**D-Dimer, CRP, MDA, and Aminotransferases levels of HIV positive pregnant women on HAART as Predictors of Neonatal Jaundice and Low Birth Weight**

**ABSTRACT**

**Background**: The administration of highly active antiretroviral therapy (HAART) during pregnancy, particularly in the third trimester, has proven effective with minimal teratogenic effects. This longitudinal study evaluates the impact of two commonly prescribed HAART regimens Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP) and Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) on specific biochemical markers in HIV positive pregnant women and their potential predictive value for neonatal jaundice and low birth weight.

**Methods**; A total of 105 pregnant women in their third trimester were enrolled: 35 HIV-negative controls and 70 HIV positive women equally distributed between the two HAART regimens. Serum levels of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), D-dimer, C-reactive protein (CRP), and Malondialdehyde (MDA) were assessed in the mothers. Total bilirubin of neonates was evaluated using a standard spectrophotometric method at 72 hours post-delivery.

**Results**: There was no significant age difference between HIV positive and control groups (32.17 ± 4.81 vs. 32.14 ± 6.22 years; p = 0.117). HIV positive women on AZT/3TC/NVP exhibited significantly higher AST levels compared to those on TDF/3TC/EFV (31.46 ± 10.64 vs. 25.20 ± 8.73; p = 0.002) and controls (31.46 ± 10.64 vs. 20.23 ± 4.59; p < 0.001). Conversely, D-dimer and CRP levels were significantly elevated in the TDF/3TC/EFV group compared to AZT/3TC/NVP (p < 0.001). Strong positive correlations were observed between maternal D-dimer (r = 0.848), CRP (r = 0.761), and age (r = 0.723) with neonatal bilirubin levels at 72 hours after birth. Multiple logistics regression analysis revealed that D-dimer (Odds Ratio [OR]: 1.003; 95% CI: 0.999 – 1.006), C-reactive protein (OR: 0.032; 95% CI: 00.004 – 0.274) and Alanine aminotransferase (OR: 1.234; 95% CI: 1.034 – 1.474) predicted an abnormal fetal outcome between third trimester females on TDF/3TC/EFV and AZT/3TC/NVP.

**Conclusion**: These findings suggest that HAART-associated biochemical changes in late pregnancy may influence neonatal outcomes. Inclusion of D-dimer, CRP, and aminotransferases as part of drug effect monitoring and routine antenatal screening, could serve as valuable predictors of adverse neonatal effects in HIV positive pregnancies.

**Keywords:** Third trimester, neonates, D-Dimer, C - reactive protein, HAART,Aminotransferases

**INTRODUCTION**

The intersection of HIV, pregnancy, and antiretroviral therapy represents a complex clinical scenario. As highly active antiretroviral therapy (HAART) becomes the standard of care for preventing mother-to-child transmission (MTCT) of HIV, the focus has shifted to understanding its broader physiological and biochemical effects on both mothers and neonates. Biochemical markers such as D-dimer, C-reactive protein (CRP), malondialdehyde (MDA), and liver enzymes (ALT and AST) have emerged as potential predictors of adverse neonatal outcomes, particularly jaundice and low birth weight (LBW). HAART is crucial for managing HIV in pregnancy, as it significantly reduces the risk of vertical transmission from mother to child. Combination regimens such as Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP) and Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) are widely used in sub-Saharan Africa due to their availability and efficacy (1). Although these regimens are generally safe, they are associated with varying degrees of hepatotoxicity, oxidative stress, and inflammatory changes, especially in the third trimester when physiological stress peaks (2).

Liver enzyme activity is a vital indicator of hepatic function. During pregnancy, particularly in the third trimester, changes in hepatic metabolism are common. In HIV positive women on HAART, these changes may be exaggerated. ALT and AST are frequently elevated in individuals on antiretroviral drugs, especially Nevirapine, which has been implicated in direct hepatocellular injury (3). A study by Floridia et al. observed a higher prevalence of elevated liver enzymes among pregnant women on Nevirapine-based regimens compared to those on Efavirenz (4). Such hepatotoxic effects could potentially influence fetal bilirubin metabolism, increasing the risk of neonatal jaundice.

D-dimer is a fibrin degradation product and is used clinically to assess thrombosis and fibrinolytic activity. During pregnancy, D-dimer levels physiologically increase, but the presence of HIV infection and HAART has been shown to amplify this response. Chronic immune activation in HIV positive individuals promotes endothelial dysfunction and a procoagulant state, resulting in elevated D-dimer concentrations (5). Kuller et al. demonstrated that elevated D-dimer levels in HIV positive adults are associated with increased mortality, suggesting its utility as a marker of systemic stress (6). In pregnancy, elevated D-dimer levels have been associated with complications such as preterm birth and low birth weight due to impaired placental perfusion (7). Thus, monitoring D-dimer in HIV positive pregnant women may provide early warning signs of compromised fetal outcomes, particularly in those receiving TDF-based regimens, which may be more inflammatory than AZT-based combinations.

