HHS Public Access

Author manuscript

Int J Gynaecol Obstet. Author manuscript; available in PMC 2019 August 01.

Published in final edited form as:

Int J Gynaecol Obstet. 2018 August ; 142(2): 207–213. doi:10.1002/ijgo.12508.

Selenium deficiency and pregnancy outcome in pregnant women with HIV in Lagos, Nigeria

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Abstract

Objective—To investigate the prevalence of maternal selenium deficiency and its effects on pregnancy outcomes in pregnant women with HIV in Lagos, Nigeria.

Methods—The present descriptive cross-sectional study enrolled women aged 15–49 years with HIV who were at 14–26 weeks of a singleton pregnancy and were attending Lagos University Teaching Hospital, Lagos, Nigeria, between August 1, 2016, and April 30, 2017. Participants were selected by consecutive sampling and baseline data were collected through interviews. Venous blood samples were obtained to measure selenium concentrations, and associations between low maternal selenium concentrations (defined as <0.89 μmol/L) and pregnancy outcomes were examined using bivariate and multivariate analysis.

Results—The final analysis included 113 patients; selenium deficiency was recorded in 23 (20.4%) patients. Women with selenium deficiency had an approximately eight-fold higher risk of preterm delivery (adjusted odds ratio 7.61, 95% confidence interval 4.37–18.89; *P*=0.031) and of delivering a term neonate with a low delivery weight (adjusted odds ratio 8.11, 95% confidence interval 3.27–17.22; *P*=0.012), compared with women with a normal selenium concentration.

Conclusion—The prevalence of selenium deficiency among pregnant women with HIV in Lagos was relatively high. The significant associations observed between maternal selenium deficiency and adverse pregnancy outcomes could have implications for the future management of HIV in pregnancy.

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AUTHOR CONTRIBUTIONS

KSO contributed to the conception and design of the study, data collection, analysis, and interpretation, and writing and revising the manuscript. OFO contributed to the conception and design of the study, data collection, and revising the manuscript. GEO contributed to data collection and analysis and revising the manuscript. SJ-O, SAA, and RIA contributed to collection, and writing and revising the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of interest

The authors have no conflicts of interest.

Keywords

CD4+ cells count; HIV; Lagos; Low delivery weight; Preterm delivery; Selenium; Viral load

1 INTRODUCTION

Micronutrient deficiencies, including selenium deficiency, are common during pregnancy, especially among women from economically disadvantaged backgrounds, whose diets tend to be low in minerals and vitamins [1]. These deficiencies are even more widespread in HIV-infected populations and are associated with impaired immune responses, weakened epithelial integrity, and accelerated HIV disease progression [1,2].

Selenium plays an important role in the maintenance of human health [3]. It is a component of several selenoproteins and is required for the activity of glutathione peroxidase, a vital intracellular antioxidant that prevents oxidative cellular damage [3, 4]. Various health problems such as nail and hair loss, gastroenteritis, and dermatitis could be associated with persistent exposure to high levels of selenium, but the most notable health effects are related to a selenium-deficient state [5]. Selenium deficiency has been linked to several pathological conditions, especially in individuals with HIV infections [4, 5]. Consequently, several studies have investigated the role of selenium in the disease progression, morbidity, and mortality of HIV-seropositive individuals [4–9]. In most of these studies, selenium supplementation improved their survival and slowed the disease progression [4, 6–8].

Micronutrient deficiencies are particularly prevalent among pregnant women in low-income countries such as Nigeria, and these deficiencies can have detrimental effects on pregnancy outcomes [1]. The demand for selenium during pregnancy is increased to support optimal fetal growth, resulting in decreased maternal blood and tissue concentrations of selenium [7]. However, data on the relationship between selenium status and pregnancy outcomes are conflicting. Moreover, few studies have examined this relationship among black African women with HIV infections.

The present study was designed to investigate the prevalence of a low maternal selenium concentration and its effects on pregnancy outcomes among pregnant women with HIV seen at Lagos University Teaching Hospital, Lagos, Nigeria.

