented to participate in the study.Those whohadknownhistologically confirmed or on treatment for vulvar cancer were excluded from the study. All participants were examinedbythe principle investigator under supervision by two senior gynecologists with experience in colposcopy. A pre-tested standardized questionnaire to capture information including social demographic and medical characteristics was administered in the language the participant was conversant with by the principal investigator/research assistant to the study participant. Vulvar screening was done in a procedural room with patient on examination bed in lithotomy position. A thorough inspection of the vulvar was done to reveal fields of redness, leukoplakia, pigmentations, ulcerations, atrophy, genital warts and invasive cancer. A freshly prepared 5% acetic acid solution was applied on the vulva for 3-5 minutes to allow vulvar lesions to show. The colposcope was then used to visualize and localize the vulvar lesions; and any abnormalities (acetowhite changes, raised lesions, discolorations) were biopsied after infiltration with a local anesthetic (1 % Lidocainewithout epinephrine). The biopsy samples were put in 10% formalin in different containers, sealed, well labeled with patient particulars and taken to the histo-pathologist at the end of the day by the principal investigator. Results were picked after one week and given to the participants. Women with vulvar intraepithelial neoplasia were managed as per the standard protocol. Histology was taken as the gold standard of diagnosis.
The dependent variable was histologically confirmed vulvar intraepithelial neoplasia. Logistic regression analysis to assess association of factors including age, age at sexual debut, multiple sexual partners, education, genital warts, menarche, alcohol, duration since diagnosisof HIV, and HPV infection with VIN was done. Results were presented in charts, graphs and tables.
P-value less than 0.05was considered statistically significant.

3. Results

3.1 Characteristics of the study population

The characteristics for the 225 participants in the study are described in Table 1. Most (211) of the study participants with the median age 37 (IQR 32-44) years didn't have VIN compared to the 14 with a median age 33 (IQR 32-36) years. Most (57.35%) of the participants without VINwere peasants who resided in the rural parts of Mbarara district with a monthly income of less than 50,000 Uganda shillings. All the participants were on ART. Of the participants without VIN 63 (29.86%), 62(29.38%) and 86 (40.76%) of the women had latest CD4 count ≤250, 251-349 and ≥350 cells/mm^3 respectively. None of the participants with VIN had a recent CD4 count of≤ 250cells/mm^3 whereas the majority (78.57%) had a CD4 count ≥ 350 cells/mm^3. The prevalence of vulva intraepithelial neoplasiaamong HIV positive women attending HIVcare clinic at MRRH was determined by the formula: Prevalence= (n/Nx100). Where n, represents the total number of HIV positive women with VIN (14) attending the ISS clinic at MRRH and N, the total number of women enrolled (225). So the prevalence of

VIN among HIV positive women attending the HIVcare clinic at MRRH = (14/225 x 100) = 6.22% (95% CI 3.44-10.22). 5 (2.22%) of the women had high grade intraepithelial neoplasia (VIN-2+) among which VIN-2 were 4 (1.78%) and only one (0.44%) had VIN-3. 9 (4%) of the women had low grade vulva intraepithelial neoplasia (VIN-1).

