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HIV/AIDS

Stabilizing HIV prevalence masks high HIV incidence rates amongst rural and urban women in KwaZulu-Natal, South Africa

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Background In mature generalized human immunodeficiency virus (HIV) epidemics, as survival from accessing antiretroviral treatment (ART) increases, HIV prevalence data may be suboptimal and difficult to interpret without HIV incidence rates.

Objective To determine the HIV incidence rate among rural and urban women in KwaZulu-Natal, South Africa.

Methods We conducted a prospective cohort study from March 2004 to May 2007. Volunteers were recruited from a rural family-planning clinic and an urban clinic for sexually transmitted infections. Consenting, HIV-uninfected women aged 14–30 years were enrolled. Demographic, clinical, sexual and behavioural data were collected using standardized questionnaires with HIV risk reduction counselling and HIV testing. Pelvic examinations were completed at quarterly visits.

Results The HIV prevalence at screening was 35.7% [95% confidence interval (CI) 32.7–38.8] amongst rural women and 59.3% (95% CI 56.5–62.0) amongst urban women. A total of 594/2240 (26.5%) enrolled women contributed to 602 person-years (PYs) of follow-up. The median age was 22 years [inter-quartile range 18–23 years]. HIV incidence rate was 6.5/100 PY (95% CI 4.4–9.2) amongst rural women and 6.4/100 PY (95% CI 2.6–13.2) amongst urban women. HIV incidence rate of 17.2/100 PY (95% CI 2.1–62.2) was highest amongst urban women <20 years of age and 10.2/100 PY (95% CI 4.1–20.9) amongst rural women $\geqslant 25$ years of age.

Conclusion HIV incidence rates are devastatingly high in young women in rural and urban KwaZulu-Natal, despite reports of stabilized HIV prevalence observed in current surveillance data. The diffuse nature of the HIV epidemic underscores the urgent need to enhance HIV prevention and treatment modalities.

Keywords HIV incidence, HIV prevalence, young women, South Africa

Introduction

South Africa has the highest burden of human immunodeficiency virus (HIV) infection in the world with an estimated 5.7 million people infected with HIV in 2008.[1] The province of KwaZulu-Natal is at the epicentre of the pandemic, and women account for >60% of infections.[2–4] The epidemic typology has been described as 'hyperendemic, generalized and mature'[5] to reflect >15.0% HIV prevalence in the general population.[2] Annual, anonymous, antenatal surveys undertaken since 1990 have served as the mainstay of HIV surveillance for monitoring trends in the evolving epidemic, for priority setting and health-service planning. Data from these surveys in the past 3 years demonstrate a stabilization of national HIV prevalence estimates.[6]

With increasing access to antiretroviral treatment (ART),[7] HIV prevalence is expected to increase resulting from increased survival.[8] Notwithstanding the challenges to increasing ART access and coverage,[7,9] knowledge of the epidemic is key to customizing responses.[5,10,11] In the early stages of the epidemic where disease burden and mortality rates are low, HIV prevalence data provide a reliable marker for monitoring the epidemic.[12] However, as the epidemic matures morbidity and mortality increases;[3,13,14] incidence rate data[8,15–17] are important to understand ongoing transmission dynamics and inform the prioritization of prevention efforts, whereas prevalence of established infections informs health service and care planning needs.[5,10]

As laboratory methods to differentiate established and new infections are being validated, cohort studies provide an option for ascertaining rates of new HIV infections. This prospective cohort study was undertaken in a rural and urban setting to better understand the stabilized HIV prevalence data in KwaZulu-Natal and to assess the feasibility of undertaking HIV prevention studies with incident HIV infections as endpoints.

Methods

Study design, setting and source population

The Centre for the AIDS Programme of Research in South Africa (CAPRISA) is an AIDS research institute in KwaZulu-Natal, South Africa conducting research that contributes to understanding HIV epidemiology, prevention and pathogenesis, as well as the links between tuberculosis and AIDS care. This prospective cohort study was undertaken at CAPRISA's two clinical research sites.

