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Effect of Platelet Indices on Pregnancy Outcome in Normotensive and Preeclamptic Women in University of Ilorin Teaching Hospital Ilorin, Nigeria

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Abstract

Background: *Preeclampsia as a disease entity is associated with maternal and perinatal morbidity and mortality especially in the developing countries. Platelet activation is pivotal to this disease entity. Therefore, platelet indices should be routinely measured to assess the severity of the disease and pregnancy outcome.*

Objectives: *To determine the effect of platelet indices on pregnancy outcome in normotensive and preeclamptic women in University of Ilorin Teaching Hospital, Ilorin.*

Study design: *A prospective case control study of consented subjects who were pregnant women at gestational age of 28 weeks and above diagnosed with preeclampsia that met the study criteria and controls who were consented healthy normotensive pregnant women at the same gestational age who also met the study criteria. Subjects and controls were matched for social status, gestational age and gravidity.*

Methodology: *A total of 140 parturient comprising 70 each from subjects and controls who satisfied the inclusion criteria were recruited for the study by purposive sampling. Subjects and controls were matched for gestational age, gravidity and social status. Social and medical histories of each parturient as well as the blood pressure and platelet indices samples were obtained. The results were analysed using SPSS version 21.0 with appropriate tables and figures generated.*

Results: *Platelet count was lower in the preeclamptic group than the control (155.47 ± 38.68 x $10^3/\mu L$ vs. 232.51 ± 53.79 x $10^3/\mu L$, p<0.001), while the other platelet indices were higher in preeclamptic group than the control namely; MPV (11.88 ± 1.05fl vs. 10.77 ± 1.22fl, p<0.001), PDW (15.53 ± 2.28fl vs. 13.94 ± 2.25fl, p<0.001) and PLCR (39.89 ± 7.73% vs. 31.81 ± 7.97%, p<0.001). Platelet count (p=0,014), PDW (p=0.036) and PLCR (p=0.002) had significant association with maternal outcome, while only platelet count (p=0,014) and PDW (p=0.008, 0.048) had significant association with fetal outcome in preeclamptic women.*

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Conclusion: *Platelet indices abnormalities and adverse pregnancy outcome were higher in preeclamptic women than their normotensive counterparts.*

Recommendation: *Platelet indices should be routinely assessed in the management of preeclampsia to evaluate the severity and outcome of the disease.*

Keywords: Platelet, Indices, Pregnancy, Outcome, Nornotensive, Preeclampsia, Women.

INTRODUCTION:

Hypertensive disorders of pregnancy are among the leading causes of maternal and perinatal morbidity and mortality, particularly in low-income countries and amount to 14% maternal deaths globally.[1-3] They complicate about 5 – 8% of pregnancies and constitute obstetric burden to both pregnant women and their babies.[4] Hypertensive disorders of pregnancy are diagnosed with the maternal blood pressure elevation of ≥ 140mmHg systolic or ≥ 90mmHg diastolic in pregnancy on two or more occasions, about four hours apart, in a woman who has been previously normotensive and in whom blood pressures may return to normal within twelve weeks of delivery or persist afterwards.[5] Hypertensive disorder in pregnancy is classified by International Society for the Study of Hypertension (ISSHP) as chronic hypertension, gestational hypertension, preeclampsia and White-coat hypertension.[6] Chronic hypertension is diagnosed when elevated blood pressure predates the pregnancy or noticed in the first half of pregnancy and persists more than 12 weeks birth. Gestational hypertension is characterized by elevated blood pressure that starts after 20 weeks gestation without proteinuria. Preeclampsia is the presence of hypertension after 20 weeks gestation with proteinuria which is spot urine protein/creatinine >30 mg/mmol (0.3mg/mg) or >300mg/day or at least 1 g/L (2+) on dipstick testing and a resolution of these symptoms usually by 6 - 12 weeks postpartum.[6] Preeclampsia can be classified as mild or severe. Chronic hypertension can be superimposed with preeclampsia. Preeclampsia without intervention can progress to eclampsia, which is the occurrence of epileptiform convulsion unrelated to other cerebral conditions with signs and symptoms of preeclampsia.[7-9] The pregnant woman may develop disseminated intravascular coagulation, acute renal failure, stroke (ischaemia, due to vasospasm and microthrombosis or even haemorrhage due to severe thrombocytopenia), acute pulmonary oedema, cerebral oedema. Other complications are placental abruption, liver haemorrhage/rupture, development of Haemolysis, Elevated liver enzymes, Low platelet count (HELLP) syndrome, transformation to chronic hypertension, or maternal mortality.[5,10] The fetal complications could be as a result of placental insufficiency and may include: pregnancy loss, fetal death in-utero, intrauterine growth restriction, premature labour.[10,11]

The most common hypertensive disorder of pregnancy is preeclampsia.[12] Majority of these conditions are asymptomatic. The associated morbidities and mortalities can be prevented with early recognition and good antenatal care.[13,14] Early assessment of its progress and severity should be known for proper intervention and prevention of further complications, but this is difficult as its pathophysiology is not well defined.[15,16]

