Greener Journal of Medical Sciences
Vol. 13(2), pp. 164-182, 2023
ISSN: 2276-7797

https://gjournals.org/GJMS

Comparative Difference in Platelet Indices Among Preeclamptics and Controls at a Tertiary Centre in Port Harcourt, Nigeria.

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ARTICLE'S INFO

Article No.: *091623094*
***Type*:** *Research*
Full Text: *PDF, PHP, HTML, EPUB, MP3*

Accepted: 16/09/2023
Published: 17/10/2023

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Keywords: *platelets, indices, pregnant, women, pre-eclampsia.*

ABSTRACT

BACKGROUND: Pre-eclampsia (PE) is a common preventable and potentially life-threatening complication of pregnancy. It is a multisystem disorder complicating 2-5% of pregnancies. The International Federation of Obstetrics and Gynaecology (FIGO) in its 2019 guidelines for combating Pre-eclampsia highlighted the fact that predicting and preventing pre-eclampsia is the solution to this global scourge.

Since the nations of the West African sub-region are generally resource-poor, there is a need to seek and ascertain other scientifically reliable but cheaper ways of screening for and predicting pre-eclampsia among pregnant women as a basis for implementing prophylactic measures. Understanding the changes in platelet indices in pregnant women with PE compared with healthy controls will be the first step towards ascertaining the predictive value of platelet indices in the development of PE which will fill the gap in this regard.

OBJECTIVES: The objectives of this study were to determine the changes in platelet indices in pregnant women with PE compared with healthy controls and to ascertain the relationship of these indices with the development of PE.

METHODOLOGY: This study was a case-control study carried out between October 2020 and June 2021 after ethical approval has been obtained from the Rivers State University Teaching Hospital Health Research Ethics Committee. It involved 50 eligible and consenting pregnant women with PE as cases and 50 healthy pregnant women as controls, all of whom either presented for routine antenatal care or presented for delivery at the labour ward of the Rivers State University Teaching Hospital. Blood samples were collected using a vacutainer and full blood count and platelet indices (platelet count, mean platelet volume and platelet distribution width) were analysed using an automated haematology analyser, Sysmex KX-21N. The socio-demographic information of the study participants was collected using a structured questionnaire. Data were analysed using the Statistical Package for Social Sciences (SPSS) version 25.

RESULTS: The sociodemographic characteristics of cases were similar to those of controls. The results found a statistically significant difference in the mean platelet count between cases (176.30 $\pm$ 67.38 fL) and controls (207.16 $\pm$ 62.07fL), p=0.019 as well as in the mean values of platelet distribution width (PDW) in both cases and controls. The PDW was significantly raised (15.53 $\pm$ 3.36fL) compared to controls (13.75 $\pm$ 2.53fL), p=.0.004. There was no significant difference in the mean platelet volume (MPV) between cases and controls. The mean value of the MPV was 11.14 ±1.33 among cases and 10.65±1.38 for controls, p=0.075. Using receiver operator characteristics (ROC) curves, the cut-off for the diagnosis of PE was 11.6fL for MPV and 14.5fL for PDW. At this value, the sensitivity of MPV was found to be 36% and specificity was 88% while the positive predictive value and negative predictive value were 73.9% and 42.9% respectively. The sensitivity and specificity of PDW at the cut-off of 14.5 were found to be 66.0%and 72.0% respectively while the positive and negative predictive values were 70.2% and 67.9% respectively.

CONCLUSION: The platelet count is significantly reduced in PE compared to controls but has very low diagnostic accuracy. The MPV is not significantly raised in PE when compared with controls. The PDW is significantly raised in PE compared with controls. Rising values of the PDW in pregnant women may be an indication of more focused care within the context of preeclampsia prevention and management.

INTRODUCTION

Preeclampsia (PE) is a multisystem disorder affecting 2-5% of pregnant women globally.[1] It is a major cause of maternal and perinatal morbidity and mortality.[1–5] It accounts for the death of 76,000 women and 500,000 babies yearly around the world.[1] Women in low-income nations are at higher risk.[6–8] Data on the overall prevalence of PE in Nigeria is lacking. However, a study carried out at the University of Calabar Teaching Hospital, Nigeria, puts the prevalence of PE at 1.2%.[7]

The pathogenesis of PE is not known.[1,9,10] However, it is believed to involve a two-stage process. The first stage is accounted for by a poor invasion of the spiral arteries by trophoblasts with the resultant poor remodelling of the spiral arteries. Two mechanisms are involved in the second stage of the disease. The first is a maternal response to endothelial malfunction. The second mechanism is an imbalance between the factors which favour angiogenesis and those unfavourable to angiogenesis. Together, these two mechanisms synergistically produce the clinical manifestations of the disease.[11,12]

Gestational hypertension is defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (dBP) ≥90 mm Hg on at least two occasions measured 4-6 hours apart occurring after the twentieth week of pregnancy in a woman previously known to be non-hypertensive.[1] International Federation of Obstetrics and Gynaecology (FIGO) adopted the International Society for the Study of Hypertension in Pregnancy (ISSHP) definition of PE. As defined by the ISSP, PE is gestational hypertension accompanied by ≥1 of the following new-onset conditions at or after 20 weeks of gestation: proteinuria (i.e. ≥30 mg/mol protein: creatinine ratio; ≥300 mg/24 hours; or ≥2 + dipstick); evidence of multiple organ abnormality manifesting as: acute kidney injury (creatinine ≥90µmol/L or 1mg/dL); liver dysfunction (elevated transaminases, e.g. alanine aminotransferase or aspartate aminotransferase >40 IU/L) plus or minus right upper quadrant or epigastric pain; neurological manifestations such as eclampsia, altered mental state, blindness, stroke, clonus, severe headaches, and persisting visual scotomata); or haematological abnormalities such as thrombocytopenia (platelet count<150,000/L), disseminated intravascular coagulopathy and haemolysis; or uteroplacental malfunction manifesting with foetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth).[1,4]

Factors which increase a pregnant woman's risk of PE include maternal age >35 at the time of delivery, nulliparity, history of PE, assisted conception, and family history of PE in the mother or siblings. Other identified risk factors include obesity (BMI>30kg/m^2), Afro-Caribbean and South Asian origin as well as the presence of comorbid conditions like diabetes mellitus, gestational diabetes mellitus, chronic hypertension, chronic kidney disease and autoimmune conditions such as systemic lupus erythematosus and antiphospholipid syndrome.[1,5] This potentially life-threatening complication of pregnancy can, in the mother lead to intracranial haemorrhage, acute pulmonary oedema, respiratory distress syndrome, placental abruption, acute renal failure, cardiovascular disease and chronic and end-stage renal disease. Sadly too, the life expectancy of women who develop PE is reduced on the average by 10 years.[1,6] Most of the foetal complications of PE are related to birth weight and gestational age at delivery.[6,12,13] These complications are largely attributed to early-onset PE.[1] Short term foetal complications of PE include foetal growth restriction, oligohydramnios, intrauterine foetal death, preterm birth, low Apgar score, non-reassuring foetal heart rate in labour and increased need for neonatal intensive care unit admission. In the long term, nervous system disorders, mental health issues, hearing and visual problems, insulin resistance, derangements of glucose metabolism, coronary artery disease and chronic hypertension could result.[1,14]

The overwhelming short- and long-term sequelae of PE on both mother and child, the huge financial burden of providing neonatal intensive care and the overall burden to the health system justify efforts aimed at effective prediction and prevention of PE. More so, accurate prediction of women likely to develop PE will create room for timely institution of prophylactic measures, appropriate antenatal surveillance and higher quality research into preventive interventions.[15]

In its 2019 Guidelines, FIGO recommends a four-pronged strategic approach for dealing with PE. This includes a public health awareness, universal screening, contingent screening, and prophylactic measures using aspirin or calcium. FIGO's public health focus is aimed at activities that create awareness, increase access, and make affordable and acceptable prenatal services for women of reproductive age. This is to be combined with raising awareness of the benefits of early prenatal visits for women of reproductive age, especially in low-resource settings. For early prediction of PE, FIGO's best model recommends a patient's risk factor assessment with assessment of Mean Arterial Pressure (MAP), Placental Growth Factor (PLGF), and Uterine Artery Pulsatility Index (UTPI).