2 MATERIALS AND METHODS

The present descriptive cross-sectional study was carried out among women who were HIV-seropositive and at 14–26 weeks of a singleton pregnancy, who attended the prenatal clinics at Lagos University Teaching Hospital, Lagos, Nigeria, between August 1, 2016, and April 30, 2017. Pregnancy duration was determined based on the last normal menstrual period and confirmed or modified based on ultrasonography dating. Eligible participants were women aged 15–49 years who were confirmed to be HIV-seropositive, had a singleton pregnancy at 14–26 weeks, and had received antiretroviral treatment (ART) for at least 3 months prior to enrollment. The exclusion criteria were a multiple pregnancy, an expected delivery date beyond August 2017, receipt of a long course of any mineral supplement during the 6

months prior to enrollment, refusal of consent at enrollment or withdrawal of consent during the course of the study, and mid-trimester pregnancy loss. Before patient recruitment, ethical approval was obtained from the study hospital's Health Research and Ethics Committee and the ethics principles of the Helsinki Declaration were applied throughout the course of the study. All participants were counselled prior to enrollment and read and signed an informed consent form. The investigators ensured strict confidentiality of participant information.

Lagos University Teaching Hospital has more than 1000 beds and is located in the metropolis of Lagos in Southwest Nigeria. The hospital provides services to patients from the neighboring states in Southwest Nigeria. It is the largest hospital in Lagos State and mainly offers clinical services, including prenatal, intrapartum, and postnatal care. Pregnant women with HIV infections are jointly managed by hematologists and HIV physicians at the hospital's AIDS Prevention Initiative Nigeria (APIN) clinic and undergo regular monitoring of their disease.

Eligible participants were selected by consecutive sampling. A structured interviewer-administered questionnaire was used to collect the following data at enrollment: maternal sociodemographic characteristics (age, parity, pregnancy duration, occupation, educational level, and tribe), time since HIV diagnosis, cumulative duration of ART, CD4+ count, and viral load. The data collected at delivery included maternal and perinatal mortality, the number of preterm deliveries (delivery <37 weeks of pregnancy), and the number of term neonates with a low delivery weight (<2500 g).

Venous blood samples were obtained at enrollment by venipuncture after an overnight fast and were collected into lithium heparin bottles; standard precautions for trace element determination were taken. Blood samples were transported to the central research laboratory of Lagos University Teaching Hospital for analysis and samples showing signs of hemolysis were discarded. Blood was centrifuged at 3000 rpm for 15 minutes at room temperature and the serum was then stored at −20 °C until the day of selenium testing. The selenium concentration was measured by an automated atomic absorption spectrophotometer (PinAAcle 900T; PerkinElmer, Shelton, CT, USA) using the hydride generation method [10]. A low selenium concentration was defined as a concentration of less than 0.89 μmol/L (70 μg/L; reference range, 0.89–1.91 μmol/L [70–150 μg/L]) [11].

The primary endpoint was the pregnancy outcome (preterm delivery; term delivery with a low delivery weight). The secondary endpoints were the maternal and the perinatal mortality.

Descriptive statistics for all data were computed using SPSS version 22.0 (IBM, Amonk, NY, USA). Quantitative data were tested for normality with the Kolmogorov–Smirnov test. Associations between continuous variables were tested using the independent sample t test (normal distribution) or the Mann–Whitney U test (skewed data), whereas categorical variables were compared using the χ^2 test or the Fisher exact test, as appropriate. This was followed by multivariate analysis using binary logistic regression models to study the effects of the major baseline characteristics on the pregnancy outcome. $P<0.05$ was considered statistically significant.

3 RESULTS

Initially, 122 patients who were HIV seropositive at 14–26 weeks of singleton pregnancies were enrolled. However, three women withdrew their consent during the course of the study for personal or cultural reasons, four women were lost to follow-up, and two women experienced mid-trimester pregnancy loss. Therefore, the final analysis included 113 women; 23 (20.4%) patients had a selenium concentration below the reference range (<0.89 μmol/L) and 90 (79.6%) with a normal selenium concentration.

Women with a low selenium concentration and those with a normal selenium level did not differ significantly in terms of age, parity, pregnancy duration, occupation, education level, tribe, time since HIV diagnosis, and cumulative duration of ART (Table 1). However, women with a low selenium concentration had a significantly lower CD4+ count ($P<0.001$) and a significantly higher viral load ($P=0.017$) compared with women with a normal selenium concentration (Table 1).