Table 1 Baseline characteristics

Variable	VIN absent N=211 (%)	VIN present N=14 (%)	Variable	VIN absent N=211 (%)	VIN present N=14 (%)
			HPV infection		
Age, median (IQR)	37 (32-44)	33 (32-36)	Present	47 (22.27)	14 (100)
			Absent	164 (77.3)	
Residence					
Rural	121 (57.35)	9 (64.29)	**On ART**	211 (100)	14 (100)
Urban	90 (42.65)	5 (35.71)			
District			**Duration since HIV diagnosis (years)**		
Mbarara	93 (44.08)	9 (64.29)			
Isingiro	45 (21.33)	3 (14.29)	≤ 5		
Kiruhura	47 (22.27)	2 (21.43)	≥6	105 (49.76)	8 (57.14)
Others	26 (12.32)	-		106 (50.24)	6 (42.86)
Marital status			**H/o cervical screening result**		
Single	36 (17.06)	1 (7.14)	Positive		
Monogamous	41 (19.43)	2 (14.29)	Negative	5 (2.37)	1 (7.14)
Polygamous	49 (23.22)	5 (35.71)	Not done	66 (31.28)	3 (21.43)
Divorced	43 (20.38)	5 (35.71)		140(63.35)	10(71.43)
Widowed	42 (19.91)	1 (7.14)			
Religion			**Recent CD4 count**		
Protestant	105 (49.76)	9 (64.29)			
Catholic	64 (30.33)	4 (28.57)	<250	63 (29.86)	-
Moslem	22	-	251-349	62 (29.38)	3 (21.43)
Others	(10.43)	1 (7.14)	>350	86 (40.76)	11 (78.57)
	20 (09.48)				
Substance use			**WHO HIV clinical stage**		
Alcohol	8 (3.79)	2 (14.29)	1	128 (60.66)	
Smoking	2 (0.95)	1	2	83 (39.34)	14 (100)
Both alcohol and smoking	-	(7.14) -	3	-	
			4	-	
No. of sexual partners Median (IQR)			**Genital warts**		
≤ 1	89 (42.18)	3 (21.43)	Present	88 (41.71)	4 (28.57)
≥ 2	122 (57.82)	11 (78.57)	Absent	123(58.29)	10 (71.43)
Education					
None	50 (23.70)	2 (14.29)	Age at menarche(years)		
Primary	65 (30.80)	8 (57.14)	Median (IQR)		
Secondary	53 (25.12)	3 (21.43)			
Tertiary	43 (20.38)	1 (7.14)		15 (14 –16)	15 (14 – 6)
Occupation			**Age of first sexual intercourse (years)**		
Business	68 (32.23)	6 (42.86)			
Peasant	77 (36.50)	5 (35.71)	≤19	96 (45.50)	2 (14.29)
Employed	66 (31.28)	3 (21.43)	≥ 20	115(54.50)	12 (85.71)
Monthly earnings (Ush)	65 (30.81)	4 (20.57)			
< 50,000/=	59 (27.96)	7 (50.00)			
50,000 - 100,000/=	45 (21.33)	2 (14.29)			
101,000-200,000/=	42 (19.91)	1 (7.14)			
> 200,000/=					

The characteristics of the 14 participants identified with VIN as described in Table 1.The median age of the study participants with VIN was 33 (IQR: 32 – 36) years. All the 14 women with VIN were found to have human papilloma virus (HPV) infection. Only one (7.14%) with VIN smoked tobacco and another (7.14%) had a positive cervical cancer screening result. Of all (14) the study participants with VIN in this study, 6 (43%) presented with vulvar itching, 4 (29%) vulvar burning sensation, 2 (14%) dyspareunia and 2 (14%) were asymptomatic (figure 2). The following factors were analysed using multivariate model: age-group: <30, OR 2.55 (95%CI0.28 - 23.17), p-value 0.29; age group 31-39 years OR 4.71 (0.84 – 26.52) p-value, 0.08; multiple sexual partner ≥ 2 OR 0.61 (0.12 – 3.16) p-value 0.56; age at sexual debut≤ 18 OR2.76 (0.48 – 15.74) p-value 0.25; and genital warts OR 1.64 (0.31 – 8.68) p-value 0.56.

Table 2A Univariate analysis of factors associated with VIN

Characteristic	**Univariate Model**	
	Unadjusted OR (95%CI)	**P-values**
Age group in years		
<30	4.75(0.90-5.04)	0.07
31-40	2.38(0.34-16.36)	0.38
≥40	1.00	
Multiple sexual partners		0.17
≤ 1	1.00	
≥ 2	0.72 (0.16 - 3.17)	
Age of sexual debut		0.13
≤ 18	2.65 (0.530 – 13.32)	
≥ 19	1.00	
Menarche		0.49
≤ 13	1.00	
≥ 14	2.17 (0.244 - 19.276)	
Duration since HIV diagnosis		0.59
≥6 years	1.00	
≤5 years	1.72 (0.23 – 2.38)	
Genital warts		0.22
No	1.00	
Yes	2.40 (0. 9 -9.82)	
Residence		0.84
Urban	1.00	
Rural	0.89 (0.27 - 2.90)	
Alcohol		0.84
No	1.00	
Yes	1.19 (0.213 - 6.694)	
Education		0.97
None	1.00	
Primary or higher	0.99 (0.48 - 2.03)	

