



## **Cord Blood Haematological Profiling Study: Predictive Markers of Neonatal Health Status at Birth in Anyigba, North Central Nigeria**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Authors Shedrack Egbunu Akor, AM, AAF and PO collected the samples and data. Author Shedrack Egbunu Akor did the laboratory and statistical analyses. Authors Shedrack Egbunu Akor, DAM, Samuel Enejo Abah, SPOA and AM participated in writing the manuscript. Author Shedrack Egbunu Akor conceived the idea and wrote the manuscript. Authors BA, DAM, SPOA and Samuel Enejo Abah proof read the manuscript. All authors read and approved the final version of this manuscript.*

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## ABSTRACT

**Background:** Neonatal mortality refers to the death of a live-born babies within the first 28 days of life remains a global public health challenge. Cord blood being the medium of communication, transmission of nutrients and wastes between mothers and fetus can reflect the health status of baby at birth if properly utilized. Owing to multiple factors involved in neonatal mortality, this study used umbilical cord blood haematological parameters to ascertain the health status of neonates at birth, the aim of this study is to use umbilical cord blood haematological parameters for management of neonates at birth.

**Methodology:** This research is a cross-sectional study carried out at the Departments of Obstetrics and Gynaecology and Medical Laboratory Department, Kogi State University Teaching Hospital, Anyigba, North Central Nigeria between January, and December, 2020. Cord blood from 164 babies delivered in Kogi State University Teaching Hospital, Grimard Catholic Hospital, and Amazing Grace Hospital between January and December, 2020 were analyzed for haematological parameters using Sysmex XP-300 automated haematology analyzer. The data obtained were expressed as mean  $\pm$  standard deviation using SPSS statistical software, version 23.0. The indicator level of statistical significance was set at  $p < 0.05$ .

**Results:** The results showed significant increase ( $p < 0.05$ ) of WBC, RBC, MCV, MCH and MCHC in unstable babies compared to the stable babies, significant decrease ( $p < 0.05$ ) in the platelets, neutrophil and mixed among unstable babies compared to the stable babies, but no significant difference in PCV, haemoglobin and lymphocyte counts of both stable and unstable babies. The results also demonstrated 25 deaths per 1000 live newborn neonates within 48hour during the period of study.

**Conclusion:** This study shows that cord blood haematological parameters at birth can be used to ascertain the health status of neonates.

*Keywords: Neonatal mortality; umbilical cord; haematological parameters; stable and unstable.*

## 1. INTRODUCTION

Neonatal mortality refers to the death of a live-born babies within the first 28 days of life remains a global public health challenge. United Nations member of states, proposed Millennium Development Goal 4 to reduce under - five global neonatal mortality rate by two thirds, between 1990 and 2015 [1]. Despite global significant achievement of 19 death per 1,000 live birth that was recorded in 2015 compared to previously 36 deaths per 1000 live births in 1990 [2], It is unfortunate to know that while some countries in East Asia, Pacific, Latin America, Caribbean, and Central/Eastern Europe have made significant progress in reducing their mortality rate, many countries in South Asia and Sub-Saharan Africa including Nigeria still have high under-five mortality [3]. Globally, Nigeria contributes 6% of neonatal deaths in 2005 and between 2000 and 2010, Nigeria was ranked from third to second after India with the highest number of neonatal deaths [4,5]. In the last few years, Nigeria has experienced increased rate of child mortality due to insecurity in some parts of the country [6]. The Under-Five Mortality Rates (U5M) Nigeria Demographic and Health Survey (NDHS) 2013 reported that approximately one in every eight

live birth in Nigeria dies before their fifth birthday which is averagely 21 times higher compared to developed nations' rate [7] Preventable diseases and several risk factors are responsible for child deaths in developing countries. Malaria, congenital infections, diarrhea and Acute Respiratory Infections (ARIs), genetically-induced malfunctions, premature births, quality of antenatal and perinatal care, post-partum care and chronic malnutrition contribute immensely to childhood morbidity and mortality among newborn [8]. Cord blood being the medium of communication, transmission of nutrients and wastes between mothers and fetus can reflect the health status of baby at birth if properly utilized.

Cord blood is the blood in the attached umbilical cord and in the placenta during pregnancy and after childbirth. This blood is collected from the umbilical cord after the baby and attached placenta have been delivered. Therefore, there is no risk to both the mother and the baby during the process of cord blood collection [9]. Plasma, platelets, red blood cells and white blood cells are present in the cord blood as in adult whole blood [10]. Compromises of fetal blood flow through the umbilical cord vessels can have

serious effects on the wellbeing of the fetus and newborn. Therefore, any damage to the umbilical cord caused by either microorganisms or chemical toxins is likely to reflect on the wellbeing of the fetus [11]. In addition, the umbilical cord contains biomolecules and electrolytes, such as proteins, lipids, carbohydrates, nucleic acids/nucleotides, enzymes, chloride, sodium, bicarbonate, potassium and trace of uric acid [12].

