

Original Research Article

Prevalence and clinical correlates of neonatal thrombocytopaenia in a tertiary healthcare facility in a low-income country

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ABSTRACT

Background: Thrombocytopaenia is known to complicate many neonatal illnesses and contributes significantly to morbidity and mortality. Early diagnosis and treatment are necessary to avoid complications. There are a few studies on the prevalence of neonatal thrombocytopaenia in South Eastern Nigeria. This study aimed to determine the prevalence and clinical correlates of neonatal thrombocytopaenia in South Eastern Nigeria.

Methods: The prospective study was carried out over a period of eight months (December 2015 to July 2016). One hundred and fifty nine neonates admitted consecutively into the Special Care Baby Unit of the Federal Medical Centre, Owerri were recruited and evaluated for thrombocytopaenia on admission and after forty-eight hours in the study. Blood platelet was analysed using Sysmex KX-21N automatic platelet analyser and manual counting. Thrombocytopenia was defined as blood platelet less than $100 \times 10^9/L$.

Results: The subjects included 89 (56%) males and 70 (44%) females. The prevalence of neonatal thrombocytopaenia was 6.3% on admission and 8.3% after forty-eight hours. Bleeding from orifices ($p=0.012$), prolonged pregnancy ($p=0.047$) and petechiae ($p=0.020$) were clinical correlates significantly associated with thrombocytopaenia. No specific clinical diagnosis was significantly associated with thrombocytopaenia, though the odds of a newborn having thrombocytopaenia was higher in certain conditions indicating increased risk.

Conclusions: The prevalence of thrombocytopaenia in this study suggests that platelet count should be done for neonates admitted into special care baby units in resource-poor settings. This should be more in neonates with bleeding from orifices, prolonged pregnancy and petechiae.

Keywords: Thrombocytopaenia, Platelet count, Special care baby unit, Sick neonate, Bleeding, Petechiae

INTRODUCTION

Thrombocytes (platelets) are important blood components primarily involved in haemostasis (to prevent excessive bleeding).¹ Thrombocytopaenia is a state of reduced circulating platelet count in blood below normal level.^{1,2} It is defined as platelet count less than $150 \times 10^9/L$ and sometimes, as less than $100 \times 10^9/L$.¹ It is considered

severe if platelet count is below $30 \times 10^9/L$, moderate if it is between $30 \times 10^9/L$ and $50 \times 10^9/L$ and mild (usually asymptomatic) if above $50 \times 10^9/L$.² It is also commonly classified as early (within the first 72 hours of life) or late (after 72 hours).^{1,2} The prevalence of thrombocytopaenia among neonates admitted into special care baby units (SCBU) ranges between 6% to 35%.¹⁻⁴ Thrombocytopaenia complicates illnesses in the neonate with significant impact on morbidity and mortality.⁵ The

morbidities that result from neonatal thrombocytopenia include intraventricular haemorrhage, periventricular haemorrhage, seizures, cortical blindness, intellectual disability and cerebral palsy.⁵ The mortality rate in severely ill neonates who have had thrombocytopenia is several times higher than those who have normal platelet count.⁶ Thus, thrombocytopenia contributes adversely to the high neonatal mortality in sub-Saharan Africa.

Neonatal thrombocytopenia is often reported to be due to underlying illnesses such as severe birth asphyxia, neonatal jaundice, neonatal sepsis, low birth weight, bleeding and anaemia.^{1,2} In majority of cases, it is found following bleeding and could be detected following thrombo-embolic events that can occur in the anti-phospholipid syndrome and sometimes in heparin-induced thrombocytopenia.^{3,4} The risk factors associated with neonatal thrombocytopenia could be maternal/perinatal, neonatal or a combination of both.¹⁻⁴ They include maternal pre-eclampsia, intrauterine growth restriction (IUGR), maternal diabetes mellitus (DM), congenital/inherited thrombocytopenia, perinatal asphyxia, perinatal disseminated intravascular coagulopathy (DIC), sepsis, necrotizing enterocolitis (NEC), low birth weight (LBW), prematurity and alloantibodies.¹⁻⁴ Some studies have shown platelet count to be slightly higher in females than in males, though the cause is not fully understood.^{7,8}

