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Original Research Article

A STUDY OF THROMBOCYTE COUNT IN NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL

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Abstract

Background: This cross-sectional investigation was carried out to estimate the prevalence of thrombocytopenia and its significance in the earlier clinical diagnosis and management of neonatal sepsis. **Materials and Methods:** Ethical clearance from the institutional ethics committee was obtained before undertaking this hospital-based cross-sectional study in the tertiary health care facility. 106 neonates who had either a sepsis screen or culture positive were chosen in succession during the study period. All enrolled neonates were subjected to various diagnostic tests and received care using the Facility-based Newborn care protocol, which was followed through to the conclusion. EpiInfo software 3.5.1 was used to analyze the data. Mean and standard deviation were used to express continuous variables while rate and ratio were used to express categorical variables. Statistical significance was defined as a P-value of <0.05. **Result:** The current study confirmed thrombocytopenia in 50.94% of septic babies, and the mortality rate was higher in the thrombocytopenic group (83.33%) than in the septic babies with a normal thrombocyte count (16.67%). The mortality rate among the thrombocytopenic group was greater in situations of severe thrombocytopenia (22.22%) than in cases of mild (3.57%) and moderate (11.76%) thrombocytopenia. **Conclusion:** The death rate was notable for cases of severe thrombocytopenia. Because neonatal thrombocytopenia is a curable and reversible illness, it calls to recognize early at-risk neonates and start the right treatment to avoid serious consequences in terms of morbidity and mortality.

INTRODUCTION

Septicaemia, meningitis, pneumonia, pyogenic arthritis, osteomyelitis, and urinary tract infections are among the systemic conditions known collectively as "neonatal sepsis" affecting neonates.[1] Clinical signs of the patient, nonspecific evidence like procalcitonin and C-reactive protein, and blood cultures are all used to make the diagnosis of neonatal sepsis which is attributed the neonatal mortality, accounting for 30 to 50 percent of all neonatal deaths in developing countries.[2,3] Thrombocytopenia, a frequent problem in neonatal critical care units that complicates the clinical course in 22–35% of intensive care admissions, is one of the early yet non-specific indications of neonatal sepsis.[4] Although bleeding is a major adverse effect of thrombocytopenia, it typically only impacts neonates with counts ≤ 30 ×109/L.[5] The fact that thrombocytopenia is one of the most trustworthy independent risk factors for sepsis-related mortality in extremely low birth weight infants emphasizes the significance of the association between thrombocytopenia and sepsis.[6]

Therefore, this study may assist healthcare providers who are working in settings where sepsis screening and blood culture are not feasible due to an array of constraints in making both clinical diagnosis and the course of neonatal sepsis earlier and to gain a better understanding of the challenges arising from it.

Objectives

To estimate the prevalence of thrombocytopenia in neonatal sepsis and to find out its association with different variables.

MATERIALS AND METHODS

Study area: The present study was conducted in the Special New Born Care Unit (SNCU) Department of Paediatrics, Bankura Sammilani Medical College and Hospital (BSMCH), Bankura, India. Period of study: The proposed study was carried out from February 2021 to July 2022. Study design: hospital-based cross-sectional descriptive Study subjects: neonates. Inclusion criteria: a. baby admitted to the SNCU with

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the diagnosis of neonatal sepsis with either a sepsis screen positive and/or a positive blood culture; and b. those carers were willing to participate in this research work. Exclusion criteria: a. neonates with a history of bleeding disorder in the family; b. mothers with a history of ITP, SLE, and other autoimmune disorders; c. maternal history of drug intake during pregnancy (sulphonamides, quinine, thiazides, tolbutamide, vancomycin, hydralazine, and heparin); and d. that carers were not willing to take part in this study. Number of participants: 106 (one hundred and six). Using the formula N= (Z)2× P(1-P)/d2, the sample was calculated. In this case, thrombocytopenia had a prevalence of 49%[7] and Z is a normal standard variate with a 95% confidence interval, d is the accepted absolute error, which in this case was 10%. Using the aforementioned formula and all of these parameters, sample 96 was obtained. The total sample size was 106 after accounting for a 10% non-response.

Study Technique: Study participants who met the eligibility requirements were chosen one after the other until the required number of samples were obtained. All enrolled neonates were subjected to various diagnostic tests and received care following the FBNC protocol8, which was carried out up until the conclusion. With the aid of a pre-designed, pre-tested interviewer-administered questionnaire, carers were questioned after receiving informed consent, and data were then recorded. Demographic information, clinical characteristics, laboratory results, clinical outcomes, and length of hospital stay were all collected on all neonates that were recruited.