The CAPRISA Vulindlela Clinical Research site (rural site) is located ~150 km north-west of Durban. This community has approximately 400 000 residents, with limited resources, infrastructure and employment opportunities accounting for high levels of poverty and unemployment.[18] Health services are provided by seven public-sector primary health-care clinics and the closest referral hospitals are ~30 km away. From March 2004 to April 2005, volunteers were recruited from the rural family planning clinic. The CAPRISA eThekwini Clinical Research site (urban site) is located in central Durban adjacent to a large public-sector primary-care clinic designated for the diagnosis and treatment of sexually transmitted infections (STIs) and tuberculosis. From July 2005 to December 2005, female volunteers were recruited from the STI clinic. Based on cross-sectional survey data, HIV incidence rates are highest in young women and establishing cohorts of young women aged 14–30 years, although this age cut-off reduces generalizability, targets women at highest HIV risk.

Study procedures

Volunteers aged 14–30 years received study information, provided written informed consent and were screened for eligibility to assess willingness to provide adequate locator data for study retention purposes, be sexually active (defined as having had vaginal intercourse at least once in the 3 months prior to screening) and test HIV negative. Women were excluded if planning to travel away from the study site for >3 consecutive months in the 12 months following enrolment; plans to migrate outside the study catchment area in the 12 months following enrolment; plans to become pregnant in the next 2.5 years post-enrolment; or enrolled in any other study of a vaginally applied product related to HIV prevention.

At enrolment and at each monthly visit, demographic, clinical, sexual and behavioural data were obtained from all women through nurse-administered interviews using structured questionnaires. Women were tested for HIV and pregnancy, received HIV and risk reduction counselling and were offered male and female condoms. At enrolment, quarterly and at study exit visits, pelvic examinations were completed and blood samples collected for archiving for retrospective confirmation of HIV endpoint. Women were reimbursed minimally at each visit for time and travel costs as per the South African National Ethics Guidelines.[19]

Laboratory testing procedures

HIV testing was performed on-site using two rapid antibody tests (Determine HIV-1/2—Abbott Laboratories, IL, USA and HIV-1/2 SmartCheck assay—Globalemed.LLC, World Diagnostics, Inc.). Women testing concordantly positive, indeterminate or discordant at follow-up visits had blood sample collected at the same visit for HIV antibody testing (Enzygnost Anti-HIV-1/2 Plus, Dade Behring, Marburg, Germany) and HIV-1 RNA polymerase chain reaction (PCR) assay [COBAS AmpliScreen HIV-1 Test, version 1.5 (Qualitative) and AMPLICOR HIV-1 MONITOR Test, v1.5 (Quantitative); Roche Molecular Systems,

Inc., Branchburg, NJ, USA]. Incident HIV infection was confirmed on positive HIV-1 RNA PCR (qualitative and quantitative) and/or HIV antibody positive, and negative on the last stored blood sample tested retrospectively. Urine pregnancy testing was performed on site (QuickVue One-Step hCG Urine Test; Quidel Corporation, San Diego, USA).

Ethical considerations

The protocol, informed consent and data collection forms were reviewed and approved by the University of KwaZulu-Natal Biomedical Research Ethics committee. The screening and enrolment visits were undertaken on different days to give eligible women sufficient time to consider their decision to participate in this study.

At both sites, community engagement processes were established through Community Research Support Groups (CRSG) consisting of stakeholders including health-service providers and traditional leaders from community structures. The community liaison officers worked closely with CRSG members on a regular basis to disseminate information on the epidemiology of HIV epidemic in South Africa, HIV prevention strategies and the rationale for conducting HIV prevention research and HIV treatment.

At screening, women identified with HIV infection were referred to the CAPRISA AIDS Treatment Program operational at both sites. Pregnant women identified during screening or follow-up were referred to local public-sector facilities for follow-up antenatal care but continued with their monthly study visits. Women diagnosed with symptomatic STIs were managed syndromically on site as per the South African Department of Health guidelines.[20] Contraceptive counselling and contraceptives were provided at both sites as part of the study visit. Women who became HIV infected were given the option of joining the CAPRISA Acute HIV-1 Infection Study or the CAPRISA AIDS Treatment Project for ongoing care and support.

