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Assessment of Platelet Indices Profile of Pregnant Women Attending University of Abuja Teaching Hospital, Nigeria

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Abstract

Platelets initiate hemostasis by aggregating at the site of injury and participate in ensuring endothelial integrity. A defect in this process could lead to intravascular blood loss. This case-control study sought to determine the platelet counts and indices among pregnant women in the University of Abuja Teaching Hospital Gwagwalada, Abuja, Nigeria. A total of 120 pregnant women as case and 60 non-pregnant women as control were enrolled for this study. Blood samples were collected in EDTA tubes, and complete platelet count and indices were carried out using an automated five-part haematology analyzer. The mean ± standard deviation of the platelets count among the pregnant women, 226.54 ± 69.76 10^9 cells/L was not significantly different from that of the non-pregnant women, 214.95 ± 52.22x 10^9 cells/L (p=0.295). There was a significant differences in mean platelets volume (MPV) of the case and control groups (p=0.036). After post-hoc test, the significant difference was between the pregnant women in 3rd trimester and the control group (p=0.014). However, there was no diffences in the mena platelets larger cell ratio and platelet distribution width in the case and control groups. Fifteen (11.0%) and 7 (12.1%) of the case and control control groups, respectively had mild thrombocytopenia. However, there was no significant association between pregnant status and thrombocytopenia (p=0.836). Based on these findngs, it can be infered that platelet count and MPV decreases while PDW increase with the progression of gestation age compared to the non-pregnant women.

Keywords

Platelet indices, Haemostasis, Coagulopathy, Nigeria.

INTRODUCTION

Pregnancy is a physiological condition and usually does not affect the general health of the pregnant woman. However, pregnancy results in hormonal, hemodynamic and haematological changes (1). These physiological changes need to be considered normal adaptations. Increased total blood volume and hemostatic changes help to combat possible consequences of haemorrhage at delivery (2).

It is often argued that altered hemostatic status is required, as the maternal coagulation system prepares for the challenges of parturition, and aims to minimize intrapartum blood loss. However, the alterations in the hemostatic system begin as early as the first trimester, suggesting a requirement for such changes in the proper progression of the early stages of pregnancy, in addition to their role in the regulation of post-partum bleeding (3). For instance, alterations in hemostasis enable the necessary changes in the uteroplacental vasculature to support the establishment of the trophoblast invasion of the spiral arteries of the uterus early in gestations (4).

The altered hemostatic status during normal pregnancy presents several physiological challenges in the vasculature and results in an increased risk of excessive thrombosis, especially within the uteroplacental circulation (5). This enhanced pregnancy-associated thrombotic risk may provide the mechanistic basis for many of the major pregnancy complications, such as pre-eclampsia, HELLP syndrome (Hemolysis, Elevated Liver enzymes and Low Platelet count) and intrauterine growth retardation (IUGR) (6).

Assessing platelet count in pregnancy is of clinical importance. It is useful in making a diagnosis of HELLP syndrome (7). The HELLP syndrome can often be a complication of pre-eclampsia and eclampsia, determining the severity of these clinical disorders and assessing response level to treatment in HELLP syndrome (8).

Pregnancy is associated with endothelial stress and increased platelet aggregation in the uteroplacental circulation resulting in a progressive decline in platelet count with increasing gestational age (9). Furthermore, the increase in plasma volume associated with pregnancy results in dilutional thrombocytopenia (10). Thus, platelet counts are generally lower in pregnancy compared to non-pregnant women, and thrombocytopenia could occur in about 10% of pregnancies (11). Rarely, this may be severe enough to cause maternal and neonatal morbidity and mortality. The elevated platelet aggregation in pregnancy has been attributed to increased formation of thromboxane A2, more intracellular calcium mobilization and reduced synthesis of cyclic adenosine monophosphate (cyclic AMP) (12). With this cognizance, the current prospective study aims to determine the values of platelet

counts and indices among pregnant women attending the University of Abuja Teaching Hospital Gwagwalada Abuja, Nigeria. Data from these could assist to also evaluate pregnant women with potential haemostatic defect and preeclampsia (MPV is useful in this regard).

