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Prior Miscarriage Prevalence Higher among HIV–Positive than in HIV-Negative Women: A Community Survey in Rural Kenya

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Abstract

Introduction: There is evidence that maternal HIV infection may increase risk of miscarriage, however estimates are challenged by underreporting in clinic-based assessments or limited comparisons in HIV-infected and uninfected populations.

Methods: In this secondary analysis, we utilized data from a household survey of recent mothers to assess the prevalence and correlates of prior miscarriage among women in rural Western Kenya.

Multivariate logistic regression was utilized to determine odds ratios.

Results and Discussion: Among 330 women with at least 2 past pregnancies and information on self-reported HIV status, 13% reported prior miscarriage, and 12% self-reported being HIV positive. The 13% prevalence of miscarriage is consistent with previous literature reporting miscarriage in 10-20% of pregnancies [1,2]. The present study findings that prior miscarriage was more frequent in HIV positive than HIV negative women (29% versus 11%, p<0.001) supports the body of literature which has found that miscarriage risk has been shown to increase with immunosuppression, symptomatic disease, or history of miscarriages [3,4]. Women had a 6% increased risk of miscarriage with each additional year of age (aOR=1.06; 95% CI: 1.00 -1.11, p =0.037). The 3-fold increased odds of miscarriage in HIV infected women compared to their HIV-negative counterparts (aOR=2.95, 95% CI; 1.30 – 6.50, p =0.007) conformed with studies from Uganda (OR=3.43) [5], South Africa (OR=3.10) [4,5]and Italy (OR 1.67) [6].

Conclusion: HIV-positive women reported significantly higher prevalence of past miscarriage than HIV- negative women did. Larger cohorts involving ART-treated women will be useful to define risk for miscarriage in the context of ART.

Keywords: HIV status; Miscarriage

Introduction

Each year approximately 210 million women become pregnant [7] of whom, 135 million deliver live born infants, while 75 million pregnancies end in miscarriage, stillbirths or induced abortion [7,8]. Miscarriage occurs in 10-20% of clinically recognized pregnancies [9] however, it remains largely invisible in global tracking, policy dialogue, and program implementation.

Causes of perinatal death are not well specified and late term miscarriage may not be distinguished from early neonatal death due to asphyxiation or stillbirth. Miscarriages may further be underreported as some women miscarry at home, without visiting a clinic.

Prior studies have noted several adverse birth outcomes associated with maternal HIV infection, including stillbirth, preterm birth, peripartum mortality, and low birth weight [1,3,4,10-13].

However, miscarriage outcomes are often combined with stillbirth or only compared within cohorts of HIV-infected women. A 1998 systematic review found four studies demonstrating spontaneous abortion risk between 2.8 to 6 times higher among HIV infected compared to uninfected women, though stating limitations in study design [14]. More recently in the United

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States, higher HIV viral load was associated with 1.59 times higher risk of miscarriage or stillbirth [13]; and a Zambian study demonstrated an association between higher viral load and stillbirth, and lower CD4 count and miscarriage, though these studies are among a cohort of HIV-infected women and not compared to the general population [3].

In 2009, we conducted a community-based assessment of uptake of antenatal and HIV service among women who delivered an infant within the past year in Western Kenya. This secondary analysis aims to assess the prevalence and correlates of miscarriage among a community-based sample of recent mothers participating in the household surveys.

Methods

Study design

This was a secondary analysis using data from a cross-sectional, community-level survey of women who had delivered an infant in the previous year. The parent study was designed to assess uptake of antenatal care and maternal HIV prevention services; this analysis assessed associations between self-reported occurrence of miscarriage, HIV status, and other sociodemographic factors.

Study setting and population

The study was conducted within Kenya Medical Research Institute (KEMRI)/ US Centers for Disease Control and Prevention (CDC) Health and Demographic Surveillance Systems (HDSS). The HDSS covers approximately 220,000 women in 385 predominantly rural villages in Western Kenya. Launched in 2001 by KEMRI and the CDC, the HDSS serves as a community-based platform for disease surveillance and health information. All women in one region of the HDSS, aged ≥ 14 years, who delivered (live or stillborn) within the previous year (2010), and were willing to give informed consent for the interview were invited to participate in the survey. For this analysis, we restricted inclusion to women who had at least one additional pregnancy before the full-term pregnancy.