Of the 113 participants, 11 (9.7%) had preterm deliveries (Table 2). The preterm delivery rate was 6.9 times higher among patients with low maternal selenium concentration than those with a normal selenium concentration ($P=0.011$). Among the 102 term deliveries, 12 (11.8%) patients had neonates with a low delivery weight, and the rate among women with a low selenium concentration 16.1 times higher than among women with a normal selenium concentration ($P=0.003$). There were 3 (2.7%) maternal deaths and 8 (7.1%) perinatal deaths recorded, and the rate did not differ between patients with low or normal selenium concentrations (Table 2). The perinatal deaths included five stillbirths and three early neonatal deaths.

After controlling for age, parity, time since HIV diagnosis, ART duration, markers of HIV infection, and other potential confounding variables, mothers with selenium deficiency had an approximately eight-fold higher risk of preterm delivery (Table 3) and an eight-fold higher risk of delivering a neonate with a low delivery weight at term, compared with women with a normal selenium concentration (Table 4). A low CD4+ cell count was also associated with increased risk of preterm delivery (Table 3), and HIV disease markers and the duration of ART were associated with increased risk of term delivery of a neonate with low delivery weight (Table 4).

4 DISCUSSION

In the present study, the prevalence of selenium deficiency among pregnant women with HIV infections in Lagos, Nigeria, was relatively high, and maternal selenium deficiency was significantly associated with preterm delivery and a low delivery weight among term neonates. These findings could have implications for the future management of HIV in pregnancy.

The prevalence of selenium deficiency in the present cohort of HIV-infected pregnant women in Nigeria was 20.4%. This figure is lower than the prevalence of 53% found by Shivakoti et al. [12] in a similar cohort from the USA; this difference could be explained by the different cutoffs for selenium deficiency used in the two studies. The cutoff value chosen

by Shivakoti et al. (1.08 μmol/L [85 μg/L]) was based on previous studies of HIV and selenium status [12], whereas the present cutoff value (0.89 μmol/L [70 μg/L]) was based on the lower limit of the reference range for normal selenium levels in a standard clinical chemistry textbook [11]. Several other studies have also found that HIV infection is associated with reduced serum selenium concentrations [8,9,13–15]. Indeed, nutritional deficiencies are common among individuals with HIV infections [16] because of factors such as the oxidative state induced by the virus, malabsorption, metabolic alterations, gut infections, and gut barrier dysfunction produced by chronic HIV infection [17].

The present study did not find any association between selenium deficiency and maternal mortality. This observation is at variance with studies into HIV-related mortality carried out among nonpregnant HIV-infected participants [18,19], but was similar to the findings of two selenium supplementation trials [20,21] carried out among pregnant women with HIV infections. Also, the present study did not demonstrate any association between selenium deficiency and perinatal mortality. However, this is at variance with findings from Kupka et al. [20], who reported an association between low maternal serum selenium concentrations and fetal death.

Literature on associations between selenium status and preterm delivery with a low delivery weight is scant. The significant association of preterm delivery with low maternal selenium levels found in the present study was in accordance with a study carried out in Tokyo, Japan [22], but at variance with findings reported from Tehran, Iran [23]. However, based on a series of bivariate and multivariate analyses, the present study indicated that a low maternal serum selenium concentration may not be an independent predictor of the neonatal delivery weight in HIV-infected mothers with low CD4+ cell count, high viral load, shorter duration of ART use or lower BMI (Table 4).

In studies from Zaire [24] and Tokyo [22] among women who, presumably, did not have HIV, the selenium levels were lower among women who delivered neonates with a delivery weight of less than 2500 g, but no such relationship was recorded in a similar study carried out in Poland [25]. However, the present study showed a strong positive relationship between selenium deficiency and a low delivery weight in term neonates. This finding could be attributable to the presence of other influencing factors such as HIV disease markers and the duration of ART use, which were not eliminated even after multivariate analyses.

The current study was hospital-based, limiting the generalizability of the findings to the entire population of HIV-infected women in Nigeria. Moreover, it was extremely difficult to extract reliable information on the intake of selenium-rich diets from the participants, and this factor could have had some direct or indirect influence on the observed association. it is also important to highlight that the association observed in the present study does not necessarily indicate causality. However, this is the second known study among black African women that examined the possible effects of a low selenium concentration on pregnancy outcomes while carefully adjusting for confounding factors. The study provides valuable information for future robust longitudinal studies and randomized controlled trials of selenium supplementation in women with HIV who are pregnant in Nigeria, which could

inform future policies on HIV care during pregnancy and on the prevention of mother-to-child transmission of the infection.

