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High incidence of asymptomatic genital tract infections in pregnancy in adolescent girls and young women: need for repeat aetiological screening

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ABSTRACT

Introduction Sexually transmitted infection (STI) prevalence and incidence estimates for pregnant adolescents are under-reported. We estimated prevalence and incidence of STIs in pregnant adolescents (15–19 years) in comparison with pregnant women 20–24 and >25 years.

Methods Pregnant women registering at primary care clinics in Umlazi, a periurban subdistrict in KwaZulu-Natal, South Africa, were enrolled in an HIV incidence cohort study during February 2017–March 2018. Women were examined for abnormal vaginal discharge, received empirical treatment, tested for HIV-1 and had vaginal swabs taken at their first and a subsequent visit in the third trimester. Vaginal swabs were stored for STI testing at completion of study and tested for *Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhoeae* and *Mycoplasma genitalium* using PCR.

Results A total of 752 HIV-negative pregnant women were enrolled at a median gestational age of 17 weeks: 180 (23.9%), 291 (38.7%) and 281 (37.4%) in the 15–19, 20–24 and >25 years age groups. Pregnant adolescents had an STI prevalence of 26.7% at baseline, not significantly lower than the 20–24 (34.7%, OR 1.4; 95% CI 1.0 to 2.1, p=0.09) and >25 years (33.8%, OR 1.4; 95% CI 0.9 to 2.1, p=0.12) age groups. *T. vaginalis* (11.1%), *C. trachomatis* (7.8%) and *N. gonorrhoeae* (4.4%) were most prevalent in adolescents, a trend similar to the other age groups. Overall, 43.4% were symptomatic and treated at baseline. Overall, 40.7% (118 of 290) of women who tested negative for an STI at baseline tested positive at the repeat visit (incidence 19.5/100 person years). STI incidence in pregnant adolescents was 23.9/100 person years and comparable with older age groups (20.5/100 person years and 16.2/100 person years). At the repeat visit, 19.0% of all women with an STI were symptomatic and treated. Performance of syndromic management was poor at baseline (negative predictive value (NPV) 68.6%, positive predictive value (PPV) 34.0%) and at repeat visit (NPV 58.4%, PPV 34.3%).

Conclusions Prevalence of asymptomatic curable STIs in pregnant adolescents is high and comparable with women >20 years old. Adolescents remain at substantial risk of asymptomatic incident STIs during pregnancy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While the high prevalence and the limitations of syndromic diagnosis of sexually transmitted infections (STIs) and bacterial vaginosis in pregnancies are well documented, pregnant adolescents have been understudied. Furthermore, it is well-known that condom use during pregnancy is inconsistent or non-existent and pregnant women, particularly pregnant adolescents, are at continued risk of incident or recurrent STIs throughout pregnancy. Such evidence for the need for repeat aetiological screening for other genital tract infections in pregnancy is lacking in low/middle-income countries.

WHAT THIS STUDY ADDS

⇒ Prevalence of largely asymptomatic genital tract infections in adolescents at antenatal registration is high. Adolescents and young women are at high risk of asymptomatic incident STIs in the third trimester of pregnancy and may be missed if aetiological screening for STIs is not repeated.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Current Centers for Disease Control and Prevention recommendations include rescreening for STIs in the third trimester of pregnancy, a strategy amiss in the WHO and South African Guidelines. We provide novel evidence for repeat aetiological testing for genital tract infections in the third trimester.

INTRODUCTION

Adolescent girls (15–19 years) bear a disproportionate burden of HIV infections compared with boys. In sub-Saharan Africa, six in seven new HIV infections among adolescents (15–19 years) are among girls.[1] Adolescent girls are also vulnerable to other sexually transmitted infections (STIs) and unintended pregnancies.[2] Adolescents are predisposed to minimal family support, age-disparate sexual relationships and financial dependency on sexual partners, and unable to negotiate condom use.[2] As of 2019, adolescents in low/middle-income countries (LMICs) had 21 million pregnancies each year.[1] In South Africa, between 2017 and 2021, the birth rate increased from 49.6 to 55.6 per 1000 girls.[3] There is also a growing concern over the high prevalence of curable STIs among adolescent girls and young women (15–24 years) in South Africa.[4] Adolescent pregnancies are considered at high

risk of adverse pregnancy outcomes and neonatal morbidity, and STIs have been associated with preterm births, low birth weight, and neonatal morbidity and mortality.[5–12] While a high prevalence of asymptomatic STIs and bacterial vaginosis (BV) in adult pregnancies (>19 years of age) is well documented,[13–15] the prevalence and clinical presentation of STIs in adolescent pregnancies are understudied.[16–18]