Data analysis: Collected data was put into the Microsoft Excel spreadsheet for analysis with the help of EpiInfo software version 3.5.1 (Developer: Centre for Disease Control and Prevention, USA). Continuous variables were expressed in terms of mean and standard deviation, whereas rate and ratio were for categorical ones. Categorical variables were again analyzed by the Chi-square test to find an association among them. A P-value of <0.05 was set as statistically significant.

Ethical clearance: Ethical clearance had been taken before the initiation of the current research.

Case definitions: Neonatal sepsis 9: We selected cases of neonatal sepsis that presented signs and symptoms of sepsis with either a reactive septic screen and/or a positive blood culture.

Positive sepsis screening: Sepsis screening was considered positive when either of the two tests were positive out of five tests: leukopenia (TLC <5000/mm3), neutropenia (absolute neutrophil count/ANC <1800/mm3), immature neutrophil to total neutrophil (IT) ratio > 0.2, micro-ESR > 15 mm in the first hour, and positive CRP (>1mg/dl).[8]

Thrombocytopenia: Platelet counts below 150 $\times 10^9$/L; mild thrombocytopenia: 150–100 $\times 10^9$/L; moderate thrombocytopenia: 100–50 ×109/L; and severe thrombocytopenia: below 50 $\times 10^9$/L.[9,10]

RESULTS

A total of 106 infants of either gender were enrolled in the current study. Of those, 52.83% of the neonates were boys and 47.17% were girls. Baby boy to female ratio was 1.12:1. Inborn births made up the majority of the population (57.55%), and government-run hospitals accounted for 83.02% of deliveries. The most frequent delivery method was a normal vaginal delivery (60.38%). There were more preterm neonates than term babies (56.60%). Only 36.79 % of births had babies with normal birth weight; the rest (63.21%) had low-birth-weight neonates. Risk factors for neonatal sepsis were present in 76.42% of neonates. Within 72 hours of birth, 57% of the neonates were admitted, and 91.51% stayed there for 7 to 14 days before the outcome, which was either survival (94.34%) or death (5.66%). The basic information of enrolled SNCU graduates is shown in Table 1.

Table 1: Basic information of study subjects.

Variable	Subgroups	Total number in each subgroup	Percentages
Gender	Boys	56	52.83
	Girls	50	47.17
Type of admission	Inborn	61	57.55
	Out born	45	42.45
Mode of delivery	*NVD	64	60.38
	**LUCS	34	32.07
	Forceps	8	7.55
Maturity	Term	46	43.40
	Preterm	60	56.60
Risk factors	Present	81	76.42
	Absent	25	23.58
Age at admission	≤3	57	53.77
(day)	4-6	24	22.64
	7 -14	15	14.15
	>14	10	9.43
Birth weight (grams)	≥2500	39	36.79
	1500-2449	33	31.13
	1000-1499	29	27.36
	<1000	5	4.72
Age at final outcome	<7	2	1.89
(day)	7-14	53	50.00

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	15-28	45	42.45
	>28	6	5.66
Duration of hospital stay	<7	4	3.77
(days)	7-14	97	91.51
	≥ 14	5	4.72
Outcome	Survived	100	94.34
	Death	6	5.66

*Normal vaginal delivery, **Lower uterine caesarian section

Clinical features: Of the neonates included in the current study, 35.85% refused to suck on their mother's breast. Other symptoms were respiratory distress, lethargy, thermal instability, jaundice, convulsion, and hypoglycemia in decreasing order of frequency as shown in Figure 1.

Hematological value and infectious marker: In the current study, the mean values for hemoglobin (gram/dl), white blood cells (×103/mm3), platelet count (×105/mm3), neutrophil and lymphocyte percentages, and ESR (mm in 1st hour) and CRP (mg/dl), respectively, were 12.17, 11.24, 1.67, 58.70, and 37.02, 29.28, and 14.44. Table 2 shows the hematological results and infectious indicators of septic neonates.