In conclusion, the present study showed a relatively high prevalence of selenium deficiency among pregnant women with HIV in Lagos. The significant associations observed between maternal selenium deficiency and adverse pregnancy outcomes could have implications in the future management of HIV in pregnancy through the use of selenium supplementation among patient with HIV as a way of reducing these adverse outcomes. However, further research is needed to answer some of the major reservations that remain from the present study, such as the overall impacts of the various identified confounders on these relationships.

Acknowledgments

KSO wishes to acknowledge the mentorship provided by Folasade Ogunsola, Deputy Vice-Chancellor, Development Services of the University of Lagos, Lagos, Nigeria, and Phillis Kanki, Harvard University School of Public Health, Boston, MA, USA, throughout the present study. The research reported in the present study was supported by the Fogarty International Center of the National Institutes of Health (award number D43TW010134). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Synopsis

The prevalence of selenium deficiency among HIV-positive pregnant women in Nigeria was high, and the maternal selenium status was significantly associated with pregnancy outcomes.

Table 1

Baseline characteristics by maternal selenium concentration (n=113). [a]

Characteristic	Low selenium (n=23)	Normal selenium (n=90)	*P* value
Age, y	35.3 ± 4.9	33.7 ± 5.9	0.193
Parity	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.940
Pregnancy duration at enrollment, wk	19.0 (16.0–22.0)	20.0 (17.8–23.0)	0.204
BMI	26.0 (22.0–29.1)	26.4 (24.1–29.5)	0.149
Occupation			0.399
Housewife	2 (8.7)	12 (13.3)	
Trader	7 (30.4)	35 (38.9)	
Artisan	4 (17.4)	6 (6.7)	
Civil servant	10 (43.5)	37 (41.1)	
Religion			0.617
Christianity	13 (56.5)	56 (62.2)	
Islam	10 (43.5)	34 (37.8)	
Education			0.330 [b]
Uneducated	2 (8.7)	2 (2.2)	
Primary	0	6 (6.7)	
Secondary	5 (21.7)	20 (22.2)	
Tertiary	16 (69.6)	62 (68.9)	
Tribe			0.600
Hausa	3 (13.0)	10 (11.1)	
Igbo	9 (39.1)	30 (33.3)	
Yoruba	9 (39.1)	31 (34.4)	
Other	2 (8.7)	19 (21.1)	
Time since HIV diagnosis, mo	93.4 ± 11.9	86.3 ± 22.1	0.081
ART duration, mo	45.9 ± 4.2	51.2 ± 8.2	0.059
CD4+ count, cells/mm^3	294.0 (222.0–302.0)	446.0 (330.8–561.5)	<0.001
Viral load, copies/mL	28 400.0 (3005.0–64 867.0)	2756.0 (250.3–12 620.0)	0.017

Abbreviations: ART, antiretroviral treatment; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

[a] Values are given as mean ± SD, median (interquartile range), or number (percentage), unless indicated otherwise.

[b] Fisher exact test.

Table 2

Bivariate analysis of maternal selenium concentrations and pregnancy outcomes. [a]

Characteristic	Total (n=113)	Low selenium (n=23)	Normal selenium (n=90)	OR (95% CI)	*P* value
Pregnancy duration at delivery					
Preterm (<37 wk)	11 (9.7)	7 (30.4)	4 (4.4)	6.85 (3.11–10.05)	0.011
Term (≥37 wk)	102 (90.3)	16 (69.6)	86 (95.6)	1.00 (ref.)	
Delivery weight for term neonates [b]					
<2500 g	12 (11.8)	9 (56.2)	3 (3.5)	16.06 (9.81–33.47)	0.003
≥2500 g	90 (88.2)	7 (43.8)	83 (96.5)	1.00 (ref.)	
Maternal death					
Yes	3 (2.7)	1 (4.3)	2 (2.2)	1.96 (0.61–7.12)	0.498 [c]
No	110 (97.3)	22 (95.7)	88 (97.8)	1.00 (ref.)	
Perinatal death					
Yes	8 (7.1)	2 (8.7)	6 (6.7)	1.29 (1.03–5.97)	0.735
No	105 (92.9)	21 (91.3)	84 (93.3)	1.00 (ref.)	

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Values are given as number (percentage) unless indicated otherwise.

[b] n=102.

[c] Fisher exact test.

Table 3

Bivariate and multivariate analyses of relationships between baseline characteristics and preterm delivery among pregnant women with HIV infection (n=113).