MATERIALS AND METHODS

Study Area

This study was conducted at the University of Abuja Teaching Hospital (UATH), Gwagwalada, Federal Capital Territory (FCT) Abuja. The laboratory investigations were carried out at the haematology laboratory of UATH.

Study Design

This was a case-control study on pregnant women who consented to be part of the study at the antenatal clinic at the University of Abuja Teaching Hospital. Controls were enrolled from the female medical students undergoing clinical postings and rotations in the hospital. This study took place from 20th April to 30th December 2018.

Selection Criteria for the Case Group

Pregnant women who gave written informed consent, and healthy with no history of diabetes mellitus, coagulation-related diseases (such as hemophilia, thalasemia), malaria, HIV/AIDS, Hepatitis-B and C viruses were enrolled as the case subjects. Their biodata alongside parity and gestational ages were extracted from their hospital folders through the assistance of the attending physicians and nurses.

Ethics approval

Ethical approval was obtained from the ethical committee of the University of Abuja Teaching Hospital (Approval number: UATH / HREC / PR / 2018 / 004.018) Gwagwalada, Abuja, Nigeria.

Consent to participate

Informed written consent was obtained from all participating subjects before recruiting into the study, following the standards of human experimentation and with the Helsinki Declaration of 1975.

Selection Criteria for the Control Group

Healthy females (>18 years) who were not pregnant in the last 12 months, with no history of diabetes mellitus, coagulation-related diseases (such as hemophilia and thalasemia), malaria, HIV/AIDS, Hepatitis-B and C viruses were enrolled as the control subjects. They provided their biodata through a short questiionnare administered to them by nurses.

Analytical Laboratory Methods

Sample collection

About 3 millileter (mL) of whole blood samples were collected from all the subjects and dispensed into EDTA (ethylenediamine-N,N,N,N-tetra acetate) tube. Blood samples were analysed in batches within 2 hours of collection until the required number (n=160) was attained.

Platelet Count and Indices

The full blood count was carried out using the Genesis HA6000 Automated Hematology Analyzer (calatog number: 9027809900) (Perlong Medical Equipment Company, China). Among other parameters, the analyzer determined platelet count and its various platelet indices (absolute platelet count, mean platelet volume, platelet distribution width and platelet larger cell ratio). Daily and per-run quality control for all the procedures for automated platelet indices analyses were ensured.

Statistical Analysis

Data were presented as mean and standard deviation on the statistical package for social science (SPSS version 26) and analyzed using student's t-test and ANOVA for a significant difference in platelet indices between groups. Also, two tailed Chi squared test was used to determine association between 2 catigorical variables. Probability ($p<0.05$) was used to determine the level of significance for all the statistical analyses.

RESULTS

In this study, one hundred and eighty (180) participants who met the inclusion criteria were successfully enrolled. Among which 120 were pregnant women (case group) and 60 non-pregnant women (control group). The demographic data obtained for the subjects showed that the most of the control group aged within 21 to 25 years (41.4%) while the majority of the pregnant women (43.2%) were within 26-30 years. Majority of the control group (58.6%) had never been pregnant, whereas (28.0%) of the case group had been pregnant at least once (Table 1). There was a statistically significant difference in age and parity, between the cases and the control groups ($p<0.0001$) (Table 1).

Although, there was an increase in mean platelet count (PLT) in the pregnant women when compared with the non-pregant group (226.54± 69.76 $x10^9$ cell/L) versus 214.95±52.22x 10^9 cell/L), the MPV, PDW, and platelet larger cell ratio were slightly lower in pregnant women than the non-pregnant group. These changes were not statistically different between the 2 study groups ($p>0.05$) (Table 2).

