International Journal of Gynecology and Obstetrics 107 (2009) 99–102

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

CLINICAL ARTICLE

Cervical dysplasia in Nigerian women infected with HIV

Patricia A. Agaba [a,*], Thomas D. Thacher [b], Chinedu C. Ekwempu [c], John A. Idoko [d]

[a] AIDS Prevention Initiative Nigeria Plus, Jos University Teaching Hospital, Jos, Nigeria
[b] Department of Family Medicine, Mayo Clinics, Rochester, MN, USA
[c] Department of Obstetrics and Gynecology, University of Jos, Nigeria
[d] Department of Medicine, University of Jos, Nigeria

ARTICLE INFO

Article history:
Received 11 February 2009
Received in revised form 25 April 2009
Accepted 3 June 2009

Keywords:
Cervical dysplasia
HIV
Immunosuppression
Nigeria

ABSTRACT

Objective: To determine the prevalence of and risk factors for cervical dysplasia in HIV-positive women receiving care at the Jos University Teaching Hospital in Nigeria. *Methods:* A total of 369 HIV-positive women had cervical cytology performed; HIV-1 RNA viral load and CD4 counts were measured. *Results:* Of 369 participants, cervical dysplasia was present in 107 (29.0%) women. However, cervical cytology was abnormal in 252 (68.3%). Among those with abnormal cytology, 145 (57.5%) women had ASCUS, 56 (22.2%) had LSIL, and 51 (20.2%) had HSIL. Median CD4 lymphocyte count was lower in women with dysplasia compared with those without (142 vs 170 cells/mm^3; $P=0.04$), while median HIV RNA viral load was higher in women with dysplasia (101 781 vs 77 479 copies/mL; $P=0.002$). Low CD4 count (<200 cells/mm^3) and evidence of HPV infection were significantly associated with cervical dysplasia. *Conclusion:* A high prevalence of cervical dysplasia was found among HIV-positive Nigerian women, which was associated with increased immune suppression.

1. Introduction

Cervical cancer is the most common malignancy in women and a leading cause of cancer mortality in Sub-Saharan Africa [1]. The global disease burden of cervical cancer is estimated at half a million new cases and 230 000 deaths every year. An estimated 79 000 new cases occur in Africa each year and the disease constitutes 25.4% of cancers in women on the continent [2]. Cervical cancer is also the leading cause of years-of-life-lost in women in Asia, Latin America, and Sub-Saharan Africa, and results in a greater reduction of a woman's life expectancy than tuberculosis, AIDS, or maternal conditions in some parts of Latin America and Europe [3]. The incidence in east and central African countries appears to have increased over time, but no increases in incidence were noted in Nigeria between 1960–1969 and 1998–1999. This lack of documented increase may be due to absence of data [2].

Since the onset of the AIDS pandemic, women consistently represent one of the fastest growing subgroups of patients with AIDS [4]. Cancer of the cervix is classified as an AIDS-defining cancer by the US Centers for Disease Control and Prevention, and it runs a more fulminant course in women infected with HIV [5,6]. Invasive cervical cancer is the end result of a continuum of consecutive stages, which begins with precursor lesions of cervical intraepithelial neoplasia (CIN) or squamous intraepithelial neoplasia [7]. Although most follow-up studies have shown spontaneous regression of both low-grade and high-grade dysplasia in HIV-negative women, a substantial proportion of dysplastic lesions progress to more advanced disease in HIV-positive women.

Cervical cancer and HIV infection are major public health problems in Nigeria and other parts of Sub-Saharan Africa [7,8]. Nigeria ranks third among all countries for the total number of people living with HIV, with 1.7–4.2 million people infected with the virus. Both CD4 lymphocyte count and HIV RNA viral load are independent predictors of the course of HIV, and the frequency of occurrence and severity of cervical dysplasia in HIV-positive women increase as CD4 count declines. Evidence also suggests a correlation between high plasma HIV RNA levels, cervical dysplasia, and oncogenic HPV infection, which is now recognized as a cause of cervical cancer [2,9]. Relative risks of association between HIV and cervical cancer are lower in Africa compared with high-resource countries because the HIV prevalence is lower in the peak age group at risk for cervical cancer [2].

