Prevalence and predictors of proteinuria in HIV-infected and uninfected pregnant women in Cameroon

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Abstract

Background. Proteinuria during pregnancy has been associated with increased pregnancy complications. Furthermore, even low-grade proteinuria has been associated with increased mortality in the general population and in non-pregnant HIV-infected women.

Methods. Urine dipstick protein was measured prospectively on HIV-infected and trace protein or more and quantified by urine protein:creatinine measurement (P:C). Logistic regression modeling was used to identify factors associated with proteinuria.

Results. About 199 human immunodeficiency virus (HIV)-infected and 190 HIV-uninfected normotensive pregnant women were evaluated. The median age was 27 years in both groups and 37% presented in the third trimester. Among HIV-infected women, median CD4 cell count was 417 cells/mm\(^3\); 27% were on combination antiretroviral therapy (cART). Proteinuria was present in 39.2% of HIV-infected and 20.9% of uninfected women (P < 0.001). HIV infection was independently associated with proteinuria [adjusted odds ratio (OR) = 2.45; confidence interval (CI) = 1.56–3.85]. Among HIV-infected pregnant women, cART was protective (adjusted OR = 0.39; CI = 0.19–0.82). Results were qualitatively similar when urine P:C was evaluated as a continuous outcome variable.

Conclusions. The prevalence of low-grade proteinuria in both HIV-infected and -uninfected Cameroonian pregnant women is high. HIV-infected pregnant women are at increased risk for proteinuria, and cART appears to exert a protective effect. Further studies are needed to elucidate the causes of increased proteinuria in African pregnant women, both HIV-infected and -uninfected.

Keywords: Cameroon; HIV; pregnancy; proteinuria

Introduction

Proteinuria during pregnancy has been associated with increased rates of pre-eclampsia/eclampsia [1–4] as well as preterm delivery [5, 6] and compromised fetal growth. Furthermore, even low-grade proteinuria has been associated with increased mortality in the general population and in nonpregnant human immunodeficiency virus (HIV)-infected women [7]. This paper describes the prevalence of proteinuria in a largely ambulatory Cameroonian cohort of HIV-infected and -uninfected pregnant women and identifies risk factors associated with proteinuria.

Materials and methods

Study population

The Cameroon Baptist Convention Health Board (CBCHB) is a consortium of five hospitals and 25 ambulatory health care centers. CBCHB antenatal and HIV treatment centers provide care to >10 000 pregnant women annually. All pregnant women aged 15–50 years presenting for prenatal care at two similar semi-urban sites were invited to participate in this study. Based on local clinical practice under the CBCHB, the majority of HIV-infected pregnant women were enrolled at an HIV treatment center, while both HIV-infected and -uninfected pregnant women were enrolled at the other site, an antenatal clinic. This study was approved by the Institutional Review Boards of CBCHB and the Mount Sinai School of Medicine. All participants provided written informed consent.

Measurements

Dipstick urinalysis was performed in participants at all prenatal visits. Participants with >trace proteinuria or more underwent urine protein:creatinine ratio measurement (P:C). Urine protein was quantified by spectrophotometry and urine creatinine by kinetic alkaline picrate reaction.

Analysis

Data were compared between groups using two sample t-tests, chi-square and Wilcoxon tests as appropriate. Proteinuria was defined as a single measure of >trace proteinuria or more, as low-grade proteinuria has been associated with increased all-cause and HIV mortality in women [7].
Crude and adjusted odds ratios (ORs) were calculated in logistic regression models to identify factors associated with proteinuria. In a separate analysis, urine P:C was evaluated as a continuous outcome variable in linear regression models with negative dipstick protein results set to ‘0’. Statistical analyses were performed using IBM® SPSS® Statistics 19.

Results

Four hundred and six pregnant women were enrolled from March 2009 through August 2010. After excluding participants with incomplete data, blood pressure $\geq 140/90$ mmHg or self-reported kidney disease, hypertension or diabetes, 389 pregnant women (199 HIV-infected and 190 HIV-uninfected) remained for analysis (Figure 1).

