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Frequency and Severity of Thrombocytopenia in Neonatal Sepsis at Bacha Khan Medical Complex/Gajju Khan Medical College, Sawabi

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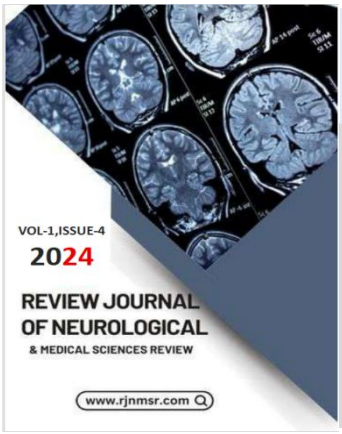
Abstract

This cross-sectional study investigates the prevalence and implications of thrombocytopenia in 333 neonates diagnosed with sepsis at Bacha Khan Medical Complex/Gajju Khan Medical College, Sawabi. The mean age of participants was 6.31 days, with a mean birth weight of 2.44 kg. The study found that 53.2% of the neonates exhibited severe thrombocytopenia (<50,000/uL), while 24.6% had moderate and 12.3% mild thrombocytopenia. Statistical analysis revealed significant associations between thrombocytopenia and respiratory distress (p=0.019) and seizures (p=0.000), indicating that these conditions are more prevalent in neonates with lower platelet counts. In contrast, no significant associations were found with pregnancy term, gender, poor feeding, fever, lethargy, or poor capillary refill. The findings underscore the critical need for vigilant monitoring of respiratory and neurological symptoms in neonates with thrombocytopenia, as these may indicate underlying complications related to sepsis. The study highlights a concerning prevalence of severe thrombocytopenia in neonates with sepsis, suggesting a potential link to respiratory and neurological complications.



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These findings warrant further investigation into the mechanisms underlying these associations and their implications for clinical management.

Keywords: thrombocytopenia, neonatal sepsis, septicemia

Introduction

In the medical field, the most vulnerable group of individuals involve two groups, one who are immunocompromised and on the other end those who are yet to develop a working robust immune system (Neonates, Infants, and children).

The Neonates are prone to various health conditions due to their weak, developing immune system; however, this when involves conditions like neonatal sepsis can lead to multiple systemic infections such as septicemia, urinary tract infections, pneumonia, and meningitis(1).

The reported incidence of neonatal sepsis ranges from 1-10 per 1000 live births(2) and the majority of affected ones are premature or low-birth-weight infants. For developing nations, neonatal septicemia accounts for about 50% of the total neonatal deaths (3) (4) , nearly 20% of neonates develop sepsis in the early phase of life(5).

Thrombocytopenia another common blood disorder in newborns (6) , with a prevalence of 20-35% increased risk in those with lower gestational age(7)(8), these range from mild to moderate on the severity scale.

As per previously published literature, an association has been observed between sepsis and thrombocytopenia, leading to an increase in bleeding risk within a day of having the infection(9)

It has been theorized that the endothelial injury triggers the reticuloendothelial system, leading to more consumption than production of platelets leading to neonates being platelets deficient and more prone to bleeding risk(10). Clinically thrombocytopenia is one of the key risk factors for sepsis-related mortalities in neonates(11).

Internationally studies like one in India provide 82.6% frequency of low platelet profile in septic neonates (<28 days)(12), At the national level, a study conducted at Islamabad showed 68.24% thrombocytopenia in septic neonates(13).

A cross-sectional study conducted at the neonatal ward of Ayub Teaching Hospital provided a 68.9% frequency of thrombocytopenia in neonates with sepsis and concluded that prompt management is warranted in these cases to avoid any further complications(14). Another cohort done among the neonates with positive septic cultures assessed them for thrombocytopenia incidence and severity, this study stated that 20% of the septic neonates developed severe thrombocytopenia. Overall, there was a 4-fold increased risk of mortality in septic neonates with thrombocytopenia(15).

There has been a scarce amount of literature on this condition locally, and no recent studies have focused on the incidence of thrombocytopenia in neonatal sepsis in this region.

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This study will provide much-needed statistics making a pathway for future studies.