Frequent condomless sex during pregnancy has been reported since 2013 in several studies in South Africa and other sub-Saharan countries[19–21] and reasons for limited condom use during pregnancy include low perception of risk, cultural myths and gender–power imbalance in relationships.[22] Given the above evidence of continued risk during pregnancy, studies reporting HIV incidence in pregnancy have provided the basis for the need for repeat testing in pregnancy with an intention to initiate antiretroviral treatment and prevent mother-to-child transmission and adverse pregnancy outcomes.[23 24] Similarly, repeat testing for syphilis and prompt treatment are widely adopted in antenatal care guidelines to prevent congenital syphilis and adverse pregnancy outcomes.[25 26] There is a paucity of incidence data for other STIs in pregnant women in general and adolescents in particular.

In this secondary retrospective data analysis of the CAP 088 HIV Incidence Cohort Study that enrolled pregnant women without HIV, we report the prevalence of asymptomatic aetiologically confirmed STIs and BV among pregnant adolescents, and pregnant women 20–24 years and >25 years of age. We further report on incident and persistent/recurrent STIs in all age groups following repeat aetiological testing of vaginal swabs collected in the third trimester and finally evaluated the test performance of syndromic management for all pregnant women.

METHODS

The CAP 088 cohort study was conducted at three primary healthcare (PHC) clinics in Umlazi, a periurban township in Durban, KwaZulu-Natal. The population of Umlazi is estimated to be between 500 000 and 800 000, residing in formal and informal housing, and whose socioeconomic status is largely low income. A prestudy facility assessment conducted in July–September 2016 revealed an average antenatal HIV prevalence of 36% (297 of 826) at the three PHC clinics in Umlazi. The STI prevalence among pregnant women with HIV in the Umlazi subdistrict was approximately 32%.[27] At the first antenatal visit, women received standard HIV counselling and testing by Department of Health staff and screened by research nurses for participation in an HIV incidence cohort study between February 2017 and March 2018. Pregnant women who tested positive for HIV, were >28 weeks of gestation, in labour or with severe obstetric complications were excluded. In addition, women who did not intend to continue antenatal care at any of study facilities or did not intend to reside in Umlazi for the study period were excluded.

At baseline (first antenatal visit), the research nurse administered a demographic and sexual behaviour questionnaire, examined the participant for symptoms of genital tract infections (GTIs) (abnormal vaginal discharge and genital blisters or sores), collected three vaginal swabs for BV and STI testing and drew 4 mL of blood (EDTA tube-plasma) for HIV testing (ELISA and point-of-care (POC) testing). Pregnant women were routinely tested for syphilis (*Treponema pallidum*) using the Macro-Vue rapid plasma reagin (RPR) qualitative card test. These procedures were repeated at a subsequent antenatal visit after 34 weeks' gestation.

HIV-1 testing with POC tests: the Rapid Anti-HIV (1 and 2) Test Card (Advanced Quality, InTec PRODUCTS, USA) was the HIV screening test at each study visit. Women who tested positive had a second POC test (TRILINE HIV-1/2 Rapid Test, ABON Biopharm, China) to confirm infection. Blood samples sent to the laboratory for storage were used to confirm HIV infection by RNA PCR (ROCHE Ampliprep-TaqMan V.2.0) and a western blot assay (Food and Drug Administration-approved BIORAD Genetics western blot kit) if POC test results were positive.