Definitions and data handling

Data were collected by trained field workers using Personal Digital Assistant (PDAs). Participants were asked about demographic information, obstetrical history including history of spontaneous abortion or miscarriage, and self-reported HIV status at the time of the interview. Our study sample was restricted to women with at least one prior pregnancy. Age in years was treated as a continuous variable, educational attainment was collapsed into none/some primary and some secondary plus, occupation of housewife, salaried job, self-employed /small business and unemployed was collapsed into "unemployed" and "salaried/self-employed". Who assisted during the delivery of the baby was collapsed into no assistance, assisted by skilled person, and assisted by unskilled person.

To measure socioeconomic status, we created wealth index using the following household asset data: ownership of cattle, television, radio, bicycles, mobile phone, fridge and roofing material. An asset index is frequently used as a measure of absolute deprivation in Demographic and Health Surveys in the place of measures of individual or household income, which may not adequately represent wealth in many settings, as validated proxies of wealth in rural Africa [15]. The above 7 items were combined into a single aggregate measure using Principal Component Analysis, and households were ranked using the index, and then divided into socio-economic position from poorest ("1") to wealthiest ("5").

Statistical analysis

Data were analyzed using Stata version 11.0 (Corporation, College Station, Texas, USA). Median and interquartile range (IQR), frequency, and percentage were used to describe continuous and categorical variables respectively. Chi-square and Fishers exact tests were used to assess the association between miscarriage and categorical variables; Mann– Whitney U was used for continuous variables since these outcomes were not normally distributed. Multivariate analysis was conducted using logistic regression model analyses, with adjusted odds ratios (AOR), 95% confidence intervals (CI). The main dependent variable was miscarriage, measured as 'Have you ever had a spontaneous abortion/miscarriage?' Two way interactions for the demographic variables were tested for the outcome of interest.

Variables with a p-value <=0.1 or set a priori in univariate analyses were included in the final multivariable model.

Ethical considerations

The University of Washington Institutional Review Board (#36022) and the Kenya Medical Research Institute Ethical Review Committee (#1714) cleared the primary study. Informed consent was obtained from all participants, and women in the community consented both to participate in the study and also to have their data from these surveys linked to their HDSS record.

Results and Discussion

Characteristics of women

Among 330 women who had at least two previous pregnancies (including the most recent one) and reported their HIV status, the median age was 26 (IQR: 22-31) (Table 1). The majority of women were in a monogamous marriage (97%), and half (50%) had never completed a primary level of education at the time of the study. The median number of pregnancies reported among these women was 4 (IQR: 3-6), and the number of live births was 4 (IQR: 3-6). Overall, 44 (13%) reported history of miscarriage and 41 (12%) women self-reported HIV positive status. The 13% prevalence of miscarriage was consistent with previous literature reporting miscarriage in 10-20% of pregnancies [1,2].

Correlates of miscarriage

In a univariate analyses, the likelihood of reporting prior miscarriage among participating women increased with each additional year of age (p<0.001). Among HIV-positive women, 12/41 (29%) reported prior miscarriage compared to 11/289 (11%) for the HIV-negative women (p<0.001). There were no significant differences in marital status, education, socio-economic status, or occupation between women reporting and not reporting miscarriage.

In multivariate analyses, age and HIV were independently associated with miscarriage (Table 2). Women had a 6% increased risk of miscarriage with each additional year of age (aOR=1.06; 95% CI: 1.00 -1.11, p =0.037). Comparing the burden of miscarriage among the HIV infected and uninfected women, we found a 3-fold increased odds of miscarriage in HIV infected women. These findings are consistent with studies from Uganda (OR=3.43)[5], South Africa(OR=3.10) [4,5] and Italy (OR 1.67) [6].

Among HIV-infected women, miscarriage risk has been shown to increase with immunosuppression, symptomatic disease, or history of prior miscarriages[3,4]. The cause of HIV-related miscarriage risk may be HIV itself or associated co-infections, and risk of miscarriage due to maternal HIV appears to decrease with antiretroviral therapy

Table 1: Demographic characteristics of recently pregnant women participating in household surveys in Siaya County, Kenya 2011 (N=330).