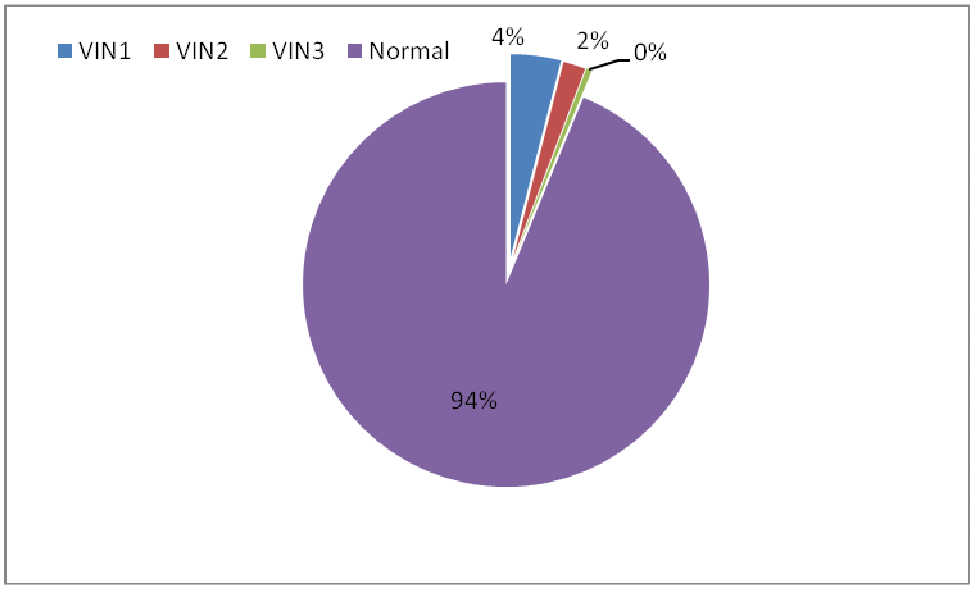
In the univariate analysis, no factors were significantly associated with VIN. Variables with p-values < 0.40 were transferred and analysed using multivariate model to check for significance.

Table 2B Multivariate analysis of factors associated with VIN

Characteristic	Multivariate Model	
	Unadjusted OR (95% CI)	P-values
Age group in years		
<30	2.55 (0.28 - 23.17)	0.29
31-40	4.71 (0.84 – 26.52)	0.08
≥40	1.00	
Multiple sexual partners		0.56
≤ 1	1.00	
≥ 2	0.61 (0.12 – 3.16)	
Age of sexual debut		0.25
≤ 18	2.76 (0.48 – 15.74)	
≥ 19	1.00	
Menarche		0.23
≤ 13	1.00	
≥ 14	3.8 0 (0.42 - 35.79)	
Genital warts		0.56
No	1.00	
Yes	1.64 (0.31 – 8.68)	

No factors were found to be significantly associated with VIN.

Figure 1 Distribution of VIN by grade.



Vulva intraepithelial neoplasia grade 1 (VIN-1) which has a low potential for development of vulvar cancer was the commonest (4%); followed by VIN-2 (1.78%) and VIN-3 (0.44%).