Vaginal swabs were collected at baseline (first and second trimesters) and repeat study visit (third trimester) and transported to the central laboratory for Gram staining to diagnose BV with Nugent's criteria (a score of 0–3 was considered BV negative, 4–6 intermediate BV and 7–10 BV positive), and the remaining swabs were stored at −70°C until the end of the cohort study. A qualified laboratory technologist read the slides to determine Nugent score. A stored vaginal swab was tested for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and *Trichomonas vaginalis* using the Roche Light Cycler 480 and Roche STI kits (Roche Diagnostics, USA).

Pregnant women symptomatic for STIs were treated empirically with single doses of azithromycin (1 g oral dose), ceftriaxone (250 mg intramuscular injection) and metronidazole (2 g oral dose) as per the National Department of Health Guidelines for STI management.[25] Women who tested positive for BV were contacted telephonically to return to the clinic for treatment (400 mg metronidazole two times per day for 7 days).

Statistical analyses

Demographic characteristics (age and occupation) and relationship/behavioural characteristics (partner's age, living together, partner's HIV status, coital frequency, concurrent sexual partners, forced to have condomless sex) were compared between pregnant adolescents (15–19 years), young women (20–24 years) and older pregnant women (>24 years) using X^2 tests for categorical data and t-tests or Mann-Whitney for numerical data. Prevalence (95% CIs) of STIs and BV was calculated at baseline as the proportion (%) of all pregnant women who tested positive for each of the STIs and BV separately and as a composite number of pregnant women with a positive test for any STI. To estimate incidence during pregnancy, each STI and BV were examined separately with follow-up time for pregnant women who first tested negative at baseline and positive at the repeat visit calculated from date of baseline visit to the repeat visit. Incidence rates in person years (py) were calculated for each STI and BV and for any STI (composite). We also present the proportion of women who tested positive for STIs at baseline and again at a subsequent visit. Using binary logistic regression to estimate OR and 95% CI, we compared the prevalence and incidence of STIs between adolescents (15–19 years) and 20–24 years and between adolescents and >24 years age group.

Women who returned for a repeat visit were compared with women who did not return (lost to follow-up) for factors that may have increased their risk of incident STIs and BV. The performance characteristics of syndromic diagnosis (sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were evaluated against laboratory diagnosis of stored specimens at end of study.

RESULTS

A total of 752 pregnant women who tested negative for HIV-1 at their first antenatal visit were enrolled at a median gestational age of 17 (IQR 12–21) weeks, among whom 180 (23.9%), 291

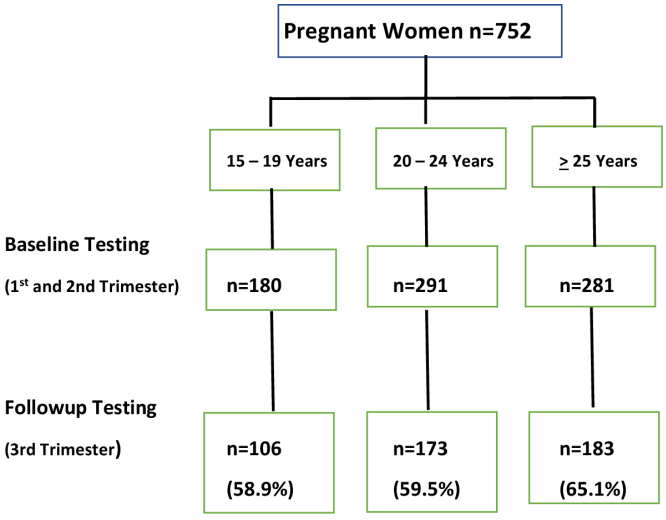

Figure 1 Cohort diagram of participant testing for GTI's.

(38.7%) and 281 (37.4%) were in the 15–19, 20–24 and >25 years age groups, respectively (figure 1).

Characteristics of pregnant women are reported in table 1. Overall, 650 (86.4%) were unmarried and not cohabiting with their sexual partner. Pregnant women reported an average of 10 unprotected sex acts in the last 3 months and 18 (2.4%) reported concurrent sexual partners. Nineteen women (2.5%) reported they were aware of their sexual partner's positive HIV status. Adolescents did not differ from their older counterparts in behavioural characteristics, except for a sexual partner who was 5 or more years older. The majority of adolescents (72.6%) and more than half of women 20–24 years old reported that their sexual partners were 5 years or older when compared with the >25 years (18.6%) age group (p<0.0001; table 1).

