Association between menopause and unprotected sex in high-risk HIV-positive women in Mombasa, Kenya

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Abstract

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Objectives: A growing number of HIV-positive women now live well beyond menopause. There is little information about condom use in postmenopausal women in sub-Saharan Africa. Postmenopausal women are no longer at risk for pregnancy, and some studies suggest that they may choose to use condoms less often than premenopausal women. Our hypothesis was that unprotected sex, defined by the presence of prostate specific antigen (PSA) in vaginal secretions, would be more common at postmenopausal visits compared to premenopausal visits.

Design: Prospective cohort study of HIV-positive women >16 years old, who reported trading sex for cash or in-kind payment in Mombasa, Kenya.

Methods: At enrollment and monthly follow-up visits, participants completed a standardized interview. A speculum-assisted pelvic examination with collection of genital samples was performed at enrollment and quarterly visits. Menopause was assessed using a clinical decision tool. The primary outcome of unprotected sex was determined by the presence of PSA in vaginal secretions.

Results: We followed 403 HIV-positive women who contributed 2753 quarterly examination visits. Detection of PSA was less frequent at postmenopausal visits compared to premenopausal visits (55/540,10.2% versus 397/2210, 18.0%; relative risk [RR] 0.57, 95% confidence interval [CI] 0.38-0.86).

Adjusting for age diminished the association between menopause and detection of PSA (adjusted RR 0.70, 95%CI 0.45-1.11). Women were more likely to report no sex in the past week at postmenopausal visits compared to premenopausal visits (RR 1.67, 95%CI 1.44-1.95). When sexually active, women reported the same rate of condom use at postmenopausal and premenopausal visits (RR 0.97, 95%CI 0.84-1.12).

Conclusions: Postmenopausal status was associated with a lower risk of unprotected sex compared to being premenopausal in this population of high-risk HIV-positive Kenyan women. The relationship between menopause and unprotected sex is likely to be contextual and may differ with varying risk groups, regions, and levels of exposure to sexual health education.

Keywords: Menopause; Condoms; Sexual Risk Behavior; Africa; HIV; Sex Workers

INTRODUCTION

The rollout of antiretroviral therapy (ART) in sub-Saharan Africa is extending survival for many people living with HIV [1]. As a result, a growing number of HIV-positive women now live well beyond menopause. While many women remain sexually active after menopause, they are not often the targets of sexual health education [2]. Postmenopausal women may view condoms primarily as a method of contraception, and healthcare providers may bring up the topic of sex less often with older women.

Most studies of the association between menopause and condom use have been conducted in industrialized countries, and the effect of menopause on condom use appears to vary in different populations. Some studies of HIV-negative women in the United States (US) and Australia have found lower condom use in postmenopausal compared to premenopausal women, and in older compared to younger women [3–7]. In contrast, a study in a US population of HIV-positive women found no difference in condom use between postmenopausal and premenopausal women [8].

There is little information about condom use in postmenopausal women in sub-Saharan Africa. In the context of the African HIV epidemic, this relationship is an important one to investigate as the population of HIV-positive postmenopausal women is growing. Female sex workers are a key population in the African HIV epidemic [9]. Women may continue in sex work after menopause, so it is important to understand how menopause influences their sexual risk behavior. The objective of this study was to test the hypothesis that unprotected sex would be more common at postmenopausal visits compared to premenopausal visits in a prospective cohort study of high-risk HIV-positive women in Mombasa, Kenya.

METHODS

Population and Procedures

Analyses were performed using data from an ongoing prospective cohort study of high-risk HIV-positive Kenyan women enrolled between October 2012 and March 2015. To be eligible for enrollment, women had to be at least 16 years old, confirmed HIV-positive, and report trading sex for cash or in-kind payment.

At enrollment and monthly follow-up visits, participants completed a standardized face-to-face interview to collect data including demographic characteristics, sexual risk behavior, obstetrical and gynecological history, and health status. Interviews were conducted in Kiswahili or English by a Kenyan study nurse. At enrollment and quarterly follow-up visits, a physical examination was performed and included a speculum-assisted pelvic examination with collection of genital specimens for detection of sexually transmitted infections (STIs) and prostate specific antigen (PSA). If a quarterly examination visit was missed, the examination was performed at the next monthly visit. The institutional review boards at Kenyatta National Hospital and the University of Washington approved the study, and all participants provided written informed consent.

