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High prevalence of abnormal Pap smears among young women co-infected with HIV in rural South Africa – implications for cervical cancer screening policies in high HIV prevalence populations

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Objective. To establish the relationship between HIV infection and cervical dysplasia in young women in rural South Africa.

Methods. This cross-sectional study was conducted at a primary health care clinic in Vulindlela, KwaZulu-Natal. Standardised questionnaires were used to collect sociodemographic and clinical presentation data from women attending family planning and other reproductive health services. Pap smears were done using standard methods. Pap smear data were linked to HIV serostatus.

Results. Four hundred and sixty-six women were included in the study. The median age was 24.3 years (range 15 - 55 years), and 80% were younger than 30 years. The HIV prevalence rate was 24.5% (95% confidence interval: 20.7 - 28.7%) and the prevalence of abnormal Pap smears was 16.9 - 6.4% ASCUS (atypical squamous cells of undetermined significance), 9.2% LGSIL (low-grade squamous intraepithelial lesions), and 1.3% HGSIL (high-grade squamous intraepithelial lesions). The association between HIV seropositivity and abnormal Pap results was statistically significant ($p < 0.05$).

Conclusion. There is a need for more data on cervical changes in HIV co-infected women and for review of guidelines on selective Pap smear screening in high HIV prevalence settings such as sub-Saharan Africa and where access to antiretroviral treatment remains limited.

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Carcinoma of the cervix is the commonest genital malignancy afflicting women in the developing world. An estimated 190 000 women die each year as a result of cervical cancer, with 80% of these deaths occurring in the developing world.¹ Rates are highest in central America, sub-Saharan Africa and Melanesia, making it one of the most important reproductive health problems of public health importance in these regions. Cervical cancer is preventable by instituting cervical cytological screening and treatment of early lesions. In countries where screening quality and coverage have been high, Papanicolaou

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(Pap) screening efforts have reduced invasive cervical cancer incidence by about 70 - 90%.²

High costs, lack of awareness and absence of adequate health infrastructure have prevented most low-resource countries from instituting population-wide Pap smear screening programmes. Only 5% of women in developing countries undergo cervical cancer screening compared with 40 - 50% in the developed world.³ Selective cervical cancer screening of women above 30 years of age at least once in their lifetime has been suggested as an alternative Pap smear screening strategy in sub-Saharan Africa and other low-resource regions.^{4,5}

Several studies⁶⁻⁸ have found the prevalence of squamous intra-epithelial lesions (SILs) among HIV-positive women to be 31 - 63%. Further, the prevalence and degree of dysplasia increases with advancing levels of immunosuppression.^{9,10} The burden of HIV infection in sub-Saharan Africa among young women under the age of 30 years is increasing.¹¹ While some clinicians working in Africa^{12,13} have expressed concern about younger age of cervical cancer presentation, little empirical data exist as to the reason for this and whether it is linked with the increasing burden of HIV infection in this region.

The purpose of this study was to assess the relationship between Pap smear findings and HIV status in young women utilising family planning services in a high HIV prevalence setting in rural South Africa.

Subjects and methods

This cross-sectional study was conducted between November 2003 and April 2005 among young women utilising family planning services at the Mafakatini Clinic, Vulindlela district. Vulindlela is a rural district in the KwaZulu-Natal midlands, about 150 km west of Durban, with approximately 400 000 residents. The Mafakatini Primary Health Care Clinic is one of seven such clinics providing comprehensive primary care services to this rural community.

All women who presented to the clinic during the study period for family planning and other reproductive health services and who consented to participation in the study were included. Sociodemographic and clinical variables including age, marital status, parity and sexual history (number of sexual partners) were collected after obtaining informed consent.

A specimen from the cervix was obtained from each participant using the Ayre's spatula. The specimen was smeared on a slide and fixed using Cytofix according to the conventional standard cytological screening procedure. Specimens were examined at the regional Department of Health cytopathology laboratories. The 1988 Bethesda II classification was used for reporting the Pap smear results.

This study was reviewed and approved by the Nelson R Mandela School of Medicine Research Ethics Committee and permission to undertake this study was obtained from the

KwaZulu-Natal Department of Health. Syndromic management of sexually transmitted infections (STIs) was provided in accordance with the South African Department of Health guidelines.¹⁴ HIV-positive patients with indications for antiretroviral treatment were enrolled into the Centre for AIDS Programme of Research in South Africa (CAPRISA) Treatment Project. Patients with abnormal Pap smears were referred for further management to the tertiary referral hospital for this district.

Data were managed in Excel and analysed using the SPSS 11.5 statistical package.

Results

Sociodemographic characteristics

Of the 479 participants eligible for this study, 13 women consented to the Pap smear but refused HIV testing and were excluded from the analysis. The mean age of the 466 women included in this analysis was 24.3 years (standard deviation (SD) 7.0, range 15 - 55 years). Most of the participants (76.0%) were single but had a stable sexual partner, 11.2% were single without a sexual partner, 7.3% were married and 4.9% were widowed.

Most participants (52.2%) had completed high school, 43.1% were secondary school students, 4.3% had only completed primary school, and 0.4% had college education.

Sexual behaviour, parity, contraception and condom use

Information was obtained on the number of sexual partners in the previous 6 months; 56.2% of participants reported having only 1 partner, 12.4% reported having 3 partners and the remainder reported 2 to 6 partners.