Data collection and statistical analysis

Data were collected on standardized case report forms (CRFs) and faxed to a dedicated study database using DataFax (Clinical DataFax Systems Inc., Hamilton, Canada). For quality assurance, all CRF entries were manually and electronically verified and the quality of the data reviewed in real time. Data analysis was undertaken with Statistical Analysis Software (SAS) statistical package (version 9.1.3; SAS, NC, USA).

The baseline variables were summarized using descriptive statistics expressed as mean or median for continuous variables and as percentages for categorical variables. For statistical testing for differences, the Fisher's exact test comparing categorical data and Wilcoxon rank sum test for continuous data were used. McNemar's agreement statistic was used for analysis of paired categorical data with two categories, Bowker's test of symmetry for paired categorical data with more than two levels and Wilcoxon signed rank sum test for paired continuous data. Missing data were not included in the comparison between baseline and 12 months. All analyses were two-sided.

HIV incidence rate was estimated on the number of confirmed seroconversions, calculated per 100 person-years (PYs) at risk. The time at risk was defined as the time from enrolment to the last negative HIV test for women who remained HIV uninfected or the first confirmed positive HIV test result for those who became infected during the study. Pregnancy rate was estimated on the number of positive urine pregnancy tests, calculated per 100 PYs. Time at risk excluded the time from a positive pregnancy test to pregnancy outcome. Confidence intervals (CIs) for HIV and pregnancy incidence rate assumed a Poisson distribution.

Results

Screening, accrual and retention

A total of 2240 (981 rural and 1259 urban) volunteers were screened. HIV prevalence was 35.7% (95% CI 32.7–38.8) amongst rural women and 59.3% (95% CI 56.5–62.0) amongst urban women; the main reason for exclusion of volunteers. At both sites, HIV prevalence was highest amongst volunteers 25 years and older compared with younger volunteers (both sites $P < 0.001$) (Table 1). Other reasons for ineligibility included volunteers being overage (13.8%), not returning for enrolment visit (5.8%), not sexually active (3.0%), requesting voluntary counselling and testing services only (1.2%), pregnancy (0.2%), planning to relocate from current address (0.1%), fear of study procedures especially pelvic examinations (0.2%), medical reasons (0.2%) and partner not agreeing to her participation in research (0.01%).

A total of 594 (26.6%) women were enrolled with a mean enrolment rate per month per site of 26 (rural) and 17 (urban) women with a screening to enrolment ratio of 1:2 and 1:10, respectively. The overall retention rate was 70.0% (95% CI 65.7–73.9) and 78.0% (95% CI 70.2–85.3) at the rural and urban sites, respectively. There were no differences in women who completed the study compared with those who did not return for follow-up with regard to demographic characteristics of age, completion of secondary schooling, relationship status, living with partner or whether they were from the rural or urban site (all $P > 0.05$). At exit, there were 477 and 117 women at the rural and urban site, respectively, with a cumulative of 602 PYs.

Demographic characteristics

All enrolled women were Black African with an overall median age of 22 years [inter-quartile range (IQR) 18–23 years]. Rural women compared with urban

Table 1 HIV prevalence and screening outcome of rural (March 2004 to April 2005) and urban (July to December 2005) women aged 14–30 years in KwaZulu-Natal, South Africa

	Overall		Rural		Urban	
HIV prevalence						
Number screened	2240		981		1259	
	n/N	**% (95% CI)**	***n/N***	**% (95% CI)**	***n/N***	**% (95% CI)**
HIV prevalence	1096/2240	48.9 (46.8–51.0)	350/981	35.7 (32.7–38.8)	746/1259	59.3 (56.5–62.0)
Age-specific HIV prevalence[a]						
<20 years	101/378	26.7 (22.4–31.5)	47/245	19.2 (14.6–24.8)	54/133	40.6 (32.3–49.5)
20–24 years	283/694	40.8 (37.1–44.6)	81/258	31.4 (25.9–37.5)	202/436	46.3 (41.6–51.1)
⩾25 years	575/870	66.1 (62.8–69.2)	85/180	47.2 (39.8–54.8)	490/690	71.0 (67.5–74.4)
Screening outcome	***n***	**%**	***n***	**%**	***n***	**%**
HIV positive	1096	48.9	350	35.7	746	59.3
Age >30 years	308	13.8	21	2.1	287	22.8
Pregnant	5	0.2	0	0.0	5	0.4
Not sexually active	68	3.0	65	6.6	3	0.2
Voluntary counselling and testing	27	1.2	0	0.0	27	2.1
Planning to move away	3	0.1	0	0.0	3	0.2
Afraid of clinical procedures	4	0.2	4	0.4	0	0.0
Medical reasons	4	0.2	0	0.0	4	0.3
Partner refusing	1	0.0	0	0.0	1	0.1
Not returning for enrolment	130	5.8	64	6.5	66	5.2