Objectives

- To determine the frequency of thrombocytopenia in neonates with neonatal sepsis
- To determine the level of severity of thrombocytopenia in these children

Operational Definitions

1. **Neonatal sepsis:** This condition primarily arises from bacterial infections and results in hemodynamic alterations, leading to significant morbidity and mortality. According to WHO guidelines for the diagnosis and management of neonatal sepsis, diagnosis is based on the following criteria:
   - Poor feeding, lethargy, or drowsiness
   - Respiratory distress
   - Elevated respiratory rate (greater than 2 standard deviations above the norm for age)
   - Vomiting
   - Increased C-reactive protein (CRP) levels
   - Fever
   - Total leukocyte counts exceeding 30,000/mm^3 or below 4,000/mm^3
2. **Early-Onset Neonatal Sepsis:** Refers to cases where neonates exhibit signs and symptoms of sepsis within the first 72 hours of life.
3. **Late-Onset Neonatal Sepsis:** Refers to cases where neonates show signs and symptoms of sepsis after 72 hours of life.
4. **Very Late-Onset Neonatal Sepsis:** Pertains to cases where symptoms of neonatal sepsis manifest after 7 days of life.
5. **Culture:** This laboratory test is conducted to confirm or rule out the presence of microorganisms, including bacteria or fungi.
6. **Thrombocytopenia:** This condition is defined as a decrease in platelet count in the blood, with an operational threshold set at fewer than 150,000 platelets per microliter (µL) in neonates. It can be classified into three categories:
   - mild (100,000–149,999/µL)
   - moderate (50,000–99,999/µL)
   - severe (<50,000/µL).(16)

Materials and Methods

This cross-sectional study was conducted in Pediatric ward at Bacha Khan Medical Complex/ Gajju Khan Medical College, Sawabi, Khyber-Pakhtunkhwa. 333 Neonates admitted with sepsis were the designated study population (sample sized was calculated using open EPI calculator). Ethical approval was obtained from the institutional ethical review board, and informed consent was signed from the parents/guardians of the eligible neonates. Data was collected using a pre-formed questionnaire containing demographics, and

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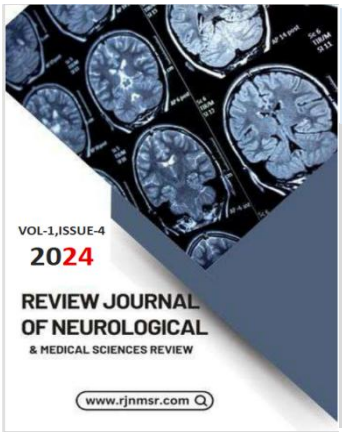
clinical symptoms such as fever, vomiting, lethargy, feeding intolerance, poor capillary refill etc. thrombocytopenia was assessed from the Blood Profile reports. The collected data was entered into analytical software for analysis.

Results

The mean age of participants is approximately 6.31 ± 6.92 days, ranging from as young as 1 day to maximum age of 29 days. The average birth weight of participants is 2.44 ± 0.60 kg, with a minimum birthweight of 1.4 kg and maximum of 4.5 kg. The mean TLC was16.17 ± 9.60 ranging from a minimum of from 1.60 to maximum of 46.80, suggesting a generally elevated total leukocyte count as expected in neonatal septicaemia. The mean CRP level of 16.37 ± 14.57 with the minimum and maximum CRP values being 1.00 and 77.00 respectively. **(TABLE 1)**

In our study, (84.4%) out 333 neonates were term pregnancies, (12.6%) were pre-term and (3.0%) post-term. (64.0%) of the neonates were male while (36.0%) were females. 22.2% of the neonates had respiratory distress, while 77.8% did not. 14.1% reported poor feeding, while (85.9%) did not have this issue. 18.3% of the participants had lethargy, while 81.7% did not show this symptom. Only 8.7% out of the 333 neonates had poor capillary refill, suggesting that this was not a common issue. 9.6% of the included neonates experienced vomiting, while the majority (90.4%) did not. A significant majority (85.0%) did not experience seizures, while 15.0% reported seizures. Out of the 333 neonates 17.7% had fever, indicating that most (82.3%) were fever-free. 9.9% had no thrombocytopenia, 12.3% of the included neonates had mild thrombocytopenia (platelet count 100,000-150,000). 24.6% had moderate thrombocytopenia (51,000-99,999) while 53.2% had severe thrombocytopenia (< 50,000). **(TABLE 2)**