The aim of the present study was to determine the prevalence of cervical dysplasia in a cohort of HIV-positive women and to identify its relationship with risk factors, CD4 cell counts, and HIV RNA levels in Jos, north central Nigeria.

2. Materials and methods

The HIV treatment clinic of the Jos University Teaching Hospital in Jos, Nigeria is a regional reference center for treatment and support of people living with the HIV virus. Patients who receive a positive HIV test from the wards, specialist clinics, stand-alone HIV counseling

* Corresponding author. Tel.: +234 803 616 3437.
E-mail address: ellagaba@yahoo.com (P.A. Agaba).

0020-7292/$ – see front matter
doi:10.1016/j.ijgo.2009.06.006

Table 1
Sociodemographic characteristics of 369 HIV-positive women in Jos, Nigeria.[a]

Characteristics	Value
Age, y	33 ± 7
Parity	2 ± 2
Lifetime sexual partners	2 ± 5
Completed high school	240 (65.0)
Unemployed	145 (39.3)
Married	147 (39.8)
Normal body mass index (18.5–24.9)	198 (53.7)
Use of HAART	114 (30.9)
Previous STI	155 (42.0)
Previous Pap smear	3 (0.8)
CD4 count, cells/mm^3	
≤200	225 (61.0)
201–499	118 (32.0)
≥500	26 (7.0)
HIV-1 RNA, copies/mL	
≥400	291 (78.9)
≤400	78 (21.1)
Cervical cytology	
Normal smear	117 (31.7)
ASCUS	145 (39.3)
LSIL	56 (15.2)
HSIL	51 (13.8)
Evidence of HPV changes	
Yes	38 (10.3)
No	331 (89.7)

Abbreviations: HAART, highly active antiretroviral therapy; STI, sexually transmitted infection.
[a] Values are given as mean ± SD or number (percentage).

and testing sites, and other health facilities are usually referred for comprehensive services. At the time of this study, the total population of the clinic was 1140 infected adults (approximately 60% were women). Following adjustment, 370 nonpregnant women presenting consecutively between November 2004 and October 2005 were recruited for this cross-sectional study.

After informed consent from each woman had been obtained, demographic data including age, marital status, parity, number of lifetime sexual partners, and history of prior sexually transmitted infections (STIs) were obtained using a questionnaire. Since the syndromic approach to management of STI is practiced in our setting, history of prior STI was elicited (self-reported treatment, prior genital discharge, and/or genital ulcers) and history of use of highly active antiretroviral therapy (HAART) was obtained. For the patients who had a positive history of HAART use at the time of the study, the regimens consisted of two nucleoside reverse transcriptase inhibitors (stavudine or zidovudine and lamivudine) and one non-nucleoside reverse transcriptase inhibitor (nevirapine). All patients on HAART were receiving first-line drugs according to national guidelines and those qualifying for HAART were subsequently placed on drugs. None of the patients was on second-line therapy. Patients were excluded from the study if they did not give consent, were pregnant or puerperal, or had received treatment for precancerous lesions of the cervix. The study was approved by the Human Research Ethics Committee of the Jos University Teaching Hospital, Nigeria.