Impaired platelet production remains the major mechanism underlying most (75%) cases of neonatal thrombocytopenia.⁹ In conditions of placental insufficiency (preeclampsia, IUGR and maternal DM), Meconium Aspiration Syndrome [MAS] and perinatal asphyxia, the concomitant hypoxia drives progenitor cells to produce erythroid cells at the expense of leucocytes and thrombocytes leading to thrombocytopenia.^{9,10} In immunological disorders (transplacental passage of maternal platelet autoantibodies) and DIC which occur in a minority of patients, consumption or sequestration is the pathophysiological mechanism.⁹ Other associated factors act through combined mechanisms to cause thrombocytopenia. For instance, bacterial infection causes both damage to vascular endothelium (which accelerates adhesion, destruction and removal of platelets) and DIC, immune-mediated destruction and bone marrow depression (decreased thrombopoiesis).^{9,11}

Thrombocytopenia is usually asymptomatic and the first manifestation may be fatal or a near fatal bleeding.⁶ Clinical manifestations such as petechiae, purpura, ecchymoses, gastrointestinal bleeding, haematoma, haematemesis, haematuria, retinal haemorrhage and intracranial haemorrhage can occur.⁶ Reliance on symptoms to make a diagnosis of neonatal thrombocytopenia may result in missed diagnosis since symptoms do not usually occur.⁶ In order to avoid complications, deliberate effort must be made to detect the presence of thrombocytopenia in neonates admitted into Special Care Baby Units.^{6,12}

Blood platelet count remains the mainstay of diagnosis and can be done manually using phase contrast microscopy or by using automated platelet analyser.¹³ In earlier studies, blood platelet counting was based on manual analysis of blood indices and mathematical derivations based on manual counts which is examiner dependent.¹⁴⁻¹⁶ In order to facilitate comparison across newer studies, it would be necessary to use more modern automated techniques.

Few studies have reported the prevalence and risk factors for neonatal thrombocytopenia unlike adult populations in tropical Africa, more so in Nigeria.^{7,14,17} The study by Utuk et al in Southern Nigeria, in 2011 notably excluded neonates.¹⁷ Additionally, platelet transfusion is not yet in active practice in many centres including Federal Medical Centre, Owerri.¹⁴⁻¹⁶ Therefore, the purpose of this study was to determine the prevalence and clinical correlates of thrombocytopenia among neonates admitted into the SCBU of Federal Medical Centre, Owerri.

METHODS

The study was carried out at the SCBU of the Federal Medical Centre, Owerri, Imo State in South Eastern Nigeria. The Federal medical centre (FMC), Owerri has 530 beds and remains the major tertiary health care facility in the state that offers specialist obstetrics and neonatal services among other health care services.

The SCBU has 16 cots and 22 incubators with total annual admissions of about 250 neonates. Of this, 60 of them are preterms. The unit has separate sections for inborn and outborn babies. There is no policy restriction on categories of illness accepted for admission. However, there are no facilities for intensive neonatal care like mechanical ventilation or parenteral nutrition. FMC Owerri has modern laboratory facilities with qualified laboratory personnel including consultant haematologists.

Sampling technique

This prospective study evaluated 159 newborns consecutively recruited over a period of eight months (December 2015 and July 2016). The study sample included all newborns (from birth to 28 days of life) admitted into the SCBU whose parents/care-givers gave informed consent. Newborns with multiple congenital malformations or who had been transfused before first sampling were excluded.

Study procedure/data collection

All newborns from birth to 28 days admitted into the SCBU who met the inclusion criteria mentioned above were recruited consecutively until the determined sample size was reached. Blood samples for platelet counting were taken on admission and after 48 hours. A case record form was completed for each neonate to obtain information on personal data, socio-demographic data, presenting complaints, duration of illness and treatments received

before presentation. Socio-economic status of the parents was determined using the social classification system described by Oyediji.¹⁸ Clinical examinations were carried out on all study subjects including anthropometric measurements. Collection of blood sample was done under aseptic conditions. A selected puncture site (peripheral vein) was cleaned using alcohol swab and allowed to dry. Two milliliters (2 ml) of blood was drawn from the recruited neonates through a peripheral vein on admission and after forty eight hours. The blood samples were put into an Ethylenediaminetetracetic acid (EDTA) bottle and sent to the haematology laboratory of the Federal Medical Centre (FMC) Owerri for platelet counting. The samples were processed immediately after collection. Samples that were not analysed immediately were refrigerated at four to eight degrees Celsius for not more than six hours.