CRP is a non-specific acute phase protein that rises in response to inflammation. Elevated CRP levels during pregnancy have been linked to adverse maternal and neonatal outcomes, including preeclampsia, premature rupture of membranes, and intrauterine growth restriction (8). In HIV-infected individuals, persistent systemic inflammation remains even during viral suppression, contributing to increased CRP levels (9). HAART can modulate this inflammatory profile. TDF/3TC/EFV regimens, for instance, have been associated with higher CRP levels than AZT-based regimens, possibly due to their interaction with lipid metabolism and mitochondrial function (10). Elevated maternal CRP levels may contribute to altered placental function, thereby increasing the risk of neonatal jaundice or LBW.

MDA is a by-product of lipid peroxidation and serves as a robust marker of oxidative stress. Oxidative stress plays a significant role in the pathophysiology of HIV and its treatment. Several studies have shown increased MDA levels in HIV positive individuals receiving HAART, indicating ongoing oxidative damage despite immune reconstitution (11). Pregnancy further increases oxidative stress due to higher metabolic demands and hormonal changes. Increased oxidative stress may impair fetal growth and disrupt normal hepatic function, leading to elevated bilirubin levels after birth. Research by Suresh et al. showed that MDA levels were significantly higher in HIV positive pregnant women than in controls, reinforcing the idea that oxidative damage contributes to neonatal complications such as jaundice and LBW (12).

Neonatal jaundice is commonly observed in infants born to HIV positive mothers, particularly those exposed to certain antiretroviral drugs. Drugs like AZT have been associated with mitochondrial toxicity and hemolysis, both of which may contribute to hyperbilirubinemia in neonates (13). Moreover, inflammation and oxidative stress during gestation may impair placental function, increasing the risk of intrauterine growth restriction and subsequent LBW. LBW is a significant predictor of neonatal morbidity and mortality. It has been linked with elevated maternal CRP and D-dimer levels, reflecting a systemic inflammatory and prothrombotic environment (14). These findings support the hypothesis that biochemical markers, altered by both HIV and HAART, can serve as predictive tools for identifying neonates at risk of complications.

The use of HAART in pregnant women has significantly reduced the incidence of MTCT of HIV. However, its impact on maternal biochemistry and neonatal outcomes warrants close scrutiny. Markers such as D-dimer, CRP, MDA, ALT, and AST offer promising insight into the physiological disruptions associated with HAART and can serve as early predictors of neonatal jaundice and low birth weight. Understanding the differences in these markers among commonly used regimens like AZT/3TC/NVP and TDF/3TC/EFV is crucial for optimizing maternal and neonatal care. Further prospective studies are needed to validate these findings and refine antenatal monitoring protocols in HIV positive populations.

**MATERIALS AND METHODS**

**Study Design and Population**

This was a hospital-based, longitudinal, observational study conducted between March and November 2024 at the General Hospital Ekpoma and Uromi, which are Secondary healthcare facilities in Nigeria. A total of 105 pregnant women in their third trimester (gestational age ≥28 weeks) were enrolled through random and consecutive sampling.

Participants were categorized into three groups:

Group 1 (HIV negative controls): 35 healthy, HIV seronegative pregnant women.

Group 2 (HAART group 1): 35 HIV positive pregnant women receiving Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP).

Group 3 (HAART group 2): 35 HIV positive pregnant women receiving Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV).

Eligibility criteria included singleton pregnancy, confirmed HIV status with HAART compliance ≥6 months, and absence of pre-existing liver disease or co-infections such as hepatitis B or C. Women with pre-eclampsia, diabetes, or other chronic illnesses were excluded.

**Biochemical and Clinical Analysis**

Maternal venous blood (5 mL) was collected aseptically into appropriate sample bottles at enrollment during the third trimester (between 28–36 weeks gestation). The various biochemical markers were analyzed at the Chemical Pathology Laboratory of Ambrose Alli University, Ekpoma, Nigeria (Cut-off values; D-dimer <500ng/mL, C-reactive protein < 4 mg/L, MDA <2.72nmol/mL, ALT<19 IU/L and AST<30 IU/L).

Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST): Measured using standard kinetic methods (Randox Laboratories Ltd, UK).

D-dimer: Quantified using an immunoturbidimetric method (Diagnostica Stago, France).

C-reactive protein (CRP): Determined via high-sensitivity immunoassay.

Malondialdehyde (MDA): Assessed using thiobarbituric acid reactive substances (TBARS) assay to evaluate lipid peroxidation levels.

All assays were performed in the chemical pathology laboratory of [insert institution] according to manufacturer protocols and quality control standards.

**Neonatal Assessment**

At 72 hours post-delivery, 2 mL of venous blood was collected from each neonate. Total serum bilirubin was measured spectrophotometrically (λ = 540 nm) using standard protocols. Neonatal birth weights were obtained within the first hour after delivery using a calibrated electronic scale, and weights <2.5 kg were classified as low birth weight.