At baseline (14–28 weeks' gestation), 244 (32.5%) tested positive for at least one STI (95% CI 29.2 to 35.9) and 280 (37.5%) tested positive for BV (95% CI 34.1 to 41.1). Thirty-two women (4.3%) tested positive for two or more STIs. The women aged 20–24 and >25 years old had a higher but comparable prevalence of STIs than adolescents (15–19 years) (26.7% vs 34.7%: OR 1.4; 95% CI 1.0 to 2.1, p=0.09 and 26.7% vs 33.8%: OR 1.4; 95% CI 0.9 to 2.1, p=0.12, respectively) (table 2). The most prevalent STIs were *T. vaginalis* (15.1%), *C. trachomatis* (9.8%) and *N. gonorrhoeae* (5.7%). In adolescents, prevalence of *T. vaginalis*, *C. trachomatis* and *N. gonorrhoeae* was 11.1%, 7.8% and 4.4%, respectively. The overall prevalence of BV was 37.5% (table 2).

At baseline, 106 (43.4%) women with an STI were symptomatic (predominantly abnormal vaginal discharge) and received empirical treatment (ceftriaxone, azithromycin and metronidazole). The sensitivity, specificity, NPV and PPV of syndromic management in this cohort in the second trimester were 43.4%, 59.4%, 68.6% and 34%, respectively (table 3).

Of 752 pregnant women enrolled in the second trimester, 462 (61.4%) women returned for their follow-up visit in the third trimester (figure 1), comprising 106 (58.9%), 173 (59.1%) and 183 (65.1%) women in the 15–19, 20–24 and >25 years age groups, respectively. Women who returned for a follow-up visit were comparable with women who did not return except for women who returned for a follow-up study visit had a significantly higher prevalence of *T. vaginalis* (18.8%) at baseline than women who did not return (9.7%) (online supplemental table).

Table 1 Demographic and behavioural characteristics of pregnant adolescents in comparison with other age categories

Variable	All women N=752	15–19 years N=180	20–24 years N=291	>25 years N=281	P value
Age, median (IQR)	23 (20–27)	18 (17–19)	22 (21–23)	28 (26–32)	—
Gestational age (weeks) at 1st booking, median (IQR)	17 (13–22)	17 (12.5–22.5)	17 (13–22)	17 (12–21)	0.532
Gravidity, mean (SD)	1.7 (0.9)	1.7 (0.8)	1.7 (0.9)	1.7 (0.9)	0.496
Occupation, n (%)					
Employed	191 (25.4)	49 (27.2)	73 (25.1)	69 (24.6)	0.919
Student	255 (33.9)	62 (34.4)	91 (31.3)	102 (36.3)	
Unemployed/at home	306 (40.7)	69 (38.3)	127 (43.6)	110 (39.1)	
Partner's age (years), median (IQR)	27 (23–31)	26 (23–30)	27 (24–31)	27 (23–32)	0.393
Partner >5 years older, n (%)	331 (44.0)	130 (72.6)	149 (51.4)	52 (18.6)	<0.0001
Relationship status, n (%)					
Living together	98 (13.0)	25 (13.9)	37 (12.7)	36 (12.8)	0.354
Not living together	650 (86.4)	155 (86.1)	251 (86.3)	244 (86.8)	
Missing data (n)	4	0	3	1	
Coital frequency in the last 3 months, mean (SD)		9.6 (10.9)	9.9 (10.2)	10.4 (11.4)	0.78
Concurrent sexual partners, n (%)	10 (10.8)	3 (2.9)	9 (5.2)	6 (4.1)	0.283
Forced to have unprotected sex, n (%)	18 (2.4)	6 (3.4)	8 (2.8)	11 (3.9)	0.738
Partner's HIV status, n (%)					
Negative	441 (58.6)	100 (55.6)	185 (63.6)	156 (55.5)	0.084
Positive	19 (2.5)	2 (1.1)	6 (2.1)	11 (3.9)	
Unknown	291 (38.7)	77 (42.8)	100 (34.4)	114 (40.6)	
Missing data	1	1	0	0	
Symptomatic for GTI at baseline, n	312	82	111	119	0.48
Abnormal vaginal discharge, n (%)	303 (97.1)	80 (97.6)	107 (96.4)	116 (97.5)	
Genital sores/blisters, n (%)	9 (2.9)	2 (2.4)	4 (3.6)	3 (2.5)	

GTI, genital tract infection.