The laboratory estimation of blood platelet concentration was done using the Sysmex KX-21N automatic platelet analyser.¹⁹ The counting principle is based on an impedance variation generated by the passage of cells through the calibrated micro aperture. The blood sample was diluted in an electrolytic diluent (current conductor). The dilution was pulled through the calibrated micro aperture. Two electrodes were placed on each side of the aperture and electric current passed through the electrodes continuously. When cells passed through the aperture, electric resistance (or impedance) between the two electrodes increased proportionately with the cell volume. Two measuring chambers and detection circuits separately carried out the analysis of WBC, and that of the platelets and red blood cells. To minimize errors, platelet count was done in triplicates, and the counts automatically averaged. If one of the triplicate counts fell outside the preset limit, it was rejected and the result was calculated based on the remaining two. In cases where two of the counts differed, the count was rejected completely and no result was given. This increased the precision and accuracy of the results.^{13,19}

Results were expressed as platelet count $\times 10^9/L$. As a quality control measure, any sample which contained a significant proportion of giant platelets, low platelet count less than $40 \times 10^9/L$ or did not show any platelet count, indicated by a flag signal from the machine, a peripheral blood smear with Leishman stain was made for manual counting.^{13,19} For this study, neonatal thrombocytopenia was defined as blood platelet count less than $100 \times 10^9/L$.

Data analysis

The collected data was entered into a computer system and analysed using the Statistical package for social sciences (SPSS) version 19. Continuous variables like age, length and weight were summarized with descriptive statistics such as mean and standard deviation.

Categorical variables were compared using Chi-squared and Fishers Exact tests. Student t- test was used to compare the means. Odds ratio with 95% confidence intervals was

calculated to measure the degrees of relationships and comparisons across groups. Probability (p) value less than 0.05 was taken as significant.

RESULTS

A total of one hundred and sixty seven newborns were recruited into this study however only one hundred and fifty nine completed the study. Eight newborns were discharged against medical advice and were excluded.

Table 1: General characteristics of the subjects.

General characteristics of the subjects	Frequency (%)
Gestational age group (weeks)	
<28	5 (3.1)
28-30	10 (6.3)
31-33	15 (9.4)
34-36	18 (11.3)
37-39	25 (15.7)
40-42	80 (50.4)
>42	6 (3.8)
Gender	
Male	89 (56.0)
Female	70 (44.0)
Place of birth	
FMC Owerri	96 (60.4)
Outside FMC Owerri	63 (39.6)
Socioeconomic class	
Upper socioeconomic class	8 (5.0)
Middle socioeconomic class	63 (39.7)
Lower socioeconomic class	88 (55.3)
Mode of delivery	
Vaginal	83 (52.2)
Spontaneous	74 (46.5)
Induced	6 (3.8)
Assisted	3 (1.9)
Caesarean Section	76 (47.8)
Emergency	74 (46.5)
Elective	2 (1.3)
Maternal age (years)	
<20	63 (39.6)
20 – 34	73 (45.9)
≥ 35	23 (14.5)
Maternal parity	
1	63 (39.6)
2 – 4	72 (45.3)
≥ 5	24 (15.1)

General characteristics of the study sample

Among the one hundred and fifty nine neonates that completed the study, 89 (56.0%) were males and 70 (44.0%) were females. The general characteristics of the subjects are shown in Table 1.

Table 2: Adverse obstetric risk factors for neonatal thrombocytopaenia.

Obstetric risk factors	Frequency (%)
Hypertensive disorders in pregnancy	26 (16.4)
Prolonged rupture of membranes	24 (15.1)
Prolonged labour	20 (12.6)
Peripartum pyrexia	16 (10.1)
Antepartum haemorrhage	7 (4.4)
Prolonged pregnancy	6 (3.8)
Maternal human immunodeficiency virus infection	5 (3.1)
Gestational diabetes mellitus	4 (2.5)
Oligohydraminous	2 (1.3)
Multiple gestation	2 (1.3)
Chorioamnionitis	1 (0.6)
Maternal hepatitis B infection	1 (0.6)

Note: Not all mothers had obstetric risk factors

Table 3: Clinical examination findings.