From our findings, the mean PLT count in the first, second and third trimester of pregnancy (228.64± 45.25 x 10^9 cell/L, 237.38± 82.39 x 10^9 cell/L and 212.48± 61.08 x 10^9 cell/L) did not differ significantly from the mean PLT count of the non-pregannt women (214.95± 52.22 x 10^9 cell/L) ($p=0.184$) (Table 3). Moreover, the mean MPV of pregnant women were lowest in 3rd trimester and significantly differ from pregnant women in their 1st, 2nd trimester and the control group ($p=0.036$) (Table 3).

The mean mean platelet volume (MPV) in the first, second and third trimester of pregnancy (10.41± 0.83 fL, 10.33± 0.92fL

and 8.73± 5.70fL) differed significantly from the mean MPV of the non-pregannt women (10.27± 1.81fL) (p=0.036) (Table 3). After post-hoc test, the significant difference was between the pregnant women in 3rd trimester and the control group (p=0.014) (Table 4). However, there was no significant differences in the platelet distribution width and platelet larger cell ratios among pregnant women of all the three trimesters and control groups (p>0.05) (Table 3).

Out of the the 180 subjects in this study, 105 (89.0%) and 53 (87.9%) of the case and control groups had normal platelet counts (150-400 x 10^9 cells/L), respectively. Moreover, 15 (11.0%) and 7 (12.1%) of the case and control groups had mild thrombocytopenia (100-150 x 10^9 cells/L), respectively. None of the 2 study groups had moderate and severe thrombocytopenia. Also, there was no significant association between pregnancy status and thrombocytopenia (p=0.836) (Table 5).

Table 1. Association between age, parity and pregnancy status of study participants

Variables	Pregnancy Status		x^2	*p*-value
	Pregnant, n (%)	Non-Pregnant, n (%)		
Age (years)				
15-20	0 (0.0%)	13 (19.0%)	52.125	<0.0001*
21-25	16 (11.9%)	24 (41.4%)		
26-30	51 (43.2%)	14 (24.1%)		
31-35	39 (33.1%)	5 (8.6%)		
36-40	14 (11.9%)	4 (6.9%)		
Parity				
0	0 (0.0%)	34 (58.6%)	52.125	<0.0001*
1	33 (28.0%)	14 (24.1%)		
2	30 (25.4%)	6 (10.3%)		
3	27 (22.9%)	1 (1.7%)		
≥4	28 (23.7%)	3 (5.2%)		

Table 2. Comparison of platelet indices between non-pregnant and pregnant women

Platelet Indices	Non-pregnant Women (n=60)	Pregnant Women (n=120)	Mean Difference	t value	*p*-value
Platelet count (x 10^9 cells/L)	214.95 ± 52.22	226.54 ± 69.76	-11.59 ±17.54	-1.119	0.295
Mean platelet volume (fL)	10.27 ± 1.81	9.74 ± 3.63	0.53 ±1.82	1.046	0.297
Platelet distribution width	13.60 ± 2.07	13.44 ± 3.60	0.16 ±1.53	0.320	0.749
Platelet larger cell ratio	29.61 ± 7.65	28.38 ± 8.33	1.23 ±0.68	0.972	0.333

Table 3. Comparison of platelet indices between non-pregnant and the various trimesters of pregnant women

Platelet Indices	Non-pregnant state (n=60)	First trimester (n=24)	Second trimester (n=52)	Third trimester (n=44)	F value	*p*-value
Platelet count (x 10^9 cells/L)	214.95± 52.22	228.64± 45.25	237.38± 82.39	212.48± 61.08	1.632	0.184
Mean platelet volume (fL)	10.27± 1.81	10.41± 0.83	10.33± 0.92	8.73± 5.70	2.913	0.036*
Platelet distribution width	13.60± 2.07	13.28± 2.17	13.48± 3.29	13.45± 4.45	0.056	0.983
Platelet larger cell ratio	29.61± 7.65	28.29± 7.74	27.90± 6.89	29.00± 10.12	0.440	0.725

Table 4. Comparison of mean platelet volume between non-pregnant and the various trimesters of pregnant women using the least significant difference (LSD) post hoc