**Statistical Analysis**

Data were analyzed using IBM SPSS Statistics version 25.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as means ± standard deviations (SD), and categorical data were presented as frequencies and percentages. Inter-group comparisons were conducted using independent-samples t-test and ANOVA where appropriate. Pearson’s correlation coefficient was used to assess relationships between maternal biochemical parameters and neonatal bilirubin levels.

Multiple logistic regression analysis and Receiver operating characteristic curve were used to identify predictors of neonatal jaundice, adjusting for potential confounders. A p-value of <0.05 was considered statistically significant.

**RESULTS**

Table 1 represents the mean distribution of age, liver enzymes, lipid peroxidation, D-dimer and inflammatory index of HIV positive HAART compliant pregnant women in their third trimester and HIV negative third trimester pregnancy as control. There was no statistically significant difference between the age of HIV positive third trimester pregnancy on HAART and HIV negative third trimester pregnancy which served as control (32.14 ± 6.22 vs 32.17 ± 4.81; p=0.117). Liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were significantly elevated in HIV positive third trimester pregnancy on HAART compared to the HIV negative control (28.33 ± 10.16 vs 20.23 ± 4.59; p<0.001, and 23.36 ± 10.11 vs 17.83 ± 5.10; p=0.003 respectively).

Malondialdehyde (MDA) levels in control was not significantly lower than HIV positive women on HAART at third trimester (2.46 ± 0.64 vs 3.00 ± 2.03; p=0.133). D-dimer was significantly elevated in HIV positive women on HAART at third trimester when compared with the HIV negative control (854.60 ± 598.92 vs 486.46 ± 268.34; p=0.001).

C-reactive protein levels of control was not significantly lower than that of HIV positive women on HAART at third trimester (4.11 ± 0.76 vs 4.90 ± 1.43; p=0.030).

**Table 1**. Mean distribution of age, liver enzymes, lipid peroxidation, D-dimer and inflammatory index of HIV positive HAART compliant pregnant women in their third trimester and control using independent sample t-test.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Control -HIV negative pregnant women at third trimester**  **(n=35)** | **HIV positive pregnant women at third trimester on HAART**  **(n=70)** | **t-value** | **p-value** |
| Age (Years) | 32.17 ± 4.81 | 32.14 ± 6.22 | 2.493 | 0.117 |
| AST (IU/L) | 20.23 ± 4.59 | 28.33 ± 10.16 | 20.093 | <0.001 |
| ALT (IU/L) | 17.83 ± 5.10 | 23.36 ± 10.11 | 9.257 | 0.003 |
| MDA (nmol/mL) | 2.46 ± 0.64 | 3.00 ± 2.03 | 2.293 | 0.133 |
| D-Dimer (ng/mL) | 486.46 ± 268.34 | 854.60 ± 598.92 | 11.975 | 0.001 |
| CRP (mg/L) | 4.11 ± 0.76 | 4.90 ± 1.43 | 9.257 | 0.030 |

**Key;** Mean values are significant p≤0.05

Table 2 represents the mean distribution of fetal (newborn) indices of both HIV negative pregnant women at third trimester which served as control and HIV positive women on HAART at third trimester. Fetal Birth weight was significantly lower in and HIV positive women on HAART at third trimester when compared with control (2.94 ± 0.49 vs 3.31 ± 0.39; p=0.044). Fetal total Bilirubin levels at 24 hours of birth was not significantly different between newborns from control and newborns from HIV positive women on HAART at third trimester (0.96 ± 0.18 vs 0.97 ± 0.17; p>0.05).

Fetal total Bilirubin levels at 72 hours after birth was significantly elevated in newborns from HIV positive women on HAART at third trimester when compared with values from newborns from control (4.43 ± 1.61 vs 1.44 ± 0.98; p <0.001).

**Table 2**: Mean distribution of newborn indices of both control HIV negative pregnant women at third trimester and HIV positive women on HAART at third trimester using independent sample t-test

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Newborn of HIV negative control**  **(n=35)** | **Newborn of HIV positive at third trimester on HAART**  **(n=70)** | t-value | p-value |
| Fetal Birth weight (kg) | 3.31 ± 0.39 | 2.94 ± 0.49 | 4.146 | 0.044\* |
| Total Bilirubin at 24 hours of birth | 0.96 ± 0.18 | 0.97 ± 0.17 | 0.323 | 0.571 |
| Total Bilirubin at 72 hours after birth | 1.44 ± 0.98 | 4.43 ± 1.61 | 52.453 | <0.001\* |

