

CHANGES IN THE HEMATOLOGICAL PARAMETERS OF NEONATES FROM MOTHERS WITH PREECLAMPSIA AND ECLAMPSIA IN SOKOTO, NIGERIA

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ABSTRACT: Background: Pregnancy is a natural physiological process in which the health of both the mother and the foetus influences neonatal outcomes. Complications such as preeclampsia and eclampsia can affect the foetal haematological parameters. This study aimed to determine and compare haematological parameters in neonates born to mothers with preeclampsia or eclampsia and in those born to normotensive mothers.

Methods: This hospital-based cross-sectional comparative study encompassed a total of 168 neonates, with 56 neonates each born to mothers diagnosed with preeclampsia, eclampsia, and normotensive conditions. Participants were recruited from the labor and preeclamptic wards of Usmanu Danfodiyo University Teaching Hospital and the Specialist Hospital, Sokoto. The preeclampsia and eclampsia groups functioned as

the study cohorts, whereas the normotensive group served as the control cohort. A complete blood count was conducted on fetal cord blood utilizing a 5-part Mythic Haematology Analyser. Reticulocyte counts were determined, and peripheral blood smears were examined. Data analysis was performed using SPSS version 27, with a p-value threshold of ≤ 0.05 deemed statistically significant.

RESULTS: In this study, the mean cord blood haemoglobin concentration was 15.15 ± 1.71 , 15.20 ± 1.67 , and 14.04 ± 1.80 g/dl for neonates born to mothers with preeclampsia, eclampsia, and normotensive conditions, respectively. The mean WBC count was significantly lower in cord blood from neonates born to mothers with preeclampsia ($9.02 \pm 1.17 \times 10^9/L$) and eclampsia ($8.70 \pm 1.15 \times 10^9/L$) than in normotensive neonates ($13.51 \pm 2.50 \times 10^9/L$). Additionally, the mean platelet count was significantly lower in cord blood from neonates born to mothers with preeclampsia ($163.16 \pm 55.43 \times 10^9/L$) and eclampsia ($162.77 \pm 52.56 \times 10^9/L$) than in cord blood from normotensive neonates ($198.18 \pm 41.55 \times 10^9/L$), with a p-value < 0.05 . There was no significant difference in the mean cord blood haematological parameters among neonates born to mothers with mild, moderate, or eclampsia.

CONCLUSION: The study reveals that neonates born to mothers with preeclampsia and eclampsia exhibit higher mean levels of haemoglobin, haematocrit, and reticulocytes. Additionally, a reduction in the mean white blood cell (specifically neutrophils) and platelet counts was observed in these neonates. Timely haematological assessments are crucial to enable the early detection and mitigation of risks such as hyperviscosity syndrome, neonatal sepsis, and bleeding. This proactive strategy can substantially decrease morbidity and improve the survival outcomes for neonatal patients.

Keywords: *Cord blood, Eclampsia, Full blood count, Preeclampsia, Neonate, Sokoto*

Introduction

Hypertensive disorders of pregnancy are categorized into chronic hypertension, gestational hypertension, [1,2] and preeclampsia-eclampsia superimposed on chronic hypertension. The preeclampsia-eclampsia syndrome has been associated with substantial maternal and perinatal morbidity and mortality. [1,2] Preeclampsia is characterised by the onset of hypertension after 20 weeks of gestation, accompanied by at least one maternal organ

dysfunction or failure. [1,3] Eclampsia is defined as the occurrence of seizures in a patient with preeclampsia. [1,3]

In preeclampsia, reduced uteroplacental blood flow leads to diminished foetal blood supply, causing local placental hypoxia, ischaemia, and necrosis. [2,3,4] The hypoxic placenta releases vasoactive substances that activate and ultimately lead to maternal endothelial damage and dysfunction.

Numerous studies have reported changes in umbilical cord blood parameters in neonates born to mothers with preeclampsia, including increased normoblasts secondary to uteroplacental hypoperfusion. While some studies observed elevated RBC count, haemoglobin, haematocrit, MCV, MCHC, RDW, and reticulocyte counts, others found no significant differences in erythrocyte indices.[5,6] Higher RDW, circulating reticulocytes, RPI, and nucleated RBCs suggest enhanced RBC production.[7] Exaggerated erythropoiesis with increased nucleated RBCs is due to heightened erythropoietin secretion induced by placental hypoxia.[5] Thus, an increased count of nucleated RBCs is considered a hypoxia marker.[5]

Increased erythropoiesis can lead to dysplastic changes, such as spherocytosis, anisocytosis, and polychromasia, in the cord blood of neonates born to mothers with preeclampsia.[6]