In low-resource settings, such as exist in the West African sub-region, a more pragmatic approach for prediction of PE is needed. Such an approach will be a prediction model that not only has a high positive predictive value but also cost-effectiveness. In this regard, several studies have shown promise using platelet indices (platelet count, PC, platelet distribution width, PDW, and mean platelet volume, MPV) as guide for the prediction of the likelihood and severity of PE.[10,16–23]

The potential role of platelet indices in prediction of PE has not been sufficiently explored. There are still gaps in what is known at the moment. Controversies exist. Some studies find statistically significant changes that are predictive and determinant of the severity of PE in all platelet indices (PC, PDW, MPV).[10,17,19,23] However, other studies

suggest either one or two of the platelet indices to be more reliable as predictor and determinant of the severity of PE.[16,18,20,21]

Such differences could possibly result from the performance of the different models of the haematology analysers used and /or the socio-demographic indices of the populations studied. The preponderance of controversies on the role of platelet indices in the prediction and determination of disease severity in PE is an indication that more studies are needed in order to reach a definitive conclusion on the role of platelet indices for predicting pre-eclampsia and determining its severity among the obstetric population.

Again, there is a dearth of studies on platelet indices among pregnant women with PE in this region. This is a huge gap in the obstetric practice in our environment, especially, given the unmet need for use of more economically pragmatic but reliable markers for the early prediction of PE.

Platelet indices are extracted from the routine measurement of full blood count using the automated haematology analyser. As such, the method for evaluating platelet indices is easy, readily available, and cost-effective. It is, therefore, necessary; to evaluate platelet indices among pregnant women with PE in Port Harcourt city as this can highlight the comparative difference with healthy pregnant controls and serve as a proxy for understanding the role of these indices in the setting of preeclampsia prevention and management in our environment.

Pre-eclampsia is a life-threatening multisystem disorder of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. It complicates about 2-5% of pregnancies globally.[1] It is sub-classified into early-onset and late-onset pre-eclampsia as well as preterm and term. Early-onset occurs before 34 weeks gestation whereas late-onset occurs after 34 weeks gestation. Preterm PE is one in which delivery occurs before 37 completed weeks while term PE is one in which delivery takes place after 37 completed weeks.[1] Women in low resource settings are adjudged to be at greatest risk.[2] African American women for example are said to have a preeclampsia-related mortality three times greater than that seen among white women due to inequalities associated with inadequate antenatal care.[3]

It is defined broadly as the presence of an elevated blood pressure of ≥140/90mmHg taken on two occasions at least 4-6 hours apart with significant proteinuria (≥300mg in a 24-hour urine sample or 2+ on dipstick) at or after the twentieth week of pregnancy in a woman not previously known to be hypertensive or proteinuric. In clinical practice, the diagnosis of PE is based on this definition.[1]

The pathophysiology of PE has not been fully elucidated.[4,13,24] However, it is currently understood that in genetically predisposed women, a combination of abnormal immune response and defective placentation lead to imbalance between pro-angiogenic factors and anti-angiogenic factors with consequent widespread maternal endothelial dysfunction, vasospasm and activation of the coagulation system.[25–27]

Peripheral vasoconstriction results in hypertension which with derangement of endothelial cell integrity causes enhanced vascular permeability and resultant generalized oedema. In the kidneys, endothelial damage leads to altered glomerular filtration and selective leakage of intermediate weight proteins such as albumin causing proteinuria.[26,28]

Endothelial damage in preeclampsia is associated with platelet activation and consumption leading to thrombocytopaenia.[29] In the liver, sub-endothelial fibrin deposition occurs with associated elevation of the liver enzymes and haemolysis. The combined, concurrent occurrence of haemolysis, elevated liver enzymes and low platelets is known as HELLP syndrome. Cerebral vasospasm and oedema are believed to be responsible for the neurological manifestations of the disease.[30]

Abnormalities of the vascular system manifesting with raised systemic vascular resistance, enhanced platelet aggregation, activation and modification of the coagulation system, and endothelial cell dysfunction are believed to contribute significantly to the pathogenesis of preeclampsia.[31–33] A gradual reduction in the platelet count is the most common observation and may be due to platelet consumption during low-grade intravascular coagulopathy. Several studies have indicated that platelets may play a critical role in the aetiopathogenesis of preeclampsia and thrombocytopenia is the most common haematological abnormality seen in PE[34]. The severity of thrombocytopenia increases with the severity of the disease. The pathogenesis of thrombocytopenia in preeclampsia is not clear; however, it may result from activation of the coagulation system and increased platelet consumption.[34] Platelet indices (PIs) are a group of parameters which are cheap to assay and are gotten from routine full blood counts. The mean platelet volume (MPV) and platelet distribution width (PDW) are the most valid and remarkable PIs and are useful for clinical research because they are readily available to clinicians.[17]

Life-threatening thrombocytopenia is associated with HELLP syndrome. Thromboxane A released by thrombocytes plays a critical role in the pathophysiology of PE. Thromboxane A enhances platelet aggregation and endothelial damage, causing platelet dysfunction and platelet consumption and ultimately thrombocytopenia. Platelet activation (by P selectin, CD 63 and PECAM) is associated with enhanced endothelial damage with microthrombi formation leading to end-organ degenerative necrosis and placental infarction.

The bone marrow responds to the decrease in platelets by release of immature, larger-size platelets having raised Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW).[25–27,29,34] MPV is a measure of platelet size while PDW is a measurement of platelet anisocytosis.