**Key;** Mean values are significant p≤0.05

Table 3 shows the comparison between HIV positive pregnant women at third trimester on HAART combination TDF/3TC/EFV versus HAART combination AZT/3TC/NVP.In comparison with theHIV negative third trimester pregnancy which served as control, there was no statistically significant difference between the age of HIV positive third trimester pregnancy on HAART combination TDF/3TC/EFV, and those on HAART combination AZT/3TC/NVP (32.17 ± 4.81 vs 32.97 ± 5.50; 32.17 ± 4.81 vs 31.31 ± 6.84; p > 0.05). Mean aspartate aminotransferase (AST) level of control participants was significantly lower in comparison with HIV positive pregnant women at third trimester on TDF/3TC/EFV (20.23 ± 4.59 vs 25.20 ± 8.73; p=0.015), and HIV positive pregnant women at third trimester on AZT/3TC/NVP (20.23 ± 4.59 vs 31.46 ± 10.64; p < 0.001). Those on TDF/3TC/EFV had significantly lower mean AST when compared with those on AZT/3TC/NVP (p=0.002).

Mean alanine aminotransferase (ALT) level of control participants was not significantly lower in comparison with HIV positive pregnant women at third trimester on TDF/3TC/EFV (17.83 ± 5.10 vs 18.69 ± 8.71; p > 0.05). HIV positive pregnant women at third trimester on AZT/3TC/NVP had significantly elevated mean ALT level than control (28.03 ± 9.30 vs 17.83 ± 5.10; p < 0.001). Those on AZT/3TC/NVP had significantly higher mean ALT when compared with those on TDF/3TC/EFV (p <0.001).

In comparison with theHIV negative control, there was no statistically significant difference between the mean MDA level of HIV positive third trimester pregnancy on HAART combination TDF/3TC/EFV, and those on HAART combination AZT/3TC/NVP (2.97 ± 0.43 vs 2.46 ± 0.64; 3.02 ± 2.86 vs 2.46 ± 0.64; p > 0.05).

The mean D-dimer level of HIV positive third trimester pregnancy on HAART combination TDF/3TC/EFV was significantly elevated in comparison with control (990.14 ± 655.86 vs 486.46 ± 268.34; p <0.001) and also significantly elevated when compared with those on HAART combination AZT/3TC/NVP (990.14 ± 655.86 vs 719.06 ± 509.89; p=0.027).

The mean C-reactive protein level of HIV positive third trimester pregnancy on HAART combination TDF/3TC/EFV was significantly elevated in comparison with control (5.52 ± 1.42 vs 4.11 ± 0.76; p <0.001) and also significantly elevated when compared with those on HAART combination AZT/3TC/NVP (5.52 ± 1.42 vs 4.27 ± 1.16 vs ; p=0.027). There is no statistically significant difference in CD4+ between HIV positive pregnant women at third trimester on HAART combination TDF/3TC/EFV and HAART combination AZT/3TC/NVP (369.29 ± 141.35 vs 413.14 ± 148.12; p=0.209).

**Table 3a**. Comparison between HIV positive pregnant women at third trimester on HAART combination TDF/3TC/EFV versus HAART combination AZT/3TC/NVP using Analysis of Variance.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **HIV negative Control at third trimester**  **(n=35)** | **HIV positive women at third trimester on TDF/3TC/EFV**  **(n=35)** | **HIV positive women at third trimester on AZT/3TC/NVP**  **(n=35)** | **F-value** | **p-value** |
| Age (Years) | 32.17 ± 4.81a | 32.97 ± 5.50a | 31.31 ± 6.84a | 0.720 | 0.489 |
| AST (IU/L) | 20.23 ± 4.59a | 25.20 ± 8.73b | 31.46 ± 10.64c | 15.779 | 0.000 |
| ALT (IU/L) | 17.83 ± 5.10a | 18.69 ± 8.71a | 28.03 ± 9.30b | 17.835 | 0.000 |
| MDA (nmol/mL) | 2.46 ± 0.64a | 2.97 ± 0.43a | 3.02 ± 2.86a | 1.145 | 0.322 |
| D-Dimer (ng/mL) | 486.46 ± 268.34a | 990.14 ± 655.86b | 719.06 ± 509.89a | 8.755 | 0.000 |
| CRP (mg/L) | 4.11 ± 0.76a | 5.52 ± 1.42b | 4.27 ± 1.16a | 15.948 | 0.000 |
| CD4+ |  | 369.29 ± 141.35 | 413.14 ± 148.12 | -1.267**#** | 0.209 |

**Key;** Mean values are significant p≤0.05;  **#,** Independent sample T-test; any two comparing mean values with different superscript a, b, c are significantly different with p≤0.05.