Various studies have been carried out in the past to develop a reliable test to predict preeclampsia.[13] Recently, several biochemical markers have been described such

as angiogenic/anti-angiogenic factors, placental proteins, etc. for predicting preeclampsia. However, their role in low-income countries is of doubt due to the financial involvement of these tests.[13] The changes that occur in the coagulation and fibrinolytic system during normal pregnancy is profound resulting in a hypercoagulable state.[6,13] Of all the haematological changes that occur in preeclampsia, low platelet count is the most commonly seen occuring in 11% to 29% of patients.[7,14,17-19] HELLP syndrome and disseminated intravascular coagulation (DIC) are known complications and are both related to change in platelet counts and may be fatal. Some of the vasoactive factors released by the platelets could have hand in the pathogenesis of preeclampsia. So, the disease entity and its severity could be due to significant abnormality in platelet indices: platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR).

The evidence to strongly demonstrate the effect of platelet indices on pregnancy outcome in normotensive and preeclamptic women in Nigeria is limited. The available studies in Nigeria are only limited to platelet counts in preeclampsia and do not include an evaluation of other platelet indices and also comparison with normotensive pregnant women.[10] Thus, to add to the body of evidence on platelet indices and pregnancy outcome there is a need to conduct this study.

METHODOLOGY

Study Area: The study was carried out in the Department of Obstetrics and Gynaecology, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria which is located at Oke-Oyi, Old Jebba Road in Ilorin. It predominantly plays the role of a teaching hospital but equally offers primary and secondary health services. It serves as a major referral centre for Kwara State and parts of the nearby states of Oyo, Osun, Ekiti, Kogi and Niger states. The hospital is approved for and undertakes undergraduate and postgraduate medical training. It is a training centre for Nursing, Post Basic Nursing in Midwifery, Accident and Emergency as well as Paediatric Nursing, Community Health Officers and Health Information Management System. The hospital has facilities for the major clinical departments i.e. Obstetrics and Gynaecology, Paediatrics, Surgery, Internal Medicine and clinical laboratories. Obstetric services are delivered by four firms; each firm consists of consultants, resident doctors and house officers.

Study Population: The study population were pregnant women at 28 week gestational age and above, with preeclampsia and equal number of healthy normotensive pregnant women at 28 week gestational age and above, attending antenatal clinics or presenting in labour ward at the University of Ilorin Teaching Hospital, Ilorin.

Inclusion Criteria: Subjects must be consented preeclamptic women at gestational age of 28 weeks and above while controls must be healthy normotensive pregnant women at gestational age of 28 weeks and above.

Study Design: The study was a prospective case control study. Consented women diagnosed with preeclampsia at the routine antenatal clinic and those admitted into the

obstetrics emergency ward of the University of Ilorin Teaching Hospital were selected. Subjects who met the criteria for the study were informed and counseled about the study. Controls were consented healthy normotensive pregnant women without any sign or history of hypertensive disorders of pregnancy. Subjects and controls were recruited consecutively till the sample size was completed. Each control was recruited as soon as possible after a case is enrolled to avoid any temporal bias, matching for gestational age and gravidity.

Study Tool: The study tool was study proforma.

Sample Size: The sample size was 140 comprising equal number of 70 participants each from consented women diagnosed with preeclampsia at 28 weeks gestational age and above as subjects and consented healthy normotensive pregnant women at 28 weeks gestational age and above as controls. It was determined by a previously validated formula for case-control study[20].

Sampling Technique: The sampling technique was by purposive sampling and consenting participants that met the inclusion criteria were recruited. Subjects and controls were recruited consecutively till the sample size was completed.

Recruitment of subjects and controls: The recruitment of patients were at the antenatal clinic and the obstetrics emergency ward where women with preeclampsia are admitted for inpatient care, while that of controls were at the antenatal clinic. Eligible women who satisfied the inclusion criteria were informed and counseled about the study in a language they understood and informed consents were obtained. A study proforma was administered. Information obtained were sociodemographic status, gestational age, history of presenting complaints, obstetric history, personal, medical and family histories including the history of bleeding disorders, hypertension, diabetes mellitus, pregnancy induced hypertension, genotype and other related history. General physical examinations were done to obtain height, weight, vital signs and exclude anaemia, cyanosis, jaundice, oedema. Recruitments were done by the researcher with assistance from the research assistants. The research assistants were four junior residents (one from each firm) who were trained about the study protocol (such as the contents of the proforma, consent form and also sample collection) daily for one week before commencement of the study.

Blood pressure measurement and Urinalysis: Blood pressure was measured with patient in comfortable sitting or supine position with the arm outstretched and supported at approximately same level as the heart, using Accoson mercury sphygmomanometer. The cuff length was at least 80% of the circumference of the upper arm and the lower edge one inch above the cubital fossa when wrapped around the arm. A second reading was taken after 4-6 hours. They were classified as mild if readings are ≥140/90mmHg or severe if ≥160/110mmHg.