Clinical examination findings	Frequency (%)
Temperature	
Hypothermia	11 (6.9)
Subnormal	37 (23.3)
Normal	84 (52.8)
Pyrexia	27 (17.0)
Jaundice	47 (29.6)
Pallor	17 (10.7)
Respiratory distress	86 (54.0)
Cyanosis	13 (8.2)
Poor motor activity	39 (24.5)
Poor primitive reflexes	52 (32.7)
Petechiae	7 (4.4)
Cephalhaematoma	1 (0.6)

Adverse obstetric risk factors for neonatal thrombocytopaenia

Hypertensive disorders of pregnancy, premature rupture of membrane (PROM), prolonged labour and peripartum pyrexia were the commonest reported adverse obstetric risk factors in 26 (16.4%), 24 (15.1%), 20 (12.6%) and 16 (10.1%) of cases respectively (Table 2).

Birth weights and clinical examination findings

The birth weights of the newborns ranged from 400 – 5,600grams with a mean birth weight of 2,703.3±987.3 g. Ninety three newborn (58.5%) had normal birth weight (2,500 – 4,000 g), 56 (35.1%) have low birth weight while 10 (6.3%) were macrosomic babies. Ten (6.3%) newborn were small for their gestational ages (SGA) and large for gestational age (LGA) respectively while 139 (87.4%) had appropriate weight for gestational age (AGA). Table 3 shows the clinical examination findings.

Table 4: Clinical diagnosis of study subjects.

Diagnosis	Frequency (%)
Neonatal sepsis	70 (44.0)
Perinatal asphyxia	64 (40.3)
Preterm	48 (30.2)
Low birth weight	45 (28.3)
Meconium aspiration syndrome	13 (8.2)
Macrosomia	5 (3.1)
Haemorrhagic disease of the newborn	4 (2.5)
Congenital pneumonia	3 (1.9)
Congenital malaria	2 (1.9)
Ophthalmia neonatorum	2 (1.3)
Laryngomalacia	2 (1.3)
Necrotizing enterocolitis	2 (1.3)
Bladder outlet obstruction	1 (0.6)
Transient tachypnoea of the newborn	1 (0.6)
Disseminated intravascular coagulopathy	1 (0.6)
Aspiration pneumonitis	1 (0.6)
Impetigo neonatorum	1 (0.6)
Respiratory distress syndrome	1 (0.6)
Meningitis	1 (0.6)

Note: Some patients had multiple diagnoses

Clinical diagnosis of the study subjects

Neonatal sepsis (44.0%), perinatal asphyxia (40.3%), prematurity (30.2%) and low birth weight (28.3%) were common diagnoses among the subjects. Four (2.5%) had haemorrhagic disease of the newborn and 1 (0.6%) had Disseminated Intravascular Coagulopathy. Table 4 shows the clinical diagnoses of the newborns.

Platelet count of the newborns

Day one platelet count of the newborn ranged from 54.0-489.0×10⁹/l with a mean platelet count of 196.2±79.8×10⁹/l while the day three count ranged from 30.0 – 400.0×10⁹/l. The incidence of thrombocytopaenia was 6.3% on day 1 and 8.3% on day 3 as shown in table 5. There was no significant increase in the proportion of newborn with thrombocytopaenia by day 3 (p=0.50). All 10 (6.3%) with thrombocytopaenia on day one had mild thrombocytopaenia while by day 3, one (0.6%) had moderate thrombocytopaenia and 12 (7.7%) had mild thrombocytopaenia (Table 5). The same neonates who were thrombocytopaenic on day 1 were also thrombocytopaenic on day 3, with 3 other neonates.

Association of thrombocytopaenia with socio-demographic variables in the newborn

Table 6 below shows the association between thrombocytopaenia and socio-demographic variables in the newborns.

Association between thrombocytopaenia and clinical symptoms

The association between thrombocytopaenia and clinical symptoms was tested in table VII. Bleeding as a symptom was significantly associated with thrombocytopaenia ($p=0.012$). (Table 7)

Association of thrombocytopaenia and adverse obstetric risk factors

Amongst all the adverse obstetric risk factors, only prolonged pregnancy was significantly associated with thrombocytopaenia ($p=0.047$).

Table 5: Comparison of day 1 and day 3 incidence of thrombocytopaenia.

	Day 1	Day 3	χ^2	P value
Platelet count				
Thrombocytopaenia	10 (6.3)	13 (8.3)	2	0.50
Normal	149 (93.7)	143 (91.7)		
Grading of platelet count (x10 ⁹)				
30-49	0 (0.0)	1 (0.6)	Fishers Exact	0.002
50-99	10 (6.3)	12 (7.7)		
100-149	40 (25.2)	64 (41.0)		
≥150	109 (68.6)	79 (50.6)		

Table 6: Association between thrombocytopaenia and socio-demographic variables.