**Table 3b.** Post hoc for comparison between HIV positive pregnant women at third trimester on HAART combination TDF/3TC/EFV versus HAART combination AZT/3TC/NVP

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **AST (IU/L)** | **ALT (IU/L)** | **D-Dimer (ng/mL)** | **CRP (mg/L)** |
| **Control**  **vs**  **HIV positive pregnant women on TDF/3TC/EFV** | 0.015 | 0.652 | 0.000 | 0.000 |
| **Control**  **vs**  **HIV positive pregnant women on AZT/3TC/NVP** | 0.000 | 0.000 | 0.056 | 0.554 |
| **HIV positive pregnant women on TDF/3TC/EFV**  **vs**  **HIV positive pregnant women on AZT/3TC/NVP** | 0.002 | 0.000 | 0.027 | 0.000 |

Table 4 represents the mean distribution of fetal (newborn) indices. Newborns of HIV negative pregnant women which served as control, had significantly higher mean fetal weight at birth when compared with Newborns of HIV positive pregnant women on TDF/3TC/EFV (3.31 ± 0.39 vs 2.77 ± 0.49; p < 0.001), but was not significantly elevated when compared with newborn of HIV positive pregnant women on AZT/3TC/NVP (3.31 ± 0.39 vs 3.10 ± 0.43; p=0.056).

Newborns of HIV positive pregnant women on TDF/3TC/EFV had significantly lower fetal birth weight when compared with newborn of HIV positive pregnant women on AZT/3TC/NVP (2.77 ± 0.49 vs 3.10 ± 0.43; p=0.002), while there was no significant difference in their men fetal bilirubin levels at birth (0.97 ± 0.18 vs 0.98 ± 0.17; p>0.05).

Mean total bilirubin at 72 hours after birth of newborns of HIV negative pregnant women (control) was lower when compared to the significantly higher mean total bilirubin levels at 72 hours after birth of newborns of HIV positive pregnant women on TDF/3TC/EFV (1.44 ± 0.98 vs 4.91 ± 4.00; p < 0.001), and newborn of HIV positive pregnant women on AZT/3TC/NVP (1.44 ± 0.98 vs 3.95 ± 1.71; p=0.007). Mean total bilirubin at 72 hours after birth of newborns of HIV positive pregnant women on TDF/3TC/EFV though more elevated than in newborns of HIV positive pregnant women on AZT/3TC/NVP, the difference was not statistically significant (p > 0.05).

**Table 4a**. Mean distribution of fetal (newborn) indices of HIV positive pregnant women on TDF/3TC/EFV and AZT/3TC/NVP using analysis of variance statistics

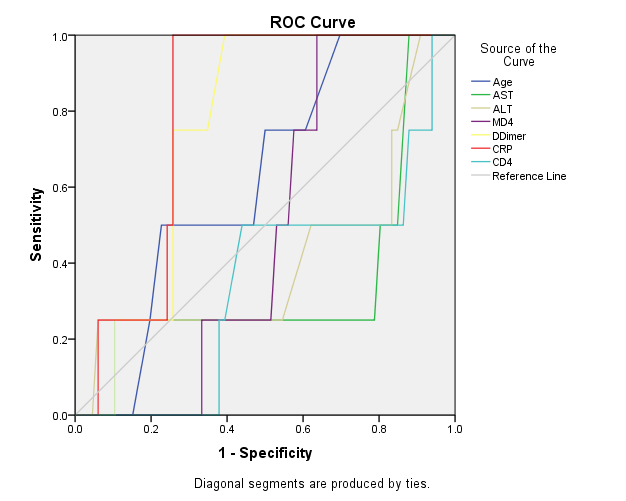
|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Newborn of HIV negative control**  **(n=35)** | **Newborn of HIV positive pregnant on TDF/3TC/EFV**  **(n=35)** | **Newborn of HIV positive pregnant women on AZT/3TC/NVP**  **(n=35)** | **F-value** | **p-value** |
| Fetal Birth weight (kg) | 3.31 ± 0.39a | 2.77 ± 0.49b | 3.10 ± 0.43a | 13.035 | 0.000 |
| Total Bilirubin at 24 hours of birth | 0.96 ± 0.18a | 0.97 ± 0.18a | 0.98 ± 0.17a | 0.085 | 0.918 |
| Total Bilirubin at 72 hours after birth | 1.44 ± 0.98a | 4.91 ± 4.00b | 3.95 ± 1.71b | 7.697 | 0.001 |

Key; any two comparing mean values with different superscript a, b, c are significantly different with p≤0.05.

Table 4b. Post hoc for mean distribution of fetal (newborn) indices of HIV positive pregnant women on TDF/3TC/EFV and AZT/3TC/NVP

|  |  |  |
| --- | --- | --- |
|  | Fetal Birth weight (kg) | Total Bilirubin at 72 hours after birth |
| **Control**  **vs**  **HIV positive pregnant on TDF/3TC/EFV** | 0.000 | 0.000 |
| **Control**  **vs**  **HIV positive pregnant on AZT/3TC/NVP** | 0.056 | 0.007 |
| **HIV positive pregnant women on TDF/3TC/EFV**  **vs**  **HIV positive pregnant women on AZT/3TC/NVP** | 0.002 | 0.296 |

Figure 1 is a Receiver operating characteristics curve which visualizes the sensitivity and specificity of the various parameters in predicting an abnormal fetal outcome. With an area under the ROC curve (AUC) of 0.619, maternal age had a moderate discriminating power in predicting abnormal fetal birth weight in HIV positive pregnant women in third trimester on HAART combination TDF/3TC/EFV and AZT/3TC/NVP. D-Dimer with an AUC of 0.752 and C-reactive protein with an AUC of 0.795 had moderate to strong sdiscriminating powers in predicting abnormal fetal birth weight in HIV positive pregnant women in third trimester on HAART combination TDF/3TC/EFV and AZT/3TC/NVP.