Several studies have evaluated the significance of platelet indices in the prediction, diagnosis and prognostication of preeclampsia.[10,17–23,32]

Likewise, raised MPV and PDW serve as important indicators of disease severity.[35]
Whereas the definitive cause for PE remains unknown, certain risk factors have been identified to be associated with increased incidence of the disease. The disease is more common in primigravidae and those with a previous personal history of PE. Pregnant women with multiple gestations, chronic hypertension or underlying kidney disease have also been noted to be at greater risk of PE.[1,2]

Advanced maternal age 35 years and above poses an increased risk of preeclampsia. Besides, hydatidiform mole, obesity (13.3% in those with BMI≥35kg/m²), thrombophilia, oocyte donation or donor insemination, urinary tract infection, diabetes mellitus also increase the risk of PE.[1] Risk factors noted in both early- and late-onset PE include older maternal age, Hispanic race and Native American race. Others are smoking, single women, and male foetus. Risk factors more strongly linked with early-onset PE than late-onset disease included black race, chronic hypertension, and congenital anomalies. Younger maternal age, nulliparity, and diabetes mellitus are more strongly linked to late-onset preeclampsia than with early-onset disease.[6]

Several studies have shown a lot of promise as regards the role of platelet indices in predicting the likelihood and severity of PE in at-risk patients.[34] In a study of sixty PE patients and sixty healthy controls, Alsheeha et al observed no significant difference in PDW and MPV between patients with PE and their healthy counterparts. However, both PC and PC to MPV ratio were significantly reduced in the women with PE compared with healthy controls. There was no significant difference in the PC, PDW, MPV, and PC to MPV ratio when women with mild and severe preeclampsia were compared. PC cut off was 248.0×10^3/μL for diagnosis of preeclampsia (p=0.019; the area under the receiver operating characteristics (ROC) curve was 62.4%). In the study, binary regression suggested that women with PC $<248.010\times10^3$/μL were at higher risk of PE (odds ratio =2.2, 95% confidence interval =1.08–4.6, P=0.03). In this study, the PC/MPV cut off was 31.2 for the diagnosis of PE (P=0.035, the area under the ROC curve was 62.2%). The researchers concluded that PC $<248.010\times10^3$/μL and PC to MPV ratio 31.2 are valid predictors of preeclampsia.[34]

In a study of one hundred Indian women, fifty of whom had PE and fifty healthy controls, Deepak et al found a difference between the PDW values in pregnant women with pre-eclampsia and that of healthy controls which was statistically significant. Though the mean platelet count in their study was decreased in comparison to controls, it lacked statistical significance. The researchers concluded that assessing the PDW and MPV, along with platelet count may be beneficial as an indicator of pre-eclampsia.[35] Priyanka G et al in their study of sixty-seven women with PE compared with an equal number of healthy controls noted that MPV was higher in women with pre-eclampsia whereas platelet count was significantly lower. Though also lower, the difference in PDW between preeclampsia patients and the control group was not significant.[36]

Abas et al in Sudan analysed platelet indices of thirty-seven women with PE compared to fifty normal healthy pregnant women and reported thrombocytopaenia in 32.4% of PE patients compared to 0% in healthy pregnant women. MPV and PDW were also significantly higher in PE patients compared to controls.[18]

To evaluate the predictive value of platelet indices in the development of PE, Dadhich, S et al in a prospective study, observed the changes in platelet indices of two hundred women from 20-24 weeks gestation up until 40 weeks and 7 days following delivery. The results showed that platelet count decreased significantly (19.4% versus 7.4%) whereas mean platelet volume and platelet distribution width increased significantly in women with PE compared to healthy controls (44.5% versus 9.22% and 47.19% versus 29.4% respectively. The decrease in platelet count in normal pregnancies was not statistically significant whereas the decline in platelet count in PE patients was statistically significant and rapid with such decline being directly proportional to the severity of hypertension. Though the MPV was raised in normal pregnancies, such rise was insignificant but a significant and consistent rise in MPV was seen among PE patients which was noticed 4-6 weeks before a notable increase in blood pressure. In this study the rise in PDW was not statistically significant in normal pregnancies up to 32weeks gestation while the rise in PDW among pregnant women with PE was statistically significant, occurring even before a significant blood pressure increase was noted. This study established a direct correlation between changes in PC, MPV and PDW and progressive rise and severity of PE as the month-wise decrease in platelet count as well as the month-wise increase in MPV and PDW were statistically significant compared to non-PE patients. The authors concluded that the evaluation of platelet indices appear to be a reliable, rapid, easy and economical way of predicting PE and its severity in early pregnancy.[19]

In a study to evaluate the relationship between platelet count, mean platelet volume (MPV) and platelet distribution width (PDW) and severity of preeclampsia and to evaluate their role in prediction of preeclampsia, Abdel-Moneim et al studied one hundred and fifty pregnant women at the Al-Azhar University Hospital, Cairo, Egypt. In their study, fifty women had severe PE; fifty had mild PE while the third group of fifty were healthy pregnant women who served as control. Their findings were in consonance with those of other researchers.[10,17–23,32] The platelet count was significantly lower in women with severe PE compared to women with mild PE and normal pregnant women groups (139.340 ± 32.610,183.940 ± 37.380 and 249.120 ± 38.350with P < 0.001) respectively. They also found that mean platelet volume and platelet distribution width were

significantly higher in women with severe PE compared to women with mild PE and normal pregnant women groups (11.07 ± 1.08 vs. 9.82 ± 0.68 and 8.50 ± 0.75with p < 0.001 for MPV and 17.09 ± 2.12 vs. 14.26 ± 1.84 and 11.01 ± 1.77 with p < 0.001 for PDW) respectively. They opined that due to increased platelet destruction and platelet turn over in patients with preeclampsia, decreasing platelet count and increasing MPV and PDW may play a role in predicting preeclampsia and concluded that Platelet indices are simple, cheap and practical tools in predicting severity of PE.[17]

The study by Tesfay et al of 79 PE patients and 140 healthy pregnant women in Ethiopia also highlighted the role of platelet indices in the prediction and prognostication of disease severity in PE. In their study, PC showed significant decrease while the MPV and PDW increased significantly with severity of PE. At cut-off value greater than 9.45fL, the MPV had a sensitivity of 83.5%, specificity of 86.4%, positive predictive value of 77.6% and negative predictive value of 90.3%. In conclusion, the authors posited that MPV and PC can be used to diagnose severe PE as well as predict and prognosticate the disease.[10]

Thrombocytopenia is the most common haematological abnormality observed in preeclampsia and it may be due to consumption of platelets during abnormal activation of the coagulation system.[35] However, Ceyhan et al in their study of fifty-six pregnant women with PE and forty-three normotensive pregnant women did not find a significant difference in the MPV and platelet count between preeclampsia patients and healthy controls.[37]

Thalor et al found no statistically significant relationship between platelet count decrease and PE but observed a significant correlation between MPV and PDW and PE. The lack of significant correlation between thrombocytopaenia and PE in that study was attributed to the low sample size as well as the fact that most of the PE patients had mild PE and at an earlier GA of between 20 and 24 weeks. MPV and PDW were however significantly raised, with the rise being directly proportional to the severity of hypertension; making the researchers conclude that these easily available and inexpensive markers could be used as predictors of preeclampsia and its severity.[20] Kashanian et al. observed that MPV alterations in the first and third trimester of pregnancy are increased in women who would ultimately develop PE, but has low predictive value and as such is not a good predictor of pre-eclampsia.[38]

