Doppler Velocimetry Indices of Human Immunodeficiency Virus-positive Pregnant Women and Their Controls at Aminu Kano Teaching Hospital, Kano

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Abstract

Background: Nigeria is among the countries having a large number of human immunodeficiency virus (HIV)-infected people in Africa with growing number of HIV-positive children, mainly infected by their mothers. Traditional tests diagnose high-risk fetuses very late. Doppler sonography has a potential for detecting high at-risk fetus at a much early stage, so that appropriate measures could be instituted to improve outcomes. This study compared umbilical artery velocimetric parameters among HIV-positive women on highly active antiretroviral therapy (HAART) and their matched controls to determine the possible abnormalities and correlates.

Methodology: This was a comparative study that was conducted among HIV-positive pregnant women and their matched controls (HIV-negative pregnant women matched for gestational age and parity) at Aminu Kano Teaching Hospital. History and physical examination, transabdominal ultrasound examination were done on each subject to obtain the basic obstetric parameters. Detailed evaluations of the umbilical arteries on gray scale and duplex Doppler protocols using a 3.5-MHz curvilinear transducer were also done. The data were analyzed using SPSS Version 19.0. Independent samples t-test was used for continuous data. Chi-square test and Fisher’s exact test were used for categorical data. P < 0.05 was considered statistically significant.

Results: The mean age ± standard deviation (SD) was 30.8 ± 5.50 and 27.6 ± 5.34 for HIV and control groups, respectively. The mean amniotic fluid indices and that of estimated fetal weight for the HIV and control groups showed no statistically significant difference between the two groups. The mean (±SD) umbilical artery diameter of the HIV-infected mothers is wider than their negative controls.

Conclusion: The study showed no statistically significant difference between the Doppler indices of HIV-positive pregnant women on HAART and their matched controls.

Keywords: Controls, Doppler velocimetry indices, human immunodeficiency virus, Nigeria, pregnant women
et la parité à l’hôpital universitaire Aminu Kano. Anamnèse et examen physique, échographie transabdominale ont été réalisés sur chaque sujet pour obtenir les paramètres obstétriques de base. Des évaluations détaillées des artères ombilicales sur des protocoles d’échelle de gris et Doppler duplex à l’aide d’un transducteur curviligne de 3,5 MHz ont également été effectuées. Les données ont été analysées à l’aide de SPSS version 19.0. Un test t d’échantillons indépendants a été utilisé pour les données continues. Le test du chi carré et le test exact de Fisher ont été utilisés pour les données catégorielles. P <0,05 était considéré comme statistiquement significatif. Résultats: L’âge moyen ± écart type (ET) était de 30,8 ± 5,50 et 27,6 ± 5,34 pour le VIH et les groupes témoins, respectivement. Les indices moyens du liquide amniotique et celui du poids fœtal estimé pour les groupes VIH et contrôle n’ont montré aucune différence statistiquement significative entre les deux groupes. Le diamètre moyen ± ET de l’artère ombilicale des mères infectées par le VIH est plus large que leurs témoins négatifs. Conclusion: L’étude n’a montré aucune différence statistiquement significative entre les indices Doppler des femmes enceintes séropositives sous HAART et leurs témoins appariés.

Mots-clés: Contrôles, indices de vélocimétrie Doppler, virus de l’immunodéficience humaine, Nigéria, femmes enceintes

Introduction
Human immunodeficiency virus (HIV) infection continues to be a burden on women of childbearing age worldwide.[1] In 2018, out of 37.9 million (32.7 million–44.0 million) people living with HIV,[2] 17.8 million were women, constituting 52%.[3] Currently, about 24.5 million (21.6 million–25.5 million) people are estimated to be receiving antiretroviral therapy (ART) in low- and middle-income countries.[2] Globally, about 6000 new infections of HIV occur each day; two out of three are in Sub-Saharan Africa with young women continuing to bear a disproportionate burden. Teenagers and young women aged 15–24 years have up to eightfold higher rates of HIV infection compared to their male peers.[4]

Nigeria is among the countries having a large number of HIV-infected people in Africa with about 1.9 million people living with HIV/AIDS and a national adult prevalence of 1.5%.[5] Women aged 15–49 years are more than twice as likely to be living with HIV than men (1.9% versus 0.9%); young women aged 20–24 years are more than three times as likely to be living with HIV as young men in the same age group.[3] In 2017, 80% of pregnant women living with HIV were receiving ART, much higher than the figure of 51% who had access to ART in 2010.[6]