Total leukocyte counts were significantly lower in neonates born to mothers with preeclampsia.[6] Neutropenia is reported in nearly 50% of preeclamptic neonates[4] and up to 80% when maternal hypertension is severe (diastolic blood pressure $\sim$ 110 mmHg).[5,8] Proposed mechanisms for neutropenia include an unidentified inhibitor of neutrophil production produced by the placenta, reduced growth factors that stimulate neutrophil production, and diminished progenitor cell responsiveness to these factors.[6] Uteroplacental insufficiency in preeclampsia, resulting in foetal hypoxia, inhibits foetal bone marrow production of the myeloid lineage, manifesting as reduced neutrophil production.[5] These neonates may be at increased risk of nosocomial infection in the first weeks of life.[6]

Thrombocytopenia recorded in neonates born to preeclamptic women might be related to intrauterine hypoxia exposure and resultant suppression of megakaryocytic

proliferation.[6] Other suggested mechanisms include the presence of an undefined placental factor transported to the baby, leading to DIC and causing thrombocytopenia in the newborn; thrombocyte adherence to damaged endothelial regions caused by segmental vasospasm and vasodilation in the placenta of hypertensive mothers; and an abnormal placental endothelial surface causing thrombocyte destruction and resultant thrombocytopenia.[6]

Studies conducted in developed and developing countries on neonates born to hypertensive women have reported inconsistent abnormalities in haematological parameters, particularly for white blood cells, red blood cells, and their indices, due to variations in ethnicity, nutrition, genetics, and environmental factors.[4,6] Additionally, data on the haematological profile of neonates born to mothers with preeclampsia and eclampsia in Nigeria are scarce. Therefore, this study aimed to determine the haematological parameters of neonates born to mothers with preeclampsia and eclampsia.

METHODS

Study type, location, and duration

This was a hospital-based comparative cross-sectional study conducted between March 2022 and November 2022 in the preeclamptic duty rooms and labour rooms of the Departments of Obstetrics and Gynaecology at UDUTH and Specialist Hospital, Sokoto State, Nigeria. The study was approved by the ethical committees of the relevant institutions, and informed consent was obtained from the mothers enrolled in the study. A convenience sampling technique was used to enrol each group of participants.

Study population

The study included 168 neonates: the case groups comprised 56 neonates delivered by mothers with preeclampsia, 56 by mothers with eclampsia, and 56 served as controls.

Inclusion criteria

Neonates born to mothers with preeclampsia or eclampsia were recruited as cases, while those born to normotensive mothers were enrolled as a control group. Preeclampsia is defined by a systolic blood pressure (BP) ≥ 140 mmHg or diastolic BP ≥ 90 mmHg on 2 occasions (at least 4 hours apart) in a previously normotensive patient. Severe

preeclampsia: systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg. Proteinuria: urine dipstick proteinuria of at least +1. Eclampsia: convulsion in a patient with preeclampsia.

Exclusion criteria

Neonates with congenital malformations and severe birth asphyxia. Neonates born to mothers with diabetes mellitus, hypertension diagnosed before 20 weeks of gestation, severe anaemia, chronic hypertension, renal disease, heart disease, and connective tissue disease. Maternal use of aspirin and neonates of mothers who are not taking folic acid.

Study procedure

Immediately after delivery, 3 mL of cord blood was collected into a vacutainer specimen bottle containing ethylene diamine tetraacetic acid (EDTA) as an anticoagulant, and a complete blood count (CBC) was performed using a 5-part differentiation MYTHIC 60 automated cell analyser. A peripheral blood smear stained with Leishman stain was examined to confirm the haemogram findings. Reticulocyte counts were determined manually using new methylene blue. The estimated counts were expressed as a percentage of reticulocytes relative to the total number of red cells.

Statistical analysis

Data Analysis and Management

Data were compiled and analysed using the Statistical Package for the Social Sciences (IBM SPSS Statistics v27). The Shapiro-Wilk test was used to assess the normality of the data distribution. Quantitative variables were presented as mean and standard deviation if normally distributed, and as median and inter-quartile range if skewed. Qualitative variables were presented as percentages. Independent-samples t-tests and ANOVA were used to compare the means of neonatal parameters. A ninety-five per cent (95%) confidence interval was used, and a p-value of ≤ 0.05 was considered significant.