[a]Missing age for 298 women.

women were younger; a higher proportion were <20 years of age and had not completed secondary schooling (all $P < 0.001$). Majority of women reported to be in a stable relationship though they were currently not living with their sexual partner (Table 2).

Sexual behaviour characteristics

Sexual behaviour data at baseline and at 12 months follow-up are presented in Table 3. Amongst rural women, there was a reduction in the mean number of sex acts reported in the 2 weeks preceding their Month 12 study visit ($P = 0.03$), increase in reported condom use with vaginal sex ($P < 0.001$), decline in the proportion reporting one sex partner in the past 3 months ($P = 0.004$) with no changes in contraceptive-use patterns ($P = 0.05$), although a higher proportion of women reported engaging in anal sex (0.8 vs 1.5%; $P = 0.18$). In contrast, among urban women there was a decline in anal-sex practice (6.8 vs 1.3%, $P = 0.03$), no decline in the mean number of sex acts in the past 2 weeks preceding their Month 12 study visit ($P = 0.17$), or the percentage of women reporting one partner in the past 3 months ($P = 0.37$), or changes in contraceptive-use patterns ($P = 0.48$) and condom use during last vaginal sex act ($P = 0.10$).

The practice of intra-vaginal substance use of water with salt, vinegar, soap or douching with antiseptics containing parachlorometaxylenol or povidone iodine products or traditional herbs was used for personal hygiene. Despite counselling on potential HIV risk, we did not observe any changes in these practices in rural women (17.6 vs 12.0%, $P = 0.07$). The self-report of STIs (genital ulceration and/or vaginal discharge) declined at 12 months amongst rural (25.4 vs 4.5%, $P < 0.0001$) and urban women (28.2 vs 5.2%, $P < 0.0001$); however, any abnormal pelvic examination finding (vaginal discharge, vaginitis, cervicitis, ulceration, abrasions, petechia, vesicles or genital warts) declined amongst rural women only (39.6 vs 15.4%, $P < 0.0001$) and not amongst urban women (36.8 vs 30.9%, $P = 0.35$).

Incidence of HIV

As shown in Table 4, a total of 39 (6.6%) women became HIV infected during the study. The HIV incidence rate was 6.5/100 PY (95% CI 4.4–9.2) amongst rural women and 6.4/100 PY (95% CI 2.6–13.2) amongst urban women. The highest rate of 17.2/100 PY (95% CI 2.1–62.2) was among urban women <20 years of age, whereas the rate of 10.2/100 PY (95% CI 4.1–20.9) was highest amongst older rural women, ⩾25 years of age. HIV incidence rate was higher amongst older rural women compared with younger women [10.2/100 PY (95% CI 4.1–20.9) vs 3.6/100 PY (95% CI 1.7–6.9), ($P = 0.03$)].

Incidence of Pregnancy

A total of 96 women (16.2%) became pregnant during the study (Table 4), out of which 74 were rural and 22 urban. The pregnancy incidence rate was 16.6/100 PY (95% CI 13.1–20.9) among rural women and 22.4/100 PY (95% CI 14.1–34.0) among urban women. The highest pregnancy incidence rate of 30.6/100 PY (95% CI 6.3–89.3) was amongst young urban women <20 years of age.

Of the women who became pregnant, 50 (52.1%) reported not having used any form of contraception, 32 (33.3%) reported relying on partners using male condoms only, 9 (17.3%) and 5 (5.2%) reported to be on injectable or oral forms of contraception, respectively. Not surprisingly, women on hormonal contraception who became pregnant reported being non-adherent to contraceptive use.