Despite this improvement in the availability of ART, 740,000 women of reproductive age became HIV positive in 2016. About 73% of these women live in only 23 countries, the vast majority of which are in Sub-Saharan Africa, and are considered as high priority for PMTCT by UNAIDS.[7]

HIV infection without antiretroviral treatment is associated with the risk of mother-to-child transmission of HIV during pregnancy, delivery, and breastfeeding in up to 25%–30%.[8] The WHO guideline now recommends the initiation of highly active antiretroviral therapy (HAART) in pregnancy and the PMTCT options for all HIV-infected pregnant women to maximize the prevention of HIV transmission and maternal and infant survival.[9] About 80% of the estimated HIV-infected pregnant women worldwide received at least some ARV drugs to prevent HIV transmission to their baby in 2020.[9] Early HAART initiation for all HIV-positive pregnant women and a widespread use of HAART among HIV-infected pregnant women have led to significant decreases in HIV transmission to the infant and decreases in maternal morbidity.[9]

However, HIV infection and the use of such medications during pregnancy may result in adverse infant birth outcomes.[10] Also, many uncertainties remain regarding the potential adverse effects of HAART initiation and its use in pregnancy in addition to the burden of the disease itself. Increased risks of prematurity, early infant mortality, high prevalence of infants with low birth weights, and preterm labor are the commonly reported adverse outcomes among HIV-infected women.[11]

The risk of facing adverse infant birth outcome was associated with maternal CD4 level, duration and time of HAART initiation, and type of HAART regimens according to many previous studies from Africa and Europe.[12] However, still, there remain controversies between different studies in different countries.

It is important to make a definite diagnosis based on the best criteria to decrease the perinatal mortality and morbidity associated with adverse outcomes among fetuses of HIV-positive pregnancies exposed to HAART. Various studies all over the world have given different modalities to diagnose fetuses at risk of poor perinatal outcomes; the latest in the series of tools for fetal surveillance antenatally is the analysis of Doppler blood flow velocity waveforms of fetal umbilical vessels.[13]

Antepartum fetal surveillance with Doppler ultrasound of umbilical artery has shown a significant diagnostic efficacy in identifying fetal compromise. Its effectiveness in decreasing perinatal mortality has been demonstrated.[14] The clinical and conventional B-mode ultrasound measurements diagnose high-risk fetuses at a very late stage when the fetus is already compromised, whereas Doppler waveform studies can detect high-risk fetus at a much early stage, so that the affected fetus can be delivered without significant compromise.[15] Doppler ultrasound gives us information directly on vascular resistance and indirectly on blood flow. The present study was aimed at evaluating measurements of fetal umbilical artery velocimetric parameters among HIV-positive women on HAART and their matched controls at Aminu Kano Teaching Hospital, Kano, Nigeria.
**Methodology**

It was a comparative study among HIV-positive pregnant women and their matched controls (HIV-negative pregnant women) at Aminu Kano Teaching Hospital from July 1, 2016, to July 31, 2017. HIV-positive pregnant women were matched for gestational age and parity with HIV-negative pregnant women. HIV-positive pregnant women with multiple gestation and chronic medical conditions such as diabetes mellitus and chronic hypertension; sickle cell anemia patients; patients with hypertensive disorders of pregnancy; and pregnant women with polyhydramnios among others, were excluded from the study. HIV-positive pregnant women who were not on HAART were also excluded from the study. All consenting pregnant women who were HIV positive and negative who qualified for the study and the control, respectively, were recruited. Ethical approval was obtained from the hospital’s ethics committee. A structured questionnaire was designed and pretested before administration. Information on sociodemographic characteristics was obtained and recorded on the questionnaire after obtaining informed consent. History concerning HIV infection and antiretroviral therapy was also recorded on the questionnaire before they were directed to the radiology units for obstetric ultrasound scan. The ultrasound and the velocimetry were performed from the second trimester to the third trimester. Each eligible patient was matched with a control for gestational age and parity before the ultrasound scan and velocimetry.

Transabdominal ultrasound examination of the gravid abdomen was done with the patient lying supine to the right of the examiner. A 3.5-MHz curvilinear transducer was used. Freeze frame capability and on-screen electronic calipers were used for measurements.