General characteristics	Thrombocytopaenic	Normal platelet count	Total	P value (chi square)
Gestational age group				
<37	2 (4.2)	46 (95.8)	48 (100.0)	0.438
37 – 42	6 (5.7)	99 (94.3)	105 (100.0)	
>42	2 (33.3)	4 (66.7)	6 (100.0)	
Gender				
Male	6 (6.7)	83 (93.3)	89 (56.0)	0.293
Female	4 (5.7)	66 (94.3)	70 (44.0)	
Place of Birth				
FMC Owerri	5 (5.2)	91 (94.8)	96 (60.4)	0.488
Outside FMC Owerri	5 (7.9)	58 (92.1)	63 (39.6)	
Socioeconomic Class				
Upper Class	3 (37.5)	5 (62.5)	8 (100.0)	1.000
Middle Class	6 (9.5)	57 (90.5)	63 (100.0)	
Lower Class	1 (1.1)	87 (98.9)	88 (100)	
Mode of Delivery				
Vaginal	5 (6.0)	78 (94.0)	83 (100.0)	0.886
Caesarean Section	5 (6.6)	71 (93.4)	76 (100.0)	
Maternal age				
<20	4 (6.4)	59 (93.6)	63 (39.6)	0.452
20 – 34	6 (8.2)	67 (91.8)	73 (45.9)	
≥35	0 (0.0)	23 (100.0)	23 (14.5)	
Parity				
<2	4 (6.4)	59 (93.6)	63 (39.6)	0.452
2 – 4	6 (8.2)	67 (91.8)	72 (45.3)	
>5	0 (0.0)	24 (100.0)	24 (15.1)	

Table 7: Association between thrombocytopaenia and clinical symptoms.

Clinical symptoms		Thrombocytopaenic	Normal platelet count	Total	P value
Fever	Yes	0 (0.0)	17 (100.0)	17 (100.0)	0.602
	No	10 (7.0)	132 (93.0)	139 (100.0)	
Poor Cry	Yes	5 (7.1)	65 (92.9)	70 (100.0)	0.694
	No	5 (5.6)	84 (94.4)	89 (100.0)	

Continued.

Clinical symptoms		Thrombocytopenic	Normal platelet count	Total	P value
Jaundice	Yes	0 (0.0)	9 (100.0)	9 (100.0)	1.000
	No	10 (6.7)	140 (93.3)	150 (100.0)	
Bleeding from orifices	Yes	3 (33.3)	6 (66.7)	9 (100.0)	0.012
	No	7 (4.7)	143 (95.3)	150 (100.0)	
Dyspnoea	Yes	1 (2.0)	48 (98.0)	49 (100.0)	0.177
	No	9 (8.2)	101 (91.8)	110 (100.0)	
Seizure	Yes	0 (0.0)	19 (100.0)	19 (100.0)	0.610
	No	10 (7.1)	130 (92.9)	140 (100.0)	
Poor Suck	Yes	1 (10.0)	9 (90.0)	10 (100.0)	0.488
	No	9 (6.0)	140 (94.0)	149 (100.0)	
Vomiting	Yes	0 (0.0)	5 (100.0)	5 (100.0)	1.000
	No	10 (6.5)	144 (93.5)	154 (100.0)	
Meconium Stainings	Yes	1 (7.1)	13 (92.9)	14 (100.0)	1.000
	No	9 (6.2)	136 (93.8)	145 (100.0)	
Eye discharge	Yes	0 (0.0)	1 (100.0)	1 (100.0)	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)	
Skin Rash	Yes	0 (0.0)	1 (100.0)	1 (100.0)	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)	

Table 8: Association between thrombocytopenia and obstetric risk factors.