Of the 96 pregnancies, 62 (64.6%) continued to full term, 20 (20.8%) were still pregnant at exit, 5 (5.2%) resulted in spontaneous abortion or had elective termination of pregnancy and in 9 (9.4%) the outcome was unknown. Should women in a trial of an investigational new drug become pregnant, for safety reasons they would be required to go off product for the duration of the pregnancy and the pregnancy time would translate to 58.7 PY.

Table 2 Socio-demographic characteristics of rural and urban women at enrolment comprising the study population in KwaZulu-Natal, South Africa

Characteristic	Overall $N=594$ %	Rural $N=477$ %	Urban $N=117$ %
Age group in years			
<20	41.1	47.6‡	14.5‡
20–24	40.6	34.8‡	64.1‡
⩾25	18.4	17.6	21.4
Median age in years (IQR)	22 (18–23)	20 (18–23)‡	22 (21–24)‡
Completed secondary education (grades 7–12)	33.0	24.3‡	68.4‡
Relationship status: stable partner including married[a]	93.4	93.9	91.5
Currently not living with partner	90.6	92.5†	82.9†

[a]Married (2.7% rural and 3.4% urban).
‡$P<0.001$; †$P=0.001$.

Discussion

In this sample of rural and urban women in KwaZulu-Natal, HIV incidence rates of 6.5/100 PY and 6.4/100 PY, respectively, are devastatingly

Table 3 Changes in sexual behaviour from enrolment and at 12 months among rural and urban women aged 14–30 years in KwaZulu-Natal, South Africa

Sexual behaviour characteristics	Rural			Urban		
	Baseline $N=477$	Month 12 $N=266$	*P*-value	Baseline $N=117$	Month 12 $N=89$	*P*-value
Mean number of vaginal sex acts in the past 2 weeks (range)	2 (0–11)	1.8 (0–18)	0.03	2 (0–20)	2 (0–8)	0.17
Mean percentage condom use with vaginal sex in the past 2 weeks (range)	30.5 (0–100)	58.0 (0–100)	<0.0001	41.9 (0–100)	61.3 (0–100)	0.10
Percentage with one sex partner in the past 3 months	98.5	94.3	0.004	82.1	92.3	0.37
Percentage reporting anal sex	0.8	1.5	0.18	6.8	1.3	0.03
Percentage not using contraception	21.8	10.9	0.05	29.1	34.6	0.48
Percentage using injectable hormonal contraception	55.1	63.9		18.8	32.1	
Percentage using oral hormonal contraception	5.9	6.8		4.3	3.7	
Percentage with any form of vaginal insertions	17.6	12.0	0.07	41.9	9.9	<0.0001
Percentage with sexually transmitted infections[a]	25.4	4.5	<0.0001	28.2	5.2	0.0002
Percentage with any abnormal[b] pelvic examination	39.6	15.4	<0.0001	36.8	30.9	0.35

[a]Genital ulceration and or vaginal discharge.
[b]Any abnormality of vaginal discharge, vaginitis, cervicitis, ulceration, abrasions, petechia, vesicles and/or warts.

Table 4 HIV incidence and pregnancy rates by age group among rural (March 2004 to May 2007) and urban (July 2005 to May 2007) women aged 14–30 years in KwaZulu-Natal, South Africa