The study by Han et al looked at changes in blood coagulation parameters and platelet indices in healthy pregnant women compared with women with mild and severe PE. The report from that study showed that MPV was significantly raised among women with PE. For this study, 174 pregnant women were recruited. Of these,79 were healthy pregnant women,53 had mild PE while 42 had severe PE. Blood samples were collected during early and late pregnancy. Coagulation and platelet indices were assessed and compared among the three different groups of women. The receiver-operating characteristic (ROC) curves of the various parameters were generated, and the area under the curve (AUC) was calculated. The predictive values of both coagulation and platelet parameters were assessed in binary regression analysis. In the later part of pregnancy activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT) and platelet count decreased in healthy pregnant women, while the fibrinogen level and mean platelet volume (MPV) were raised compared to early pregnancy (p<0.05). On the other hand, in women with PE raised APTT, TT, MPV and D-dimer (DD) during the third trimester was observed. It was also observed that TT showed the largest AUC (0.743) and high predictive value in all participants. In women with PE, MPV showed the largest AUC (0.671) and ideal predictive efficiency irrespective of the severity. The researchers concluded that thrombin time and MPV may serve as early monitoring markers for the onset and severity of PE, respectively.[21]

Based on observations from a retrospective study of 284 pregnant women at a tertiary hospital in Istanbul, Turkey (composed of 49 with mild PE, 70 with severe PE and 165 healthy women serving as control group) over a three-year period, Dogan K et al recommended that PC, MPV, and the PC/MPV ratio are useful indices for predicting the risk of PE. They observed a statistically significant difference between pregnant women with PE and healthy controls in terms of PC (p = 0.023; p<0.05), MPV (p = 0.023; p<0.05), PC/MPV ratio (p = 0.005; p<0.01). However, no difference was observed between women with severe PE and those with mild PE. Cut-off values for MPV and PC were 9 and 90 respectively for the diagnosis of PE (p<0.01) whereas the odds ratios were 1.999 and 1.932 for MPV and PC respectively. In the study, the PC/MPV ratio was significantly lower in subjects with PE than healthy controls (p = 0.001). A significant relationship between PE and a cut-off level of 19.9 for the PC/MPV ratio was evident from the study (p< 0.01). The study highlighted a 2.4-fold higher risk of PE in women with PC/MPV ratios of ≥19.9 with an odds ratio of 2.422 (95% CI: 1.449–4.048).[32]Viana-Rojas et al demonstrated from their study of 64 women with PE and 70 normotensive pregnant women that the MPV was significantly raised in PE and even more so in severe PE compared with normotensive pregnancies and concluded that the MPV is a cheap and easily accessible marker of PE and its severity.[39] Many other studies have also highlighted the effectiveness of MPV as a marker of PE.[22,23,40]

Raised MPV indicates enhanced platelet activation which may result from poor utero-placental circulation. Kanat-Pektas et al studied 200 women at 11- 14 weeks gestation to determine the predictive value of MPV in the late first trimester in detecting women who could develop PE. MPV was significantly higher in pregnant women who subsequently developed PE (P = 0.001). The study concluded that MPV values of 10.5 fL or more could predict pre-

eclampsia with 66.7% sensitivity and 63.8% specificity.[41]

Reddy et al in a prospective study of 235 PE patients and 203 healthy pregnant women demonstrated that the PC, MPV and PDW values had diagnostic and prognostic values for PE. While the PC decreased, the MPV and PDW increased. The MPV particularly demonstrated prognostic significance as the degree of increase in the MPV correlated with the degree of severity of PE. MPV at cut-off values of 10.95fL had a sensitivity of 80% and a specificity of 75%. In the study, a cut-off value of 10.95f L for MPV was found to have significant predictive value for disease progression in PE.[42]

In a retrospective case-control study of fifty PE patients and fifty healthy controls, Amita K et al reported no statistically significant increase in MPV in PE patients as compared with healthy controls. However, they noted that platelet count was a reliable index for diagnosing PE and predicting its severity. They also observed a statistically significant increase in PDW and concluded that this was also another reliable index for diagnosis of PE but recommended that its role in determining the severity of preeclampsia need to be explored.[43]

To ascertain normal platelet indices in the city of Port Harcourt, Pughikumo, et al studied the platelet indices of 126 healthy pregnant women and those of 102 non-pregnant women of reproductive age using the automated haematology analyser, PCE-210 (N), ERMA. They reported a progressive decline in platelet count and PDW with advancing gestation compared to non-pregnant controls, but the finding was not statistically significant. The MPV in their study was higher in pregnant women but this, again, was not statistically significant. The mean platelet count for the pregnant women was 212.74 ± 63.28 x 10^9/L; the mean MPV 9.99 ±1.94fL while the mean PDW was 12.68 ± 1.91fL.[44]

To establish normal haematological values in healthy pregnant women in the city of Port Harcourt, Amah-Tariah et all studied the values of platelet count, mean platelet volume and platelet distribution width, in the three trimesters of pregnancy among two hundred and twenty healthy pregnant women. Of that number, seventy-three were in the first trimester, seventy-five in the second and seventy-two in the third trimester. Platelet count, mean platelet volume and platelet distribution width, were all determined by flow cytometry using the Swelab Alfa Basic model haematological analyser (Boule Medical AB, Stockholm, Sweden). Their study showed that the average PC across the three trimesters varied from 289.4±21.68 x10^3/µL (87.00-594.00) in the first trimester to 259.93± 98.6 x 10^3/µL (71.00-558.00) in the second trimester and 279.63± 107.97 x 10^3/µL (117.00-693.00) in the third trimester. Average values for the MPV (fL) were 8.45±0.79(6.60-10.90), 8.65±0.76(7.00-10.2) and 8.69±0.75(7.00-10.70) in the first, second and third trimesters respectively. The PDW(%) averages were 9.93±1.40 (6.90-14.4), 10.10±1.46(6.90-13.40), and 9.86±1.37(7.70-14.90) for the first, second and third trimesters respectively.[45] Unamba in a study of 65 pregnant women with PE at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria looked at “Haematological indices and the Effects of Thrombocytopenia on maternal and Perinatal Outcome in women with preeclampsia in Port Harcourt, Nigeria” and reported no thrombocytopaenia among the study population using a cut-off mark of 150 x 10^9/L. The researcher concluded that platelet count may not be a reliable index for predicting and prognosticating disease severity and risk for foetal-maternal complications in pregnant women with PE in Nigeria. The author further asserted that the probability of using thrombocytopaenia to ascertain the prognosis of pre-eclampsia is not feasible in our environment and should not be advocated for.[46] However, the author attributed the absence of thrombocytopaenia among the study population in this particular study to possible early intervention before the onset of thrombocytopaenia. Again, since this was not a comparative study, it is difficult to rely on the conclusion from this study as the study did not consider what the platelet indices were in the healthy pregnant population. Also, in this study, proteinuria was pegged at 1+ on urine dipstick. However, FIGO definition of significant proteinuria is 2+ on urine dipstick. This could have also affected the results of this study which contradicts the findings of similar studies showing a progressive decline in platelet count even before the onset of a rise in blood pressure. From the foregoing, it is clear that the potential role of platelet indices has not been sufficiently explored. There are still gaps in what is known at the moment. Controversies exist. Some studies find statistically significant changes that are predictive and determinant of the severity of PE in all platelet indices (PC, PDW, MPV).[10,17,19,23] However, other studies suggest either one or two of the platelet indices to be more reliable as predictor and determinant of the severity of PE.[18,21,22,32,47] Such differences could possibly result from the performance of the different models of the haematology analysers used and /or the socio-demographic indices of the populations studied. The preponderance of controversies on the role of platelet indices in the prediction and determination of disease severity in PE is an indication that more studies are needed in order to reach a definitive conclusion on the role of platelet indices for predicting pre-eclampsia and determining its severity among the obstetric population.