**Figure 1.** Receiver operating characteristics of age, D-dimer, aminotransferases, MDA, CD4 and CRP in predicting abnormal fetal birth weight in HIV positive pregnant women in third trimester on HAART combination TDF/3TC/EFV and AZT/3TC/NVP.

**Table 5**. Values for receiver operating characteristics of age, D-dimer, aminotransferases, MDA, CD4 and CRP in predicting abnormal fetal birth weight in HIV positive pregnant women in third trimester on HAART combination TDF/3TC/EFV and AZT/3TC/NVP.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Area Under Curve | 95% CI | Asymptotic Sig. |
| Age (Years) | 0.619 | 0.405 – 0.834 | 0.109 |
| AST (IU/L) | 0.343 | 0.022 – 0.664 | 0.294 |
| ALT (IU/L) | 0.413 | 0.083 – 0.743 | 0.561 |
| MDA (nmol/mL) | 0.485 | 0.330 – 0.639 | 0.919 |
| D-Dimer (ng/mL) | 0.752 | 0.621 – 0.883 | 0.092 |
| CRP (mg/L) | 0.795 | 0.676 – 0.915 | 0.048 |
| CD4+ | 0.348 | 0.86 – 0.611 | 0.311 |

Table 6 shows the factors predicting abnormal fetal outcome between study participants on TDF/3TC/EFV or AZT/3TC/NVP, using a Multiple Logistics Regression model. The analysis revealed that D-dimer (Odds Ratio [OR]: 1.003; 95% CI: 0.999 – 1.006), C-reactive protein (OR: 0.032; 95% CI: 00.004 – 0.274) and Alanine aminotransferase (OR: 1.234; 95% CI: 1.034 – 1.474) were predictors of abnormal fetal outcome between third trimester females on TDF/3TC/EFV and AZT/3TC/NVP (An odds ratio >1 implies that there is a significant likelihood that there will be an abnormal fetal outcome).

**Table 6.** Factors predicting abnormal fetal outcome between TDF/3TC/EFV users or AZT/3TC/NVP use by HIV positive pregnant women at third trimester using a Multiple Logistics Regression model

|  |  |  |  |
| --- | --- | --- | --- |
| **Factors** | **Odds ratio (95% Confidence Interval)** | **Wald** | **p-value** |
| ALT | 1.234 (1.034 – 1.474) | 5.417 | 0.020 |
| C-reactive protein | 0.032 (0.004 – 0.274) | 9.868 | 0.002 |
| D-Dimer | 1.003 (0.999 – 1.006) | 2.761 | 0.047 |

**Table 7** Correlations between maternal indices of pregnant women on HAART and fetal birth weight

|  |  |  |
| --- | --- | --- |
|  | **Pearson’s (r) Correlation Coefficient** | **p-value** |
| Age (Years) | -0.653\*\* | <0.001 |
| MDA (nmol/mL) | -0.270\* | 0.024 |
| D-Dimer (ng/mL) | -0.818\*\* | <0.001 |
| CRP (mg/L) | -0.836\*\* | <0.001 |
| CD4+ | -0.566\*\* | <0.001 |
| Fetal bilirubin at 72 hours | -0.741\*\* | <0.001 |

Key: \*\*. Correlation is significant at the 0.01 level (2-tailed).

\* .Correlation is significant at the 0.05 level (2-tailed).

**Table 8**. Correlations between maternal indices of pregnant women on HAART and fetal bilirubin at 72 hours

|  |  |  |
| --- | --- | --- |
|  | **Pearson’s (r) Correlation Coefficient** | **p-value** |
| Age (Years) | 0.723\*\* | <0.001 |
| AST (IU/L) | 0.372\*\* | 0.002 |
| ALT (IU/L) | 0.322\*\* | 0.007 |
| MDA (nmol/mL) | 0.302\* | 0.011 |
| D-Dimer (ng/mL) | 0.848\*\* | <0.001 |
| CRP (mg/L) | 0.761\*\* | <0.001 |
| CD4+ | 0.499\*\* | <0.001 |

Key: \*\*. Correlation is significant at the 0.01 level (2-tailed).

\* .Correlation is significant at the 0.05 level (2-tailed).