Parameter	Groups		Mean Difference	*p*-value
	Non-pregnant state	First trimester		
Mean platelet volume (fL)	10.27± 1.81	10.41± 0.83	-0.14± 0.79	0.861
	Non-pregnant state	Second trimester		
Mean platelet volume (fL)	10.27± 1.81	10.33± 0.92	-0.06± 0.59	0.917
	Non-pregnant state	Third trimester		
Mean platelet volume (fL)	10.27± 1.81	8.73± 5.70	1.55± 0.62	0.014*

Table 5. Incidence and severity of thrombocytopenia in non-pregnant and pregnant women

Variables	Pregnancy Status		x^2	*p*-value
	Pregnant, n (%)	Non-Pregnant, n (%)		
Platelet Count				
Normal (150-400 x 10^9 cells/L)	105 (89.0%)	53 (87.9%)	0.043	0.836
Mild (100-<150 x 10^9 cells/L)	15 (11.0%)	7 (12.1%)		
Moderate (50-<100 x10^9cells/L)	0 (0.0%)	0 (0.0%)		
Severe (<50 x 10^9 cells/L)	0 (0.0%)	0 (0.0%)		

DISCUSSION

Platelet indices studies in pregnancy have become of great interest owing to the recurrent hypercoagulability crisis accompanied by pregnancy. This study showed that there are changes in the various platelet indices in pregnancy and the mean values of these parameters differ from the control group (non-pregnant women). However, the absolute platelet count (PLT) did not significantly change in pregnant women compared to the contril subjects. This is not in agreement with an earlier study by Boehlen *et al*. (13) where significant platelet counts decrease was reported among pregnant women. Physiological changes in haematological parameters during pregnancy was reported to have significantly decreased the platelet count in pregnant women (13). Our findings were also not similar to those of Fahmi *et al*. (14) where they noted that thrombocytopenia was caused by either increased platelet destruction or decreased platelet production.

In pregnancy, increased platelet destruction may be mediated by

immunological mechanisms, abnormal platelet activation, or platelet consumption. Increased destruction or utilization of platelets during pregnancy occurs in microangiopathies (affecting small blood vessels) such as thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome, haemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, and pre-eclampsia (14). Another study agrees with the physiologic findings in pregnancy where platelet counts decrease possibly due to haemodilution, which majorly occurs in the third trimester (15). However, the difference in platelet count reported in our study compared to others could be attributed to the nature of sampling techniques or variation in laboratory analytical protocols, as these might have impacted on the results (16). Indeed, there are various hematology analyzers with different technologies and principles of operations (such as the impedance, optical methods and immunofluorescence) current used to count the platelets. Besides, platelet counts are seldom subjected to variations due to artifacts that needed to be ruled out before validation of protocol (16). However, the 5-part automated hematology analyser used in our study is insignifcanly affected by these factors as it uses the latest hematology analysis technology with the best performance caharcteristics (17).

These data emphasize the need for additional studies to accurately describe the course of platelet counts throughout normal pregnancies, to document the period platelet counts begin to decrease, and to determine the range of platelet counts among normal women during pregnancy.

Findings from this study showed non-significant decreased levels of MPV, PCT and PDW in pregnant women compared to the control subjects (p>0.05). These changes might be related to the blood volume expansion and hemodilution that occurs during pregnancy. During pregnancy, platelet count decreases gradually from the 1st till the 3rd trimester. In addition, hemodilution has been shown to accelerate platelet consumption which may contribute to a decline in platelet count throughout gestation (9). Interestingly, platelet activation can occur several weeks prior to the clinical onset of pre-eclampsia and increased mean platelet volume (MPV) in the late first trimester of gestation are suggestive of IUGR and PE (9). Our findings was similar to an earlier study by Babah *et al*. (18), where decreased MPV and PCT in pregnancy was highlighted (18). Findings from our study are also in consonance with that of Nooh and Abdeldayem (19) where they also reported a decrease in the level of MPV, PCT and PDW during pregnancy.