Table 2 Prevalence of genital tract infections at baseline in adolescents in comparison with other age categories

					20–24 vs 15–19 years (ref)	≥25 vs 15–19 years (ref)
	All women (n=752)	15–19 years (n=180)	20–24 years (n=291)	≥25 years (n=281)	OR (95% CI) P value	OR (95% CI) P value
Trichomonas vaginalis, n (%) (95% CI)	115 (15.1) (13.0 to 18.2)	20 (11.1) (7.0 to 16.9)	50 (17.2) (13.0 to 22.0)	45 (16.0) (12.1 to 21.1)	1.6 (0.9 to 2.8) 0.09	1.5 (0.9 to 2.7) 0.17
Neisseria gonorrhoeae, n (%) (95% CI)	43 (5.7) (4.3 to 7.7)	8 (4.4) (2.0 to 8.7)	17 (5.8) (3.4 to 9.2)	18 (6.4) (3.9 to 10.0)	1.3 (0.6 to 3.1) 0.57	1.5 (0.6 to 3.4) 0.42
Chlamydia trachomatis, n (%) (95% CI)	73 (9.8) (7.9 to 12.1)	14 (7.8) (4.4 to 12.9)	33 (11.3) (7.9 to 15.6)	26 (9.3) (6.2 to 13.4)	1.5 (0.8 to 2.9) 0.27	1.2 (0.6 to 2.4) 0.62
Mycoplasma genitalium, n (%) (95% CI)	26 (3.5) (2.4 to 5.1)	9 (5.0) (2.4 to 9.4)	7 (2.4) (1.0 to 4.9)	10 (3.6) (1.8 to 6.5)	0.5 (0.2 to 1.3) 0.19	0.7 (0.3 to 1.8) 0.48
Treponema pallidum, n (%) (95% CI)	4 (0.5) (0.2 to 1.4)	0 (0.0)	1 (0.3) (0.01 to 1.9)	3 (1.1) (0.2 to 3.1)	N	N/A
Any STI, n (%) (95% CI)	244 (32.5) (29.2 to 35.9)	48 (26.7) (20.4 to 33.8)	101 (34.7) (29.3 to 40.5)	95 (33.8) (28.3 to 39.7)	1.4 (1.0 to 2.1) 0.09	1.4 (0.9 to 2.1) 0.12
Bacterial vaginosis, n (%) (95% CI)	280 (37.5) (34.1 to 41.1)	63 (35.0) (28.4 to 42.9)	107 (36.8) (31.4 to 42.9)	110 (39.2) (33.7 to 45.4)	1.1 (0.7 to 1.6) 0.77	1.2 (0.8 to 1.8) 0.37

STI, sexually transmitted infection.

At the repeat visit, 66 of 170 (38.8%) pregnant women who tested positive for at least one STI at baseline subsequently tested positive, comprising 11 (37.9%), 27 (40.9%) and 28 (37.3%) women in the 15–19, 20–24 and >25 years age categories, respectively (table 4). The most recurrent or persistent infections were *T. vaginalis* (11.5%), *C. trachomatis* (12.0%) and *N. gonorrhoeae* (9.4%). Overall, 38.8% tested positive again at the repeat visit. Thirty-eight (57.6%) women with persistent infections at the repeat visit were asymptomatic at baseline and did not receive empirical treatment.

Overall, 40.7% (118 of 290) who tested negative for any STI at baseline tested positive for an STI at the repeat visit in late pregnancy over a cumulative period of 605 months, with an incidence rate of 19.5 per 100 py. Incidence rates of any STI during pregnancy were 23.9/100 py, 20.5/100 py and 16.2/100 py in the 15–19 years, 20–24 years and >25 years age categories, respectively (table 4). When compared with the adolescents (15–19 years), the odds of incident STIs in the 20–24 (OR 1.1; 95% CI 0.6 to 1.9, p=0.88) and >25 years (OR 0.8; 95% CI 0.5 to 1.5, p=0.54) age categories were not significant.