Enrolment and follow-up	**Overall**					**Rural**				**Urban**		
Number enrolled	594					477				117		
Person-years at risk (PYs)	602.0					492.8				109.2		
Retention rate	71.4% (95% CI 67.5–75.0)					69.8% (95% CI 65.4–73.9)				77.8% (95% CI 69.0–84.7)		
HIV incidence rate	***n***	**Cases**	**PY**	**Per 100 PY (95% CI)**	***n***	**Cases**	**PY**	**Per 100 PY (95% CI)**	***N***	**Cases**	**PY**	**Per 100 PY (95% CI)**
Overall	594	39	602.0	6.5 (4.6–8.9)	477	32	492.8	6.5 (4.4–9.2)	117	7	109.2	6.4 (2.6–13.2)
<20 years	244	11	260.7	4.2 (2.1–7.6)	227	9	249.1	3.6 (1.7–6.9)	17	2	11.6	17.2 (2.1–62.2)
20–24 years	241	20	249.5	8.0 (4.9–12.3)	166	16	174.8	9.2 (5.2–14.9)	75	4	74.7	5.4 (1.5–13.7)
⩾25 years	109	8	91.8	8.7 (3.8–17.2)	84	7	68.9	10.2 (4.1–20.9)	25	1	22.9	4.4 (0.1–24.4)
Pregnancy rate	***n***	**Cases**	**PY[a]**	**Per 100 PY (95% CI)**	***n***	**Cases**	**PY[a]**	**Per 100 PY (95% CI)**	***N***	**Cases**	**PY[a]**	**Per 100 PY (95% CI)**
Overall	594	96	543.4	17.7 (14.3–21.6)	477	74	445.3	16.6 (13.1–20.9)	117	22	98.1	22.4 (14.1–34.0)
<20 years	244	51	227.2	22.5 (16.7–29.5)	227	48	217.4	22.1 (16.3–29.3)	17	3	9.8	30.6 (6.3–89.3)
20–24 years	241	36	229.0	15.7 (11.0–21.8)	166	19	162.5	11.7 (7.0–18.3)	75	17	66.5	25.6 (14.9–40.9)
⩾25 years	109	9	87.2	10.3 (4.7–19.6)	84	7	65.4	10.7 (4.3–22.1)	25	2	21.8	9.2 (1.1–33.1)

[a]Excludes time pregnant.

high, yet similar to the 7.2/100 PY reported for self-identified female sex workers in Durban,[21] 6.0/100 PY among women in rural Hlabisa, northern KwaZulu-Natal, and 5.0/100 PY amongst urban women in Durban.[22] Regardless of the stabilizing HIV prevalence observed in the antenatal[6] and population-based surveys,[2] these high HIV incidence rates are disturbing. In contrast, HIV incidence rates from many southern African countries are comparatively lower, ranging from 1.3/100 PY in Moshi, Tanzania, to 2.6/100 PY in Lusaka, Zambia,[22,23] to 4.2/100 PY in Lilongwe, Malawi, 4.5/100 PY in Blantyre, Malawi, to 4.8/100 PY in Harare, Zimbabwe.[24,25] Of note in all of these studies is that these high incidence rates are being reported in the context of substantial amounts of counselling and promotion of abstinence, behaviour change, condom use and know-your-HIV-status paradigm. In the absence of this intensity of counselling and prevention support, the reported incidence rates are likely to be even higher.

At screening, a large number of women older than age 25 years were already infected with HIV and were unaware of their HIV status. For many women this was their first opportunity to have an HIV test. This highlights the importance for increasing provider-initiated HIV counselling and testing services.[26] The high HIV prevalence in both rural and urban women provides an indication of the enormous AIDS care and treatment needs and anticipated disease burden on health-care services.

HIV prevalence has been used to measure burden of disease and to track epidemiological changes over time. However, increasing access to ART over time makes prevalence data less reliable in understanding transmission dynamics, which are better understood by measuring the rates of new HIV infections.[15,16] Despite the benefits of ART to enhance quality of life, increase survival and more importantly its potential impact as a prevention tool to lower the HIV incidence rate, the wide-scale implementation of ART has been challenging.[9]

In South Africa, limited numbers of studies have directly measured HIV incidence rates, although these studies have consistently shown high rates over time, yet vary by age, gender and geographic area.[3,37] HIV incidence rates have remained high, with >5.0% amongst urban and rural women from the general population[22] and women at high risk in Durban[21] highlighting the diffuse nature of the epidemic. Modelling the national HIV incidence rates amongst pregnant women attending public-sector clinics, HIV incidence increased from 0.58% in 1990, peaked to 6.45% in 1997 and declined to 5.41% in 2006, with the KwaZulu-Natal province experiencing the highest rate of 8.0%.[27] Using the BED-HIV-1 capture enzyme immunoassay (BED-CEIA) to measure HIV incidence, the 2005 South African National HIV Household Survey estimated the HIV incidence of