Menopausal status was assessed at enrollment and annual follow-up visits using a clinical decision tool. We considered women to be postmenopausal if they were over 40 years old and reported 12 months or more of amenorrhea from the time of their last menstrual period. Exclusions from postmenopausal status, regardless of age and duration of amenorrhea, included pregnancy, breastfeeding, post-partum status (within 9 months of delivery), and use of unopposed progesterone contraception such as depot medroxyprogesterone acetate or progesterone only oral contraceptive pills. Once a woman was classified as postmenopausal, she was considered postmenopausal for the remainder of the study.

The primary outcome was detection of semen in vaginal secretions by PSA test, a biological marker of exposure to semen within the past 24-48 hours [10–12]. Additional biological markers for unprotected sex included sperm detected in cervical or vaginal secretions and the presence of STIs.

Self-reported sexual risk behavior was assessed at enrollment and monthly follow-up visits. Unprotected sex in the past week was considered to be present if participants' frequency of vaginal intercourse was greater than their frequency of vaginal intercourse with condoms. Abstinence was defined as the participant reporting zero vaginal sex acts in the past week. Consistent (100%) condom use, number of vaginal sex acts, and number of different sex partners were restricted to women who were not abstinent

during the past week. Consistent condom use was defined as reported frequency of vaginal intercourse with condoms being equal to frequency of vaginal intercourse in the past week. Anal sex was reported very infrequently in this cohort. Thus, we did not incorporate anal sex into our measurements of self-reported sexual risk behavior outcomes.

Covariates in these analyses included socio-demographic characteristics, psychosocial risk factors, and clinical factors. The socio-demographic characteristics were collected at enrollment and included age (continuous), education (≤8 vs. >8 years), marital status (ever vs. never married), age at first sex (continuous), and place of work (bar, nightclub, home, or other). The psychosocial risk factors were collected at enrollment and follow-up visits. Depression was assessed every 6 months by the Patient Health Questionnaire (PHQ-9) [14,15]. Scores were dichotomized, with a score of ≥5 indicating at least mild depressive symptoms. Disclosure of HIV status was determined during the interview at enrollment and every 6 months by asking if women had shared their HIV test results with anyone. Alcohol use was assessed annually by the Alcohol Use Disorders Identification Test (AUDIT) [13], which categorizes individuals based on their score as no risk (0), minimal risk (1-6), moderate risk (7-15), or high risk (16-40). Intimate partner violence in the last year was determined annually through an adapted version of the World Health Organization survey on Violence Against Women, which has demonstrated high internal consistency in a wide variety of settings [16]. Clinical factors were collected at enrollment and monthly follow-up visits and included self-reported ART use and Karnofsky performance score. The Karnofsky performance score is an indicator of physical function ranging from 0 to 100 and has been found to have good reliability and validity [17].

Laboratory Methods

Semen in vaginal secretions was detected by PSA test (ABACard, Abacus Diagnostics, West Hills, CA). Sperm was detected through vaginal wet prep, vaginal gram stain, or cervical gram stain. We tested for the presence of *Neisseria gonorrhoeae, Chlamydia trachomatis,* and *Trichomonas vaginalis* using a nucleic acid amplification test (Aptima, Gen-Probe/Hologic, San Diego, CA). An automated method (FACS Count, Becton Dickinson, Forest Lakes, NJ) was used to measure CD4 count.

Statistical Analyses

Log-binomial generalized estimating equation (GEE) models, with working independence correlation structure and robust standard errors, were used to evaluate the association between menopause and detection of PSA in vaginal secretions. Relative risks (RRs) and 95% confidence intervals (CI) were calculated. Several variables were collected less frequently than every month, as detailed in the Population and Procedures section. Values for these variables were filled forward until the next visit when the variable was updated. If a woman's menopausal status transitioned from premenopausal to postmenopausal, this transition was assumed to occur at the midpoint of the relevant time interval.

Age was pre-specified as a potential confounding factor, and it was included *a priori* in all multivariable models. Education, marital status, age at first sex, place of work, alcohol use, depression, intimate partner violence, HIV disclosure status, baseline CD4 count, ART use, and Karnofsky performance score were considered as additional potential confounding factors based on our hypothesized causal model. Bivariate regression analyses were conducted with each of these covariates and the primary outcome. Associations with $p<0.1$ were considered for inclusion in the multivariable model in descending order of the magnitude of their effect on the outcome. Variables that changed the primary effect estimate by ≥10% on the relative risk scale were retained in the model. Since no other variables met this threshold for inclusion, only age was retained in the final multivariable model.