The most common new infections were *T. vaginalis* (9.6/100 py), *N. gonorrhoeae* (9.3/100 py) and *C. trachomatis* (11.6/100 py). The 15–19 years age group had a higher incidence of *T. vaginalis* (14.2/100 py) than the other age groups. At the repeat visit, 19.0% (35 of 184) with any STI were symptomatic and received empirical treatment. The specificity, NPV and PPV of syndromic management in the third trimester were 75.7%, 58.4% and 34.3%, respectively (table 3).

There were seven (1.5%) HIV seroconversions in late pregnancy: one (0.9%) adolescent, five (2.9%) in the 20–24 years age group and one (0.5%) in the >25 years age group. The overall HIV incidence rate during pregnancy was 1.2/100 py. The highest HIV incidence rate was reported among the 20–24 years age group (2.2/100 py) (table 3). Of the seven pregnant women who seroconverted, two (28.6%) tested positive for *N. gonorrhoeae*, two (28.6%) for *T. vaginalis*, one (14.3%) for *C. trachomatis* and four (57.1%) for BV. All infections were detected at baseline. None of the seroconvertors tested positive for an STI at the repeat visit.

DISCUSSION

Our retrospective cohort data analysis confirms high prevalence of asymptomatic STIs and BV in pregnant women not living with HIV. Overall, one-third of the pregnant women tested positive for at least one STI at their first antenatal visit in the first or second trimester, the common STIs being *T. vaginalis* (15.1%), *C. trachomatis* (9.8%) and *N. gonorrhoeae* (5.7%). One in four (26.7%) adolescents (15–19 years) tested positive for an STI at their first antenatal visit, not significantly lower than older counterparts 20–24 years (34.7%) and >25 years (33.8%). Consistent with other studies, 56.6% of women with a GTI were asymptomatic and not treated, while 40.6% of pregnant women received syndromic treatment unnecessarily. Our cohort study is one among a handful of studies that reports a high incidence of asymptomatic STIs in pregnant women who returned for their third trimester visit.[14 18 28] Overall, 40.7% of pregnant women tested positive for an STI for the first time at repeat testing. Pregnant adolescents (15–19 years) had a high incidence of STIs in the third trimester (23.9/100 py) but not significantly higher than the women 20–24 years old (20.5/100 py) and women >25 years (16.2/100 py). When compared with baseline, a much higher proportion (>70%) of all pregnant women with a positive STI result at repeat testing were asymptomatic and not treated. Our study further reports a lower HIV incidence rate (1.2/100 py) in pregnancy when compared with a meta-analysis of earlier studies (7.4/100 py). Adolescent girls had a lower HIV incidence than the pregnant women 20–24 years old (0.7/100 py vs 2.2/100 py).

Table 3 Sensitivity, specificity, NPV and PPV of syndromic management of genital tract infections at baseline and third trimester of pregnancy

	Sensitivity (%)	Specificity (%)	NPV	PPV
Baseline (12–28 weeks)	106/244 (43.4)	302/508 (59.5)	302/440 (68.6)	106/312 (34.0)
Repeat visit (>28 weeks)	35/184 (19.0)	209/276 (75.7)	209/358 (58.4)	35/102 (34.3)

NPV, negative predictive value; PPV, positive predictive value.