Obstetric risk		Thrombocytopenic	Normal platelet count	Total	Odd ratio	P value
Hypertension in pregnancy	Yes	3 (11.5)	23 (88.5)	26 (100.0)	2.35	0.211
	No	7 (5.3)	126 (94.7)	133 (100.0)		
Peripartum pyrexia	Yes	2 (12.5)	14 (87.5)	16 (100.0)	2.41	0.265
	No	8 (5.6)	135 (94.4)	143 (100.0)		
Prolonged rupture of membranes	Yes	1 (4.2)	23 (95.8)	24 (100.0)	0.61	1.000
	No	9 (6.7)	126 (93.3)	135 (100.0)		
Antepartum haemorrhage	Yes	1 (14.3)	6 (85.7)	7 (100.0)	2.65	0.371
	No	9 (5.9)	143 (94.1)	152 (100.0)		
Chorioamnionitis	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
Gestational diabetes mellitus	Yes	0 (0.0)	4 (100.0)	4 (100.0)	0.00	1.000
	No	10 (6.5)	145 (93.5)	155 (100.0)		
Oligohydraminous	Yes	0 (0.0)	2 (100.0)	2 (100.0)	0.00	1.000
	No	10 (6.4)	147 (93.6)	157 (100.0)		
Maternal HIV Infection	Yes	1 (20.0)	4 (80.0)	5 (100.0)	4.03	0.280
	No	9 (5.8)	145 (94.2)	154 (100.0)		
Multiple gestation	Yes	0 (0.0)	2 (100.0)	2 (100.0)	0.00	1.000
	No	10 (6.4)	147 (93.6)	157 (100.0)		
Prolonged pregnancy	Yes	2 (33.3)	4 (66.7)	6 (100.0)	6.38	0.047
	No	8 (5.2)	145 (94.8)	153 (100.0)		
Prolonged labour	Yes	1 (5.0)	19 (95.0)	20 (100.0)	0.76	1.000
	No	9 (6.5)	130 (93.5)	139 (100.0)		

Table 9: Association of Thrombocytopenia with clinical findings in the newborn.

Clinical examination findings	Thrombocytopenic	Normal platelet count	Total	P value
Temperature				
Hypothermia	1 (9.1)	10 (90.1)	11 (100.0)	

Continued.

Clinical examination findings		Thrombocytopaenic	Normal platelet count	Total	P value
Subnormal		3 (8.1)	34 (91.9)	37 (100.0)	
Normal		2 (2.4)	82 (97.6)	84 (100.0)	
Pyrexia		4 (14.8)	23 (85.2)	27 (100.0)	
Jaundice	Yes	2 (4.3)	45 (95.7)	47 (100.0)	0.724
	No	8 (7.1)	104 (92.9)	112 (100.0)	
Pallor	Yes	3 (17.6)	14 (82.4)	17 (100.0)	0.076
	No	7 (4.9)	135 (95.1)	142 (100.0)	
Respiratory distress	Yes	4 (4.9)	77 (95.1)	81 (54.0)	0.529
	No	6 (7.7)	72 (92.3)	78 (100.0)	
Apnoea	Yes	1 (20.0)	4 (80.0)	5 (100.0)	0.280
	No	9 (5.8)	145 (94.2)	154 (100.0)	
Cyanosis	Yes	2 (15.4)	11 (84.6)	13 (8.2)	0.191
	No	8 (5.5)	138 (94.5)	146 (100.0)	
Poor motor activity	Yes	3 (7.7)	36 (92.3)	39 (100.0)	0.708
	No	7 (5.8)	113 (94.2)	120 (100.0)	
Poor primitive reflexes	Yes	5 (9.6)	47 (90.4)	52 (32.7)	0.228
	No	5 (4.7)	102 (95.3)	107 (100.0)	
Petechiae	Yes	2 (50.0)	2 (50.0)	4 (100.0)	0.020
	No	8 (5.2)	147 (94.0)	155 (100.0)	
Cephalhaematoma	Yes	0 (100.0)	1 (100.0)	1 (100.0)	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)	
Crepitations	Yes	0 (0.0)	4 (100.0)	4 (100.0)	1.000
	No	10 (6.5)	145 (93.5)	155 (100.0)	

Table 10: Association between thrombocytopaenia and clinical conditions/diagnoses.