Just like any other human tissue or organ, the umbilical cord can also be subjected to both internal and external pathological conditions. Such internal conditions include torsion, knots and inflammation, while external factors such as virus, bacteria and fungi invasion can also occur. Inflammation of umbilical cord, also known as funisitis, is a common cord pathological finding. In funisitis neutrophils move out of fetal circulation in response to endotoxin and chemokines under the influence of chemical (chemotactically) towards infected amniotic fluid [13]. Therefore, the present study uses haematological biomarkers to ascertain the health status of a neonate. The aim of this study is to use haematological parameters of umbilical cord blood for clinical management of fetus and neonates.

## **2. MATERIALS AND METHODS**

### **2.1 Study Setting**

The study was carried out at the Departments of Obstetrics and Gynaecology, and Medical Laboratory Department, Kogi State University Teaching Hospital, Anyigba, North Central Nigeria between January and December, 2020. Cord blood samples and data were collected from three Hospitals within Anyigba Metropolis, North Central Nigeria namely: Kogi State University Teaching Hospital, Grimard Catholic Hospital and Amazing Grace Hospital for the study.

### **2.2 Study Design**

This research is a cross-sectional study of newborn babies whose umbilical cord blood was assessed for haematological biomarkers.

### **2.3 Study Population and Sampling**

A total of one hundred and sixty four [164] babies were enrolled into the study.

### **2.4 Data Collection**

Parent/guardian gave their permission to be enrolled into the study and written informed consent was properly filled and signed. Vital information such as baby's weight, 48 hours observation, gestational age (number of weeks), mothers' parity, mothers' educational status, duration of labor, route of delivery and mothers' age were obtained from each participant.

### **2.5 Forty-Eight (48) Hours Baby Observation and Clinical Presentations**

Newborn participants delivered at these hospitals were subjected to direct nursing observation for the first 48hours and these observations were reviewed to classify the babies into stable and unstable based on further medical information. Babies classified as stable were those with APGAR (Appearance, Pulse, Grimace, Activity and Respiratory) scores above 6 while babies with APGAR scores below 5 score were classified as unstable. Babies with clinical presentations such as intermittent jerking, excessive crying, poor sucking reflex, petechial, conjugated jaundice, sepsis, haemolytic anaemia, hepatosplenomegaly and death within 48 hours observation were also classified as unstable participants.

### **2.6 Sample Collection**

Umbilical cord blood of each baby was collected after delivery. Small area of the cord, adjacent to the clamp was sanitized and a needle was inserted into the umbilical cord artery with a syringe, 4.5 mL of the umbilical cord blood was collected into a 5mL specimen EDTA collection tubes. The EDTA tube was inverted 8-10 times to ensure adequate anticoagulation of the specimen.

### **2.7 Haematological Assay**

The haematological analysis of umbilical cord blood was done within two hours of collection using SYSMEX XP-300 automated hematology analyzer, which provides parameters such as white blood cell, red blood cell, haemoglobin, packed cell volume, mean cell volume, mean cell haemoglobin and mean cell haemoglobin concentration, platelet and three parts differential percentage of neutrophil, lymphocyte and mixed (monocyte, eosinophil, basophil).

### 2.8 Statistical Analysis

The data obtained were expressed as mean  $\pm$  standard deviation using SPSS statistical software, version 23.0. The indicator level of statistical significance was set at  $p < 0.05$ .

### 3. RESULTS

The results showed significant increase ( $p < 0.05$ ) in the WBC ( $17.8 \pm 5.3 \times 10^9/L$ ), RBC ( $4.3 \pm 1.4 \times 10^{12}/L$ ), MCV ( $112.8 \pm 15.9$  fL), MCH: ( $35.3 \pm 8.6$  pg) and MCHC ( $31.0 \pm 3.4$  g/dl) of the unstable babies compared to the stable babies WBC ( $8.3 \pm 3.2 \times 10^9/L$ ), RBC ( $3.4 \pm 1.0 \times 10^{12}/L$ ), MCV ( $110.1 \pm 11.3$  fL), MCH ( $32.9 \pm 4.5$  pg) and MCHC ( $29.7 \pm 1.8$ g/dl); significant decrease ( $p < 0.05$ ) in the platelets ( $95.8 \pm 52.0 \times 10^9/L$ ), neutrophil ( $47.6 \pm 11.9\%$ ) and mixed ( $13.4 \pm 4.7\%$ ) of the unstable babies compared to the stable babies platelets ( $143.5 \pm 87.4 \times 10^9/L$ ), neutrophil ( $50.7$

$\pm 17.1\%$ ) and mixed ( $15.0 \pm 14.5\%$ ). However, no significant difference in haemoglobin, PCV and lymphocyte counts of the stable babies compared to unstable babies. The results also demonstrated 25 deaths per 1000 live newborn neonates within 48hour during the period of study (Table 2).

