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Some Blood Cell Changes and Alteration in Renal and Hepatic Function in Pre-eclampsia: A Study in Owerri Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Authors PNA, FIB and CSA designed the study. Author PNA performed the statistical analysis, managed the analyses of the study and literature searches. Authors PNA and CSA wrote the protocol while author PNA wrote the first draft of the manuscript and incorporated all corrections from co-authors. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aims: We studied some blood cell changes and alterations in renal and hepatic functions in pregnancy and pre-eclampsia and determined baselines for the population in owerri, south east Nigeria.
Study Design: It was a cross sectional case control study conducted prospectively among antenatal women attending clinic at Holy Rosary, Federal Medical Centre and General Hospitals Owerri. The study included fifty non-pregnant, fifty pre-elampsia and fifty normotensive pregnant women of singleton gestation in their third trimester
Place and Duration of Study: Sample: Antenatal unit of Holy Rosary, Federal Medical Centre and General Hospitals Owerri between May 2009 and June 2010.
Methodology: The study included fifty (50) non-pregnant women, fifty (50) pregnant normotensive women and fifty (50) pre-eclamptic women of singleton gestation in their third trimester. Full blood count, liver function enzymes assay and some kidney function parameters was determined in all subjects. The subjects were selected under defined

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criteria. PE patients were at 28 to 42 wks of single-diastolic pressure of 110mmHg or more or two measurements of 90mmHg or more on two consecutive occasions of 6hours or more apart, urinary protein 2+ or more. The exclusion criteria include history of hypertension and proteinuria before conception or before 20wks of gestation, a history of antioxidant vitamins therapy during the last one year and smoking.

Results: The result showed a significant (P = 0.05) decrease in Red cell distribution width coefficient of variance (RDW-CV), mean cell haemoglobin (MCH), platelet count (PC) and mean platelet volume- platelet count (MPV-PC) ratio in pre-eclampsia comaperd to normal pregnancy. Significant increases (P= 0.05) in red blood cell count, haemoglobin concentration, haematocrit, mean cell volume, mean platelet volume, platelet distribution width (PDW) and circulating large platelet ratio (PLCR) were found among the pre-eclamptic women. There was a significant (P = 0.05) increase in ALT, AST, ALP and LDH activities in pre-eclampsia when compared to both the normal and the pregnant controls. Urea, Creatinine and Uric acid concentrations had a significant increase (P = 0.05) in pre-eclampsia when compared to normal and pregnant controls

Conclusion: The significant variation seen in these red cell parameters between the PC and NPC is attributable mainly to pregnancy than to pre-eclampsia. Pre-eclampsia though resulted in a marked platelet usage with a resulting shorter platelet life-span. A burden on the liver and kidney resulting from pre-eclampsia could have adversely affected protein metabolism which in turn may have affected erythropoesis. Results indicate that renal function is impaired in the presence of pre-eclampsia.

Keywords: Pre-eclampsia; red cells; platelet; liver and kidney; reference.

1. INTRODUCTION

Hypertension is a common complication of pregnancy, occurring with a frequency of 10 to 15 percent. Its development is due to a number of different and distinct etiological and pathophysiological mechanisms, many of which are poorly understood. Pre-eclampsia the world's most common glomerullar disease complicates about 5 to 10 percent of hypertensive pregnancies and remains a major cause of maternal and neonatal morbidity and mortality [1]. Normal pregnancy is associated with a transient hypercoagulable state, which most likely evolved in response to the dangers of post-partum hemorrhage. This prothrombotic state is balanced by adaptations in the fibrinolytic pathway. Activation of these systems may be more marked in the uteroplacental circulation than in the systemic circulation in both normotensive and pre-eclamptic pregnancies [2]. When a major pathological crisis occurs in pregnancy, such as pre-eclampsia, this delicate balance is disturbed. In addition to hypertension, there appears to be platelet activation, as well as endothelial damage and dysfunction, with the consequences of thrombosis, low birth weight, fetal loss, and maternal morbidity and mortality.

Oxidative stress has been shown to be a significant contributor in the pathogenesis and white cell changes in pre-eclampsia [3]. Contribution by stress could constitute a load on the hepatic and renal functions and factors resulting in white cell changes. This could affect the red cell and platelet indices. The aim of this study is to compare some blood cell (RBC and platelets) changes and alterations in renal and hepatic functions in non-pregnant women, in pregnancy and in pre-eclampsia. The result obtained could serve as reference ranges and/or diagnostic tools to assess the magnitude of these changes and to identify abnormal changes in women in Owerri south-eastern Nigeria.