Chi-square test was applied to identify any associations between thrombocytopenia and different independent variables to assess the association between thrombocytopenia and various factors. A chi-square test P-value of 0.209 indicates that there is no significant association between pregnancy term (pre-term, term, post-term) and thrombocytopenia status. Similarly, no significant association between gender (male, female) and thrombocytopenia status was found (P-value=0.553). A significant association was found between respiratory distress and thrombocytopenia status. The p-value of 0.019 (<0.05) suggests that individuals with respiratory distress are more likely to have thrombocytopenia compared to those without respiratory distress. A significant association was found between seizures and thrombocytopenia status with a p-value of 0.000, indicating a potential relationship between neurological symptoms and thrombocytopenia. Further analysis indicated that there is no significant association between thrombocytopenia and Feeding intolerance, lethargy, fever, poor capillary refill and vomiting (p-values of 0.665, 0.752, 0.137, 0.693 and 0.052 respectively). **(TABLE 3)**



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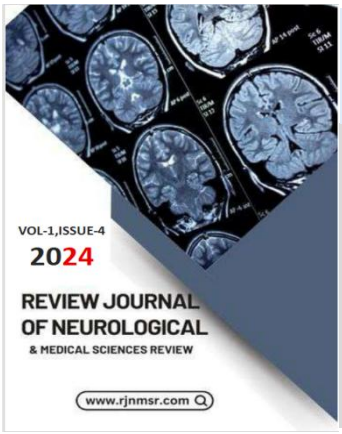
Descriptive Statistics

VARIABLE	N	minimum	maxiimum	MEAN	STD. DEVIATION
AGE (in days)	333	1.00	29.00	6.3063	6.91749
Birth Weight (in kg)	333	1.40	4.50	2.4420	.60343
TLC count	333	1.60	46.80	16.1680	9.59714
CRP	333	1.00	77.00	16.3720	14.57418

Table 1
DESCRIPTIVE STATISTICS

S. No	SYMPTOMS		FREQUENCY (N=333)	PERCENTAGE (%)	VALID PERCENTAGE
1	Pregnancy term	Pre-term	42	12.6	12.6
		Term	281	84.4	97.0
		Post-term	10	3.0	100.0
2	Gender	Male	213	64.0	64.0
		Female	120	36.0	100.0
3	Respiratory Distress	Yes	74	22.2	22.2
		No	259	77.8	100.0
4	Poor Feeding	Yes	47	14.1	14.1
		No	286	85.9	100.0
5	Lethargy	Yes	61	18.3	18.3
		No	272	81.7	100.0
6	Poor capillary refill	Yes	29	8.7	8.7
		No	304	91.3	100.0
7	Vomitting	Yes	32	9.6	9.6
		No	301	90.4	100.0
8	seizures	Yes	283	85.0	85.0
		No	50	15.0	100.0
9	Fever	Yes	59	17.7	17.7
		No	274	82.3	100.0
10	Thrombocytopenia Status	None (>150,000/uL)	33	9.9	9.9
		Mild (1,00,000-149,999/uL)	41	12.3	22.2
		Moderate (50,000-99,999/uL)	82	24.6	46.8



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	Severe(<50,000/uL)	177	53.2	100.0