Analyses of the secondary outcomes were conducted using the same approach described for the primary outcome. In an additional analysis of the effect of age on sexual risk behavior, age at visit was transformed to evaluate each 10-year increment in age. All analyses were conducted using Stata 13.0 (StataCorp, College Station, TX).

RESULTS

Study participants

Between October 2012 and March 2015, 403 women contributed 2753 quarterly examination visits where the primary outcome was measured and 6104 monthly visits where secondary outcomes were assessed. The median number of quarterly visits per participant was 8 (interquartile range: 3, 11). Analyses based on quarterly visits included 605.3 person-years of follow-up time, while those based on monthly visits included 628.0 person-years of follow-up time. Baseline demographic, psychosocial, and clinical characteristics of the women are provided by menopausal status in Table 1.

Associations between menopause and sexual risk behavior

In contrast to the primary hypothesis, detection of PSA was less frequent at postmenopausal visits compared to premenopausal visits (55/540,10.2% versus 397/2210, 18.0%; RR 0.57, 95%CI 0.38-0.86) (Table 2). The effect of menopause was attenuated and no longer statistically significant after adjusting for age (adjusted RR [aRR] 0.70, 95%CI 0.45-1.11).

Postmenopausal status was similarly associated with lower risk of detecting sperm in genital secretions (RR 0.56, 95%CI 0.32-0.98). As with PSA detection, adjusting for age diminished the effect of menopause on detection of sperm in genital secretions (aRR 0.73, 95%CI 0.36-1.45). Detection of STIs did not differ significantly in postmenopausal versus premenopausal women (RR 0.73, 95%CI 0.38-1.38).

Women were more likely to report no sex in the past week at postmenopausal visits compared to premenopausal visits (RR 1.67, 95%CI 1.44-1.95). They were less likely to report unprotected sex in the past week at postmenopausal visits (RR 0.54, 95%CI 0.29-1.02), although this association did not reach statistical significance. At visits when women reported sex in the past week, there was no difference in the rate of 100% condom use between postmenopausal versus premenopausal visits (RR 0.97, 95%CI 0.84-1.12).

Because age was a strong confounding factor in these analyses, the effect of age on sexual risk behavior was also assessed. For each 10-year increase in age, there was a significantly lower risk of detecting PSA (RR 0.75, 95%CI 0.64-0.88). This effect remained statistically significant when adjusted for menopausal status (aRR 0.65, 95%CI 0.46-0.91).

DISCUSSION

In this prospective cohort analysis of high-risk HIV-positive Kenyan women, postmenopausal status was associated with less unprotected sex using the primary biological outcome, detection of PSA in vaginal secretions. Women had sex less frequently at postmenopausal visits compared to premenopausal visits. However, when they were sexually active, women reported the same rate of condom use at postmenopausal and premenopausal visits. Our adjusted data suggest that lower rates of unprotected sex at postmenopausal visits are largely a reflection of lower rates of unprotected sex in women who are older.

The results of this study parallel those of studies of HIV-positive women conducted in the US Women's Interagency HIV Study (WIHS) cohort. The WIHS investigators detected no association between menopause and condom use, but observed a decline in unprotected sex and any sexual activity (vaginal and anal) in the last 6 months among postmenopausal compared to premenopausal women [4,8]. In contrast to this study of HIV-positive Kenyan women, a number of studies of HIV-negative women in the US and Australia have demonstrated a significant association between menopause, older age, and decreased condom use [3,5–7].

This study had a number of important strengths. First, the primary outcome (PSA in vaginal secretions) was a biological marker rather than a self-reported behavior, which eliminates potential reporting biases due to social desirability and recall. Second, a single, pre-specified analysis of our primary hypothesis was conducted, reducing the risk of falsely identifying significant associations as a result of making multiple comparisons. Third, complementary secondary outcomes allowed triangulation of the findings from the primary analysis and exploration of mechanisms that help to explain these findings.

This study also had limitations. Importantly, age and menopause are collinear which made it difficult to disentangle the two when measuring their effect on unprotected sex. As a result, some of the effect of menopause may have been adjusted away when models were adjusted for age. Secondary outcomes relied on self-report, and comparison to the PSA data does suggest that women may be underreporting unprotected sex. Notably, PSA may also be positive when condoms fail or are used incorrectly. These results from a cohort of women who reported transactional sex should not be interpreted as generalizable to all postmenopausal women. However, they represent a key population in terms of HIV transmission in sub-Saharan Africa.