Findings from this revealed an increase in the platelet count in the first and second

trimester of pregnancy. However, there was a decrease in platelet count among subject in their 3rd trimester when compared with the control group. These are similar to the findings by Babah *et al*. (18) where they reported a statistically non-significant increase in platelet count in the first to the third trimester of pregnancy. These observations could be attributed to the feeding habit of the subject (7). It is known that supplements or diet rich in vitamins, iron and folate could enhance erythropoietic activities in the bone marrow, which could assist in boosting platelet counts during pregnancy (20). In most low- and middle-income settings, pregnant women consistent consumption of iron/folate tablets reduces with gestation age (poor adherence) (21, 22). Nevertheless, the progressive fall in platelet count with an increase in gestation did not cause thrombocytopenia in all trimesters of pregnancy as the values were within the normal range (150–450 × 10^9/L).

There was a significant increase in mean platelet volume among subjects in the first and second trimester when compared with the control group. But a significant decrease was observed in the third trimester when compared with the control group. Mean platelet volume (MPV) and platelet distribution width (PDW) were reported to increase during platelet activation (23). Essentially, the decline in the third trimester could be attributed to the physiologic haemodilution.

In normal pregnancy, there is often an increase in platelet aggregation and a decrease in the number of circulating platelets with gestation (24). As the platelet lifespan decreases, the MPV increases minimally during pregnancy (24). Thus, the MPV is an accurate measure of platelet size and its considered a biomarker of platelet function (25). Hence, larger platelets with higher MPV counts are reactive and raise higher amounts of the prothrombotic factor thromboxane A_2, increasing the tendency to thrombosis (25).

The PDW values appeared to have reduced in the three groups of pregnant women, which were statistically non-significant. On the contrary, an increase in PDW was reported by Omorogiuwa and Aigborhuan (26), which was attributed to physiologic compensation for the decreasing platelet count and volume with progression in gestation age (26). Platelets having denser granules are bigger and metabolically active (27), hence PDW is more specific than MPV in the identification of platelet activity. It is a simple and specific marker for enhanced coagulation (23).

There was a statistically non-significant increase in the mean of mean± SD of MPV in the first and second trimester among the case group when compared with the mean± SD value of the control group. However, in the

third trimester, there was a significant decrease in MPV among pregnant women. On the contrary, a longitudinal study by Giles (28) showed that MPV increased with gestational age in a statistically non-significant manner. The decline in MPV in the third trimester could be attributed to platelet consumption and hemodilution, conditions common in the third trimester.

Findings from this study showed mild thrombocytopenia among the pregnant women when compared with the control group. This explains the normal physiologic changes in pregnancy where hemodilution effects overwhelm the erythropoietic activities of the bone marrow (30). However, pregnant women with thrombocytopenia may be at a higher risk of coagulopathy.

CONCLUSION

This study is not without limitation. The heterogenous nature of the biodata (especially age) of the case and control groups might signify a bias in subjects selection which could influence the statistics of some analytes. Also, the concurrent analyses of certain platelet factors (such as fibrinogen and Von Willebrand) would have provided more information about the coagulation profile of the pregnant women with low platelet counts and MPV. It is worthy to follow up the pregnant women and neonates with higer risk of developing coagulation complication so that approparite therapeutic interventions could be made available to arrest possible complications.

AUTHOR CONTRIBUTIONS

Amos Dangana: conceptualization, formal analysis, investigation, supervision, writing - original draft, writing - review & editing. Anthony Uchenna Emeribe: formal analysis, methodology, writing - original draft, writing - review & editing. Hezekiah Alkali Isah: writing - original draft, writing - review & editing. sanusi musa: writing - original draft, writing - review & editing. Joel Monday Abu: writing - original draft, writing - review & editing. Solomon Oloche Onoja: writing - original draft, writing - review & editing. Nkechi Onukegbe: writing - original draft, writing - review & editing. Idris Nasir Abdullahi: conceptualization, formal analysis, investigation, methodology, supervision, writing - original draft, writing - review & editing.

CONFLICT OF INTEREST

None declared by authors.

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