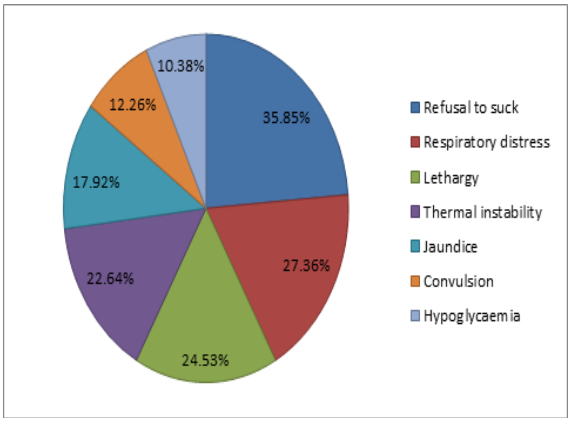

Figure 1: shows the Clinical features of septic neonates

Table 2: Hematological value and infective marker

Variables	Normal value	Mean ±*SD	Number of abnormal values (%)
Hemoglobin (gram/dl)	15-22	12.17±3.75	87 (82.08)
**WBC (×103/mm3)	9.1–34.0	11.24±3.13	24 (22.64)
Platelets (×105/mm3)	1.5–4.5	1.67 ±1.02	54 (50.94)
Neutrophil %	32–67	58.09±10.87	7 (6.6)
Lymphocytes %	25–37	36.05±11.50	24 (22.64)
†ESR (mm in 1st hour)	0-20	29.28±12.71	84(79.25)
††CRP (mg/dl)	<1mg/dl	13.42±7.31	101 (95.28)

*Standard deviation, **White blood corpuscles, †Erythrocyte sedimentation rate, †† C-reactive protein

Grading of thrombocytopenia: The grading of the thrombocytopenia in the current study is shown in Table 3. The death rate was higher (22.22%) in neonates with severe thrombocytopenia compared to neonates with normal platelet count (1.93%), mild (3.57%), and moderate (11.76%) thrombocytopenia, even though the Chi-Square test did not produce a statistically significant P value (<0.05).

Table 3: Grading of thrombocytopenia

Grading of platelet count	Total (%)	Survived (%)	Death (%)	P value
Normal (1.5 – 4.5×105/mm3)	52 (49.06)	51(98.07)	1(1.93)	0.06
Mild (1- <1.5×105/mm3)	28(26.42)	27 (96.43)	1(3.57)	
Moderate (0.5 -1×105/mm3)	17(16.04)	15 (88.24)	2 (11.76)	
Severe (<0.5 ×105/mm3)	9 (8.49)	7 (77.78)	2 (22.22)	

In the present research work, to find out the association of thrombocytopenia with other variables such as gender, type of admission, risk factors, maturity, birth weight in gram, type of sepsis, status of blood culture and status of gram stain, and outcome, a Chi-Square test was run. The P values of 0.02, 0.012, 0.011, and 0.03 were seen in the variables of maturity, birth weight, status of culture, and type of sepsis, respectively, and were statistically significant (P-value <0.05) as shown in Table 4.

Table 4: Association of thrombocytopenia with different variables

Variable	Subgroups	Thrombocytopenia		Total	P value
		Present (%)	Absent (%)		
Gender	Boys	29 (51.79)	27(48.21)	56	0.86
	Girls	25 (50.00)	25 (50.00)	50	
Type of admission	Out born	27 (60.00)	18 (40.00)	45	0.22
	Inborn	28 (45.90)	33 (54.10)	61	
Risk factors	Present	46(56.79)	35 (43.21)	81	0.034
	Absent	8(32.00)	17(68.00)	25	
Maturity	Preterm	37(61.67)	23 (38.33)	60	0.013
	Term	17(36.97)	29 (63.03)	46	
Birth weight (gram)	<2500	38(62.3)	23(37.7)	61	0.007

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	≥2500	16 (35.56)	29 (64.44)	45	
Type of sepsis	*LONS	31(63.27)	18 (36.73)	49	0.02
	**EONS	23 (40.35)	34 (59.65)	57	
Status of blood	Positive	17 (77.27)	5(22.73)	22	0.005
culture	Negative	37(44.05)	47 (55.95)	84	
Type of culture positive	Negative	10 (83.33)	2 (16.67)	12	0.51
(Gram)	Positive	7 (70.00)	3 (30.00)	10	
Outcome	Survived	49 (49.00)	51 (5.00)	100	0.13
	Death	5(83.33)	1 (16.67)	6	

*Late onset sepsis, **Early onset sepsis

DISCUSSION

For neonatal survival and neurodevelopmental results in septicemia in newborns, timely diagnosis and treatment are essential. Since ill, preterm, and full-term neonates typically have low platelet counts, platelet count may serve as an early indicator for the identification of septicaemia.[11] Combining the parameter of thrombocytopenia with the current sepsis screen may improve its sensitivity and specificity.