	All Women	Miscarriage (Yes)	Miscarriage (No)	Miscarriage Prevalence
		44 (13%)	286 (87%)	
Variable level	N(%) or Median (IQR)	N(%) or Median (IQR)	N(%) or Median (IQR)	%
HIV status (n=330)				
Negative	289 (88)	32 (73)	257 (90)	11.1
Positive	41 (12)	12 (27)	29 (10)	29.1
Age in years	26 (22-31)	29 (25-33)	25 (22-30)	
Socio-economic quintile[¥] (n=370)				
Poorest	84 (26)	9 (20)	75 (26)	11.8
Very poor	64 (20)	15 (9)	57 (20)	11.0
Poor	80 (24)	10 (23)	70 (25)	12.2
Less poor	32 (10)	5 (11)	27 (10)	15.2
Least poor	68 (21)	13 (30)	55 (19)	19.4
Education (n=364)				
None/Some primary	289 (87)	38 (86)	251 (88)	13.4
Some secondaryplus	40 (12)	6 (14)	34 (12)	14.6
Occupation (n=372)				
Unemployed	182 (55)	27 (62)	155 (54)	15.2
Salaried/self-employed	148 (45)	17 (39)	133 (46)	11.2
Number of Pregnancies	4 (3 – 6)	5 (4 – 6)	4 (3 – 6)	
Number of Live Births	4 (3 – 6)	5 (3 – 5)	4 (3 - 6)	
Number of Miscarriages	44 (13)			

Table 2: Correlates of miscarriage among recently pregnant women participating in householdsurveys in Siaya County, Kenya 2011 (N= 327)[Φ].

	Total			Miscarriage		
	(N=327)	UadOR		Prevalence[¥]	aOR	
	n (%)	95% CI	p-value		95% CI	p-value
HIV status						
Negative	287 (88)	Ref		11		
Positive	40 (12)	3.32 (1.54, 7.15)	0.002	26	2.95 (1.33, 6.50)	0.007
Age in years		1.06 (1.01, 1.11)	0.013		1.06 (1.00, 1.11)	0.037
Socio-economic position						
Poorest	83 (25)	Ref		10		
Very poor	64 (20)	0.92 (0.36, 2.38)	0.869	10	0.99 (0.33, 2.90)	0.991
Poor	80 (24)	1.04 (0.43, 2.49)	0.922	11	1.23 (0.42,3.06)	0.804
Less poor	32 (10)	1.33 (0.43,4.13)	0.611	14	1.55 (0.45, 5.30)	0.484
Least poor	68 (21)	1.81 (0.78, 4.18)	0.165	18	2.06 (0.78, 5.42)	0.142
Education						
None/ Some primary	287 (88)	Ref		12		
Some secondary plus	40 (12)	1..11 (0.44, 2.79)	0.824	11	0.94 (0.34, 2.56)	0.899
Occupation						
Un-employed	180 (55)	Ref		14		
Salaried/ self-Employed	147 (45)	0.70 (0.38, 1.31)	0.266	10	0.70 (0.35, 1.40)	0.315

[¥]Adjusted miscarriage prevalence rates.
[Φ]The three observations were dropped due to missing v.

(ART)[16,17]. However, there are conflicting data on ART and peripartum outcomes in general, with some studies noting increased adverse outcomes (preterm birth, low birthweight) with ART[17-19]. Most of these studies do not include data on miscarriages because enrollment into the studies occurred during pregnancy, often after the first trimester when most miscarriages occur. As more women become pregnant on ART, it will be important to compare risk of miscarriages in this group of women to HIV-uninfected or HIV-positive previously untreated women to discern potential influence of ART or specific regimens.

Our study had strengths and limitations. Using a household-based survey enabled us to evaluate prior pregnancy outcomes, including those that were not reported to clinics. The sampling structure in the parent study was restricted to women with at least one full-term pregnancy. For this analysis, we included only women with at least two pregnancies. While this allowed us to evaluate miscarriages, the study population may limit generalizability and underestimate miscarriage because of exclusion of women who never had a term pregnancy.HIV status was self-reported and may have included some misreported status due to stigma or may not reflect HIV status at the time of the prior miscarriage, and finally we did not gather data on other extraneous factors associated with miscarriage, including ART status among those women who reported being HIV-positive. This would be expected to bias our results to the null and suggests potentially even higher risk of maternal HIV infection.

Conclusions

In conclusion, we found a significant increase in miscarriage prevalence among HIV-positive women compared to HIV-negative women in this household survey. Further studies in larger cohorts involving ART treated women will be useful to better define risk for miscarriage in the context of ART and Option B+ interventions.

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Author's Contribution

PK, JO, GO, JK and GJS contributed substantially to the conceptualization and development of the research study and its implementation.

GO, and PK were involved significantly in the analysis and interpretation of data. VA provided critical reviewing and input during the write up.

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