**DISCUSSION**

This study investigated the potential of maternal biochemical markers including D-dimer, C-reactive protein (CRP), malondialdehyde (MDA), and aminotransferases (AST and ALT) as predictors of neonatal jaundice and low birth weight among HIV positive pregnant women in their third trimester who were compliant with HAART regimens. The findings demonstrate a significant relationship between maternal inflammatory and hepatic biomarkers and adverse neonatal outcomes, particularly in women receiving the TDF/3TC/EFV combination. Elevated levels of AST and ALT observed among HIV positive women, especially those on AZT/3TC/NVP, are consistent with prior reports that antiretroviral therapy may induce hepatocellular injury or hepatic enzyme induction during pregnancy (15, 16, 17). While ALT was a significant predictor of abnormal neonatal outcome in logistic regression analysis, AST, although elevated, did not show a statistically significant predictive value in this context. The ALT elevation in the AZT/3TC/NVP group may reflect a higher degree of hepatic stress or mitochondrial toxicity associated with zidovudine based therapy (18).

D-dimer and CRP were markedly elevated in the TDF/3TC/EFV group and exhibited strong positive correlations with elevated neonatal bilirubin levels and low birth weight. These findings align with literature suggesting that elevated maternal D-dimer and CRP levels reflect systemic inflammation and hypercoagulability, which are known to compromise placental perfusion and fetal growth (19-21). The ROC curve analysis confirmed their utility as moderate-to-strong predictors of adverse neonatal outcomes, with CRP (AUC = 0.795) showing the strongest discriminative ability.

The significant increase in total bilirubin at 72 hours among neonates born to HIV positive mothers on HAART, particularly those on TDF/3TC/EFV, supports the hypothesis that maternal systemic inflammation may influence fetal hepatic bilirubin metabolism or enterohepatic circulation. Although total bilirubin at 24 hours did not differ significantly between groups, the sharp rise at 72 hours indicates delayed clearance, which may be attributable to subclinical hepatic immaturity or oxidative stress linked to HAART exposure (22, 23). Previous studies have linked maternal viral infection to intrauterine fetal disorders (24).

Interestingly, MDA levels were not significantly different between HAART and control groups, yet a modest correlation was found with fetal bilirubin and birth weight. MDA is a marker of lipid peroxidation, and its association with neonatal outcomes, though less pronounced, warrants further exploration, especially considering previous studies linking oxidative stress in pregnancy with low birth weight and neonatal jaundice (25, 26).

CD4 count did not differ significantly between HAART groups, suggesting that immune status was relatively balanced; however, its significant correlations with both fetal birth weight and bilirubin at 72 hours suggest that maternal immunologic competence may still influence neonatal outcomes. Prior evidence indicates that lower maternal CD4+ counts are associated with increased risk of intrauterine growth restriction and neonatal morbidity, even in HAART compliant individuals (27), and decline in CD4+ count in women with HIV during pregnancy has been attributed to gestational haemodilution (28).

Taken together, these findings support the clinical value of routinely monitoring D-dimer, CRP, and aminotransferases during the third trimester in HIV-positive pregnancies. Their predictive ability for low birth weight and neonatal hyperbilirubinemia underscores their relevance in risk stratification and perinatal planning. Moreover, the differential impact observed between the two HAART regimens suggests a potential need for regimen-specific monitoring protocols.

This study has a few limitations. First, the sample size, although sufficient for preliminary inference, may not be adequately powered to generalize findings across diverse populations. Secondly, the study did not stratify for other potential confounders such as nutritional status, co-infections, or socioeconomic variables, which could affect both maternal biomarker levels and fetal outcomes. Lastly, the absence of longitudinal neonatal follow-up data limits insights into the long-term consequences of these early life biochemical alterations.

**CONCLUSION**

In conclusion, this study highlights the predictive value of D-dimer, CRP, and ALT in identifying HIV positive pregnant women at risk for delivering neonates with jaundice and low birth weight. These markers can serve as useful adjuncts to routine antenatal care in resource limited settings, particularly when tailored to the specific HAART regimen in use.

**ETHICAL APPROVAL & CONSENT**

Ethical approval was obtained from the ethics committee of the State Hospital Management Board, and all participants provided written informed consent.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models, etc., have been used during the writing or editing of manuscript.