Demographic and clinical characteristics of the study population are shown in Table 1. Median age was 27 years in both HIV-infected and -uninfected women. HIV-infected women presented later [median estimated gestational age (EGA) 27 versus 24 weeks, $P = 0.003$], although the distribution by trimester of pregnancy did not differ significantly. Among HIV-infected women, median CD4 cell count was 417 cells/mm$^3$ (IQR: 288–616); 27% were on combination antiretroviral therapy (cART). Proteinuria was present in 39.2% of HIV-infected and 20.9% of -uninfected women ($P < 0.001$). In a sensitivity analysis evaluating the prevalence of $\geq 1+$ proteinuria, trends remained similar though failed to reach statistical significance.

Among the 204 women with repeated urinalyses, proteinuria was reproducible in 21/48 (44%) of those with >trace proteinuria or more at the initial visit. Among participants with proteinuria at the initial visit, the median urine P:C was 70 mg/g (IQR: 10–140), and 67% (79/118) had a P:C $>30$ mg/g. Overall, 4.6% of participants had a P:C $>200$ mg/g [8, 9].

Birth outcome data were available on 116 (30%) of the women followed up postpartum. Aside from two pregnancies which resulted in intrauterine fetal demise (IUFD), the remaining were live births. In multivariate analysis controlling for age, EGA and family history of kidney disease, HIV infection remained an independent predictor of proteinuria [adjusted OR = 2.45; confidence interval (CI) = 1.56–3.85] (Table 2). Results were qualitatively similar when P:C was evaluated as a continuous outcome variable ($P < 0.001$).

Among HIV-infected women, cART use was found to be protective (adjusted OR = 0.39; CI = 0.19–0.82).

Discussion

This prospective study demonstrated a high prevalence of proteinuria among both healthy and HIV-infected normotensive pregnant women in Cameroon. Among healthy HIV-uninfected pregnant women in our study, 20.9% had trace or greater proteinuria. Early North American studies have shown a rate of <10% trace proteinuria during normal pregnancy [10].

No studies to date have evaluated proteinuria in HIV-infected pregnant women. Our study found 39.2% of HIV-infected pregnant women to have trace or greater, and

<table>
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<tr>
<th>Table 1. Demographic and clinical characteristics of study subjects at enrollment ($n = 389$)</th>
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<tbody>
<tr>
<td>HIV+ ($n = 199$)</td>
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<tr>
<td>Age, years</td>
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<td>1st trimester</td>
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<td>Trace or greater</td>
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<td>1+ or greater</td>
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<td>Urine protein:creatinine $&gt; 200$ mg/g</td>
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aData are reported as median (interquartile range) for continuous variables and n (%) for categorical variables. P-values from Wilcoxon test for continuous variables and chi-square test for categorical variables. N/A, not applicable.

bP-value confirmed comparing means between groups: mean systolic blood pressure (±SD) = 103.2 (±11) and 100.7 (±10.9) in HIV+ and HIV− groups, respectively.
15.6% to have 1+ or greater proteinuria. A recent report from Rwanda evaluated proteinuria in HIV-infected and -uninfected nonpregnant women and found high rates of proteinuria (1+ or greater) in both (9 and 7.2%, respectively) [11]. In addition, previous studies have reported high rates of proteinuria in HIV-infected individuals in Africa [12, 13] and HIV-infected women in the USA [14]. In our study, current use of cART appears to be protective against proteinuria, consistent with prior studies which have shown cART to improve renal function in African HIV-infected individuals [15].

Our study was limited by the lack of repeated measures in all participants, reflective of resource-limited settings where multiple prenatal visits are not often possible. In addition, we were unable to perform 24-h urine collection for protein. Therefore, we may have overestimated the true prevalence of proteinuria. Another limitation was the recruitment of HIV-infected and -uninfected participants at separate sites. Though the sites were close in proximity with a similar demographic, this may have led to selection bias. A third limitation was the lack of complete and accurate data on parity and birth outcomes. Additionally, the birth outcome data available on our participants may be biased for two reasons: (i) women whose pregnancy resulted in IUFD, still birth or death of the neonate peripartum may have been less likely to be followed up postpartum and (ii) in HIV-infected pregnant women, because of the need to have their babies tested for HIV, may have been more likely to be followed up for their postpartum visit than HIV-uninfected pregnant women. Further studies are needed to validate our findings and elucidate the causes and consequences of increased proteinuria in pregnant African women, both with and without HIV infection.

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Conflict of interest statement. None declared.

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