#### 3.1 Calculation of Early Neonatal Mortality Rate at 48 Hours during the Period of Study

(Number of resident neonatal deaths in 48 hours / Number of resident live births in 48 hours) x 1,000

$$(4/160) \times 1,000 = 25$$

This demonstrated 25 deaths per 1000 live newborn neonates in 48 hours during the period.

**Table 1. Frequency distributions of stable and unstable babies**

	Frequency	Percent	Valid Percent	Cumulative Percent
Stable	122	74.4	74.4	74.4
Unstable	42	25.6	25.6	100.0
Total	164	100.0	100.0	

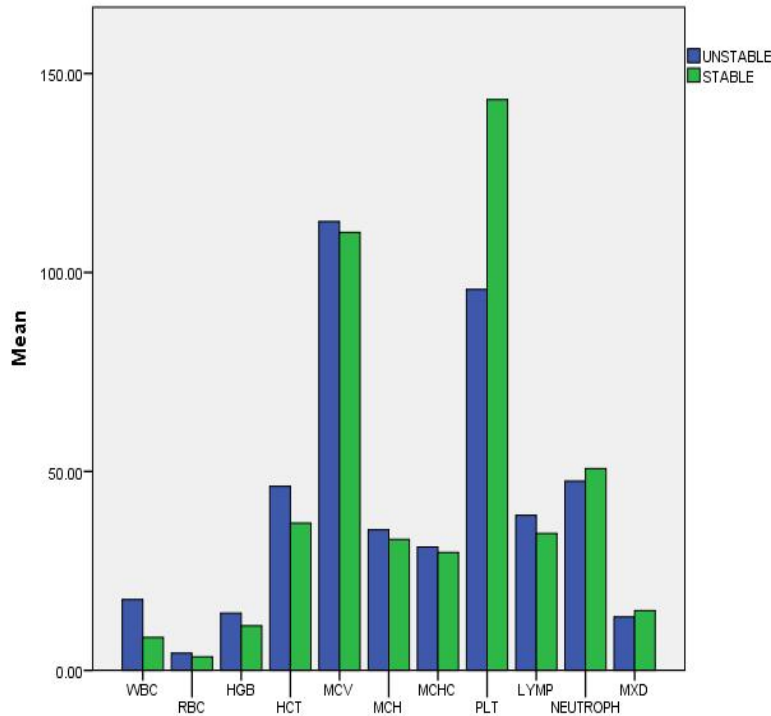
**Table 2. Frequency distributions of stable, unstable and dead babies**

	Frequency	Percent	Valid Percent	Cumulative percent
STABLE	120	73.2	73.2	73.2
UNSTABLE	40	24.4	24.4	97.6
DEAD	4	2.4	2.4	100.0
TOTAL	164	100.0	100.0	

**Table 3. Haematological parameters of stable and unstable babies**

Parameters	Stable (n=122)	Unstable (n=42)	p-value
WBC ( $\times 10^9/L$ )	8.3 $\pm$ 3.2	17.8 $\pm$ 5.3	.037
RBC ( $\times 10^{12}/L$ )	3.4 $\pm$ 1.0	4.3 $\pm$ 1.4	.045
Haemoglobin (g/dl)	11.2 $\pm$ 3.2	14.4 $\pm$ 2.9	.296
PCV (%)	37.0 $\pm$ 10.8	46.3 $\pm$ 9.7	.282
MCV (fl)	110.1 $\pm$ 11.3	112.8 $\pm$ 15.9	.007
MCH (pg)	32.9 $\pm$ 4.5	35.3 $\pm$ 8.6	.002
MCHC (g/dl)	29.7 $\pm$ 1.8	31.0 $\pm$ 3.4	.000
Platelets ( $\times 10^9/L$ )	143.5 $\pm$ 87.4	95.8 $\pm$ 52.0	.000
Neutrophil (%)	50.7 $\pm$ 17.1	47.6 $\pm$ 11.9	.007
Lymphocyte (%)	34.4 $\pm$ 13.2	38.9 $\pm$ 12.1	.927
Mixed (%)	15.0 $\pm$ 14.55	13.4 $\pm$ 4.7	.007