**REFERENCES**

1. World Health Organization. Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. Geneva: WHO; 2012.
2. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. AIDS. 2007;21(8):1019–1026.
3. Mirochnick M, Capparelli E. Pharmacokinetics of antiretrovirals in pregnant women. Clin Pharmacokinet. 2004;43(15):1071–1087.
4. Floridia M, Tamburrini E, Ravizza M, et al. Hepatotoxicity during pregnancy in HIV-infected women: the role of highly active antiretroviral therapy. Clin Infect Dis. 2006;42(3):385–386.
5. Neuhaus J, Jacobs DR, Baker JV, et al. Markers of inflammation, coagulation, and renal function are elevated in adults with HIV infection. J Infect Dis. 2010;201(12):1788–1795.
6. Kuller LH, Tracy R, Belloso W, et al. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. PLoS Med. 2008;5(10):e203.
7. Kobayashi T, Araki S, Maeda S. D-dimer levels and pregnancy outcomes. Thromb Res. 2014;134(6):1232–1236.
8. Ferguson KK, McElrath TF, Chen YH, Mukherjee B, Meeker JD. Longitudinal profiling of inflammatory markers during pregnancy. Am J Reprod Immunol. 2014;72(3):326–336.
9. Tenorio AR, Zheng Y, Bosch RJ, et al. Soluble markers of inflammation and coagulation but not T-cell activation predict non-AIDS-defining morbid events during suppressive antiretroviral treatment. J Infect Dis. 2014;210(8):1248–1259.
10. Kintu K, Malaba TR, Nakiboneka-Ssenabulya D, et al. Inflammatory responses to efavirenz-based HAART in pregnant women. AIDS Res Hum Retroviruses. 2015;31(5):460–465.
11. Elbim C, Pillet S, Prevost MH, et al. Redox and activation status of monocytes from human immunodeficiency virus-infected patients: relationship with viral load. J Virol. 1999;73(6):4561–4566.
12. Suresh DR, Annam V, Pratibha K, Prasad BV. Oxidative stress and antioxidant status in HIV positive pregnant women. Indian J Clin Biochem. 2010;25(3):242–246.
13. Blanche S, Tardieu M, Rustin P, et al. Persistent mitochondrial dysfunction and perinatal exposure to antiretroviral nucleoside analogues. Lancet. 1999;354(9184):1084–1089.
14. Paternoster L, Evans DM, Nohr EA, et al. Maternal CRP and risk of low birth weight. Int J Epidemiol. 2011;40(4):1092–1100.
15. Mehta U, Durrheim DN, Blockman M, et al. Adverse drug reactions in adult medical inpatients in a South African hospital serving a community with a high HIV/AIDS prevalence: prospective observational study. Br J Clin Pharmacol. 2008;65(3):396-406.
16. Kamga HLF, Assob JCN, Nde PF, et al. The effects of antiretroviral treatment on liver function enzymes among HIV infected outpatients attending the Central Hospital of Yaoundé, Cameroon. Afr J Clin Exp Microbiol. 2010;11(3):174-178.
17. Strauss K-LE, Phoswa WN, Mokgalaboni K. The Impact of Antiretroviral Therapy on Liver Function among Pregnant Women Living with HIV in Co-Existence with and Without Pre-Eclampsia. Viruses. 2025; 17(1):28. 10.3390/v17010028.
18. Moyle GJ. Mitochondrial toxicity of antiretroviral drugs: leading to lactic acidosis, hepatic steatosis and lipodystrophy. HIV Med. 2000;1(2):77-81.
19. Rizk DEE, El-Said M, Al-Marzouqi AH, et al. Maternal plasma D-dimer concentrations in pregnancy, labor, and the puerperium. Int J Gynaecol Obstet. 2001;74(3):225–231.
20. Costantine MM, McNeer E, Garovic VD, et al. Inflammatory and thrombotic markers in women with preeclampsia and fetal growth restriction. Obstet Gynecol. 2012;119(5):1121–1128.
21. Kramer MS, Kahn SR, Rozen R, et al. Vasculopathic and thrombophilic risk factors for spontaneous preterm birth. Int J Epidemiol. 2009;38(3):715–723.
22. Maisels MJ, Newman TB. Neonatal hyperbilirubinemia and kernicterus—not gone but sometimes forgotten. Pediatrics. 2012;129(4):770–773.
23. Olusanya BO, Kaplan M, Hansen TW. Neonatal hyperbilirubinemia: a global perspective. Lancet Child Adolesc Health. 2018;2(8):610–620.
24. Dubucs C, Groussolles M, Ousselin J, et al. Severe placental lesions due to maternal SARS-CoV-2 infection associated to intrauterine fetal death. Hum Pathol.2022;121, 46-55. 10.1016/j.humpath.2021.12.012.
25. Jain SK, Wise R. Relationship between elevated lipid peroxides and decreased birth weight in pregnancies complicated by preeclampsia. J Am Coll Nutr. 1995;14(6):643–647.
26. Tadesse S, Alemu A, Ayele T, et al. Malondialdehyde and vitamin E levels in preterm and full-term neonates: evidence from a case–control study. Ital J Pediatr. 2019;45:70.
27. Ndirangu J, Newell ML, Bland RM, et al. Maternal HIV infection associated with increased risk of low birth weight and prematurity: a meta-analysis. J Infect Dis. 2012;206(5):687–694.
28. Chilaka VN, Konje JC. HIV in pregnancy- An update. Eur J Obstet Gynecol Reprod Biol. 2021. 256, 484-491.10.1016/j.ejogrb.2020.11.034