The relationship between menopause and unprotected sex is likely to be contextual. Further studies to examine this association in different risk groups, diverse regions, and populations with varying levels of exposure to sexual health education will be important to develop a comprehensive understanding of the effect of menopause on sexual risk behavior.

Author contribution

MSG and RSM designed the study. MSG analyzed the data and drafted the manuscript. RSM and BAR reviewed drafts of the manuscript and statistical analyses. RSM provided oversight of study procedures and data collection at our research clinic.

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Table 1: Baseline characteristics, by baseline menopausal exposure status[1]

	Postmenopausal N=63	**Premenopausal N=340**
	n(%) or Median (IQR)	n(%) or Median (IQR)
Demographic factors		
Age	47 (42, 52)	38 (31, 42)
Primary school or less education (≤ 8 years)	46 (73.0)	188 (55.3)
Ever married	55 (87.3)	254 (74.7)
Age at first sex	17 (15, 18)	17 (15, 19)
Place of work		
Bar	45 (71.4)	190 (55.9)
Night club	5 (7.9)	95 (27.9)
Home based	2 (3.2)	8 (2.4)
Other	11 (17.5)	47 (13.8)
Psychosocial risk factors		
Alcohol - AUDIT score category[2]		
No risk (0)	44 (69.8)	154 (45.6)
Minimal risk (1-6)	14 (22.2)	101 (29.9)
Moderate risk (7-15)	3 (4.8)	71 (21.0)
High risk (16-40)	2 (3.2)	12 (3.5)
Depression - PHQ-9 ≥ 5	17 (27.0)	99 (29.1)
IPV in last year	9 (14.3)	60 (17.7)
HIV status disclosure to anyone[3]	42 (66.7)	215 (63.4)

Clinical characteristics		
CD4	492 (379, 713)	448 (316, 616)
Not Taking ART[4]	19 (30.7)	143 (42.2)
Karnofsky Performance Score[2]	90 (90, 100)	90 (90, 100)

[1]15 women transitioned from pre to postmenopausal during the course of the study. These women are categorized as premenopausal in this table (their status at baseline).
[2] Analyzed only among 63 postmenopausal and 338 premenopausal women.
[3] Analyzed only among 63 postmenopausal and 339 premenopausal women.
[4] Analyzed only among 62 postmenopausal and 339 premenopausal women.

Table 2: Associations between menopause and sexual risk behavior

	Postmenopausal		Premenopausal					
Outcomes	#/total visits	(%)	#/total visits	(%)	RR (95% CI)	p value	aRR[1] (95% CI)	p value
Positive PSA	55/540	(10.2)	397/2210	(18.0)	0.57 (0.38, 0.86)	0.007	0.70 (0.45, 1.11)	0.1
Sperm detected	24/513	(4.7)	183/2181	(8.4)	0.56 (0.32, 0.98)	0.044	0.73 (0.36, 1.45)	0.4
Any STI[2]	33/534	(6.2)	187/2201	(8.5)	0.73 (0.38, 1.38)	0.329	1.66 (0.80, 3.46)	0.2
Self-reported behaviors in the past week								
Abstinent	919/1266	(72.6)	2095/4834	(43.3)	1.67 (1.44, 1.95)	<0.001	1.16 (0.96, 1.40)	0.1
Unprotected sex	70/1265	(5.5)	493/4836	(10.2)	0.54 (0.29, 1.02)	0.057	0.76 (0.39, 1.46)	0.4

100% condom use[3]	276/346	(79.8)	2246/2,39	(82.0)	0.97 (0.85, 1.12)	0.700	0.97 (0.84, 1.12)	0.7
# vaginal sex acts (>2) [3]	65/347	(18.7)	953/2739	(34.8)	0.54 (0.32, 0.92)	0.022	0.85 (0.47, 1.52)	0.6
# sex partners (>1) [3]	90/347	(25.9)	1157/2742	(42.2)	0.61 (0.34, 1.13)	0.115	0.94 (0.51, 1.76)	0.9

[1]Adjusted for age at visit.
[2] STIs included: Neisseria gonorrhoeae, Chlamydia trachomatis, and Trichomonas vaginalis.
[3]Restricted to visits where the participant was not abstinent in the past week.