Fig.2 Distribution of the clinical presentation with VIN

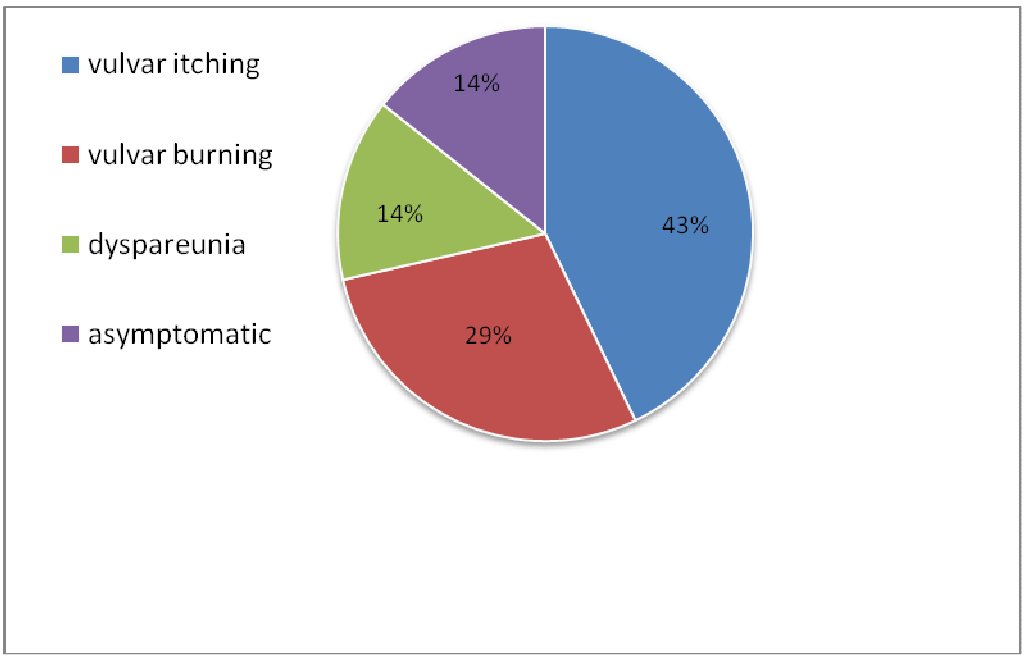
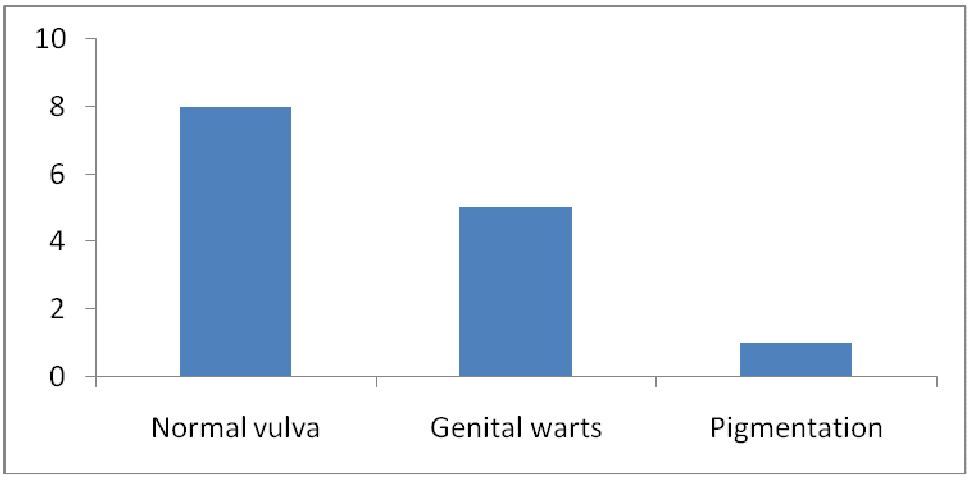


Fig 3 Clinical findings in participants with VIN.



Among patients with VIN, 8 (57.14%) had normal vulva, 5 (35.71%) had genital warts, and only one (7.15%) had vulva pigmentation.

4. Discussion

4.1 Prevalence of vulva intraepithelial neoplasia (VIN)

Limited data are available on the prevalence of vulva intraepithelial neoplasia (VIN) in HIV-positive women therefore there are only a few studies for comparison. In this study, the prevalence of vulva intraepithelial neoplasia among HIV-positive women attending ISS clinic at MRRH was found to be 6.22% (95% CI 3.44-10.22). Byrne and colleagues (1989) found the prevalence of VIN to be 16% among eighteen HIV-positive

women in St. Mary's Hospital, London. The difference with that in this study could be due to the different settings and patients profiles. Also, the sample size in our study was larger than that used by Bryne.

The prevalence of vulva intraepithelial neoplasia (VIN) in this study was also lower than that of a study done by Korn AP et al (1998) where they found the prevalence of VIN to vary from 9% to 37%. This was a compilation of prevalence of VIN from different colposcopy clinics in Africa. They only included mothers with abnormal results of cytological examination who were referred for colposcopy thus they may have had selection bias. Our study took into consideration all women who were HIV positive without subjecting them to cytological examination which would have otherwise left out those with VIN in this population.