AIM AND OBJECTIVES

This study aimed to compare the platelet indices between pregnant women with and without preeclampsia and determine the relationship between platelet indices and the occurrence of preeclampsia.

PATIENTS AND METHODS

The subjects for this study were from the antenatal clinic attendees and labour ward parturients. Routine

examinations and investigations carried out at the booking antenatal visit and the labour ward for unbooked patients include weight, height, and blood pressure measurements. Others are full blood count, retroviral screening, hepatitis B virus screening, venereal disease research laboratory test, haemoglobin genotype, ABO blood group and rhesus typing and urinalysis. This study was a case-control study involving pregnant women with PE and healthy pregnant women at a gestational age of 20 completed weeks and above being seen at the ante-natal clinic or labour ward of the Rivers State University Teaching Hospital.

Socio-demographic information of participants was collected using a structured questionnaire by the principal investigator and trained designated house officers. Physical examination was carried out by the principal investigator. Pregnant women were initially advised to sit and relax for five minutes before having their blood pressure taken. The participants were then instructed to take off their extra clothes and sit up straight with their left arm resting on the bench. Blood pressure readings of participants were then taken by designated trained midwives using OMRON automated blood pressure monitor, Model M3 and finally crosschecked by the principal investigator. A urine sample was collected using a clean dry specimen bottle to check for proteinuria. This aspect of the study which was carried out by designated trained midwives involved dipping a Meditest Combi-2 test strip into the urine sample for one minute and then checking for colour change which indicated the presence of proteinuria. A colour change from yellow to green which is equivalent to 2+ proteinuria in addition to a raised blood pressure of ≥140/90mmHg on at least two occasions four hours apart was used to make the diagnosis of preeclampsia. A woman who meets the inclusion criteria was briefly counselled on the procedure for blood sample collection. She sits down with her arm rested on a table. A tourniquet is then applied to the upper arm 8cm-10cm above the antecubital fossa. The area over the cubital vein is cleaned with a spirit-soaked piece of cotton wool. The vacutainer needle on a holder with the bevel facing up was used to puncture the vein and a properly labelled vacutainer tube prefilled with K2 EDTA applied. When blood flow starts, the tourniquet was removed and three (3ml) of blood collected. After sample collection, a piece of dry cotton wool was placed on the venepuncture site, the needle removed, and gentle pressure applied by the participant for about two minutes to prevent bleeding. The vacutainer tube was then inverted 8-10 times for proper mixing with the anticoagulant and then kept in a temperature-controlled carrier (Versapak Insulated Sample Carrier) and subsequently transferred to the laboratory for analysis. Sample collection from the study participants was done by either a phlebotomist, a trained house officer or the principal investigator. Platelet indices (platelet count, mean platelet volume and platelet distribution width) were analysed using automated haematology analyser, Sysmex KX-21N by a dedicated laboratory scientist at the haematology laboratory. Pregnant women at or after 20 weeks gestational age with blood pressure of ≥140/90mmHg measured on two occasions at least 4 hours apart with proteinuria (≥2 + dipstick) constituted the cases while pregnant women at or after 20 weeks gestational age who were normotensive and had no proteinuria constituted the control group. Pregnant women with pre-gestational hypertension, chronic kidney disease, urinary tract infection, patients on aspirin therapy or who do not meet the inclusion criteria above.

Data Analysis

Data were entered and cleaned using Microsoft Excel and then exported to IBM Statistical Package for Social Sciences (SPSS) version 25 for statistical analysis. Socio-demographic characteristics of participants were collected and presented as frequencies and percentages in tables. Descriptive statistics included means and standard deviation for variables of the ratio scale of measurement e.g., platelet count, etc. Nominal variables were summarized using frequencies and proportions. The mean platelet indices between preeclampsia and controls were compared using independent t-test. The platelet indices were recorded into normal and abnormal categories. The relationship between platelet indices and preeclampsia were determined using Chi-square statistics. The predictive value of the platelet indices (platelet count, MPV, and PDW) for forecasting preeclampsia were determined using the Receiver Operator Characteristics (ROC) Curve. The Area Under the Curve (AUC) values with the 95% confidence intervals were calculated. Validity tests of the platelet indices in relation to preeclampsia were determined using sensitivity, specificity, and positive and negative predictive values. Statistical significance was set at alpha level of 0.05.

Ethical Approval

This was obtained from the Rivers State University Teaching Hospital Health Research Ethics Committee.

RESULTS

Table 1 shows that the highest proportion 16 (32%) of the cases were aged 31-35 years; 12 (24%) were aged 36-40 years, 12 (24%) within the 26–30-year age group and 6 (12%) within the 19–25-year age group. while 4 (8%) were aged 41-46 years. The age distribution was similar among the controls since they were age-matched with the cases.

Most participants were married as observed among cases 47 (94%) and controls 49 (98%), while 3(6%) among cases and 1 (2%) among controls were single.

Table 1: Socio-demographic characteristics of cases and controls

Variables	Study group: Cases N = 50 n (%)	Study group: Controls N = 50 n (%)	Total N = 100 n (%)
Age category			
19 – 25 years	6 (12.0)	6 (12.0)	12 (12.0)
26 – 30 years	12 (24.0)	12 (24.0)	24 (24.0)
31 – 35 years	16 (32.0)	16 (32.0)	32 (32.0)
36 – 40 years	12 (24.0)	12 (24.0)	24 (24.0)
41 – 46 years	4(8.0)	4 (8.0)	8 (8.0)
	Chi Square =5.316; p-value = 0.256		
Marital status			
Married	47 (94.0)	49 (98.0)	96 (96.0)
Single	3 (6.0)	1 (2.0)	4 (4.0)
	Fisher's exact p-value = 0.617		
Occupation			
Civil servant/ Professional	15 (30.0)	8 (16.0)	23 (23.0)
Trader/ Business	26 (52.0)	34 (68.0)	60 (60.0)
Housewife	7 (14.0)	4 (8.0)	11 (11.0)
Student	2 (4.0)	4 (8.0)	6 (6.0)
	Chi Square = 4.682; p-value = 0.197		
Level of education			
Primary	2 (4.0)	1 (2.0)	3 (3.0)
Secondary	21 (42.0)	18 (36.0)	39 (39.0)
Tertiary	27 (54.0)	31 (62.0)	58 (58.0)
	Fisher's exact test = 0.924; p-value = 0.650		
Religion			
Christianity	48 (96.0)	46 (92.0)	94 (94.0)
Islam	2 (4.0)	4 (8.0)	6 (6.0)
	Fisher's exact test = 1.604; p-value = 0.678		
Tribe			
Hausa	2 (4.0)	2 (4.0)	4 (4.0)
Yoruba	0 (0.0)	4 (8.0)	4 (4.0)
Igbo	18 (36.0)	25 (50.0)	43 (43.0)
Ijaw	7 (14.0)	5 (10.0)	12 (12.0)
Others	23 (46.0)	14 (28.0)	37 (37.0)
	Fisher's exact test = 7.471; p-value = 0.099		

Among cases 13(26.0%) had a past history of preeclampsia while only 1(2.0%) of controls had a history of preeclampsia and this was statistically significant (p = 0.001). (Table 2).

