employees. The South African National Departments of Health and Social Development and the Gauteng Department of Health and the Employees Wellness Program (EWP) also provided important support.

This project was funded by the Foreign Assistance Agencies of Australia (AusAID), the UK (DFID), and the United States of America (USAID), and by the United Nations Development Programme (UNDP) of South Africa. Technical assistance was provided by the Joint Economics AIDS and Poverty Programme (JEAPP), an affiliate of the African Asian Society (AAS).

References

1. Shisana O Rehle T, Simbahi L, *et al. South African National HIV Prevalence, HIV Incidence, Behaviour and Communication Survey*, 2005. Cape Town, HSRC Press, 2005.
2. Shisana O, Hall EJ, Maluleke R, Chauveau J, Schwabe C. HIV/AIDS prevalence among South African health workers. *S Afr Med J* 2004; 94: 846-850.
3. Auvert B, Males S, Puren A, Taljaard D, Carael M, Williams B. Can highly active antiretroviral therapy reduce the spread of HIV? A study in a township of South Africa. *J Acquir Immune Defic Syndr* 2004; 36(1): 613-621.
4. Shisana O, Peltzer K, Zungu-Dirwahi N, *et al. The Health of our Educators: A Focus on HIV/AIDS in South African Public Schools, 2004/5 Survey.* Cape Town: Human Sciences Research Council, 2005.
5. Rehle T, Shisana O. Estimates of eligibility for antiretroviral treatment (ART) and projected ART impact on AIDS mortality among South African educators. *Journal of Social Aspects of HIV/AIDS* 2006; 2(3): 304-310.
6. Evian C, Fox M, MacLeod W, Slotow SJ, Rosen S. Prevalence of HIV in workforces in southern Africa, 2000-2001. *S Afr Med J* 2004; 94: 125-130.
7. Wilkinson D, Gilks CF. Increasing frequency of tuberculosis among staff in a South African district hospital: impact of the HIV epidemic on the supply side of health care. *Trans R Soc Trop Med Hyg* 1998; 92(5): 500-502.
8. World Health Organization. *WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children.* Geneva: WHO, 2006: 1-48.
9. Department of Health, Republic of South Africa. *National Antiretroviral Treatment Guidelines.* Pretoria: DOH, 2004: 1-56.
10. Department of Health, Republic of South Africa. *A National Human Resource Plan for Health.* Pretoria: DOH, 2006: 1-72.

Accepted 2 November 2006.

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

Asheber Gaym, May Mashego, Ayesha B M Kharsany, Jenny Walldorf, Janet Frohlich, Quarraisha Abdool Karim

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.

S Afr Med J 2007; 97: 120-123.

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

Faculty of Medicine, Addis Ababa University, Ethiopia, and Centre for the AIDS Programme of Research in South Africa (CAPRISA), University of KwaZulu-Natal, Durban
Asheber Gaym, MD

CAPRISA, University of KwaZulu-Natal, Durban
Mary Mashego, MB ChB
Ayesha B M Kharsay, PhD
Janet Frohlich, PhD

CAPRISA, University of KwaZulu-Natal, Durban, and Albert Einstein School of Medicine, New York, USA
Jenny Walldorf, MD

CAPRISA, University of KwaZulu-Natal, Durban, and Department of Epidemiology, Columbia University, New York, USA
Quarraisha Abdool Karim, PhD

Corresponding author: *Q Abdool Karim (abdoolq2@ukzn.ac.za)*

(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 studies[6-8] 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 intrauterine 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.

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

Pap result	Age group (years) 0 - 29	30 - 60	Total
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.

Data from other studies[19-21] 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 studies[23] 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-

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.

The researchers were supported by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) and Columbia University, USA. CAPRISA is part of the Comprehensive International Program of Research on AIDS (CIPRA) and is supported by the National Institute of Allergy and Infectious Disease (NIAID), the National Institutes of Health (NIH) and the US Department of Health and Human Services (DHHS) (grant # 1 U19 AI51794). Support was also provided by the Columbia University-Southern African Fogarty AIDS International Training and Research Program (grant # D43 TW00231). We thank the clinic staff at Mafakatini Clinic who assisted in these surveys and the women who participated.

Particular thanks to all the CAPRISA staff at Mafakatini Clinic for their help in conducting the study, and to Mrs Cheryl Baxter for assistance with manuscript preperation.

Dr Asheber Gaym Belay was a recipient of a World Health Organization (WHO) research training grant while conducting the study. Dr Jenny Walldorf was an Albert Einstein International Research Trainee based at CAPRISA at the time of the study.