Table 4 Repeat and incident genital tract infections at follow-up visit (third trimester of pregnancy) by age category

N/A	All women (n=462) Pos/tested (%)	15–19 years (n=106) Pos/tested (%)	20–24 years (n=173) Pos/tested (%)	>25 years (n=183) Pos/tested (%)	20–24 vs 15–19 years OR (95% CI) P value	>25 vs 15–19 years OR (95% CI) P value
Trichomonas vaginalis						
Repeat infection	10/87 (11.5)	1/10 (10.0)	3/38 (7.9)	6/39 (15.4)	0.8 (0.1 to 8.3) 1.00	1.6 (0.2 to 15.4) 1.00
New infection	58/375 (15.5)	19/96 (19.8)	25/135 (18.5)	14/144 (9.7)	0.9 (0.5 to 1.8) 0.87	0.4 (0.2 to 0.9) 0.03*
Incidence rate	9.6/100 py	14.2/100 py	11.1/100 py	5.7/100 py		
Neisseria gonorrhoeae						
Repeat infection	3/32 (9.4)	0/5 (0)	2/12 (16.7)			N/A
New infection	56/430 (13.0)	14/101 (13.9)	22/161 (13.7)	20/168 (11.9)	0.9 (0.5 to 2.0) 1.0	0.8 (0.4 to 1.7) 0.71
Incidence rate	9.3/100 py	10.5/100 py	9.8/100 py	8.1/100 py		
Chlamydia trachomatis						
Repeat infection	6/50 (12.0)	1/10 (10.0)	2/23 (8.7)	3/17 (17.7)	0.9 (0.1 to 10.7) 1.00	1.9 (0.2 to 21.5) 1.00
New infection	70/412 (17.0)	12/96 (12.5)	27/150 (18.0)	31/166 (18.7)	1.5 (0.7 to 3.2) 0.29	1.6 (0.8 to 3.3) 0.23
Incidence rate	11.6/100 py	9.0/100 py	12.0/100 py	12.6/100 py		
Mycoplasma genitalium						
Repeat infection	0/19	0/6	0/6	0/7	N/A	N/A
New infection	21/443 (4.7)	2/100 (2.0)	8/167 (4.8)	5/176 (2.8)	2.5 (0.5 to 11.8) 0.33	1.4 (0.3 to 7.5) 1.00
Incidence rate	3.5/100 py	1.5/100 py	3.6/100 py	2.0/100 py		
*Treponema pallidum**						
Missing results	157	32	65	60	N/A	N/A
Repeat infection	0/1	0	0	0/1		
New infection	1/304 (0.3)	0/74 (0.0)	0/108 (0.0)	1/122 (0.8)	N/A	N/A
Incidence rate	0.2/100 py	0	0	0.4/100 py		
Women positive for any STI at baseline and at repeat visit	66/170 (38.8)	11/29 (37.9)	27/66 (40.9)	28/75 (37.3)	1.1 (0.5 to 2.8) 0.82	0.9 (0.4 to 2.4) 1.00
Women negative for any STI at baseline and positive at repeat visit	118/292 (40.4)	32/77 (41.6)	46/107 (43.0)	40/108 (37.0)	1.1 (0.6 to 1.9) 0.88	0.8 (0.5 to 1.5) 0.54
Incidence rate	19.5/100 py	23.9/100 py	20.5/100 py	16.2/100 py		
HIV-1						
New infection	7/462 (1.5)	1/106 (0.9)	5/173 (2.9)	1/183 (0.5)	3.1 (0.4 to 21.1) 0.41	0.6 (0.04 to 9.3) 1.00
Incidence rate	1.2/100 py	0.7/100 py	2.2/100 py	0.4/100 py		

*Missing results for repeat visits; depended on facility-based routine testing.
py, person years; STI, sexually transmitted infection.

High prevalence of asymptomatic STIs in pregnancy has been commonly reported in LMICs and higher prevalence of *T. vaginalis, N. gonorrhoeae* and *C. trachomatis* reported in Southern Africa.[13] In our study, 27% of adolescents tested positive for any STI at antenatal registration and although the prevalence was lower than their older counterparts, we report a notably higher prevalence than other studies of adolescent pregnancies (11%–19%).[9 16 29] While adolescents had a lower prevalence of *T. vaginalis* (11.1%), *N. gonorrhoeae* (4.4%) *and C. trachomatis* (7.8%) in comparison with their older counterparts, *M. genitalium* was more prevalent in pregnant adolescents (5.0%; 95% CI 2.4% to 9.4%) than in other age categories (2.4% and 3.6%).