Diagnosis/conditions		Thrombocytopaenia (%)	Normal platelet count (%)	Total (%)	Odd ratio	P value
NNS	Yes	6 (8.6)		70 (100.0)	1.99	0.338
	No	4 (4.5)	85 (95.5)	89 (100.0)		
Perinatal Asphyxia	Yes	3 (4.7)	61 (95.3)	64 (100.0)	0.62	0.741
	No	7 (7.4)	88 (92.6)	95 (100.0)		
Preterm	Yes	2 (4.2)	46 (95.8)	48 (100.0)	0.56	0.724
	No	8 (7.2)	103 (92.8)	111 (100.0)		
Low Birth Weight	Yes	2 (4.4)	43 (95.6)	45 (100.0)	0.62	0.726
	No	8 (7.0)	106 (93.0)	114 (100.0)		
MAS	Yes	1 (7.7)	12 (92.3)	13 (100.0)	1.27	0.585
	No	9 (6.2)	137 (93.8)	146 (100.0)		
NNJ	Yes	1 (8.3)	11 (91.7)	12 (100.0)	1.39	0.555
	No	9 (6.2)	138 (93.8)	147 (100.0)		
Macrosomia	Yes	1 (20.0)	4 (80.0)	5 (100.0)	4.03	0.280
	No	9 (5.8)	145 (94.2)	154 (100.0)		
HDN	Yes	1 (25.0)	3 (75.0)	4 (100.0)	5.41	0.231
	No	9 (5.8)	146 (94.2)	155 (100.0)		
ABO incompatibility	Yes	1 (33.3)	2 (66.7)	3 (100.0)	8.17	0.178
	No	9 (5.8)	147 (94.2)	156 (100.0)		
Congenital Pneumonia	Yes	0 (0.0)	3 (100.0)	3 (100.0)	0.00	1.000
	No	10 (6.4)	146 (100.0)	156 (100.0)		
Laryngomalacia	Yes	0 (0.0)	2 (100.0)	2 (100.0)	0.00	1.000
	No	10 (6.4)	147 (93.6)	157 (100.0)		
Congenital malaria	Yes	0 (0.0)	2 (100.0)	2 (100.0)	0.00	1.000
	No	10 (6.4)	147 (93.6)	157 (100.0)		

Continued.

Diagnosis/conditions		Thrombocytopenia (%)	Normal platelet count (%)	Total (%)	Odd ratio	P value
Ophthalmia neonatorum	Yes	0 (0.0)	3 (100.0)	3 (100.0)	0.00	1.000
	No	10 (6.4)	146 (100.0)	156 (100.0)		
NEC	Yes	1 (100.0)	0 (0.0)	1 (100.0)	Infinity	0.069
	No	10 (6.3)	148 (93.7)	158 (100.0)		
BOO	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
TTN	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
DIC	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
Impetigo neonatorum	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
RDS	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		
Meningitis	Yes	0 (0.0)	1 (100.0)	1 (100.0)	0.00	1.000
	No	10 (6.3)	148 (93.7)	158 (100.0)		

However, the odd that newborns of women that had hypertensive disorders in pregnancy, peripartum pyrexia, antepartum haemorrhage, HIV infection and prolonged pregnancy were 2.35, 2.41, 2.65, 4.03 and 6.38 times higher than those who do not have them. This suggests that the risk of neonatal thrombocytopenia is higher in these conditions even though they were not statistically significant. (Table 8).

Association of thrombocytopenia with clinical findings

Table 8 shows the association between thrombocytopenia and examination findings. Petechiae patches was the only examination finding significantly associated with thrombocytopenia ($p=0.020$).

Association of thrombocytopenia with clinical conditions and diagnoses

Thrombocytopenia was not significantly associated with any of the specific clinical diagnosis in this study, however the odds that newborns with neonatal sepsis, meconium aspiration syndrome, neonatal jaundice, haemorrhagic disease of the newborn, ABO incompatibility and NEC were 1.99, 1.27, 1.39, 5.41, 8.17 and infinity times higher. This indicates that the risk of neonatal thrombocytopenia is increased in these conditions even though they were not statistically significant (Table 9).

DISCUSSION

The prevalence of neonatal thrombocytopenia in this study was found to be 6.3% on the first day on admission and 8.3% on the third day on admission. This is similar to reports from earlier studies which ranged from 6 to 35%.^{5,20,21} This high prevalence could be as a result of the fact that only neonates who were sick enough to be

admitted were recruited and neonatal illnesses pose a risk for thrombocytopenia.^{5,20,21} Hence, there is immense need to check blood platelet at the point of admission into the Special Care Baby Unit in resource-poor settings. This finding is however higher than the study by Ogundeyi et al in Sagamu, Nigeria, where no neonate had thrombocytopenia.²² The marked difference may be because only healthy neonates were studied in Sagamu, while the subjects of the current study were neonates who were ill enough to be admitted into the Special care baby unit.

Manual platelet counting method is burdensome, examiner dependent and prone to errors especially when large samples are involved.¹³ The prevalence reported in this study was much lower than 53% found by Jeremiah et al.¹⁴ The difference probably resulted from the manual platelet counting method (methodology) used in the study by Jeremiah et al which may have accounted for higher prevalence.¹⁴ It is also possible that the manual counting was not done by one person, hence introducing inter-observer variation in the values.