References

1. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. *Int J Cancer* 1999; 83(1): 18-29.
2. Gustafsson L, Ponten J, Zack M, Adami HO. International incidence rates of invasive cervical cancer after introduction of cytological screening. *Cancer Causes Control* 1997; 8(5): 755-763.
3. Chirenje ZM, Rusakaniko S, Kirumbi L, *et al*. Situation analysis for cervical cancer diagnosis and treatment in east, central and southern African countries. *Bull World Health Organ* 2001; 79(2): 127-32.
4. Murthy NS, Agarwal SS, Prabhakar AK, Sharma S, Das DK. Estimation of reduction of lifetime risk of cervical cancer through one life-time screening. *Neoplasma* 1993; 40(4): 255-258.
5. Mandelblatt JS, Lawrence WF, Gaffikin L, *et al*. Costs and benefits of different strategies to screen for cervical cancer in less-developed countries. *J Natl Cancer Inst* 2002; 94(19): 1469-1483.
6. Leroy V, Ladner J, De Clercq A, *et al*. Cervical dysplasia and HIV type 1 infection in African pregnant women: a cross sectional study, Kigali, Rwanda. The Pregnancy and HIV Study Group (EGE). *Sex Transm Infect* 1999; 75(2): 103-106.
7. La Ruche G, You B, Mensah-Ado I, *et al*. Human papillomavirus and human immunodeficiency virus infections: relation with cervical dysplasia-neoplasia in African women. *Int J Cancer* 1998; 76(4): 480-486.
8. Abercrombie PD, Korn AP. Lower genital tract neoplasia in women with HIV infection. *Oncology (Williston Park)* 1998; 12(12): 1735-1739; discussion 1742, 1745, 1747.
9. Gichangi PB, Bwayo J, Estambale B, *et al*. Impact of HIV infection on invasive cervical cancer in Kenyan women. *Aids* 2003; 17(13): 1963-1968.
10. Chirenje ZM, Loeb L, Mwale M, Nyamapfeni P, Kamba M, Padian N. Association of cervical SIL and HIV-1 infection among Zimbabwean women in an HIV/STI prevention study. *Int J STD AIDS* 2002; 13(11): 765-768.
11. UNAIDS. *UNAIDS Fact Sheet 2004*. Geneva: World Health Organization, 2004.
12. Rogo KO, Omany J, Onyango JN, Ojwang SB, Stendahl U. Carcinoma of the cervix in the African setting. *Int J Gynaecol Obstet* 1990; 33(3): 249-255.
13. Lancaster EJ, Banach L, Lekalakala T, Mandiwana I. Carcinoma of the uterine cervix: results of Ka-Ngwane screening programme and comparison between the results obtained from urban and other unscreened rural communities. *East Afr Med J* 1999; 76(2): 101-104.
14. South African Department of Health. *Syndromic Case Management of Sexually Transmitted Diseases – Guide for Decision-makers, Health Care Workers and Communicators*. Pretoria: Department of Health, 2000. http://www.cadre.org.za/pdf/pdf/WHO_STD.pdf (accessed 13 December 2006).
15. Cohen MS, Pilcher CD. Amplified HIV transmission and new approaches to HIV prevention. *J Infect Dis* 2005; 191: 1391-1393.
16. Quinn TC, Wawer MJ, Sewankambo N, *et al*. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000; 342(13): 921-929.
17. Wawer MJ, Gray RH, Sewankambo NK, *et al*. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005; 191: 1403-1409.
18. Wright TC jun, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. *JAMA* 2002; 287(16): 2120-2129.
19. Östör AG. Natural history of cervical intraepithelial neoplasia: a critical review. *Int J Gynecol Pathol* 1993; 12(2): 186-192.
20. Nasiell K, Roger V, Nasiell M. Behavior of mild cervical dysplasia during long-term follow-up. *Obstet Gynecol* 1986; 67(5): 665-669.
21. Lonky NM, Navarre GL, Saunders S, Sadeghi M, Wolde-Tsadik G. Low-grade Papanicolaou smears and the Bethesda system: a prospective cytohistopathologic analysis. *Obstet Gynecol* 1995; 85(5 Pt 1): 716-20.
22. Fonn S, Bloch B, Mabina M, *et al*. Prevalence of pre-cancerous lesions and cervical cancer in South Africa – a multicentre study. *S Afr Med J 2002*; 92(2): 148-156.
23. Berek JS. Cervical and vaginal cancer. In: Berek JS, Hillard, PJA, Adashi EY, ed. *Novak's Gynecology*. 13th ed. Philadelphia: Lippincott Williams & Wilkins, 2002: 1207.
24. Goff BA, Atanasoff P, Brown E, Muntz HG, Bell DA, Rice LW. Endocervical glandular atypia in Papanicolaou smears. *Obstet Gynecol* 1992; 79(1): 101-104.
25. Boon ME, Baak JP, Kurver PJ, Overdiep SH, Verdonk GW. Adenocarcinoma in situ of the cervix: an underdiagnosed lesion. *Cancer* 1981; 48(3): 768-773.

Accepted 6 October 2006.