RESULTS

Details of obstetric and neonatal characteristics are shown in Table 1. The gestational age at delivery in the preeclampsia and eclampsia groups was lower than in the normotensive group. There was a significant difference in gestational age at delivery between the

preeclampsia and eclampsia groups (37.04 ± 0.7 and 36.7 ± 0.5 weeks, $p=0.007$), and between the eclampsia and normotensive groups (36.70 ± 0.5 and 37.23 ± 0.47 weeks, $p<0.001$). However, the gestational age at delivery between the preeclampsia and normotensive groups was similar ($p=0.153$). Apgar scores at the first and fifth minutes were significantly lower in the preeclampsia and eclampsia groups compared with the normotensive group ($p<0.05$). Birth weight in the preeclampsia and eclampsia groups was significantly lower than in the normotensive group ($p<0.001$), but was similar between the preeclampsia and eclampsia groups ($p=0.130$).

Table 1: Obstetric and neonatal variables of the study participants, n=50 for each group

Variable	Study participants			ANOVA	
	Preeclampsia Mean (SD)	Eclampsia Mean (SD)	Normotensive Mean (SD)	F- test	p-value
Mean maternal age in years (SD)	24.18 (6.23)	24.21 (5.25)	24.20 (4.51)	12.261	0.038
Parity	1.86 (1.26)	1.27 (0.80)	1.84 (1.05)	6.06	0.003
ANC visits	1.43 (0.50)	1.31 (0.47)	1.71 (0.46)	10.570	<001
SBP (mmHg) at presentation	159.59 (11.8)	206.07(17.6)	111.75 (12.0)	629.10	<0.001
DBP(mmHg) at presentation	107.6 (9.6)	122.4 (6.5)	65.3 (7.5)	774.70	<0.001
EGA at delivery	37.04 (0.7)	36.7 (0.5)	37.23 (0.47)	12.30	<0.001
Apgar score					
At 1 min	5.95 (0.75)	5.77 (0.71)	7.50 (0.63)	103.78	<0.001
At 5 min	8.43 (1.01)	8.00 (0.89)	9.68 (0.51)	61.69	<0.001
Neonatal birth weight	2.43 (0.34)	2.28 (0.29)	3.30 (0.50)	110.23	<0.001

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure

The comparison of cord blood haematologic parameters across study groups and controls is presented in Table II. Neonates of mothers with preeclampsia and eclampsia had significantly higher mean haematocrit values than those of normotensive mothers, $p<0.001$. The neonates of mothers with preeclampsia and eclampsia had mean Hct, MCV and RDW values that were not significantly different. However, their MCV and RDW differed significantly from those of neonates of normotensive mothers. The cord blood reticulocyte count for neonates of mothers with preeclampsia and eclampsia was

significantly higher than that of normotensive mothers, $p < 0.001$. Neonates of mothers with preeclampsia and eclampsia had significantly lower mean WBC, neutrophil and platelet values than those of normotensive mothers, $p < 0.001$.

Table II: Cord blood Haematological parameters

Variables	Study participants			ANOVA	
	Preeclampsia	Eclampsia	Normotensive	F-test	p-value
Hb (g/dl)	15.15 (0.71)	15.20 (0.67)	14.02 (0.80)	47.08	<0.001
Hct (%)	46.72 (1.71)	46.62 (1.60)	43.20 (2.35)	61.07	<0.001
WBC ($\times 10^9/L$)	9.02 (1.17)	8.70 (1.15)	13.51 (2.50)	135.68	<0.001
PLT ($\times 10^9/L$)	163.16 (55.43)	162.77 (52.56)	198.18 (21.55)	11.03	<0.001
Neutrophils ($\times 10^9/L$)	2.68 (0.62)	2.63 (0.56)	6.17 (1.61)	210.52	<0.001
Lymphocytes ($\times 10^9/L$)	4.92 (0.99)	4.82 (1.01)	5.44 (1.43)	3.76	0.025
MCV (fl)	110.67 (9.36)	110.51 (9.36)	108.17 (9.30)	0.98	<0.001
MRDW-CV (%)	12.79 (1.48)	12.77 (1.79)	12.88 (1.46)	0.72	0.931
RETIC (%)	6.31 (0.64)	9.37 (1.23)	2.95 (0.37)	530.48	<0.001

WBC, White Blood Cells; MCV, Mean Corpuscular Volume; RDW-CV, Red cell Distribution Width -Corpuscular Volume; g/dL, gram/deciliter; %, percent; fl, femtoliter; p -values are significant at < 0.005 , p -values < 0.05

DISCUSSION

Preeclampsia and eclampsia are associated with abnormal placentation, oxidative stress and endothelial dysfunction, which can lead to impaired blood flow to the foetus. This can result in foetal growth restriction, preterm birth, intrauterine growth retardation and altered foetal blood parameters.