Risk factor	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Age, y		0.992		
<35 (n=55)	0.97 (0.44–5.11)		NA	
≥35 (n=58)	1.00 (ref.)		NA	
Parity		0.026		0.110
Nulliparous (n=52)	0.34 (0.73–3.26)		0.81 (0.40–6.01)	
Multiparous (n=61)	1.00 (ref.)		1.00 (ref.)	
Occupation		0.082		
Professional (n=47)	1.46 (1.25–7.68)		NA	
Nonprofessional (n=66)	1.00 (ref.)		NA	
Education		0.777		
≥High school (n=103)	1.21 (0.32–4.55)		NA	
<High school (n=10)	1.00 (ref.)		NA	
BMI		0.618		
≤24.9 (n=45)	1.51 (1.16–9.49)		NA	
≥25.0 (n=68)	1.00 (ref.)		NA	
Duration of HIV diagnosis, mo		0.012		0.087
>12 (n=88)	4.71 (1.33–7.61)		1.34 (0.96–19.34)	
≤12 (n=25)	1.00 (ref.)		1.00 (ref.)	
ART duration, mo		0.007		0.161
<10 (n=10)	4.18 (2.24–7.83)		3.14 (2.11–33.59)	
≥10 (n=103)	1.00 (ref.)		1.00 (ref.)	
CD4+ count, cells/mm^3		0.003		0.027
<350 (n=50)	9.46 (3.33–15.18)		8.11 (4.21–15.50)	
≥350 (n=63)	1.00 (ref.)		1.00 (ref.)	
Viral load, copies/mL		0.139		
≥1000 (n=34)	3.11 (1.22–29.47)		NA	
<1000 (n=79)	1.00 (ref.)		NA	
Selenium level		<0.001		0.031
Low (n=23)	11.04 (8.84–21.9)		7.61 (4.37–18.89)	
Normal (n=90)	1.00 (ref.)		1.00 (ref.)	

Abbreviations: OR, crude odds ratio; CI, confidence interval; aOR, adjusted odds ratio; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); ART, antiretroviral treatment.

Table 4

Bivariate and multivariate analysis of relationships between baseline characteristics and low delivery weight in term neonates by patients with HIV (n=102).

Risk factor	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Age, y		0.111		
<35 (n=49)	1.68 (0.79–11.24)		NA	
≥35 (n=53)	1.00 (ref.)		NA	
Parity		0.075		
Nulliparous (n=44)	3.34 (1.53–17.26)		NA	
Multiparous (n=58)	1.00 (ref.)		NA	
Occupation		0.332		
Professional (n=43)	0.88 (0.45–9.68)		NA	
Nonprofessional (n=59)	1.00 (ref.)		NA	
Education		0.096		
≥High school (n=94)	2.36 (1.12–7.55)		NA	
<High school (n=8)	1.00 (ref.)		NA	
BMI		0.002		0.038
≤24.9 (n=41)	11.51 (2.18–22.45)		6.42 (3.33–9.11)	
≥25.0 (n=61)	1.00 (ref.)		1.00 (ref.)	
Duration of HIV diagnosis, mo		0.042		0.099
>12 (n=83)	3.71 (2.14–9.79)		1.11 (0.78–11.43)	
≤12 (n=19)	1.00 (ref.)		1.00 (ref.)	
ART duration, mo		0.016		0.004
<10 (n=7)	10.07 (4.24–17.83)		7.23 (6.21–12.12)	
≥10 (n=95)	1.00 (ref.)		1.00 (ref.)	
CD4+ count, cells/mm^3		0.037		0.016
<350 (n=48)	7.15 (3.33–21.18)		4.11 (2.29–7.08)	
≥350 (n=54)	1.00 (ref.)		1.00 (ref.)	
Viral load, copies/mL		0.039		0.001
≥1000 (n=28)	13.11 (3.22–19.47)		9.35 (2.22–13.76)	
<1000 (n=74)	1.00 (ref.)		1.00 (ref.)	
Selenium level		0.009		0.012
Low (n=17)	14.04 (10.12–25.92)		8.11 (3.27–17.22)	
Normal (n=85)	1.00 (ref.)		1.00 (ref.)	

Abbreviations: OR, crude odds ratio; CI, confidence interval; aOR, adjusted odds ratio; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); ART, antiretroviral treatment.