2. MATERIALS AND METHODS

2.1 Study Design

It was a cross sectional case control study conducted prospectively among antenatal women attending clinic at Holy Rosary, Federal Medical Centre and General Hospitals Owerri. The study included fifty non-pregnant, fifty pre-elampsia and fifty normotensive pregnant women of singleton gestation in their third trimester.

2.1.1 Selection criteria

The subjects were selected under defined criteria. PE patients were at 28 to 42 wks of single-diastolic pressure of 110mmHg or more, or two measurements of 90mmHg or more on two consecutive occasions of 6hours or more apart, urinary protein 2+ or more. The exclusion criteria include history of hypertension and proteinuria before conception or before 20wks of gestation, a history of antioxidant vitamins therapy during the last one year and smoking. As cohort control, age and socio-economically matched healthy normotensives at 28 to 42 wks of singleton gestation with no urinary protein were recruited by convenience. The non-pregnant controls were consisted of 50 healthy normotensive subjects. They were matched by group percent of age, education and income. Ethical clearance was obtained from relevant committees.

2.2 Blood Collection

Venous blood was collected from each case and control subjects. 4 ml of the collected sample was added into a bottle (8ml) containing 80µl of ethylene diamine tetra-acetic acid (EDTA). The full blood count was done with the Erma automatic multi-parameter blood cell counter for in vitro diagnostic use in clinical laboratories. Blood (2ml) for chemistry analysis was separately put in plain containers and allowed to clot for 45 min at room temperature. Serum was separated by centrifugation at 600×*g* for 15 min and analyzed for various biochemical parameters

2.3 Full Blood Count

To measure FBC parameters, automated blood counter Erma automatic multi-parameter blood cell was used after calibration [3].

2.4 Biochemical Assays

Determination of ALT and AST activity was based on the method of Reitman and Frankel [4]. The ALP assay was based on the method as described in Tietz [5]. The LDH assay procedure was by a modification of the method of Wacker [6]. Urea, creatine and uric acid concentrations were determined spectrometrically (Turner Model390) using commercially available Biosystems kits (Biosystems S.A. costa Brava Barcelona Spain).

2.5 Statistical Analysis

Data obtained from the study were analyzed by the use of one-way analysis of variance (ANOVA), all results were given as Mean±SD and values for P = 0.05 were considered statistically significant.

3. RESULTS AND DISCUSSION

Our result (Table 1) showed that red cell count, haemoglobin and haematocrit were significantly (p=0.001) higher in the blood of PE women than pregnant controls (PC). These parameters were significantly lower in the blood of PC than NPC. The significant variation seen in these red cell parameters between the PC and NPC could be attributed to pregnancy. In normal pregnancy there is an increase in erythropoietic activity. However, an increase in plasma volume occurs and this results to a fall in haemoglobin concentration, haematocrit (%) and red blood cell count. It is therefore suggestive that pre-eclampsia contributed to the significant difference observed among PE subjects and the PC. The increase in haematocrit which was observed could imply a possible interference with the processes leading to increased plasma volume. Haematocrit had been shown to correlate with mean arterial blood pressure and peripheral vascular resistance [7]. The possible effects of the alterations in these haematological parameters on blood flow through the intervillous circulation are thought to be the clinical implications in this study.

Table 1. Effect of pre-eclampsia on red blood cell parameters

	Non-pregnant controls	Pregnant controls	Pre-eclampsia	P-value
Red Blood Cell count ($X10^{12}$ / L)	4.23±0.71	3.40±0.80[a]	3.78±0.38	0.0005
Heamoglobin (g/dl)	10.86±2.30	9.65±2.10[b]	10.91±1.78	0.0085
haemotocrit (%)	36.33±4.80	29.18±6.93	36.55±5.42	0.0000
Mean Cell Volume (MCV) (fl)	89.03±24.64	86.09±7.50	97.14±14.19[b]	0.0009
Mean Cell Haemoglobin (MCH)(pg)	25.61±4.05	29.66±6.05[a]	28.78±2.50	0.0021
Mean Cell Haemoglobin Concentration (MCHC) (g/dl)	32.06±2.51	32.74±1.79	32.59±1.33	0.2037
RDW-SD	42.77±5.38	43.32±9.00	43.69±2.66	0.8232
RDW-CV	15.29±2.66	14.59±2.20	13.36±0.75[a,b]	0.0060

p = 0.05 was considered significant

Mean cell volume in pre-eclamptic group was significantly elevated when compared to the pregnant control. However, there was no significant difference between non-pregnant control group and the pre-eclamptic group. Since pre-eclampsia could result in decreased erythrocyte membrane fluidity [3] as a result of stress, it could reduce RBCs ability to withstand osmotic changes and oxidative damages. Pre-eclampsia induces haemolysis [3] resulting in the production of young red blood cells as a compensatory measure. This may give rise to the observed elevation in MCV.