Urinalysis was done using dipstick measurement with Combi 2 urinalysis strips and it was read as negative, trace, 1+ (30mg/dl), 2+ (100mg/dl), 3+ (300-1999mg/dl) and 4+ (>2g). A clean catch or catheter sample was used for the tests.

Blood Sample Collection: After application of tourniquet and taking all aseptic precautions, 3ml of venous blood was collected by venepuncture from the median antecubital vein of all participants using 22 Gauge size needle and 5ml disposable syringe. It was deposited into a sample bottle containing ethylene diamine tetraacetate (EDTA) and thorough mixing done to prevent clot formation. Sample was analyzed with an automated cell counter using Sysmex KX21, an autoanalyzer.

Patients Follow Up: Patients were followed up till delivery. The preeclampsia group was categorized as mild or severe based on their blood pressures on admission, urinalysis and clinical features.

Data Analysis: The data was analyzed using the Statistical Package for Social Sciences Software (SPSS) version 21.0 Chicago, Illinois, USA. The data was presented in frequency tables and chart. Chi-square analysis was used to test relationships between categorical variables while continuous variables were analyzed with Independent Samples T test and Analysis of Variance (ANOVA). Spearman correlation was used to determine the platelet indices and severity of preeclampsia while Receiver Operating Curve (ROC) was used to determine the association criterion of the platelet indices in differentiating severity of preeclampsia as well as in predicting pregnancy outcomes. Probability (p) values less than 0.05 was accepted as statistically significant.

Ethical Consideration: An institutional approval for this study has been obtained from the Ethical Review Committee of University of Ilorin Teaching Hospital, Ilorin. Informed written consent was obtained from each participant after adequate counselling and the data obtained from the study were treated with confidentiality and used solely for the purpose of the study.

Study Limitations:

1. The study was done in a single center thus was limited in terms of participants' heterogeneity.
2. Larger sample size would be more representative of what is obtainable in this environment.
3. The study only described findings and outcomes in selected cases of preeclampsia at 28 weeks and above with exclusion of other hypertensive disorders in pregnancy.
4. Samples were taken at point of diagnosis of preeclampsia; serial samples would have allowed detection of a possible trend and changes in platelet indices in preeclampsia and normal pregnancy.

RESULTS:

The study on 140 participants comprising 70 participants in each arm was carried out over a period of 9 months (July 2017 to March 2018).

Table 1: Socio-Demographic Variables, Booking Status Gravidity and Blood Pressure Measurements of Study Participants

Variable	Group		Total	χ^2/t	*p* value
	Preeclamptic n = 70 (%)	Normotensive n = 70 (%)			
Age group (years)					
< 25	18 (25.7)	10 (14.3)	28 (20.0)	5.467	0.243
25 – 29	26 (37.1)	21 (30.0)	47 (33.6)		
30 – 34	16 (22.9)	25 (35.7)	41 (29.3)		
35 – 39	8 (11.4)	11 (15.7)	19 (13.6)		
≥ 40	2 (2.9)	3 (4.3)	5 (3.6)		
Mean ± SD	28.16 ± 4.62	29.59 ± 4.92		-1.776[t]	0.078
Range	22 - 40	22 – 43			
Marital status					
Single	7 (10.0)	0 (0.0)	7 (5.0)	5.414[Y]	0.020*
Married	63 (90.0)	70 (100.0)	133 (95.0)		
Education					
None	7 (10.0)	1 (1.4)	8 (5.7)	15.403[Y]	0.002*
Primary	9 (12.9)	1 (1.4)	10 (7.1)		
Secondary	21 (30.0)	12 (17.1)	33 (23.6)		
Tertiary	33 (47.1)	56 (80.0)	89 (63.6)		
Employment status					
Unemployed	24 (34.3)	21 (30.0)	45 (32.1)	18.789	<0.001*
Self employed	40 (57.1)	22 (31.4)	62 (44.3)		
Employed	6 (8.6)	27 (38.6)	33 (23.6)		
Religion					
Christianity	15 (21.4)	14 (20.0)	29 (20.7)	0.043	0.835
Islam	55 (78.6)	56 (80.0)	111 (79.3)		
Ethnicity					
Yoruba	53 (75.7)	59 (84.3)	112 (80.0)	8.223[Y]	0.042*
Hausa	11 (15.7)	1 (1.4)	12 (8.6)		
Igbo	2 (2.9)	6 (8.6)	8 (5.7)		
Others	4 (5.7)	4 (5.7)	8 (5.7)		
Gravidity					
1	19 (27.1)	15 (21.4)	34 (24.3)	0.674	0.714
2 – 4	39 (55.7)	41 (58.6)	80 (57.1)		
> 4	12 (17.1)	14 (20.0)	26 (18.6)		
Booking status					
Booked	21 (30.0)	59 (84.3)	80 (57.1)	42.117	<0.001*
Unbooked	49 (70.0)	11 (15.7)	60 (42.9)		
Blood Pressure					
SBP(mmHg)	174.14 ± 23.23	115.29 ± 19.13		16.289	<0.001*
DBP(mmHg)	113.00 ± 14.66	74.71 ± 11.44		17.156	<0.001*
MAP(mmHg)	170.99 ± 20.02	113.10 ± 16.80		18.450	<0.001*

χ^2: Chi square test, [Y]: Yates corrected, t: Independent samples T test, *: *p* value < 0.05 (statistically significant) SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure

Table 1 showed the socio-demographic variables, gravidity, booking status and blood pressure measurements of the study participants.