Each examination took at least 15 min. Scanning was done after application of copious amount of transonic gel to displace air which would otherwise cause interference. The following measurements were determined from the ultrasound scan:

- Gestational age using biparietal diameter, femur length, head circumference, and abdominal circumference [Figure 1]
The scanning of the umbilical artery (uterine artery) was done in the transverse, longitudinal, and oblique to visualize the free-floating loop of umbilical cord. Color Doppler was used to locate the UA and the Doppler spectral waveforms were measured within 5 cm of the umbilical cord insertion into the fetal abdomen. The peak systolic velocity (PSV) and end diastolic velocity (EDV) were measured [Figures 2 and 4]. Henceforth, the systolic diastolic (SD) ratio, resistance index (RI) and Pulsatility index (PI) were driven and recorded using the following formulae.

\[ SD \text{ ratio} = \frac{PSV}{EDV} \]

\[ RI = \frac{PSV - EDV}{PSV} \]

\[ PI = \frac{PSV - EDV}{Mean Velocity} \]

The placental thickness was taken at the level of the umbilical cord insertion in the longitudinal direction and a mean of three readings was taken, with the patient in supine position.

The data were analyzed using Statistical Package for the Social Sciences (SPSS) Version 19.0 (SPSS Inc., Chicago, IL, USA). Independent samples \( t \)-test was used for continuous data and Chi-square test and Fisher’s exact test were used for categorical data. \( P < 0.05 \) was considered statistically significant.

### Results

During the period under review (from July 1, 2016, to July 31, 2017), 31 HIV-positive pregnant women and their matched controls were studied. The HIV-positive pregnant women were all on HAART following the diagnosis. The mean age ± SD was 30.8 ± 5.50 years and 27.6 ± 5.34 years for HIV and control groups, respectively.

The mean gestational ages of the two groups were 30.0 ± 6.48 and 29.5 ± 4.70 weeks, respectively. There was no statistically significant difference (\( t = 0.404, df = 60, P = 0.68, 95\% \) confidence interval [CI]: −2.295 to +3.457). Similarly, the mean parity was 3.3 ± 2.15 and 2.2 ± 2.48, respectively. There was no statistically significant difference (\( t = -2.295, df = 60, P = 0.68, 95\% \) CI: −0.0884 to 0.1706).

The mean amniotic fluid indices ± SD for the HIV and control groups were 18.7 ± 5.21 and 16.9 ± 4.79, respectively. There was no statistically significant difference between the two groups (\( t = 1.179, df = 46, P = 0.244, 95\% \) CI: −1.256 to +4.812).

The mean EFW ± SD for the HIV and control groups were 1.7 ± 0.83 kg and 1.49 ± 0.67 kg, respectively. There was no statistically significant difference between the two groups (\( t = 0.814, df = 53, P = 0.420, 95\% \) CI: −0.267 to +0.632).

The mean (±SD) umbilical artery diameter of the HIV-infected mothers is wider than their negative controls, measuring 5.8 ± 2.17 mm and 2.8 ± 2.12 mm, respectively (\( t = 5.052, df = 52, P = 0.00, 95\% \) CI: 1.782–4.129).

The mean PSV ± SD of the HIV and control groups were 49.1 ± 18.89 mm and 51.2 ± 23.76 mm, respectively. These differences were not statistically significant between the two groups (\( t = -0.379, df = 58, P = 0.706, 95\% \) CI: −13.184 to 8.984).

The mean EDV ± SD was 18.1 ± 8.56 for the HIV group and 19.0 ± 10.08 for the control group. Also, there was no statistically significant difference between the two groups (\( t = 0.363, df = 57, P = 0.718, 95\% \) CI: −0.5754 to +3.986).

The mean systolic diastolic (SD) ratio ± SD was 2.9 ± 0.76 and 2.7 ± 0.58 for study and control groups, respectively. Similarly, there was no statistically significant difference between the two groups (\( t = 0.960, df = 59, P = 0.341, 95\% \) CI: −0.181 to 0.514).

The mean resistive indices ± SD for the study and control groups were 0.65 ± 0.10 and 0.63 ± 0.07, respectively. There was no statistically significant difference between the two groups (\( t = 0.952, df = 60, P = 0.345, 95\% \) CI: −0.0227 to +0.064).

The mean pulsatility indices ± SD for the study and control groups were 1.00 ± 0.22 and 0.96 ± 0.19, respectively. There was no statistically significant difference between the study and control groups (\( t = -0.642, df = 39, P = 0.524, 95\% \) CI: −0.0884 to 0.1706).

As shown in Table 1, higher proportion (8; 25.8%) of HIV-positive pregnant women had RI of ≤0.57 when compared with the control (5; 16.1%). However, this difference was not statistically significant (\( P = 0.349 \)).

