Gestational thrombocytopaenia among pregnant women in Lagos, Nigeria

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ABSTRACT

Background: Thrombocytopaenia is a common haematologic abnormality during pregnancy. Pregnant women with thrombocytopenia have a higher risk of bleeding excessively during or after childbirth, particularly if they need to have a caesarean section or other surgical intervention during pregnancy, labour or in the puperium. The aim of this study was to determine the prevalence of gestational thrombocytopaenia among pregnant women reporting for antenatal care at tertiary health care centres in Lagos. Materials and Methods: Platelet count was analyzed in 274 consecutive pregnant women who gave informed consent and 70 non-pregnant female staff of the hospitals. Platelet count was performed on each sample using the Sysmex KN-21N automated haematology analyzer. The study design was cross-sectional, proportions were analyzed for statistical significance with the chi-square, and Odds ratio was also calculated. Thrombocytopaenia is classically defined as a platelet count of less than $150 \times 10^9/L$.^{3.4} Counts from 100 to $150 \times 10^9/L$ are considered mildly depressed, 50 to $100 \times 10^9/L$ are moderately depressed and less than $50 \times 10^{\circ}$ /L are severely depressed. **Results:** Thirty-four (13.5%) pregnant women were thrombocytopaenic compared with three (4.3%) non-pregnant women. This was statistically significant; P = 0.03; Odds ratio: 3.5 (95% Cl 1.03-11.82). Out of the 37 pregnant women who were thrombocytopaenic, most of them (78%) had mild thrombocytopenia, only 6% had severe thrombocytopaenia. Conclusion: The prevalence of gestational thrombocytopaenia in this study was 13.5%. Although majority of the pregnant women had mild thrombocytopaenia, healthcare providers should screen all pregnant women routinely for thrombocytopaenia to avoid excessive bleeding during or after childbirth.

Key words: Gestational thrombocytopaenia, platelet count, haemorrhage

INTRODUCTION

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Platelets are non-nucleated cells derived from megakaryocytes in the bone marrow and normally live in the peripheral circulation for as long as 10 days. Platelets play a critical initiating role in the haemostatic system.¹

Thrombocytopaenia is second only to anaemia as the most common haematologic abnormality during pregnancy.² Thrombocytopaenia is classically defined as a platelet count of less than 150×10^9 /L.^{3,4} Counts from

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| | DOI: 10.4103/0300-1652.129647 |

100 to 150×10^9 /L are considered mildly depressed, 50 to 100×10^9 /L are moderately depressed and less than 50×10^9 /L are severely depressed.⁵

The overall incidence of thrombocytopaenia in pregnancy is 8%, but when patients with obstetric or medical conditions are excluded, the incidence drops to 5.1%.²

Some causes are unique to pregnancy, whereas others can be serious medical conditions that have been previously undiagnosed. The most common cause is gestational thrombocytopaenia,³ which accounts for almost threefourths of all cases. Hypertensive disorders account for 21%.³ Thrombocytopaenia occurs more commonly in patients with eclampsia (30%) than in patients with both mild and severe forms of preeclampsia (15-18%).² Of the patients who have severe preeclampsia, 4-12% will manifest criteria for HELLP syndrome (haemolysis, elevated liver enzymes and low platelet counts).² Immunemediated thrombocytopaenia, including idiopathic thrombocytopaenic purpura and neonatal alloimmune thrombocytopaenia, is responsible for 4.1% of cases,³ which is a proportionally small number. These conditions, however, can cause considerable morbidity and mortality and must be managed closely. Other, less common causes include rheumatologic disease (e.g. systemic lupus erythematosis), disseminated intravascular coagulation, thrombotic thrombocytopaenia purpura, fatty liver, antiphospholipid syndrome, human immunodeficiency virus (HIV) infection and medications.⁶