Maternal age: The participants in the preeclamptic group were within the age range of 22–40years (mean age of 28.16years ± 4.62), while the normotensive participants were 22 – 43 years (29.59years ± 4.92) which was not statistically significant (p= 0.078). The highest percentage of participants were in the age group of 25-29years 47(33.6%) while the least number of participants were greater than 40years 5(3.6%) in both groups.

Marital status: Majority of the participants, 95% (133) were married, of these, 63(90%) were in the preeclamptic group and 70(100%) in normotensive group while 5% of the participants were single.

Educational status: Eighty nine participants (63.6%), had tertiary level of education, 33(47.1%) in the preeclamptic group and 56(80%) in the normotensive group. Eight participants (5.7%) had no formal education, 7(10%) in the preeclamptic group and 1(1.4%) in the normotensive group and this was statistically significant (p= 0.002)

Employment status: Twenty four (34.3%) women were unemployed in the preeclamptic group while 21(30.0%) were unemployed in the normotensive group. Also, 40 (57.1%) and 22 (31.4%) participants were self-employed in the preeclamptic and normotensive group respectively. Employed participants in the preeclamptic and normotensive group were 6 (8.6%) and 27 (38.6%) respectively.

Religion: Most of the participants 111(79.3%) were Muslims; 55(78.6%) in the preeclamptic group and 56(79.3%) in the normotensive group. Fifteen (21.4%) women in the preeclamptic group and 14(20%) in the normotensive group were Christians. There was no statistically significant difference (p= 0.835) in the distribution of participants by their religion among the two groups.

Ethnicity: Majority of the participants in both study groups were of Yoruba ethnicity; 53 (75.7%) of these from the preeclamptic and 59(84.3%) from the normotensive group.

Gravidity: Majority of the participants in both arms of the study were multigravida, 80(57.1%). There were 19(27.1%) and 15(21.4%) primigravida in the preeclamptic and normotensive groups respectively and the difference was not significant (p= 0.714).

Booking: Most of the women 59 (84.3%) in the normotensive group booked antenatal at the study centre while only 21(30%) preeclamptics booked at the place of study and it was statistically significant (p<0.001).

Blood Pressure: The mean systolic blood pressure in the preeclamptic group was 174.14 ± 23.23mmHg, while that of the normotensive group was 115.29 ± 19.13mmHg; (p= <0.001). The mean diastolic blood pressure in the preelamptic group was 113.00 ± 14.66mmHg and that of the normotensive group was 74.71 ± 11.44mmHg and the difference was statistically significant (p= <0.001).

There were more cases of severe preeclampsia than mild preeclampsia, 48 (68.6%) and 22(31.4%) respectively.

Table 1: Comparison of Feto-Maternal Outcomes in the Study Group and Controls

Feto-Maternal Outcomes	Group: Preeclamptic n = 70 (%)	Group: Normotensive n = 70 (%)	Total	χ^2/t	*p* value
MATERNAL					
Estimated Blood loss(ml) at delivery					
Mean ± SD	506.15 ± 291.35	216.13 ± 72.87		7.613	<0.001*
Range	150 – 1500	150 – 600			
Abruptio placenta					
Yes	4 (5.7)	0 (0.0)	4 (2.9)	2.316[Y]	0.128
No	66 (94.3)	70 (100.0)	136 (97.1)		
Mode of delivery					
SVD	36 (51.4)	56 (80.0)	92 (65.7)	12.861	<0.001*
CS	34 (48.6)	14 (20.0)	48 (34.3)		
ICU Admission					
Yes	2 (2.9)	0 (0.0)	2 (1.4)	0.507[Y]	0.476
No	68 (97.1)	70 (100.0)	138 (98.6)		
Postpartum stay					
≤ 72 hours	16 (22.9)	69 (98.6)	85 (60.7)	84.120	<0.001*
> 72 hours	54 (77.1)	1 (1.4)	55 (39.3)		
FOETAL					
GA at delivery (weeks)					
Mean ± SD					
Range	34.37 ± 3.47	38.16 ± 1.35		-8.138	<0.001*
Birth weight(Kg)	28 – 40	33 – 41			
Mean ± SD	2.21 ± 0.79	3.22 ± 0.51		-8.558	<0.001*
Range	0.80 – 3.60	2.10 – 4.20			
NICU Admission					
Yes	29 (41.4)	1 (1.4)	30 (21.4)	33.261	<0.001*
No	41 (58.6)	69 (98.6)	110 (78.6)		
Apgar score (1st minute)					
< 7	40 (57.1)	9 (12.9)	49 (35.0)	30.173	<0.001*
≥ 7	30 (42.9)	61 (87.1)	91 (65.0)		
Apgar score (5th minute)					
< 7	33 (47.1)	3 (4.3)	36 (25.7)	33.654	<0.001*
≥ 7	37 (52.9)	67 (95.7)	104 (74.3)		