Table 2: Past medical history of cases and controls in the study

Variables	Study group: Cases N = 50 n (%)	Study group: Controls N = 50 n (%)	Total N = 100 n (%)
History of preeclampsia			
Yes	13 (26.0)	1 (2.0)	14 (14.0)
No	37 (74.0)	49 (98.0)	86 (86.0)
	*Chi Square =11.960; p-value = 0.001**		
History of high blood pressure			
Yes	3 (6.0)	0 (0.0)	3 (3.0)
No	47 (94.0)	50 (100.0)	97 (97.0)
	Chi Square =3.093; p-value = 0.079		
History of diabetes			
Yes	0 (0.0)	1 (2.0)	1 (1.0)
No	50 (100.0)	49 (98.0)	99 (99.0)
	Chi Square =1.010; p-value = 0.315		
History of Kidney disease			
Yes	0 (0.0)	0 (0.0)	0 (0.0)
No	50 (100.0)	50 (100.0)	100 (100.0)
	Chi Square =0.00; p-value =1.000		
History of infertility			
Yes	1 (2.0)	0 (0.0)	1 (1.0)
No	49 (98.0)	50 (100.0)	99 (100.0)
	Chi Square =1.010; p-value = 0.315		

Table 3 shows that 5(10%) of cases had a family history of PE whereas 1(2%) of controls had such history. In both cases and controls, the history of PE was more in the sister.

Table 3: Family and social history of cases and controls

Variables	Study group: Cases N = 50 n (%)	Study group: Controls N = 50 n (%)	Total N = 100 n (%)
Relative with history of preeclampsia			
Yes	5 (10.0)	1 (2.0)	6 (6.0)
No	45 (90.0)	49 (98.0)	94 (94.0)
	Chi Square =2.837; p-value = 0.092		
Exact relationship with relative with history of preeclampsia			
Mother	1 (2.0)	0 (0.0)	1 (1.0)
Sister	4 (8.0)	1 (2.0)	5 (5.0)
Nil	45 (90.0)	49 (98.0)	94 (94.0)
	Fisher's exact =2.755; p-value = 0.204		
History of tobacco intake			
Yes	0 (0.0)	1 (2.0)	1 (1.0)
No	50 (100.0)	49 (98.0)	99 (99.0)
	Chi Square =1.010; p-value = 0.315		
History of alcohol intake			
Yes	4 (4.0)	7 (14.0)	11 (11.0)
No	46 (92.0)	43 (86.0)	89 (89.0)
	Chi Square =0.919; p-value =0.338		

The highest proportion of the participants were para 1 and above 32 (64%) for cases and 36(72%) for controls. Most of the cases and controls had history of delivery of babies with normal birth weight (Table 4).

Table 4: Obstetrics and gynaecological history of cases and controls in the study

Variables	Study group: Cases N = 50 n (%)	Study group: Controls N = 50 n (%)	Total N = 100 n (%)
Gravidity			
1	6 (12.0)	7 (14.0)	13 (13.0)
2-3	21 (42.0)	25 (50.0)	46 (46.0)
4-5	17 (34.0)	16 (32.0)	33 (33.0)
>5	6 (12.0)	2 (4.0)	8 (8.0)
	Chi Square =2.455; p-value = 0.483		
Parity			
Nulliparous	16 (32.0)	13 (26.0)	29 (29.0)
Para 1-4	32 (64.0)	36 (72.0)	68 (68.0)
>Para 4	2 (4.0)	1 (2.0)	3 (3.0)
	Fisher's exact =0.963; p-value = 0.630		
Birth weight of previous babies (N=71)			
< 2.5kg	6 (20.0)	1 (2.4)	7 (9.9)
2.5 – 3.9kg	21 (70.0)	30 (73.2)	51 (71.8)
> 3.9kg	3 (10.0)	10 (24.4)	13 (18.3)
	*Fisher's exact =7.038; p-value = 0.026**		
History of miscarriage			
Yes	15 (30.0)	17 (34.0)	32 (32.0)
No	35 (70.0)	33 (66.0)	68 (68.0)
	Fisher's exact =2.006; p-value =0.397		
G.A at miscarriage (n=27)			
1-10wks	5 (33.3)	6 (50.0)	11 (40.7)
11-20wks	6 (40.0)	4 (33.3)	10 (37.0)
21-30wks	4 (26.7)	2 (16.7)	6 (22.2)
	Fishers exact =0.886; p-value = 0.692		
Babies died in womb			
Yes	6 (12.0)	1 (2.0)	7 (7.0)
No	44 (88.0)	49 (98.0)	93 (93.0)
	*Chi square =3.840; p-value = 0.050**		
Babies died within 28 days of delivery			
Yes	5 (10.0)	3 (6.0)	8 (8.0)
No	45 (90.0)	47 (94.0)	92 (92.0)
	Chi square =0.543; p-value = 0.461		
Method of GA determination			
LMP	45 (90.0)	45 (90.0)	90 (9.0)
First trimester	5 (10.0)	5 (10.0)	10 (10.)
Ultrasound scan	0 (0.0)	0 (0.0)	0 (0.0)
	Fisher's exact =0.996; p-value = 1.000		

**Statistically significant*

There is no significant difference in the systemic and general examination of cases and controls as table 5 shows.

Table 5: Systemic and general examination of cases and controls in the study

Variables	Study group: Cases N = 50 n (%)	Study group: Controls N = 50 n (%)	Total N = 100 n (%)
Respiratory system			
Normal	46 (92.0)	50 (100.0)	96 (96.0)
Abnormal	4 (8.0)	0 (0.0)	4 (4.0)
	*Chi Square =4.167; p-value = 0.041**		
Blood pressure			
Normal	0 (0.0)	50(100.0)	50 (50.0)
Hypertension	50 (100.0)	0 (0.0)	50 (50.0)
	*Chi Square =88.395; p-value = 0.0001**		
Pulse rate			
Normal	31 (62.0)	50 (100.0)	81 (81.0)
Tachycardia	19 (38.0)	0 (0.0)	19 (19.0)
	*Chi Square =23.457; p-value = 0.0001**		
Foetal heart rate			
Normal	45 (90.0)	49 (98.0)	94 (94.0)
Abnormal	5 (10.0)	1 (2.0)	6 (6.0)
	Chi Square =2.837; p-value =0.092		
Fundal height			
Compactible with G. A	49 (98.0)	47 (94.0)	96 (96.0)
<G. A	1 (2.0)	1 (2.0)	2 (2.0)
>G. A	0 (0.0)	2 (4.0)	2 (2.0)
	Fisher's exact =1.911; p-value =0.745		
Glycosuria			
Absent	50 (100.0)	50 (100.0)	100 (100.0)
Present	0 (0.0)	0 (0.0)	0 (0.0)
	Chi Square =; p-value =		
Proteinuria			
Absent	0 (00.0)	50 (100.0)	50 (50.0)
Present	50(100.0)	0 (0.0)	50 (50.0)
	*Chi Square =81.818; p-value =0.0001**		
Conjunctiva			
Normal	45 (90.0)	49 (98.0)	94 (94.0)
Pale	5 (10.0)	1 (2.0)	6 (6.0)
	Chi Square =2.837; p-value =0.092		
Pedal oedema			
Present	37 (74.0)	4 (8.0)	41 (41.0)
Absent	13 (26.0)	46 (92.0)	59 (59.0)
	*Chi Square =45.019; p-value =0.0001**		
Jaundice			
Present	0 (0.0)	0 (0.0)	0 (0.0)
Absent	50 (100.0)	50 (100.0)	100 (100.0)

**Statistically significant*

As shown in table 6, there was a significant difference in the mean BMI of cases (33.44±5.33) and controls (30.95±4.76). p = 0.015. This is an indication that obesity is a risk factor for the development of PE.