Gestational thrombocytopaenia is a diagnosis of exclusion, use of automated blood counters in routine pre-natal screening has resulted in an increased diagnosis and the following five characteristics make it more likely: (1) the degree of thrombocytopaenia is usually mild to moderate, usually remaining greater than 70×10^9 /L (however, the lower level has never been established); (2) patients are asymptomatic with no history of bleeding; (3) there is no pre-conception history of thrombocytopaenia; (4) an early gestation or preconception platelet count is normal and (5) the platelet count returns to normal within 2-12 weeks postpartum.⁷

The cause of gestational thrombocytopaenia is unclear, although it might be secondary to accelerated platelet consumption and the increased plasma volume associated with pregnancy.⁷ Anti-platelet antibodies have been detected in the serum, but this finding does not differentiate it from idiopathic thrombocytopaenic purpura, and the presence of anti-platelet antibodies is not specific for gestational thrombocytopaenia.⁶

Gestational thrombocytopaenia essentially poses no risk to either the mother or foetus-neonate. A prospective cohort study by Burrows and Kelton⁴ of 756 women with a diagnosis of gestational thrombocytopaenia showed that none of the mothers and only 1 infant, which had congenital bone marrow dysfunction diagnosed later, had any bleeding complication. In another study by Nagey *et al.*,⁸ of 730 pregnancies with platelet counts of less than 150×10^9 /L, no neonate had a platelet count of less than 100×10^9 /L, and no bleeding complications were observed. Thus, it appears that mildly to moderately depressed platelet counts from gestational thrombocytopaenia are not associated with any adverse effects to the foetus, neonate or mother, and no management is necessary other than periodic monitoring.⁶

It is known that pregnant women with thrombocytopaenia have a higher risk of bleeding excessively during or after childbirth, particularly if they need to have a caesarean section or other surgical intervention during pregnancy, labour or in the puperium. Such bleeding complications are more likely when the platelet count is less than $50 \times 10^9/L^9$ Healthcare providers must weigh the benefits of interventions in relation to cost and morbidity against the risk of maternal and foetal bleeding complications. This study was designed to determine the prevalence of gestational thrombocytopaenia among pregnant women reporting for antenatal care at tertiary healthcare centres in Lagos.

MATERIALS AND METHODS

This was a cross-sectional study of 274 pregnant women attending the Lagos University Teaching Hospital (LUTH) and Lagos State University Teaching Hospital (LASUTH) antenatal clinics (situated at Orile Agege and Isolo general hospitals). During the study period between February and September 2012 all pregnant women who gave informed consent and satisfied the study inclusion criteria were recruited into the study. Thrombocytopaenia is classically defined as a platelet count of less than 150×10^9 /L.^{3,4} Counts from 100 to 150×10^{9} /L are considered mildly depressed, 50 to $100 \times$ 10^{9} /L are moderately depressed and less than 50×10^{9} /L are severely depressed.⁵ Data collected from them was entered into a data sheet. All study participants were on routine ferrous sulphate tablet 200 mg three times daily, folic acid tablets 5 mg daily and vitamin B complex tablets three times daily.

The research was approved by the Ethics Review Committees of both LUTH and LASUTH.

Inclusion criteria

Among the pregnant women who gave informed consent, only those who had normotensive blood pressure less than or equal to 140/90 mmHg were recruited at various gestational ages.

Exclusion criteria

Pregnant women with the following conditions were excluded from the study: bleeding disorders, women on non-steroidal anti-inflammatory drugs such as aspirin, splenomegaly, connective tissue disease such as systemic lupus erythematosus (SLE), hypertension, HIV and hepatitis B infection. Information such as drug history, presence of splenomegaly and HIV/hepatitis B status were extracted from the clinical notes.

Sample size was estimated using the sample size expression: $^{\rm 10}$

$$n = \frac{Z^2 p q}{d^2}$$

Where *n* = the desired sample size.