Foetal death					
Yes	13 (18.6)	0 (0.0)	13 (9.3)	14.331	<0.001*
No	57 (81.4)	70 (100.0)	127 (90.7)		

χ^2: Chi square test, ^{Y}: Yates corrected, t: Independent samples T test, *: *p* value < 0.05 (statistically significant)

Table 2 showed the comparison of feto-maternal outcomes in the study group and controls

Estimated Blood Loss at Delivery: The estimated blood loss postpartum was 506.15 ± 291.35ml and was 216.13 ± 72.87ml for the preeclamptic and normotensive participants respectively and the difference was significant (p= <0.001).

Abruptio Placenta: There were 4(5.7%) cases of abruption placenta in the preeclamptic group and this complication was not present in the normotensive group, this was found to be insignificant (p=0.128).

Mode of Delivery: Vaginal delivery was the mode of delivery in 36(51.4%) in the preeclamptic group and in 56(80.0%) patients in the normotensive group, others delivered abdominally. The difference was statistically significant (p= <0.001). Caesarean deliveries were 34(48.6%) in the preeclamptic group compared to 14(20.0%) in the control and the difference was statistically significant (p= <0.001).

ICU Admission: There were 2(2.9%) cases of ICU admission in the preeclamptic group, while none in the normotensive group with the difference not statistically significant (p= 0.472).

Postpartum Stay: Duration of postpartum stay was ≤ 72 hours in 16(22.9%) and >72hours in 54(77.1%) in preeclamptic group whereas ≤ 72 hours in 69(98.6%) and >72hours in just 1(77.1%) in normotensive group and this difference was found to be statistically significant (p= <0.001).

Gestational Age at Delivery: The mean gestational age at delivery for the preeclamptic group was 34.37 ± 3.47weeks while that of normotensive was 38.16 ± 1.35weeks and this difference was statistically significant (p= <0.001).

Birth Weight: The mean birth weight in the preeclamptic group was 2.21 ± 0.79Kg while it was 3.22 ± 0.51Kg in the control group with statistically significant difference (p= <0.001). **NICU Admission:** Twenty nine (41.4%) of the neonates had NICU admission in the test group while only 1(1.4%) had NICU admission in the control group and the difference is statistically significant (p = <0.001).

Apgar Scores: The 1st minute Apgar score was <7 in 40(57.1%) and ≥7 in 30(42.9%) of the neonates in the test group and these were <7 in 9(12.9%) and ≥7 in 61 (87.1%) in neonates in the control group (p<0.001). The 5th minute Apgar score was <7 in 33(47.1%) and ≥7 in 37(52.9%) neonates in the test group and while in 3 (4.3%) and 67 (95.7%) neonates in the control group, 5thApgar scores were <7 and ≥7 respectively (p = <0.001).

Foetal Death: There were 13 (18.6%) foetal demise in the preeclamptic group but none in the normotensive group (p<0.001). The fetal demises were fresh still birth.

Table 3: Platelet Count, MPV, PDW and PLCR in Preeclamptics and Normotensive Pregnant Women

Variable	Preeclamptic	Normotensive	T	*p* value
Platelet Count (x 10^3/µL)				
Mean ± SD	155.47 ± 38.68	232.51 ± 53.79	-9.603	<0.001*
Range	109 - 254	150 – 365		

MPV (fl)				
Mean ± SD	11.88 ± 1.05	10.77 ± 1.22	5.622	<0.001*
Range	9.5 – 13.7	8.1 – 12.6		
PDW (fl)				
Mean ± SD	15.53 ± 2.28	13.94 ± 2.25	4.003	<0.001*
Range	10.4 – 19.3	9.9 – 20.0		
PLCR (%)				
Mean ± SD	39.89 ± 7.73	31.81 ± 7.97	5.911	<0.001*
Range	20.9 – 52.3	14.2 – 46.7		

t: Independent samples T test, *: p value < 0.05 (statistically significant)

Table 3 showed the Platelet Count, MPV, PDW and PLCR in preeclamptics and normotensive pregnant women.

There were statistically significant differences in all the platelet indices between the preeclamptic and normotensive pregnant women. Apact from the main platelet count that was lower in the preeclamptic group all other indices were higher in the women with preeclampsia than those without the disease. Mean platelet count (155.47 ± 38.68 x 10^3/µL vs. 232.51 ± 53.79 x 10^3/µL; p<0.001), MPV (11.88 ± 1.05fl vs. 10.77 ± 1.22fl; p<0.001), PDW (15.53 ± 2.28fl vs. 13.94 ± 2.25fl; p<0.001) and the PLCR (39.89 ± 7.73% vs. 31.81 ± 7.97%; p<0.001).