The mean cell haemoglobin (MCH) in pregnant control (PC) was significantly higher than non-pregnant control (NPC), while the pre-eclamptic group (PE) was significantly higher than the non-pregnant control. However, no significant (P= 0.1) differences exist between the pre-eclamptic group and the pregnant control. This was in agreement with findings from Turkey [8]. The reason for the moderate increase experienced in normal pregnancy and pre-eclampsia is not certain but it should be observed that values of MCH are still within the normal ranges.

The mean cell haemoglobin concentration (MCHC) and red cell distribution width-standard deviation (RDW-SD) were found not to have statistical difference between the groups. The findings agrees with reports of Makuyana and other workers [9,7] who also found no

significant difference among the healthy pregnant women and those with pre-eclampsia. This could be understood as the absence of anaemia both in the case study and the control groups as RDW-SD and MCHC are indicative of anaemia and anisocytosis. This observation is not out of place since our pregnant groups are singleton gestation. Depletion of nutrients is known to occur in multi-gravida and multi-para but uncommon in singleton pregnancy. MCHC is also an indicator of accuracy of the haemoglobin and haematocrit estimation as increased MCHC is associated with inaccurate haemoglobin or haematocrit.

The red cell distribution width-coefficient of variance (RDW-CV) was significantly decreased in pre-eclamptic women when compared to the normal and pregnant controls. However, no significant difference was found to exist between PC and NPC. This observation implied that pre-eclampsia led to a little degree of anisocytosis which has become significant enough to effect a change in the mean cell volume.

Ceyhan and coworkers [8] found no significant difference between the platelet count of pre-eclamptic women and the pregnant control women; this is however at variance with the result of the present study. The result of this study showed a lower platelet count among the PC women and much lower platelet count among the PE in agreement with earlier studies [10,11,12]. This study confirms the postulation that normal pregnancy is associated with a lower mean platelet count than non-pregnancy. It is also suggestive that pre-eclampsia could lead to a reduction in platelet function.

Pre-eclampsia affected the platelet distribution width (PDW) in that the PDW was significantly higher in pre-eclampsia when compared with the non-pregnant control and pregnant control. However, no statistical difference existed between NPC and PC. Although this parameter has not been studied by other researchers, this variation could be explained as resulting from the endothelia dysfunction seen in pre-eclampsia and consequently the production of young platelets to compensate for the reduction in platelet.

In this study a higher mean platelet volume (MPV) was seen in pre-eclampsia compared to pregnant control women. These findings agreed with those of Boriboonhirusam and coworker [13,14] but differed from the findings of Ceyhan [8], who found no significant difference between the pre-eclamptic and pregnant control women. Increase in MPV values in pre-eclampsia compared to their pregnant control could be attributed to increase consumption of peripheral platelet caused by endothelia dysfunction and subsequent production of young platelets. This could be a useful tool in differentiating pre-eclamptic cases from normal pregnancy.

The effect of pre-eclampsia on circulating large platelet ratio (P-LCR) (Table 2) showed that there was no difference between the PC and NPC. There was a significant increase of P-LCR in pre-eclampsia ($P = 0.001$) when compared to the controls. A positive correlation was found between P-LCR and PDW ($r = 0.995$). This could represent a marked platelet usage and localized platelet deposition in the utero-placental microvasculature, possibly secondary to defective endothelia with a resulting shorter platelet life-span and may be the cause of the effects seen in pre-eclampsia.