Similarly, there were more HIV-positive pregnant women (23; 74.2%) with normal PI (≤1.42) than in the

### Table 1: Doppler indices of human immunodeficiency virus-positive pregnant women and their matched controls

| Variable | Frequency (%) | \( \chi^2 \), Df, P |
|----------|---------------|----------------------|
| RI       |               |                      |
| Normal (≤0.57) | 8 (25.8) | 5 (16.1) | 0.876, 1, 0.349 |
| High (>0.57) | 23 (74.2) | 26 (83.9) | 31 (100.0) |
| PI       |               |                      |
| Normal (≤1.42) | 23 | 18 (58.1) | 1.80, 1, 0.180 |
| High (>1.42) | 8 | 13 (41.9) | 31 (100.0) |

HIV=Human immunodeficiency virus, RI=Resistance Index, PI=Pulsatility Index, Df=Degrees of freedom
control group (18; 58.1%). However, there was no statistically significant association ($P = 0.180$).

**DISCUSSION**

Umbilical artery Doppler assessment is used in surveillance of fetal well-being in the third trimester of pregnancy, especially fetuses at risk of or suspected to have intrauterine growth restriction. Abnormal Doppler indices are markers of uteroplacental insufficiency and consequent intrauterine growth restriction or suspected preeclampsia. In this study, the indices obtained from the Doppler studies of both HIV-infected women and their matched controls were within normal limits.

The resistivity index is a measure of pulsatile blood flow that reflects the resistance to blood flow caused by microvascular bed distal to the site of measurement commonly not more than 0.6 at 30 weeks of gestational age.[18] The RI was 0.65 ± 0.10 for the HIV-infected women and 0.63 ± 0.07 for the control group though not statistically significant. These values are similar to those obtained by Adekanmi et al.,[19] where RI was 0.6 and 0.53 at second and third trimesters, respectively. This is also comparable to the values obtained by Chanprapaph et al.,[20] in Thailand, where RI was 0.756, 0.72, 0.679, and 0.62 at 21, 25, 31, and 35 weeks of gestational age. This value tends to decrease with gestational age. The slight differences might be due to different sample sizes used by the authors and different equipment used.

Pulsatility index is a measure of resistance to flow in a blood vessel. The value obtained in this study was 1.00 ± 0.22 in the HIV-infected group and 0.96 ± 0.19 in the control group. This was also not statistically significant. These values are similar to those obtained by Adekanmi et al.,[19] in Ibadan of 1.00 and 0.80 in the second and third trimesters, respectively, and those found by Chanprapaph et al.[20] of 1.27, 1.256, 1.11, and 0.958 at 21, 25, 31, and 35 weeks of gestational age, respectively. These values are, however, higher than those obtained by Kurmanavicius et al.[21] of 0.82, 0.77, and 0.73 at 25, 31, and 35 weeks of gestational age, respectively. Acharya et al.,[22] in India recorded slightly higher values of 1.9, 1.62, 1.47, and 1.39 at 21, 25, 31, and 35 weeks of gestational age, respectively. The reason for these higher values could be racial or environmental.

PSV signifies the amount of blood flow through a vessel. It is inversely related to the total cross-sectional area of the blood vessel. The values obtained in these studies though not statistically significant were 49.1 ± 18.89 in the HIV-infected group and 51.2 ± 23.76 in the control group. There was a paucity of data in determining its values in other studies. It was, however, found not to correlate with adverse perinatal outcome.[23]

The mean amniotic fluid index of 18.7 ± 5.21 in the HIV-infected group and 16.9 ± 4.79 obtained in the control group was not statistically significant, but could be related to the wider mean umbilical artery diameter obtained in the HIV-infected group of 5.8 ± 2.17, compared to 2.8 ± 2.12 in the control group, which was statistically significant. The wider mean umbilical artery diameter could also account for the higher mean EFW in the HIV-infected group compared to the control group (1.7 ± 0.83 and 1.49 ± 0.67) even though these values were not statistically significant.

**CONCLUSION**

This study showed a statistically significant difference in the mean umbilical artery diameter between HIV-infected women and their matched controls, significance of which is undetermined. There was, however, no statistically significant difference between the Doppler indices of HIV-infected pregnant on HAART and their matched controls.

**Limitation**

The small sample size could have influenced the results of no statistical difference in the measured indices.

This was a comparative study and the patients with the matched controls were not followed up till delivery to determine birth weight and correlate it with the measured indices.

There was a paucity of data regarding umbilical artery diameter and therefore its significance could not be ascertained.

**Recommendation**

A follow-up study is recommended to determine fetal outcomes at delivery and correlate it with the Doppler indices measured.

More studies should be done among HIV-infected women and controls with larger sample sizes to determine the significance of Doppler studies in predicting adverse outcomes among them.

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**Conflicts of interest**

There are no conflicts of interest.

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