Table 4: Comparison of Platelet Indices in Normotensive Women and Severity of Disease in Preeclamptics

Variable	Normotensive	Mild Pre-eclampsia	Severe Pre-eclampsia	F	p value
Platelets Count (x 10^3/µL)					
Mean ± SD	232.51 ± 53.79	181.68 ± 44.42	143.46 ± 29.09	55.013	<0.001*
Range	150 – 365	109 – 254	109 – 248		
MPV (fl)					
Mean ± SD	10.77 ± 1.22	11.24 ± 0.92	12.19 ± 0.97	22.738	<0.001*
Range	8.1 – 12.6	9.5 – 13.7	9.5 – 13.7		
PDW (fl)					
Mean ± SD	13.94 ± 2.25	14.99 ± 2.22	15.78 ± 2.29	8.986	<0.001*
Range	9.9 – 20.0	10.4 – 19.2	10.4 – 19.3		
PLCR (%)					
Mean ± SD	31.81 ± 7.97	39.27 ± 7.90	40.19 ± 7.72	17.466	<0.001*
Range	14.2 – 46.7	22.4 – 52.3	20.9 – 52.3		

F: Analysis of Variance (ANOVA), *: p value < 0.05 (statistically significant)

Table 4 showed the comparison of platelet indices in normotensive women and severity of disease in preeclamptics.

This table described the platelet indices of normotensive women and those with mild and severe preeclampsia. It was found that platelet count declined with severity of preeclampsia, while MPV, PDW and PLCR elevated as disease severity increased. The differences in the platelet indices in the three groups were statistically significant. The mean platelet count declined across normotensive, mild, and severe preeclamptic

groups respectively as follows; 232.51 ± 53.79 x 10^3/µL, 181.68 ± 44.42 x 10^3/µL and 143.46 ± 29.09 x 10^3/µL. The mean MPV increased from the normotensive category, through mild preeclampsia and severe preeclampsia; 10.77 ± 1.22fl, 11.24 ± 0.92fl and 12.19 ± 0.97fl respectively. The mean PDW was 13.94 ± 2.25fl, 14.99 ± 2.22fl and 15.78 ± 2.29fl for the normotensive, mild preeclampsia and severe preeclampsia respectively. While the PLCR was 31.81 ± 7.97%, 39.27 ± 7.90% and 40.19 ± 7.72% for the normotensive, mild preeclampsia and severe preeclampsia respectively. The differences were significant for all the indices ($p<0.001$).

Table 5: Association between Platelet indices and Feto-Maternal Outcomes

Maternal Platelet indices	**Preeclamptic**			**Normotensive**		
Duration of maternal admission	**Postpartum stay**			**Postpartum stay**		
	≤ 72 hours	**> 72 hours**	***p* value**	**≤ 72 hours**	**> 72 hours**	***p* value**
PlateletCount (x 10^3/µL)	176.06±50.25	149.37±32.67	**0.014***	232.53±54.22	231.00	0.978
MPV (fl)	11.41±1.28	12.01±0.96	0.061	10.75±1.23	11.80	0.400
PDW (fl)	14.39±2.17	15.82±2.24	**0.036***	13.94±2.27	14.10	0.945
PLCR (%)	34.21±7.51	41.37±7.15	**0.002***	31.73±8.01	36.80	0.533
Apgar score	**5th minute score**			**5th minute score**		
	< 7	**≥ 7**	***p* value**	**< 7**	**≥ 7**	***p* value**
Platelets (x 10^3/µL)	143.58±33.91	166.08±40.00	**0.014***	229.50±2.12	232.60±54.65	0.937
MPV (fl)	12.09±1.27	11.69±0.76	0.121	10.90±0.14	10.76±1.24	0.879
PDW (fl)	16.07±2.59	15.01±1.84	0.054	13.95±0.07	13.94±2.29	0.997
PLCR (%)	41.62±8.70	38.26±6.40	0.073	32.95±1.48	31.77±8.10	0.839
NICU admission	**NICU admission**			**NICU admission**		
	Yes	**No**	***p* value**	**Yes**	**No**	***p* value**
Platelets (x 10^3/µL)	154.66±33.89	156.05±42.14	0.883	228.00	232.58±54.22	0.933
MPV (fl)	11.92±0.89	11.86±1.17	0.823	10.90	10.77±1.23	0.915
PDW (fl)	16.36±2.20	14.90±2.17	**0.008***	14.10	13.94±2.27	0.945
PLCR (%)	40.49±8.36	39.45±7.31	0.590	32.20	31.81±8.04	0.961

*: *p* value < 0.05 (statistically significant)
NB: *p* value of Independent Samples T test

Table 5 showed the association between platelet indices and feto-maternal outcome

Maternal Intensive Care Unit admission: None of the women in the normotensive group had ICU admission, while 2 women in the preeclamptic group had ICU admission, with a mean platelet count of 127.00 ± 0.01 x 10^3/µL. Mean values of other parameters in the 2 preeclamptics were MPV 13.25 ± 0.64fl, PDW 16.20 ± 0.4fl and PLCR 40.15 ± 0.35%. The indication for the ICU admission was poor recovery from anaesthesia.