Our result (Fig. 1) showed that pre-eclampsia resulted in a marked increase in hepatic enzyme activity. Increases in liver enzyme activities are however normal in pregnancy, but significant increases in hepatic enzyme activity observed in pre-eclampsia when compared with normal pregnancy indicate that the integrity of hepatic membranes may have been compromised [15], resulting in damages to the hepatocytes/hepatic parenchyma. Oxidative

stress being part of this disease process [3] may have been contributory to the observed damage. The liver forms part of the reticuloendothelial system. Injury to the liver adversely affects protein metabolism [15] which in turn could affects erythropoesis. Reduction in red blood cell count and platelet may be a consequence of the burden on the liver.

Table 2. Effect of pre-eclampsia on platelet blood cell parameters

	Non pregnant controls	Pregnant controls	Pre-eclampsia	P-value
Platelet count (x10^9/L)	151.44±74.31	122.92±44.89	108.0±30.02[b]	0.000
PDW (fl)	11.50±2.17	11.32±0.84	12.04±1.70[a,b]	0.248
MPV (fl)	8.79±0.86	8.83±0.59	9.52±0.75[a,b]	0.000
PLCR (%)	18.91±5.53	19.83±2.94	22.92± 5.74	0.004

p = 0.05 was considered significant

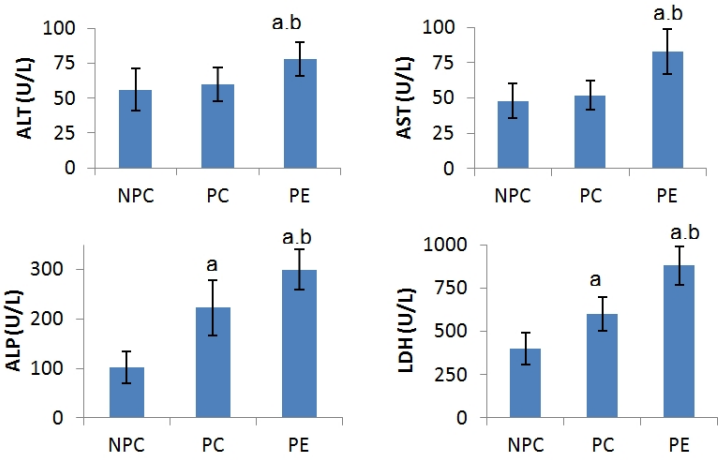

Fig. 1. Effect of Pre-eclampsia on some markers of hepatic toxicity
a – significant difference with NPC, b - significant difference with PC, (p = 0.05), n = 50

The renal system undergoes many changes in pregnancy to accommodate increased metabolic and circulatory requirements. The result of our study (Table 3) showed that pregnancy did not significantly affect renal function. The little drop in the concentrations of urea and creatinine in preganancy observed in this study are consistent with the normal increase in renal clearance of many substances resulting in lower-than-normal serum concentrations of urea and creatinine. The increase in the concentration of urea, creatinine and Uric acid observed in pre-eclampsia which is significant (p = 0.05) when compared to the pregnant and normal controls indicates that renal function is impaired in the presence of pre-eclampsia.

Table 3. Effect of Pre-eclampsia on some renal parameters

	Non-pregnant Control (NPC)	Pregnant Control (PC)	Pre-eclampsia (PE)
BUN (mg/dl)	10.2±0.8	9.0±1.2	12.2±1.3[ab]
CREATININE (mg/dl)	0.86±0.23	0.8±0.3	1.0±0.2[ab]
URIC ACID (mg/dl)	5.1±0.62[b]	3.5±1.3[a]	7.3±1.1[ab]

a – significant difference with NPC, b - significant difference with PC, (p = 0.05), n = 50

4. CONCLUSION

The significant variation seen in these red cell parameters between the PC and NPC could be attributed to pregnancy. This study confirms the postulation that normal pregnancy is associated with a lower mean platelet count. It is also suggestive that pre-eclampsia could lead to a reduction in platelet function. Pre-eclampsia may have resulted in a marked platelet usage with a resulting shorter platelet life-span and may be the cause of the effects seen in pre-eclampsia. Injury to the liver adversely affects protein metabolism which in turn may have affected erythropoesis. Reduction in red blood cell count and platelet may be a consequence of the burden on the liver. Pre-eclampsia tend to overcome the renal changes in pregnancy in preparation to accommodating increased metabolic and circulatory requirements. The changes in some parameters in this study in pre-eclampsis compared to normal and pregnant controls could serve as veritable tool or baseline to monitor prognosis and onset of pre-eclampsia in this region.

CONSENT

All authors declare that 'written informed consent was obtained from the patients for publication of this study'.

ETHICAL APPROVAL

We hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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