Table 6: Comparison of mean weight, height, and BMI between the two groups

Variables	Cases Mean ± SD	Controls Mean ± SD	T	p-value
Weight	1.57±0.07	1.59±0.08	1.625	0.107
Height	82.80 ± 14.93	79.07 ± 13.86	1.295	0.198
BMI	33.44 ± 5.33	30.95 ± 4.76	2.466	0.015*

SD – Standard deviation *Statistically significant

The results found a statistically significant difference in the mean platelet count between cases (176.30 ± 67.38) and controls (207.16 ± 62.07), p = 0.019, as well as in the mean values of PDW in both cases and controls. The PDW was significantly raised (15.53 ± 3.36) compared to controls (13.75 ± 2.53), p = 0.004. (Tables 7 and 8).

Table 7: Comparison of mean blood indices among the two groups

Variables	Cases Mean ± SD	Controls Mean ± SD	t	p-value
PCV	34.44 ± 4.55	32.22 ± 2.69	2.950	0.004*
WBC count	11.48 ± 5.44	8.20 ± 2.06	3.979	0.0001*

SD – Standard deviation *Statistically significant

Table 8: Comparison of MPV and PDW among the two groups of the study

Variables	Cases Mean ± SD	Controls Mean ± SD	t	p-value
MPV	11.14 ± 1.33	10.65 ± 1.38	1.799	0.075
PDW	15.53 ± 3.36	13.75 ± 2.53	2.987	0.004*
PC	176.30±67.38	207.16±62.07	2.390	0.019*

SD – Standard deviation *Statistically significant

Figure 1 is the Receiver Operator Characteristics (ROC) Curve of the platelet indices (PC, MPV and PDW).

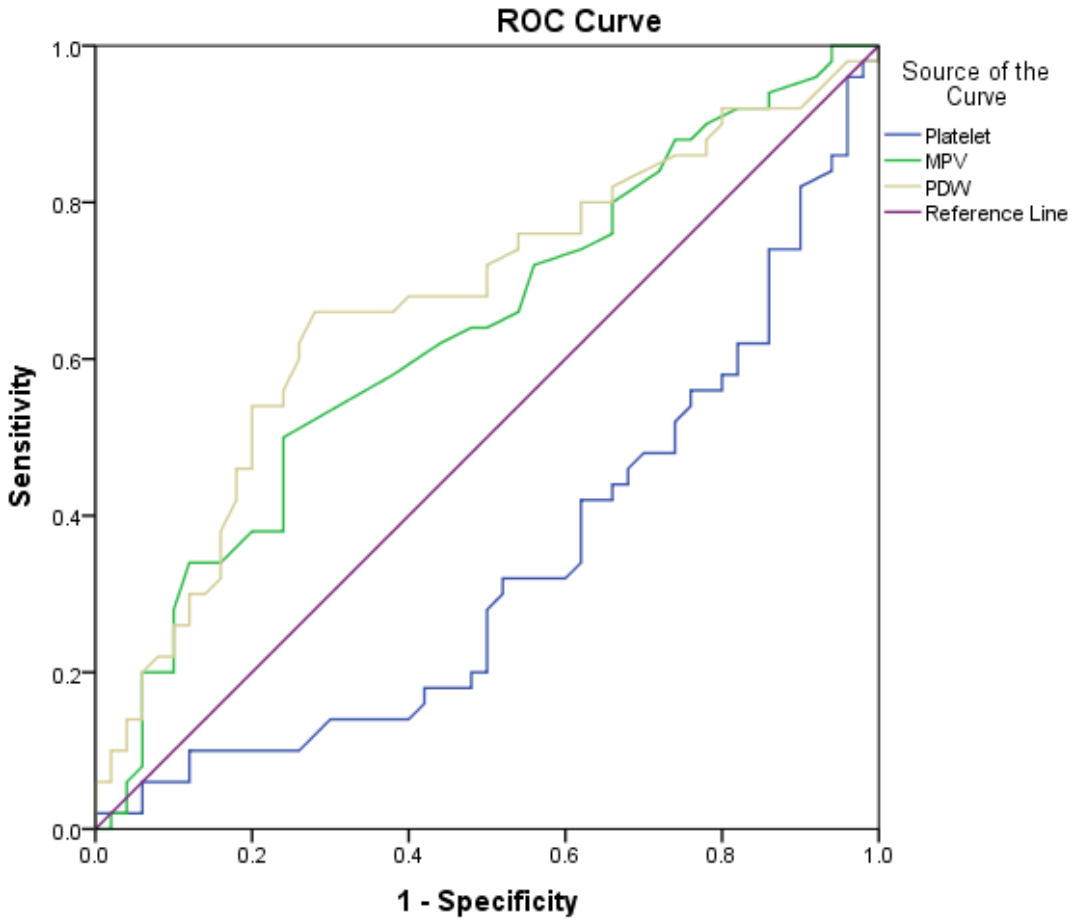

Figure 1: Receiver Operator Characteristics (ROC) Curve of the platelet indices (PC, MPV and PDW)

Table 9 shows that the Area under the Curve of the Receiver Operator Characteristics indicates that PDW has a greater area under the curve and is significant whereas the MPV shows moderate evidence of a correlation with preeclampsia.

Table 9: ROC Curve outputs [Area under the Curve (AUC) values and optimal cut-off value of platelet indices]

		95% CI			
Variables	**AUC**	**Lower**	**Upper**	**p-value**	**Optimal cut-off**
Platelet count	0.336	0.229	0.443	0.005*	**
MPV	0.634	0.525	0.743	0.021*	11.60
PDW	0.672	0.565	0.779	0.003*	14.50

*Statistically significant **Not determined due to poor diagnostic accuracy of test