In a study carried out by Olamide Dosekun and colleagues (2013) among HIV-positive women attending the vulval dermatology clinic at St. John's Institute of Dermatology, St. Thomas' Hospital, London from January 2007 to August 2012, the prevalence of vulva intraepithelial neoplasia was found to be 57% out of 14 HIV-positive women identified. This is much higher than the prevalence of VIN in this study. Our sample size was 16 times higher than that used by Olamide Dosekun et al., 2013.

In another study conducted among 343 patients referred with an abnormal genital intraepithelial lesion or cytology to the University of Tennessee, West Clinic gynecology oncology division between June 2006 and December 2009 (Wendy Likes et al.,2013), the prevalence of VIN among immuno-compromised patients was found to be 76% (N=33). This is much higher than that in this study and could be explained by the following: Firstly, Likes and colleagues determined VIN in all immuno-compromised patients whereas our study was specific to only HIV-positive women. Secondly, these immuno-compromised patients already had abnormal genital lesions and cytology with high possibility of being VIN.

4.2 Clinical features of vulva intraepithelial neoplasia

The symptoms of vulva intraepithelial neoplasia in this study included vulvar itching, vulvar burning sensation and dyspareunia. These symptoms are not unique to VIN and often under looked. Patients may therefore present late with VIN or vulvar cancer. However, no studies were available to compare with the above.

4.3 Factors associated with vulva intraepithelial neoplasia (VIN)

The factors associated with vulva intraepithelial neoplasia (VIN) in various studies include HPV infection (Conley LJ et al., 2002,Massad LS et al., 2004, De Vuyst H et al., 2009), smoking (Dahling JR et al., 1992; Brinton LA et al., 1990; Massad LS et al., 2012), history of abnormal papanicolaou test (Massad LS et al., 2004 and Brinton et al., 1990), multiple sexual partners, young age at first sexual intercourse (Ho L et al., 1993, Kiviat NB et al., 1989, and Brinton et al., 1990), and genital warts (Brinton LA et al., 1990).

In this study, 14 (100%) participants with VIN were found to have human papilloma virus (HPV) infection. This is in agreement with the following studies which found out that HPV was significantly associated with VIN (Conley LJ et al., 2002, Massad LS et al., 2004, and De Vuyst H et al., 2009). Human papilloma virus (HPV) infection in this study was determined by histology rather than Polymerase Chain Reaction (PCR).

Various studies have shown that the age of the women developing vulva intraepithelial neoplasia, which was historically judged to be postmenopausal, had decreased during several decades (Sturgeon SR et al., 1992; Kaufman RH et al 1995; Jones RW et al., 1997; De Vuyst H et al., 2009; Dutta et al., 2012). Conley LJ and colleagues (2002) found the median age of HIV-positive women who developed vulva intraepithelial neoplasia in a prospective cohort study done in USA to be 38 years (IQR 33–40). In this study, the median age of HIV-positive women with VIN was 33 years (IQR 32-36) which is lower than that found by Conley and colleagues (2002).

Although smoking tobacco was found to be highly associated with vulva intraepithelial neoplasia in various studies (Dahling JR et al., 1992; Brinton LA et al., 1990; Massad LS et al., 2012), only one of the 14 participants with VIN in this study smoked tobacco.

Age at first sexual intercourse and having multiple sexual partners were not significantly associated with VIN in this study. This is contrary to the findings of Ho L et al., (1993), Kiviat NB et al., (1989) and Brinton et al., 1990. This variance might be that the women did not tell the truth. Genital warts were not also significantly associated with VIN in this study. However, Brinton LA and colleagues (1990) found that genital warts were strongly associated with VIN.

In this study only one of the participants with VIN had history of previous abnormal cervical cancer screening result and thus couldn't determine its association with VIN. However, studies by Massad LS et al., 2004 and Brinton et al., 1990 found out that history of abnormal papanicolaou test was highly associated with VIN.

4.4 Limitations

Due to the lower prevalence and limited time we were not able to get enough sample size for determination of the factors associated with VIN among HIV positive women at MRRH.