2.4% amongst men and women aged 15–48 years. Young women in the age group 20–29 years had the highest rate of 5.6% compared with 0.9% amongst men in the same age group.[17] Several studies[17,21,22,27] and this study confirm the persistently high steady-state HIV incidence rates, demonstrating the underlying transmission dynamics despite the scaled-up prevention and treatment efforts, which have failed to address the HIV prevention needs of young women. This study highlights the importance of augmenting HIV prevalence data with incidence rate data to get a more accurate indication of trends of HIV infection.[16] Although these studies are expensive and may not be feasible to undertake at the same frequency as cross-sectional surveys, it is important in mature HIV epidemics to supplement HIV prevalence data with HIV incidence rate data to minimize complacency emanating from a stabilized prevalence and to provide a more informative and sensitive marker of the state of the epidemic.[27]

The sexual-behavioural data highlight the complexity of HIV risk and prevention for women across their life course. Although marriage is rare, many women are sexually active and the duration of their relationships vary substantially. In these settings where economic options for women are limited and their survival is dependent on having a man in their life, child-bearing is an important facet of their identity. In this context, the traditional 'ABC' (abstinence, be faithful, condom use) prevention approach is misleading and has limited applicability.[11,28] The higher abnormal pelvic examination findings in urban women is not surprising given that they were recruited from the STD clinic and are likely to be at higher risk of acquiring and reporting STIs. The strengthening of sexual reproductive health services, including comprehensive pregnancy prevention counselling, provision of services for reducing HIV transmission to infants and reducing maternal mortality rates has been gaining increasing attention;[29–34] and in the context of HIV programme planning,[33,34] is as important for primary and secondary HIV prevention.

Although this study has some important findings, the benefit of longitudinal data and rigorous endpoint ascertainment, it also has several limitations. A key limitation is the retention rate in the study as HIV risk behaviours of those lost to follow-up are likely to be different from those completing the study. As these are research-naïve cohorts, the potential challenges in undertaking longitudinal studies underscore the importance of placing more effort on retention for future studies.[35,36] HIV risk behaviours were assessed using self-report and even though the staff received substantial training to minimize socially desirable responses, there is no guarantee for valid self-reported data.[37] The anal sex reporting rates, for example, could be indicative of women's response to information received from study staff in the HIV risk-reduction counselling session on the additional increased risk of HIV acquisition through anal sex compared with vaginal sex and could partially account for the lower reported rates of anal sex in these study populations compared with other reported studies from this region.[21,22] Given its potential confounding effect in testing efficacy of vaginal products, accurate measurement of anal sex practice is important.[35]

Pregnancies were determined using chemical testing and could be an overestimate of real pregnancy rates.[38] The potential bias with selecting women not intending to fall pregnant could impact HIV incidence rates substantially; however, only 0.2% of the pregnant volunteers were excluded at screening and none excluded as a result of planning to become pregnant, and this should have minimal impact on HIV incidence in this study. It is also clear that self-reported intention not to fall pregnant does not correlate with actual intentions and the importance of the selection criteria used. Although external validity is important, the strategy used is not generalizable even though it is important for identifying women at high risk of acquiring HIV infection. While the pregnancy rates were high but lower than when contraceptives are not provided by study sites,[39–41] women in the rural site recruited from the family-planning clinic were more likely to already be on a reliable form of contraceptive in contrast to urban women recruited from the STD clinic. A key lesson for future clinical trials of investigational new drugs is the importance of counselling and on-site provision of contraceptive services to support fertility control and maintain the scientific integrity of the trial through minimizing product hold. Lastly, the urban HIV incidence rate is less stable than the rural estimate given the smaller size of the cohort and the shorter duration of follow-up.

Notwithstanding these study limitations and the HIV prevalence appearing to be stabilizing,[2,6,27] these results highlight the uniquely diffuse, generalized, hyperendemic nature of the epidemic in South Africa and the unprecedented high HIV prevalence and incidence rates across rural and urban KwaZulu-Natal. Although these populations are not representative of all HIV epidemics, the high prevalence and incidence rate data underscore the importance and appropriateness of including these cohorts for testing new HIV prevention modalities. The public health imperative for the conduct of pivotal prevention trials in this select population in this region is particularly important to alter HIV epidemic trajectories in this region and globally.

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Conflicts of interest: None declared.

KEY MESSAGES

- The HIV incidence rates are disturbingly high among young women in rural and urban KwaZulu-Natal, South Africa, despite reports of stabilized HIV prevalence observed in current surveillance data.
- The diffuse nature of the epidemic highlights the need to enhance HIV prevention and treatment modalities for young women.

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