WBC: total white cell count; RBC: red blood cell; PCV: packed cell volume, MCV: mean cell volume; MCH: mean cell haemoglobin; MCHC: mean cell haemoglobin concentration, MIXED: (monocyte, eosinophil, and basophil)



**Fig. 1. Mean count of WBC, RBC, HGB, HCT (PCV), MCV, MCH, MCHC, platelets, neutrophil, lymphocyte and mixed of participants**

#### 4. DISCUSSION

Haematological parameters such as WBC, RBC, PCV, MCV, haemoglobin, MCH, MCHC, neutrophil, lymphocyte, platelets and mixed (monocyte, eosinophil, basophil) are widely used as biomarkers to evaluate patients' health status. Early assessment of fetus and neonates health status could be a daunting challenge owing to multiple factors involved. The major strength in this study is the well-defined clinical and laboratory procedures put in place to use umbilical cord blood haematological parameters to assess neonates' health status at birth.

This present study showed clearly the significantly higher values of haematological parameters analysed between stable and unstable subjects. However, the haemoglobin, PCV and lymphocyte showed no significant difference between the two groups. The significantly increased WBC of unstable babies compared to stable babies may indicate the release of cytokines following an increase polymorphonucleated (PMN) cells activation or granulocytes colony stimulating factor activation during infections as a result of the defensive mechanism WBC offers to the umbilical cord to

fight against placenta pathogens and toxic materials as previously reported [14,15].

The decrease in platelet turnover also known as thrombocytopenia in unstable babies compare to stable babies in this study is a well-known clinical indicator associated with neonatal infection [16, 17] while neutropenia (decrease in neutrophil) and decreased mixed (monocyte, eosinophil, basophil) obtained from the samples of unstable babies compare to stable ones indicates movement of neutrophil and other granulated cells out of fetal circulation in response to endotoxin and chemokine under the influence of chemical towards infected amniotic fluid thereby causing low level of neutrophil and mixed in circulatory cord blood which is in accordance with the report of Harvey [13].

The observed increased RBC in unstable babies compared to stable babies in this present study suggested congenital heart disease among members of unstable group as increased RBC is one of the diagnostic biomarkers of congenital heart disease which is in accordance with the report of Binh et al. [18]. Also, the significantly higher value of other indices such as MCV and MCH obtained from unstable babies compared

with the results of stable ones could be an indicative of Macrocytic anaemia due to either Vitamin B12 or Folate deficiencies [19], also Increased level of MCHC observed among unstable babies compared to stable babies is an indicator of more haemoglobin including fetal haemoglobin (HbF) among unstable group than stable ones. Usually fetal haemoglobin is normally present in neonates as a factor that is needed to slow down the development rate of pathogens, therefore, more fetal haemoglobin (HbF) may be present in cord blood of unstable babies in response to invaded pathogens compared to stable babies [20]. Four deaths were recorded among the babies during 48hours of direct nursing observation. This revealed 25 deaths per 1000 live newborn neonates within 48hours (table 2), According to Nigeria Demographic and Health Survey (DHS) of 2013, the neonatal mortality rate was 37 per 1000 live births, therefore this report indicated an improved neonatal cares in these facilities.

This well-defined clinical and laboratory study is very important in clinical management of babies at birth in resource and skill limited communities. It shows that cord blood haematological parameters should be carefully studied in the neonate with obvious clinical risk features. This study also shed some light on the promising benefits of cord blood haematological biomarkers in clinical management of neonate to reduce early infant mortality and these procedures can easily be carried out in poor resource district hospitals.

## 5. CONCLUSION

This study shows that cord blood haematological parameters can be used to ascertain the health status of neonates at birth. It has been shown that instability observed in unstable babies causes cord blood leukocytosis, thrombocytopenia, neutropenia and with increased RBC, MCV, MCH and MCHC due to micronutrients deficiency and inflammatory response. Early assessment of neonate health status at birth using cord blood haematological parameters is therefore advocated.

## 6. RECOMMENDATION

This report looks at neonatal health status in general rather than assessing the effect of each risk factors (Malaria, congenital infections, diarrhea, Acute Respiratory Infections (ARIs) and malnutrition). It will be important to look into the

effect of each factors on cord blood haematological markers in subsequent studies.

## ETHICAL APPROVAL AND CONSENT

Ethical approval for the study was obtained from the Research and Ethical Committee of Kogi State University Teaching Hospital (KSUTH), Nigeria. Parent/guardian permission (informed consent) was obtained from all participating subjects as recommended by WHO (TDR, 2003). This was done via an informed consent form duly completed by all the subjects Parent/Guardian.

## AVAILABILITY OF DATA AND MATERIALS

The study data is available on personal request to the corresponding author.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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