Duration of Post-partum Stay: Platelet indices for the preeclamptic group in those that stayed ≤ 72 hours on admission were platelet count of 176.06 ± 50.25 x 10^3/µL,

MPV of 11.41 ± 1.28fl, PDW of 14.39 ± 2.17fl and PLCR of 34.21 ± 7.51% as against those participants that stayed > 72 hours with platelet count of 149.37 ± 32.67 x 10^3/µL, MPV of 12.01 ± 0.96fl, PDW of 15.82 ± 2.24fl and PLCR of 41.37 ± 7.15%. The differences were statistically significant for these platelet indices except for MPV (*p* value of Independent Samples T test, p<0.061). For the normotensive group, there were less marked changes in these parameters and all were not statistically significant. Indications for the preeclamptics that had prolonged hospital stay were mode of delivery(C/S) and poor BP control.

Fifth Minute Apgar score: In the preeclamptic group, for the babies with <7 Apgar score at 5th minute of life, the maternal platelet count was 143.58±33.91 x 10^3/µL and 166.08±40.00 x 10^3/µL for those with ≥ 7 APGAR scores at 5th minute of life, (*p*= 0.014). Although, maternal MPV, PDW and PLCR were lower at Apgar scores ≥7 with regards to babies of preeclamptics, there was no significant association when compared with same parameters at scores ≤7 (p>0.05).

NICU Admission: Out of all platelet parameters in preeclamptics whose babies had NICU admission, only PDW had significant association. The mean PDW in the preeclamptic mothers whose babies were admitted into NICU was 16.36 ± 2.20fl, while 14.90 ± 2.17fl for those whose babies were not admitted into NICU with statistical significant difference (p=0.008). The mean platelet count in preeclamptic mothers whose babies had NICU admission was 154.66 ± 33.89 x 10^3/µL, while those without NICU admission was 156.05 ± 42.14 x 10^3/µL but the difference was not statistically significant (p= 0.883). The mean MPV for those preeclamptic mothers whose babies were admitted was 11.92 ± 0.89fl and 11.86 ± 1.17fl for those that were not admitted with no statistically significant difference (p= 0.823). The mean PLCR in the preeclamptic mothers whose babies were admitted into NICU was 40.49±8.36%, while 39.45±7.1% for those whose babies were not admitted into NICU with no statistical significant differences (p=0.590). The indications for NICU admissions were prematurity and low Apgar scores.

Table 6: Association between Platelet Indices and Foetal Outcome (Foetal death)

Maternal	**Preeclamptic**			
Platelet indices	**Foetal death**			
	Yes (n = 13)	**No (n = 57)**	**t**	***p* value**
Platelets Count (x 10^3/µL)	143.46 ± 31.95	158.21 ± 39.80	-1.245	0.217
MPV (fl)	12.00 ± 1.45	11.86 ± 0.95	0.440	0.662
PDW (fl)	15.79 ± 2.23	14.40 ± 2.26	2.019	**0.048***
PLCR (%)	40.392 ± 10.23	39.776 ± 7.13	0.256	0.798

t: Independent Samples T test; *: p value <0.05

Table 6 showed the association between platelet indices and fetal outcome (Fetal death)

There was statistically significant difference in the mean values of PDW in preeclamptics with and without fetal demise: mean values of 15.79 ± 2.23fl vs. 14.40 ± 2.26fl (p = 0.048) respectively. Other parameters were not significantly associated with fetal deaths in preeclamptics.

DISCUSSION

The remarkable findings in this study were significant differences in platelet indices values between the preeclamptic participants and the normotensive controls, increase severity of preeclampsia with increase platelet indices abnormalities and more adverse pregnancy outcome in the preeclamptic participants as oppossed to the normotensive women.

The platelet indices of 140 participants comprising 70 participants from each arm of the study were analyzed. The mean platelet count in the preeclamptic group was significantly lower than in the normotensive group while the MPV, PDW and PLCR were significantly higher in the preeclamptic group than the normotensive group. The mean platelet count in the normotensive group in this study agreed with reports from other parts of Nigeria and also lower than non-pregnant values by some authors.[10,21,22] Similarly, the mean values of MPV and PDW were also consistent with findings of other authors which were higher than values in non-pregnant women.[13,21,23] However, The PLCR of the normotensive group was found to be higher than findings of Ammar et al and Biva et al in Egypt and India respectively and consistent with elevation in pregnancy.[23,24] This was as a result of bone marrow compensation for the rapid turnover of platelets; the release of younger and larger platelets which increase MPV, PDW and PLCR, which were indices of measurements of average platelet size.[25] Differences in sample size, number of controls and type of haematological autoanalyzer may explain the little difference in mean PLCR in this study and other reports.[23,24] Hence, it is important to have baseline values of platelet indices in our environment so as to serve as reference values and also using appropriate study designs that are multicentered with large sample sizes wound be of help.