All patients had their HIV-status confirmed by western blot (Immunetics Inc, Boston, MA, USA) following presentation of a positive screening test. HIV-1 RNA viral load was determined by nucleic acid amplification (Roche-Ampliclor HIV-1 Monitor Test, version 1.5; Roche Diagnostics, Branchburg, NJ, USA), and results were expressed as the number of RNA copies per milliliter of plasma (copies/mL). Values of 400 copies/mL or fewer were regarded as undetectable. CD4 count was measured using flow cytometry (Cyflow; Partec, Germany) and reported as cells per cubic milliliter of blood (cells/mm^3). Following visual inspection, the cervix was assessed for gross lesions and abnormal discharge. All pelvic examinations were performed by a trained family physician. We collected ectocervical and endocervical specimens using a plastic spatula and cytobrush, respectively. Smears from both the endocervix and ectocervix were placed on one prelabeled slide for convenience and immediately fixed using alcohol spray.

The slides were stained according to the Papanicolaou (Pap) staining technique. The fixed slides were stained in Harris hematoxylin. The smear was decolorized with acid alcohol and rinsed in Scott's tap water. They were then stained in orange G stock solution and finally stained with Eosin Azure 50. The slides were further rinsed in 2 changes of 95% alcohol, cleared in xylene, and mounted in a neutral synthetic resin medium. To ensure quality assurance, a cytotechnologist and histopathologist screened and examined the Pap smears using standard checks. Cytology was reported using the Bethesda system terminology.

Blood samples for CD4 count and viral load assays were taken on the same day as the Pap smears. Women with abnormal smears were referred for further evaluation in the gynecology clinic of the hospital. All patients with atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL) were referred.

Data were entered and analysis was performed using Epi Info 3.3.2 (CDC; Atlanta, GA, USA). The *t* test was used to compare differences in normally-distributed continuous variables between subjects with and without dysplasia. Non-normally distributed variables were compared using the Mann-Whitney test. Univariate analysis using the χ^2 statistic was performed to identify risk factors associated with dysplasia. Multivariate logistic regression was used to identify independent risk factors for dysplasia. Variables were entered in the model if their *P* value on univariate analysis was 0.25 or less. $P<0.05$ was considered significant.

3. Results

Of the 370 women who participated in the study, one woman declined a Pap smear at the point of examination and was excluded from the analysis. The mean age of the 369 women was 33 ± 7 years (range, 21–60 years). Median number of lifetime sexual partners was 2 (range, 0–100), and 155 (42.0%) women reported having had an STI (Table 1). The patients who reported no sexual partners may have acquired HIV through other means besides sexual intercourse. A total of 114 (30.9%) women were on HAART, with a mean duration of use of 14 ± 1 month (range, 1–40 months). Some of the patients had been on HAART for over 36 months before recruitment into the study and this may account for the variability in the duration of use among the patients. The predominant HAART regimen was stavudine, lamivudine and nevirapine (75.4%), while zidovudine, lamivudine and nevirapine was the regimen used by 24.6% of the patients. Median CD4 cell count was 161 cells/mm^3

Table 2
Demographic characteristics and selected risk factors between women with and without dysplasia (n = 369).[a]

Parameter	Dysplasia [b] (n = 107)	No dysplasia [c] (n = 262)	*P* value
Age, y	35 ± 8	33 ± 6	0.008
Parity	2 ± 8	2 ± 2	0.12
Lifetime sexual partners	2 ± 3	2 ± 6	0.72
Mean duration of contraception use, mo.	24 ± 27	25 ± 32	0.77
Mean duration on HAART, mo.	15 ± 11	13 ± 11	0.26
Genital ulcers, %	12.1	15.6	0.38
Genital warts, %	14.9	11.0	0.30
Post coital bleed, %	9.3	1.9	0.21
Previous STI, %	45.8	40.5	0.34
HPV changes, %	36	2	<0.001
Median CD4 count, cells/mm^3	142	170	0.04
Median HIV RNA level, copies/mL	101 781	77 479	0.002

[a] Values are given as mean ± SD, percentage, or median unless otherwise indicated.
[b] Dysplasia group consists of those with LSIL (n = 56) and HSIL (n = 51).
[c] No dysplasia group consists of those with normal smears (n = 117) and those with ASCUS (n = 145).