Table 10: Validity tests for MPV based on optimal cut-off of 11.60FL

		Pre-Eclampsia		
		Yes	**No**	**Total**
MPV	**≥ 11.6 FL**	17 *True positive*	6 *False positive*	23
	< 11.6 FL	33 *False negative*	44 *True negative*	77
	Total	50	50	100

$$Sensitivity = \frac{TruePositive}{TruePositive+FalseNegative} \text{ x } 100$$

$$= \frac{17}{50} \text{ x } 100 = 34.0\%$$

$$Specificity = \frac{TrueNegative}{TrueNegative+FalsePositive} \text{ x } 100$$

$$\frac{44}{50} \text{ x } 100 = 88.0\%$$

$$Positive\ Predictive\ Value\ (PPV) = \frac{True\ Positive}{TruePositive+False\ Positive} \text{ x } 100$$

$$\frac{17}{23} \text{ x } 100 = 73.9\%$$

$$Negative\ Predictive\ Value\ (NPV) = \frac{True\ Negative}{TrueNegative+False\ Negative} \text{ x } 100$$

$$= \frac{44}{77} \text{ x } 100 = 42.9\%$$

$$Overall\ Accuracy = \frac{True\ Positive+True\ Negative}{Total} \text{ x } 100$$

$$= \frac{17 + 44}{100} \text{ x } 100 = 61.0\%$$

Table 11: Validity tests for PDW based on optimal cut-off of 14.5%

		Pre-Eclampsia		
		Yes	**No**	**Total**
PDW	**≥ 14.5%**	33 *True positive*	14 *False positive*	47
	< 14.5%	17 *False negative*	36 *True negative*	53
	Total	50	50	100

$$Sensitivity = \frac{TruePositive}{TruePositive+FalseNegative} \text{ x } 100$$

$$= \frac{33}{50} \text{ x } 100 = 66.0\%$$

$$Specificity = \frac{TrueNegative}{TrueNegative+FalsePositive} \text{ x } 100$$

$$\frac{36}{50} \text{ x } 100 = 72.0\%$$

$$Positive\ Predictive\ Value\ (PPV) = \frac{True\ Positive}{TruePositive+False\ Positive} \text{ x } 100$$

$$\frac{33}{47} \text{ x } 100 = 70.2\%$$

$$Negative\ Predictive\ Value\ (NPV) = \frac{True\ Negative}{TrueNegative+False\ Negative} \text{ x } 100$$

$$= \frac{36}{53} \text{ x } 100 = 67.9\%$$

$$Overall\ Accuracy = \frac{True\ Positive + True\ Negative}{Total} \times 100$$

$$= \frac{69}{100} \times 100 = 69.0\%$$

Table 12 shows that at a cut-off mark of ≥11.6 FL, MPV has a sensitivity of 34% and a specificity of 88% while the positive predictive value and negative predictive value are 73.9% and 34.2% respectively. It also shows that at a cut-off value of 14.5% the sensitivity of PDW is 66.0% while the specificity is 72.0%. The positive predictive value for PDW is 70.2 while the negative predictive value is 67.9%. This implies that whereas the predictive value MPV is low, PDW is has a high predictive value for PE.

Table 12: Validity findings on MPV and PDW indices

Variables	Sensitivity	Specificity	PPV	NPV	Overall accuracy
MPV	34.0%	88.0%	73.9%	42.9%	61.0%
PDW	66.0%	72.0%	70.2%	67.9%	69.0%

DISCUSSION

Pre-eclampsia is a life-threatening multisystem disorder of pregnancy and a leading cause of maternal and perinatal morbidity and mortality complicating about 2-5% of pregnancies globally.[1]Its pathophysiology is not fully understood. However, widespread endothelial damage with associated increased platelet activation and consumption leading to thrombocytopaenia (the most common haematological abnormality seen in PE) have been implicated in its pathophysiology.[4,13,24] The objectives of this study were to: compare platelet indices (platelet count, MPV and PDW) between preeclampsia and healthy controls in RSUTH, determine the relationship between platelet indices and occurrence of preeclampsia among pregnant women in RSUTH and ascertain the predictive value of platelet indices (platelet count, MPV and PDW) in the development of PE among the study population.

There were no significant differences in the sociodemographic indices of the study participants. The study demonstrated significant reduction in PC in PE compared to controls. The mean platelet count in cases was 176.30 × 10^9/L± 67.38 but 207.16 × 10^9/L ± 62.07 for controls (P=0.019). However, the PC displayed very low diagnostic accuracy when the three parameters were evaluated on the ROC curve. The PDW was significantly raised (15.53 ± 3.36) compared to controls (13.75 ± 2.53) (P=0.004). The area under the curve (AUC) of the ROC Curve for PDW was 0.672(0.565-0,779), CI 95% P=0.003 at a cut-off level of 14.50. This means that at PDW cut-off value of 14.5, there was ahigh risk of developing PE. Though also raised, the difference in MPV between women with PE and the healthy controls in this study was not significant. Furthermore, the MPV in this study displayed very low sensitivity.

The mean values for PC in this study are lower than those obtained by Alsheeha et al where the mean value for PE subjects was 248.0×10^9/L. Again, unlike the findings in this study, Alsheeha et al assessed and reported no significant difference in the PDW and MPV between pregnant women with PE and healthy controls.[34] Some findings of this study are closer to those by Gopi-Arun et al who found statistically significant difference in the PDW values of PE patients compared with healthy controls.[49] In that study, PDW was observed to be significantly raised in PE compared to healthy controls but the MPV and PC showed no difference between the two groups.
Several studies reported statistically significant difference among women with PE compared with healthy control in all three parameters (marked reduction in platelet count and elevation of the PDW and MPV).[10,17–19,42,43] However, this was not the case in this study as only the PC and PDW showed statistically significant difference in PE subjects compared to the healthy group of women. Other studies reported findings congruent with the findings in this study with just one or two parameters displaying significant differences among cases and controls.[32,39,41] The findings of this study are, however, completely at variance with the findings by Ceyhan et al who reported no significant difference in all three platelet indices among cases with PE and controls.[37] Reddy et al in a prospective study of 235 PE patients and 203 healthy pregnant women reported that the MPV demonstrated prognostic significance as the degree of rise in MPV correlated with the disease severity in PE at a cut-off value of 10.9fL and a sensitivity and specificity of 80% and 75% respectively. The authors concluded that MPV had predictive value for disease progression in PE and all three indices have diagnostic and prognostic values for PE. In this study however, MPV at a cut off value of 11.6fL had a sensitivity of 34% and a specificity of 88%.[42]

The dissimilarities in the various studies on the performance of platelet indices can be attributed to two major factors. First, it could possibly be due to

differences in the sociodemographic characteristics of the various study populations. Secondly, it could be due to functional differences in the various versions of the automated haematology analysers used for analysing blood samples for full blood count by the various researchers.

CONCLUSION

The platelet count is significantly reduced in PE compared to controls but has a very low diagnostic accuracy. The MPV is not significantly raised in PE when compared with controls. The PDW is significantly raised in PE compared with controls. Rising values of the PDW in pregnant women may be an indication of more focused care within the context of preeclampsia prevention and management.

LIMITATION

The small sample size, the study design being a case-control and its single-centre profile limits the findings of this study. A prospective cohort study with a large sample of pregnant women initiating antenatal care in the first trimester would have provided more robust data for analysing the performance of platelet indices as predictive markers for PE.

RECOMMENDATIONS

The PDW values in pregnant women should be carefully noted by caregivers as this could be an indication of more focused care within the context of pre-eclampsia prevention and management. Future research should adopt a prospective cohort study design with a large sample of healthy pregnant women initiating antenatal care in the first trimester to corroborate the findings of this study. Again, large scale, multicentre prospective cohort studies with the same version of haematology analyser could be carried out among pregnant women with similar baseline characteristics to ascertain the generalisability of the findings of this study for clinical decision-making in resource-poor settings like ours.

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Cite this Article: Ela, GM; Ikechebelu, JI; Kua, PL; Omunakwe, H; Jumbo-Cleopatra, T (2023). Comparative Difference in Platelet Indices Among Preeclamptics and Controls at a Tertiary Centre in Port Harcourt, Nigeria. *Greener Journal of Medical Sciences*, 13(2): 164-182.