4.5 Conclusion

The prevalence of VIN among HIV-positive women attending HIV care clinic at MRRH was low. All participants with VIN had HPV infection; common symptoms included vulva itching, vulva burning sensation and superficial dyspareunia. Majority of women with VIN had no physical findings therefore were only identified on vulvoscopy.

Since all cases of VIN had HPV infection we recommend that HPV vaccination should be included in HIV care to prevent VIN and consequently vulva cancer. We also recommend that all women with vulva itching, vulva burning and superficial dyspareunia should be screened for VIN. Vulvoscopy should be included in reproductive healthcare since majority present with no symptoms. Finally we recommend a big study to determine the factors associated with VIN.

References

Brinton LA, Nasca PC, Mallin K, et al: Case-control study of cancer of the vulva. ObstetGynecol 75:859, 1990.

Byrne MA, Taylor-Robinson D, Munday PE, Harris JR. (1989) The common occurrence of human papillomavirus infection and intraepithelial neoplasia in women infected by HIV. AIDS 3:279

Chiasson MA, Ellerbrock TV, Bush T et al. (1997). Increased prevalence of vulvovaginalcondyloma and vulvar intraepithelial neoplasia in women infected with the human immunodeficiency virus. ObstetGynecol; 89:690.

Conley LJ, Ellerbrock TV, Brush TJ et al. (2002). HIV-1 infection and risk of vulvovaginal and perianal condylomataacuminata and intraepithelial neoplasia: A prospective cohort study. Lancet 359:108.

De Vuyst H, Clifford GM, Nascimento MC, et al. (2009). Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: a meta-analysis. Int J Cancer; 124:1626–36.

DuttaD.C. Text book of Gynaecology 6th edition (2012). Vulva intraepithelial neoplasia Chapter 22 page 304.

Ferenczy A, Coutlee F, Franco E, Hankins C (2003). Human papillomavirus and HIV coinfection and the risk of neoplasias of the lower genital tract: a review of recent developments. CMAJ [Review] 169(5):431–434.

Hart WR. (2001). Vulvar intraepithelial neoplasia: historical aspects and current status.Gynecol Path. 20(1):16-30.

Ho L, Tay SK, Chan SY, Bernard HU: (1993). Sequences of variants of HPV type 16 from couples suggest sexual transmission with low infectivity and polyclonality in genital neoplasms. J Infect Dis 168:803.

Jones RW, BaranyaiJ,Stables S: (1997). Trends in squamous cell carcinoma of the vulva: The influence of vulvar intraepithelialneoplasia.ObstetGynecol 90:448.

Jones RW, Rowan DM, Stewart AW (2005). Vulvar intraepithelial neoplasia: aspects of the natural history and outcome in 405 women. Obstet Gynecol. 106 (6):1319–1326.

Joura EA, Losch A, Haider-Angeler MG, et al. (2000). Trends in vulvar neoplasia. Increasing incidence of vulvar intraepithelial neoplasia and squamous cell carcinoma of the vulva in young women.J Reprod Med; 45:613–15.

Judson PL, Habermann EB, Baxter NN, et al. (2006). Trends in the incidence of invasive and in situ vulvar carcinoma.Obstet Gynecol. 107(5):1018–1022.

Kiviat NB, Koutsky LA, Paavonen JA, et al: (1989). Prevalence of genital papilloma virus infection among women attending a college student health clinic or a STD clinic. J Infect Dis 159:293.

Klapper, A, DelPriore, G, et al: (2011). Vulvar Intraepithelial NeoplasmsGlob. libr. women's med.,(ISSN: 1756-2228); DOI 10.3843/GLOWM.10258

Korn AP, Abercrombie PD, Foster A. (1998). Vulvar intraepithelial neoplasia in women infected with human immunodeficiency virus in Africa. Cancer; 82: 2401-8.

Koutsky L. (1997). Epidemiology of genital human papillomavirus infection. Am J Med. 102:3–8.

Maiman M, Fruchter RG, Clark M, et al. (1997). Cervical cancer as an AIDS-defining illness.ObstetGynecol; 89:76.

Maiman M, Fruchter RG, Serur E, Remy JC, Feuer G, Boyce J. (1990). Human immunodeficiency virus infection and cervical neoplasia.Gynecologic Oncology. 38(3):377–382.