In the present study, 50.94% of septic babies developed thrombocytopenia. Of these, 26.42%, 16.04%, and 8.49% of babies were graded as having mild, moderate, and severe thrombocytopenia, respectively. This observation is congruent with the study done by Ree IMC et al,[7] from the Netherlands and Parmar D et al,[12] from Gujrat, India. The frequency of thrombocytopenia in neonatal sepsis ranges from 24.1% to 83.55%, as reported by different authors across the globe.[13-15] Due to both increased consumption and decreased synthesis of platelets during septicemia, thrombocytopenia develops, typically progressing to severe thrombocytopenia.[16]

The current study found no statistically significant relationship between gender and thrombocytopenia (P-value = 0.855), which is consistent with the studies conducted by Iranian researchers Eslami Z et al.[17]

Thrombocytopenia was found to be more common in LONS than EOS in the current study (63.27% vs. 40.35%), and this finding was statistically significant (P value = 0.03). This observation is in line with PH Rabindran et al.'s study from Andhra Pradesh, India.[18] Their research showed that thrombocytopenia is more common in LONS than EONS (57% vs. 48%). The different etiological factors that cause both types of neonatal sepsis may account for the discrepancies in the prevalence of thrombocytopenia in LONS and EONS and it needs further in-depth investigation. Infectious agents found in the maternal vaginal tract are what cause early-onset illnesses, whereas, organisms growing in the external environment of the house or hospital are what cause late-onset septicemia in neonates.

Prematurity was linked to extremely severe thrombocytopenia in investigations by Charoo BA et al. and Hanoudi BM.[19,20] According to the current study, thrombocytopenia was statistically significantly more prevalent in preterm infants than term infants (61.67% vs. 36.97%) and was statistically significant (P-value = 0.02). This finding is consistent with research by Sharma A et al,[21] which found that 58.2% of preterm infants experienced thrombocytopenia. However, a study by Khetavath G.S. et al,[22] from Telangana, India, found that thrombocytopenia affects 66.7% of preterm neonates, which is greater than the percentage found in the current study. It can be a result of the different research populations. Our study participants were selected from the SNCU and NICU, as opposed to Khetavath G.S. et al., who only used the NICU for their subject selection.

In the current study, it was discovered that thrombocytopenia was more frequently found in low-birth-weight babies, accounting for 62.3% of them. This finding was consistent with a study conducted by Tirupati K et al,[16] in Maharashtra, India, which found that 62.5% of infants had thrombocytopenia. The prevalence of thrombocytopenia is higher in low-birth-weight infants, according to Goudar VR et al.[23] Because of their inability to fully compensate for the faster breakdown of platelets, LBW newborns exhibited statistically significant thrombocytopenia, according to Gupta AK et al.[24] Babies with low birth weight have impaired placental transport of IgG from maternal to fetal circulation, which increases their risk of developing sepsis.[25]

The current study found that thrombocytopenia was more prevalent in gram-negative sepsis (83.33%) than in gram-positive sepsis, however, this difference was not statistically significant (P value = 0.82). This study's observations corroborate those made in a study by Alazem EAA et al.[26] However, this discovery was made before, and the ability to release endotoxins was given responsibility for it.

The study's participants' mortality rate (n = 6) was 5.66%, whereby 83.33% (n = 5) of the neonates experienced thrombocytopenia. On the other hand, only 49.0% of babies (n = 100) developed thrombocytopenia in those who survived. In comparison to infants with a normal platelet count (1.93%), mild (3.57%), and moderate (11.76%) thrombocytopenia, infants with severe thrombocytopenia had a higher mortality rate (22.22%). Previous research has also revealed an increasing rise in mortality in neonatal cases of thrombocytopenia, particularly in severe forms.[7,27,28] The higher mortality is a result of DIC, which leads to consumptive thrombocytopenia and severe thrombocytopenia, which in turn results in bleeding symptoms.

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Limitations of the study: This study has selection bias because it was a hospital-based single-center cross-sectional study with a small sample size. Therefore, it cannot be applied to the entire community. However, multiple studies with a larger sample size carried out in different locations are required to generalize the conclusion and apply it to all cases of neonatal sepsis.

CONCLUSION

The current study showed that 50.94% of septic neonates had thrombocytopenia, and that group had a greater mortality risk (83.33%) than those with normal thrombocyte counts (16.67%). In the thrombocytopenic group, instances of severe thrombocytopenia (22.22%) had a higher mortality rate than those of mild (3.57%) or moderate (11.76%) thrombocytopenia. Henceforth, thrombocytopenia in neonates with sepsis can be employed as a diagnostic and prognostic indication. Because neonatal thrombocytopenia is a disorder that may be treated and reversed, it's crucial to recognize neonates who are at risk and start the right therapy to stop severe bleeding and possibly serious morbidity.

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