Z = the standard normal deviation, usually set at 1.96, which correspond to the 95% confidence interval.

p = the proportion in the target population estimated to have a particular characteristic. In this case, a reasonable

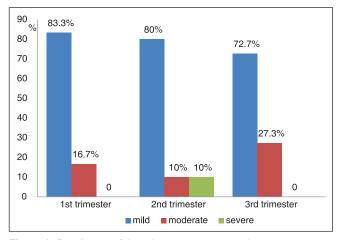
estimate will be 0.15 (15.3%). This reasonable estimate will be chosen based on prevalence of 15.3% in the literature. 11

Q = 1.0-p = 1.0-0.15 = 0.85D = degree of accuracy, usually set at 0.05. n = 196. However, 274 participants were recruited.

Blood specimen was withdrawn with minimal stasis from the ante-cubital vein using a dry sterile disposable syringe and needle. Four and half millilitres of blood was collected and dispensed into ethylenediamine tetraacetic acid ethylenediamine tetraacetic acid (EDTA) anticoagulant tubes. The specimens were labelled with subject's age, sex and identification number. The EDTA samples were kept at room temperature until processed within 4 hours of collection. Full blood count was performed using the Sysmex KN-21N, (manufactured by Sysmex corporation Kobe, Japan) a three-part auto analyzer able to run 19 parameters per sample including haemoglobin concentration, packed cell volume, red blood cell concentration and platelets. Standardization, calibration of instrument and processing of samples were done according to manufacturer's instructions. Well mixed blood sample was aspirated, by letting the equipment sampling probe into the blood sample and then pressing the start button. Approximately 20 µl of blood was aspirated by the auto analyzer. Result of analysis is displayed after about 30 s. A printout copy of result is released on the thermal printing paper.

Statistical analysis

Data were analyzed using SPSS version 16.0 (Statistical Package for Social Sciences, Inc., Chicago, IL). The descriptive data were given as means \pm standard deviation (SD). The Pearson chi-squared test was used for analytic assessment and the differences were considered to be statistically significant when the *P* value obtained was <0.05.





RESULTS

A total of 274 pregnant women and 70 non-pregnant controls were recruited. Thirty-seven (13.5%) pregnant women were thrombocytopaenic, compared with three (4.3%) control subjects (P = 0.03); Odds ratio: 3.5 (95% confidence interval 1.0305-11.8225). Majority of the participants (183 of 274; 66.8%) were in their second trimester as at the time of the study, followed by third trimester participants (53 of 274; 19.3%) and first trimester patients (38 of 274; 13.9%).

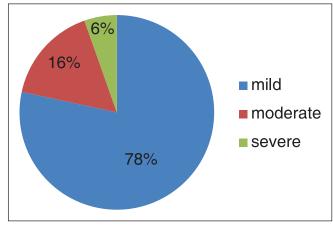
The overall platelet mean was $228.29 \pm 65.6 \times 10^{9}$ /L. A statistically significant relationship could not be established between platelet counts and various trimesters of pregnancy *P* = *0.998*, neither could it be established between platelet counts and gestational age in weeks *P* = 0.296, nor between platelet counts and parity *P* = 0.992.

Figure 1 shows the distribution of thrombocytopenia among pregnant women at different trimesters. In the first trimester, 83.3% of pregnant women who were thrombocytopenic had mild thrombocytopenia, compared with 80% and 72.7% in the second and third trimesters, respectively. No pregnant woman in the first trimester had severe thrombocytopaenia.

Figure 2 illustrates the severity of thrombocytopaenia among pregnant women. Out of the 37 pregnant women who were thrombocytopaenic, most of them (78%) had mild thrombocytopenia. However, all the thrombocytopaenic control subjects had mild thrombocytopaenia.

DISCUSSION

This work was designed to determine the prevalence of gestational thrombocytopaenia in pregnant women attending antenatal care at tertiary health centres in Lagos. Significantly more pregnant women in this study





were thrombocytopaenic compared with non-pregnant healthy controls. Pregnant women were at least three times more likely to be thrombocytopaenic compared with controls.