Parity of participants ranged from 1 to 7; 31.5% of participants were nulliparous and 47.7% were para 1. Depo-Provera injectable contraceptive was the most commonly used family-planning method (60.1%), while 6.2% used combined hormonal pills for birth control, none of the participants used an intra-uterine device or surgical sterilisation methods of contraception, 8.4% were not on any form of contraception, and 25.3% reported use of male condoms.

HIV status and Pap smear results

Data on Pap smear results and HIV status are presented in Table I. The frequency of abnormal Pap smears was 16.9% (79/466). LGSIL (low-grade squamous intraepithelial lesions) were the most common abnormality identified (9.2%), and 1.3% of the participants had HGSILs (high-grade squamous intraepithelial lesions). HIV status was not known for 13 participants. The HIV prevalence in this cohort was 24.5%. There was a statistically significant association between HIV infection and abnormal Pap smear findings (10.3% among HIV-negative women v. 36% among HIV-positive women (chi-square 52.6,

**Table I. HIV serostatus and Pap smear results for family planning clients in Vulindlela, KwaZulu-Natal, 2004/2005**

Pap smear results	HIV-positive (N)	HIV-negative (N)	HIV? (N)	Total (N)
Normal	73	304	10	387
ASCUS	12	18	0	30
LGSIL	24	17	2	43
HGSIL	5	0	1	6
Total	114	339	13	464

$p < 0.05$; odds ratio (OR) 0.20, 95% confidence interval CI: 0.12 - 0.34).

The age distribution of clients in relation to Pap smear results is presented in Table II. Overall age distribution of Pap smear results is similar within each age category. Of note is that almost all cases of HGSILs were detected in young women co-infected with HIV.

Discussion

The high prevalence of abnormal Pap smears in young sexually active women co-infected with HIV utilising family planning services in Vulindlela, KwaZulu-Natal, is of concern. While this is a fairly modest, cross-sectional study, it highlights the need for more studies of HIV-infected populations and a re-examination of criteria being used for cervical cancer screening in high HIV prevalence countries where the prevalence of cervical cancer is also high and access to antiretroviral treatment remains limited.

All the HGSILs in this study occurred in women younger than 30 years of age, which is much lower than the usual age distribution for high-grade lesions (around 35 - 40 years of age). Almost all cases of HGSILs occurred among HIV-infected women, suggesting a strong association between HIV infection and cytological changes. These findings are similar to those of other studies^{6,8,9} that have demonstrated a clear association between HIV infection and abnormal Pap smears. Management of HGSILs requires immediate follow-up with colposcopy-directed biopsy.

Higher HIV viral loads are associated with more efficient HIV transmission.¹⁵⁻¹⁷ A substantial increase in HIV shedding

has been observed in HIV-positive women treated for pre-cancerous lesions.¹⁸ Counselling and HIV risk-reduction support for women after treatment of the pre-cancerous lesions is important. Abstinence and/or use of male condoms during coitus while the cervix heals is important to reduce both the risk of HIV transmission and exposure to HIV.

Data from other studies¹⁹⁻²¹ on further evaluation of ASCUS (atypical squamous cells of unknown significance) findings demonstrate a cervical intra-epithelial neoplasia (CIN)-1 rate of 10 - 20% and a CIN-2 and CIN-3 rate of 3 - 5%. CIN-2 and CIN-3 have a 5% risk of progression to invasive cancer.¹⁸ Hence a finding of ASCUS on Pap smear signifies a small but significant morbidity risk to the patient.

The prevalence of LGSILs reported in this study is substantially higher than the 1.6 - 2.4% reported in the literature from population-based surveys.²² This higher rate could reflect the bias of the family planning population. A 20% association between LGSIL and CIN2/3 has been noted in other studies.²² Hence women with LGSIL on Pap smear screening are likely to have a higher probability of progressing to invasive cancer than women with ASCUS results. The high rate of LGSIL among HIV co-infected young women found in this study needs further investigation in similar settings as the high HIV prevalence in this age group could be reversing the age trends of cervical cytological abnormalities.

Recent cervical carcinoma studies²³ demonstrate a 5 - 28% increase in the proportion of adenocarcinoma of the cervix compared with squamous cell carcinoma. Much of this increase is attributed to the high incidence of adenocarcinoma of the cervix in women in their 20s and 30s. Hence early detection of cervical adenocarcinoma using ASGUS (atypical glandular cells) in the Pap smears is becoming increasingly important^{24,25} and needs to be understood better in resource-constrained settings with a high HIV prevalence. As the majority of the lesions detected in these young women, who are ordinarily not screened because of the age selection criteria utilised, are early precursor lesions for cervical cancer, they lend themselves to intervention at an earlier stage thus potentially reducing individual and health-sector costs.

Worth noting is an important quality-limiting factor when Pap smears are taken using the Ayre's spatula, viz. that a lim-

Table II. Age distribution of Pap smear clients in Vulindlela, KwaZulu-Natal, 2004/2005

Pap result	Age group (years)		Total
	0 - 29	30 - 60	
Normal	313	73	386
ASCUS	23	7	30
LGSIL	30	12	42
HGSIL	5	1	6
Total	371	93	466

Pearson's chi-square = 2.460, $p = 0.483$.



ited number of endocervical cells are collected. It is therefore possible that what we have identified in this study is an underestimate of the true prevalence of abnormal cervical lesions in this population.

The high prevalence of HIV infection in young women may result in high incidence of cervical epithelial pathology in this subgroup of women thereby creating the need for expansion of the overall resources allocated for the cervical cancer screening programme.

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