The mean platelet count in preeclamptics was significantly lower than the mean value in the controls. This was similar to findings of Onuigwe et al in Sokoto, Ammar et al in Egypt, Sultana et al in Bangladesh and Amita et al in India.[10,13,17,23] However, Santos et al in Turkey found no significant difference.[26] The further significant reduction in platelet count in preeclamptics could be linked to increased production of thromboxane A_2 that induces supplementary platelet aggregation and endothelial damage, contributing to platelet dysfunction and promoting platelet consumption resulting in low platelet count, which is an important sign of preeclampsia.[27]

The mean MPV for the preeclamptic group was significantly higher than in the normotensive group. This was in agreement with findings in similar studies.[23,26] However, Studies by Amita et al and Ceyhan et al though found increase in MPV in preeclamptics, but were not statistically significant.[13,28] These studies used varying sample sizes and some were multicentred based studies compared to what was obtained in this study. Bone marrow produces and releases large platelets due to increased consumption of platelets leading to increase MPV in preeclampsia.[13]

The mean PDW in the preeclamptic group was significantly higher than in the normotensive group, similar to study by Ammar et al in Egypt, and other similar studies.[13, 23,29] The increase in PDW was due to platelet turnover which would support the fact that platelet survival time was decreased leading to increased destruction of platelets.[13] The mean PLCR was significantly lower than mean value of normotensive controls. This finding was similar to study by Ammar et al in Egypt.[23]

Furthermore, comparison of mean platelet count in normotensive women and mild to severe preeclamptics showed a significant inverse relationship between the count and degree of severity. This is in agreement with other similar studies.[14,23] This was due to the fact that the platelet numerical and functional anomalies worsen with the severity of the disease.[27]

The mean MPV in normotensive women and those with mild and severe preeclampsia showed increasing values from normotensive ones to severe preclamptics. This proportionate increase with degree of severity was similar to findings of Ammar et al in Egypt, but different from reports of Amita et al probably because of the differences in gestational age, Amita et al used cases at earlier gestational age.[13,23] In the same vein, mean PDW and PLCR also increased with severity of disease. This was consistent with findings from earlier studies.[13,23]

There were more of caesarean deliveries in preeclamptic women than the normotensives. This was because some pregnancies were terminated in the preeclamptic group with severe disease and unfavourable cervix using abdominal delivery as the fastest and safest route of delivery. Blood loss was significantly more in the preeclamptic group compared to the normotensive group and this could be explained by the fact that about half of the parturient in this group were delivered by caesarean section. Thus, specifically designed study on platelet indices and blood loss in preeclampsia will be needed to assess their relationship.

More parturient in the preeclamptic group had greater length of stay on admission (> 72 hours) compared to the control group and this was statistically significant. Also this might have been as a result of the fact that a significant number of these parturient had Caesarean delivery and poor BP control. Test of association between the platelet indices in the preeclamptics that had longer hospital stay (>72hours) compared to those with less stay (≤72 hours) revealed that the differences in the indices were significant except for the MPV. This was similar to maternal outcome found in study by Ammar et al in Egypt.[23]

Babies in the preeclamptic group were delivered at a lower gestational age compared to those in the normotensive group which was found to be significant. This was as a result of the fact that some of the preeclamptic women had their pregnancy terminated as a result of difficulty in controlling their disease (BP), anticipated complications or with evidence of worsening disease state. This also explained the lower mean birth weight in the preeclamptic group compared to normotensive group as the mean gestational age at delivery was lower in the preeclamptic controls. A significant number of newborns in the preeclamptic group were admitted into the NICU compared to those in the normotensive group (41.4% vs. 1.4%). This was as a result of prematurity and poor Apgar scores in significant number of their newborns necessitating NICU admission. Platelet indices in those preeclamptics whose babies were admitted into NICU revealed that the platelet count was lower and MPV, PDW and PLCR were higher than in those without NICU admission. However, changes in PDW were the only significant ones. In contrast, Ammar et al found significant changes in all these platelet parameters.[23]

As expected, the Apgar scores were better in babies of controls than the preeclamptic mothers. However, only mean platelet count was significantly higher in preeclamptics whose newborns had better 5th minute Apgar score than those whose newborns had lower 5th minute Apgar score. The MPV, PDW and PLCR were not

significantly different. This was unlike the study by Ammar et al in Egypt who found significant changes in all these platelet parameters.[23]

There were 18.6% fetal demise in the preeclamptic group and none in the normotensive group and this was statistically significant. This study also found that platelet count was lower and MPV, PDW and PLCR were higher in the women with fetal demise compared to those without fetal death. Although, only the differences in PDW was statistically significant. Ammar et al in Egypt found significant differences in all the indices.[23] This suggests variable or indefinite associations between fetal outcome and platelet indices, unfortunately, there were few studies on this subject and further research works are needed.

CONCLUSION

Platelet indices abnormalities and adverse pregnancy outcome were higher in preeclamptic women than their normotensive counterparts.

RECOMMENDATIONS

1. Close monitoring should be ensured in the preeclamptics with suggestive platelet indices results.
2. Multicenter studies in platelet indices in normal pregnancies and preeclamptics should be carried out to establish the reference values in this environment.
3. Further studies should be carried out to determine the prognostic values of each platelet indices.
4. Studies on serial platelet indices in pregnancy should be carried out to establish reference values across trimesters.

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