Massad LS, Silverberg MJ, Springer G. et al. (2004). Effect of antiretroviral therapy on theincidence of genital warts and vulvar neoplasia among women with the human immunodeficiency virus. Am J Obstet Gynecol. 2004 May; 190(5):1241-8.

Massad LS, XianhongXie, Teresa Darragh et al.(2011).Genital Warts and Vulvar Intraepithelial Neoplasia: Natural History and Effects of Treatment and Human Immunodeficiency Virus Infection.Obstet Gynecol. 118(4): 831–839.

OlamideDosekun, PippaFarrugia, Fiona Lewis and GulshanSethi. (2013). Vulval disease in HIV-positive women attending a tertiary vulval dermatology clinic over a five-year period.International Journal of STD & AIDS; 24(10) 834–836.

Robinson WR, Barnes SE, Adams S, Perrin MS. (1997). Histology/cytology discrepancies in HIV-infected obstetric patients with normal pap smears.GynecolOncol. 65:430.

Spitzer M. (1999). Lower genital tract intraepithelial neoplasia in HIV-infected women: guidelines for evaluation and management.ObstetGynecolSurv. 54:131.

Skapa P, Zamecnik J, Hamsikova E, et al. (2007). Human papillomavirus (HPV) profiles of vulvar lesions: possible implications for the classification of vulvar squamous cell carcinoma precursors and for the efficacy of prophylactic HPV vaccination. Am J SurgPathol. 31:1834–1843.

van der Avoort IAM, Shirango H, Hoevenaars BM, et al. (2006). Vulvar a multifactorial disease following two separate and independent pathways. International Journal of Gynecological Pathology. 25(1):22–29.

vanSeters M, van Beurden M, de Craen AJ. (2005). Is the assumed natural history of vulvar intraepithelial neoplasia III based on enough evidence? A systematic review of 3322 published patients.GynecolOncol. 97(2):645–651

Wendy Likes, Joseph T. Santoso, Jim Wan Arch. (2013). A cross-sectional analysis of lower genital tract intraepithelial neoplasia in immune-compromised women with an abnormal Pap.GynecolObstet 287:743–747 DOI 10.1007/s00404-012-2637-3

Competing interests

Authors did not have any conflict of interest

Authors' contributions:

1. Andrew Oryono.MD, Principal investigator, conceived the idea, developed the concept, involved in data collection, entry, analysis and manuscript writing
2. Mayanja Ronald.MD, involved in data collection, entry, analysis and manuscript writing
3. Ngonzi Joseph.MD, involved in development the concept, data management and manuscript writing
4. Prof. YarineFajardo.pHD, involved in development the concept, data management and manuscript writing
5. Dr. Wasswa Ssalongo, Senior Consultant(obs/gyn), involved in development the concept, data management and manuscript writing

Authors' information:

1. Andrew oryono, MBChB(Gulu University), Senior resident (Mbarara University of Science and Technology
2. Mayanja Ronald, MBChB(MUST), MMed O&G(MU), Lecturer, Department of obstetrics and Gynaecology, Mbarara University of Science and Technology, Uganda
3. Ngonzi Joseph, MBChB(MUST), MMed O&G(MUST), PhD candidate, Senior lecturer, Chair Department of obstetrics and Gynaecology, Mbarara University of Science and Technology, Uganda
4. Prof. YarineFajardo.PhD
5. Dr. Wasswa Ssalongo, Senior Consultant(obs/gyn)

Acknowledgements
My lecturers; Prof. Yarine Fajardo, Dr. Kayondo Musa, Dr. Wasswa Ssalongo, Dr. Godfrey Mugyenyi, Dr. Julius Mugisha, others Dr Samson Okello , Dr Francis Bajunirwe for the statistical input and Prof. Damaris Latiffa for the histopathological work. I am indebted to my research assistants Sr Alexcer Namuli, Sr Alice Najjuma and Sr Susan Asiimwe. Lastly all the study participants, staff of ISS/CCP clinics. I acknowledge my classmates Abdul Namugongo, Ayol Mac Ayol, Damulira Adam, Inzama Wilfred, Muhumuza Joy, and Nanzira Rachael Samantha. Finally my regards go to my sponsor ONCOLOGY FOR AFRICA for the financial support.