The study compared cord blood haematological parameters in neonates delivered to mothers with preeclampsia, eclampsia, and normotension. In this study, there was no

significant difference in the mean age of the preeclampsia, eclampsia, and normotensive mothers, $p=0.048$.

Preeclampsia is associated with premature delivery and low birth weight. This study found that the birth weights of neonates with preeclampsia and eclampsia were significantly lower than those of normotensive neonates ($p<0.001$). A similar finding was reported by Ahmet et al.[6] In preeclampsia, placental insufficiency due to reduced nutrient supply to the baby leads to IUGR.[6] The mean gestational age was lower in the preeclampsia and eclampsia groups compared with their normotensive counterparts. This difference was statistically significant between the eclampsia and normotensive neonates. Kooffreh et al. reported a similar finding in Calabar, South-South Nigeria.[9] Preeclampsia is a progressive disorder, and in some cases delivery is required to halt progression and benefit the mother and fetus.[10] Therefore, premature delivery and its consequences are recognised neonatal presentations of preeclampsia and eclampsia.[11,12]

According to a study by Roudil et al., erythrocytosis, thrombocytosis, and leucopenia are common haematological disorders in premature neonates.[13] Haemoglobin concentration was significantly higher in neonates of mothers with preeclampsia and eclampsia. This is comparable to the findings of Elgari et al.[14] and Bolat et al.[6] By contrast, Catarino et al. reported no significant difference in haemoglobin and RBC count in neonates of mothers with preeclampsia compared with those of normotensive mothers.[15] In this study, the haematocrit in neonates of mothers with preeclampsia and eclampsia was higher than in those of normotensive mothers. Kurlat et al. have shown that the risk of polycythaemia was 12.6-fold higher in babies of hypertensive mothers compared with their normotensive counterparts.[6] However, the Hct values of the neonates in this study were within the normal reference range. The reticulocyte count in neonates of mothers with preeclampsia and eclampsia was significantly higher than in normotensive neonates. A previous study by Bolat et al. has shown a significantly higher reticulocyte count in neonates of hypertensive mothers.[6] The significantly higher haemoglobin and reticulocyte percentage in neonates of mothers with preeclampsia and eclampsia at the time of delivery have been proposed to result from uteroplacental failure due to hypoperfusion and increased erythropoiesis due to hypoxia.[6]

In this study, the mean WBC count was significantly lower in the study groups than in the control group. Previous studies by Mouna et al. and Elgari et al. have shown significantly lower WBC counts in neonates of preeclampsia.[5,14] The mean neutrophil count was significantly reduced in the study group compared with the control group. However, none of the neonates recorded a value below $1.5 \times 10^9/L$. The mechanisms that result in low WBC counts, especially neutrophils, include the presence of a yet-to-be-identified inhibitor of neutrophil production elaborated by the placenta, a decrease in growth factors that stimulate neutrophil production, and a reduced response of progenitor cells to these factors.[6] Other factors include utero-placental insufficiency with a resultant hypoxic state, which occurs in preeclampsia.[5,10] This inhibits foetal bone marrow production of the myeloid lineage, manifesting as reduced neutrophil production.[5,10] Neonates with neutropenia may be at greater risk of nosocomial infection in the first weeks of life.[6] Management of neonatal neutropenia involves the use of G-CSF, G-M-CSF, intravenous immunoglobulin (IV IG) and corticosteroids.[16]

The neonates of mothers with preeclampsia and eclampsia had a significantly lower mean platelet count than those of normotensive mothers ($p < 0.001$). Low platelet counts have been reported in several studies.[5,6,14] Reduced platelet counts have been attributed to intrauterine hypoxia and consequent suppression of megakaryocytic proliferation.[5,6,17] It has also been reported that an abnormal placental endothelial surface caused thrombocyte adherence to the damaged endothelial region, resulting from segmental vasospasm and vasodilatation.[6] It has also been reported that an undefined factor that leads to DIC was transported to the baby by the placenta, causing thrombocytopenia in the newborn.[6] This finding suggests that preeclampsia and eclampsia are risk factors for thrombocytopenia in neonates. Thrombocytopenia is managed by treating the underlying conditions and the judicious use of platelet transfusions.[18]

CONCLUSION

This study has shown that neonates of mothers with preeclampsia and eclampsia are more likely to be delivered prematurely. They also have an increased risk of developing high mean haemoglobin, haematocrit, and reticulocyte count. This study also showed that neonates of mothers with preeclampsia and eclampsia have an increased risk of having low WBC, neutrophil, and platelet counts than neonates of normotensive mothers.

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