Consistent with several studies conducted in sub-Saharan Africa, the prevalence estimates of predominantly asymptomatic STIs in our study further support the need for POC testing and targeted treatment during pregnancy.[10 15 30] The WHO, while acknowledging that syndromic management is simple and assures rapid, same-day treatment, is also cognisant of disadvantages of syndromic management in the overtreatment and missed treatment as the majority of STIs are asymptomatic.[31] We report suboptimal sensitivity (43%) and PPV (34%) of syndromic diagnosis in the first or second trimester. Moreover, we report 30% of pregnant women without any STI or BV received antibiotic treatment unnecessarily in the second trimester. Syndromic diagnosis in the third trimester had a much lower sensitivity (19%), although a lower proportion (24%) of pregnant women without an STI received antibiotic treatment unnecessarily. Our findings further support the need for aetiological rescreening for STIs prior to delivery.

Repeat testing for STIs revealed a high incidence of predominantly asymptomatic STIs (19.5/100 py) with a comparably high incidence rate among pregnant adolescents (23.9/100

py) versus women 20–24 years (20.5/100 py) and >25 years (16.2/100 py). Adolescents had a higher incidence of *T. vaginalis* (14.2/100 py) than women 20–24 years (11.1/100 py) and >25 years (5.7/100 py). In an urban adolescent pregnant cohort in the USA, rescreening in the third trimester yielded 9% (9 of 95) and 3% (3 of 95) recurrent *C. trachomatis* and *N. gonorrhoeae* infections, respectively, while 4% (4 of 95) had new *C. trachomatis* and *N. gonorrhoeae* infections.[18] At repeat testing, we detected new *T. vaginalis*, *N. gonorrhoeae* and *C. trachomatis* infections in 19.8%, 13.9% and 12.5% of adolescents, respectively. Our findings further support the conclusion of others that adolescents continue to have unprotected sex during pregnancy and therefore at continued risk of acquiring STIs and HIV-1.[22 23] In a secondary data analysis from the MIRA Study conducted between 2003 and 2006 in South Africa and Zimbabwe, the study reported an incidence rate of 9.2/100 py for *T. vaginalis* in pregnant women not living with HIV, similar to our study finding (9.6/100 py).[28] However, our study reports a higher incidence of *C. trachomatis* (11.6/100 py) and *N. gonorrhoeae* (9.3/100 py) than the MIRA Study (9.9/100 py and 4.9/100 py, respectively), therefore emphasising the need for rescreening and targeted treatment later in pregnancy. Current Centers for Disease Control and Prevention recommendations include rescreening for STIs in the third trimester, a strategy absent in the WHO and South African Guidelines.[26 31 32]

Repeat POC testing for HIV-1 in the third trimester in our study cohort as per national guidelines revealed seven HIV seroconversions (1.5%), including one adolescent (0.9%) and the majority in the 20–24 years age group (2.9%). Incidence of syphilis in our study was unexpectedly low with only one new syphilis case (0.9%) in older women in the third trimester. The HIV seroconversion rate in our pregnant cohort like that of recent cohort studies in Uganda and Kenya is relatively low, hence limiting the power to ascertain an association between STIs and HIV acquisition.[24 33]

While our study provides some novel evidence that could change public health practice, it is not without limitations. First, we depended on routine testing for syphilis. At the PHCs, an RPR test was conducted by PHC staff and we did not confirm with laboratory-based TPHA testing. Second, only 60% of pregnant women returned for their subsequent study visit, hence limiting generalisability of findings. Lastly, we were unable to differentiate recurrent from persistent infections at repeat testing. Furthermore, we did not collect partner STI data to confirm recurrent infections in pregnant women at the repeat visit.

CONCLUSIONS

Prevalence of largely asymptomatic GTIs in adolescents at first antenatal registration is high but comparable with older women, thus necessitating aetiological screening tests for all antenatal attendees. Adolescents and young women are at risk of asymptomatic incident STIs in the third trimester. We provide novel evidence supporting repeat testing for STIs in pregnancy.

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Patient consent for publication Not required.

Ethics approval This study involves human participants and institutional regulatory oversight was provided by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE 194/18). Women were asked to provide written informed consent for participation in the study and for storage of biological specimens for future research.

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