The prevalence of gestational thrombocytopaenia in our study was 13.5%. This figure is similar to that of 15.3% reported by Edeghonghon *et al.*,¹¹ in Ghanaian pregnant women. However, it is higher than figures of 11.6% reported by Boehlen *et al.*, in 2006¹² and 7.2% reported by Sainio *et al.*, in 2000 in the Western world.¹³ The fact that in this study, majority of the pregnant women were in the second trimester could explain the higher prevalence.

From our findings, gestational thrombocytopaenia occurred across the three trimesters, this was against the report of Crowther *et al.*,¹⁴ who reported that gestational thrombocytopaenia in pregnancy is a disorder that develops primarily in the late second or third trimester. These observations suggest that pregnancy is associated with a mild and generally unappreciated decrease in the circulating platelet count.

Most of the cases of thrombocytopenia (78.4%) in our study were mild with platelet counts above 100×10^9 /L; this agrees with the finding of Boehlen¹² who reported that gestational thrombocytopenia is usually mild.

In accordance with previous studies on early versus late antenatal booking, this study reported a preponderance of the participants registered for antenatal clinic (ANC) in second trimester, followed by the third and only 13.87% of the participants registered early for ANC. This finding tallies with various studies from different regions in Nigeria, which reported that most pregnant women registered above 20 weeks.¹⁵⁻¹⁸

This study reported a decline in platelet count as pregnancy advances; this is also consistent with the study of Akingbola *et al.*¹⁹ Due to haemodilution secondary to expansion of plasma volume, platelet count in normal pregnancies may decrease by approximately 10%, most of this decrease occurs during the third trimester^{3,20-22}, though the absolute platelet count remains within normal reference range in most patients.^{3,4,21,22}

The trimester-specific platelet counts obtained in this study also tallies with what Akingbola *et al.*,¹⁵ reported in Ibadan, Nigeria in 2006 but slightly higher than what Onwukeme *et al.*,²³ reported in Jos, Nigeria in 1990.

It is obvious from various studies^{3,4,21,22} that majority of pregnant women still have levels within the normal range; however, if pre-pregnancy levels are border-line, or there is a more severe reduction, the level may fall below the normal range. The mechanisms for this are thought to be dilutional effects and accelerated destruction of platelets passing over the often scarred and damaged trophoblast surface of the

placenta.²⁴ Platelet counts may also be lower in women with twin compared with singleton pregnancies, possibly related to greater increase of thrombin generation.²⁵ Although most cases of thrombocytopaenia in pregnancy are mild, with no adverse outcome for mother or baby, occasionally a low platelet count may be part of a complex disorder with significant morbidity and may (rarely) be life-threatening.

Overall, about 75% of cases of thrombocytopaenia in pregnancy are due to gestational thrombocytopaenia; 15-20% secondary to hypertensive disorders; 3-4% due to an immune process and the remaining 1-2% made up of rare constitutional thrombocytopaenias, infections and malignancies.⁴

CONCLUSION

Majority of pregnant women have platelet counts within the non-pregnant normal range, the prevalence of thrombocytopenia in this study was 13.5%. This rather high figure could be as a result of majority of the pregnant women being in the second trimester in the study.

Since gestational thrombocytopenia is usually mild or moderate, pregnant women found to have severe thrombocytopenia should be investigated to exclude other causes of thrombocytopenia in pregnancy such as autoimmune diseases and pre-eclampsia. Care should be taken during delivery of women with thrombocytopenia especially if severe to avoid bleeding complications.

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How to cite this article: Ajibola SO, Akinbami A, Rabiu K, Adewunmi A, Dosunmu A, Adewumi A, *et al.* Gestational thrombocytopaenia among pregnant women in Lagos, Nigeria. Niger Med J 2014;55:139-43.

Source of Support: Nil, Conflict of Interest: None declared.

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