Several studies have shown that multiple factors acting through impaired production, consumption, sequestration and multiple mechanisms are associated with thrombocytopenia.^{9-11,23} In this present study, thrombocytopenia was found to be associated with neonatal sepsis, perinatal asphyxia, prematurity, low birth weight, necrotizing enterocolitis, ABO Incompatibility and neonatal jaundice. This is comparable to the findings by Jeremiah et al in Port Harcourt, Nigeria who reported thrombocytopenia to be more commonly associated with severe birth asphyxia, neonatal jaundice, neonatal sepsis and low birth weight.¹⁴ Sonam et al in India also reported the highest prevalence of thrombocytopenia in neonates who were diagnosed with prematurity, neonatal sepsis, meconium aspiration syndrome and birth asphyxia.²⁴ The

clinical conditions found to be associated with thrombocytopaenia in the present study were not statistically significant; however, the odd that newborns with these clinical conditions will have thrombocytopaenia was high.

Prolonged pregnancy leads to hypoxia which drives progenitor cells to produce erythroid cells at the expense of leucocytes and thrombocytes.^{10,25} A significant association was found between neonatal thrombocytopaenia and prolonged pregnancy ($p=0.047$), similar to a report by Sharma et al in India.²⁵ However, Khalessi et al in Iran and Patil et al in Gulbarga did not document a significant association between neonatal thrombocytopaenia and prolonged pregnancy.^{11,26} The difference may be due to variations in the definitions of prolonged pregnancy. In the present study, prolonged pregnancy was defined as pregnancy that has extended beyond 42 weeks of gestation, while the Khalessi et al and Patil et al used gestational age above 40 weeks.^{11,26} This implies the subjects in this study with prolonged pregnancy had longer duration of hypoxia in utero.

Thrombocytopaenia, often reported to be due to an underlying cause, is usually asymptomatic and fatal or near-fatal bleeding may be the initial manifestation.^{1,3} Clinical features of bleeding from orifices ($p=0.012$) and petechiae ($p=0.020$) were significantly associated with thrombocytopaenia in this study. This finding implies that history of bleeding and clinical finding of petechiae are pointers to neonatal thrombocytopaenia. However, it is surprising that none of the clinical conditions or diagnoses was significantly associated with thrombocytopaenia including cephalhaematoma and DIC – conditions known to have bleeding manifestations. Nevertheless, the odds that newborns with neonatal sepsis, meconium aspiration syndrome, neonatal jaundice, haemorrhagic disease of the newborn, ABO incompatibility and NEC were 1.99, 1.27, 1.39, 5.41, 8.17 and infinity times higher indicating that the risk of neonatal thrombocytopaenia is increased in these conditions even though they were not statistically significant.

No significant gender difference in platelet counts was seen in the neonates studied. This is similar to the observation by Ogundeyi et al and Onwukeme et al but in contrast to observations by Taylor et al in Dublin, Ireland.^{15,22,27} Taylor et al found a higher platelet count in girls than boys.²⁷ The reason for this difference may be related to the age and race. Whereas, the present study, Ogundeyi et al and Onwukeme et al were limited to African neonates, Taylor et al studied Adolescent Caucasian children.^{15,22,27} It is documented that in older children, the haematologic parameters including platelet count tend towards adult values with its gender differences (higher platelet counts in females) and racial differences.^{8,27} The peri-pubertal rise which occurs in girls is related to the onset of menstruation and increase in oestrogen release which triggers pro-platelet formation in megakaryocytes.^{8,27}

Manual platelet count was not done on all study subjects but only on those noted to be thrombocytopaenic. It may have helped to compare automated with manual platelet counting among the subjects and this was identified as one limitation of the study.

CONCLUSION

The prevalence of thrombocytopaenia among neonates admitted into the SCBU of Federal Medical Centre, Owerri was found to be 6.3% on the first day and 8.3% on the 3rd day on admission and suggests that platelet count should be done for sick neonates in resource-poor settings. This should be more in neonates with bleeding from orifices, prolonged pregnancy and petechiae. Newborn babies with neonatal sepsis, meconium aspiration syndrome, neonatal jaundice, haemorrhagic disease of the newborn, necrotizing enterocolitis have higher odds ratio of developing neonatal thrombocytopaenia than those without them.

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