Table 2

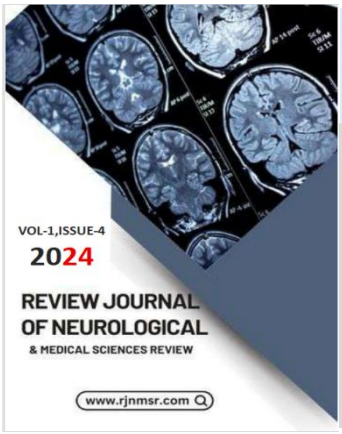
Statistical Analysis

		Thrombocytopenia Status				Chi Square P-Value
		None >150,000/uL	Mild 100,000-149,99/uL	Moderate 50,000-99,999/uL	Severe <50,000/uL	
Pregnancy term	Pre-term	4	8	10	20	0.209
	Term	29	32	66	154	
	Post-term	0	1	6	3	
Gender	Male	23	27	55	107	
	Female	10	13	27	70	0.553
Respiratory Distress	Yes	23	25	67	144	
	No	10	16	15	33	0.019
Poor Feeding	Yes	26	36	71	153	
	No	7	5	11	24	0.665
Fever	Yes	27	29	66	152	
	No	6	12	16	25	0.137
Lethargy	Yes	28	33	34	147	
	No	5	8	18	30	0.752
Poor capillary refill	Yes	29	36	76	163	
	No	4	5	6	14	0.693
Vomiting	Yes	33	40	73	155	
	No	0	1	9	22	0.052
Seizures	Yes	10	10	18	12	
	No	23	31	64	165	0.000

Table 3

Discussion

Our study analyzed 333 neonates, revealing a mean age of 6.31 ± 6.92 days (range: 1-29 days) and an average birth weight of 2.44 ± 0.60 kg (range: 1.4-4.5 kg). Mean total leukocyte count (TLC) was elevated at 16.17 ± 9.60 (range: 1.60-46.80), and mean CRP levels were 16.37 ± 14.57 (range: 1.00-77.00), consistent with neonatal septicemia. Among participants, 84.4% were term, 12.6% pre-term, and 3.0% post-term; 64.0% were male. Respiratory distress was present in 22.2%, lethargy in 18.3%, with 8.7% showing poor capillary refill. Notably, 15.0% reported seizures, and 17.7% had fever. Thrombocytopenia levels varied, with 53.2% classified as severe. Chi-square



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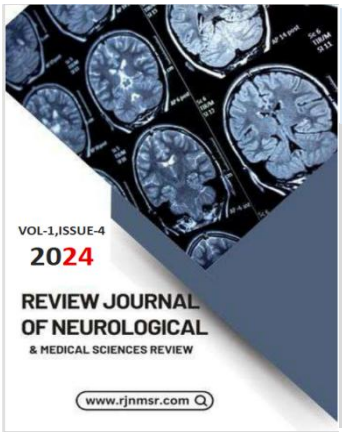
tests indicated no significant associations between thrombocytopenia and pregnancy term (P=0.209) or gender (P=0.553). However, significant associations were found between thrombocytopenia and respiratory distress (P=0.019) and seizures (P=0.000). No significant links were detected between thrombocytopenia and feeding intolerance, lethargy, fever, poor capillary refill, or vomiting (p-values greater than 0.05).

In comparison, This study by H Malik et al. aimed to determine the frequency of thrombocytopenia in neonatal sepsis at King Edward Medical University, Mayo Hospital Lahore, it involved neonates with a clinical diagnosis of sepsis in the neonatal intensive care unit. Platelet counts were measured using an automated analyzer and verified with peripheral smear examination. Of the 90 neonates analyzed, 75% exhibited thrombocytopenia, with a statistically significant p-value of less than 0.05. The study concluded that thrombocytopenia is prevalent in neonatal sepsis and serves as a sensitive indicator for the condition (16) . Similarly, another study by Arabdin et al., investigated the prevalence and severity of thrombocytopenia in neonates suffering from sepsis at Khyber Medical University, Pakistan. Out of 170 neonates, primarily males with a mean age of 12 days, 65.29% displayed thrombocytopenia—20% mild, 25.3% moderate, and 20% severe. Symptoms like fever and feeding reluctance were common. Notably, lower platelet levels were observed in neonates with positive blood cultures, with gram-negative organisms associated with significantly lower platelet counts compared to gram-positive ones. The findings underscore the relationship between sepsis and thrombocytopenia in newborns, highlighting a concerning prevalence of severe cases linked to gram-negative septicemia(17). Another study by F Adil et al. aimed to assess the frequency of thrombocytopenia in neonatal sepsis, conducted at Ayub Teaching Hospital, involving 119 infants under one month with positive blood cultures and weights between 1-4 kg. Excluded were infants with birth asphyxia, blood transfusions, preterm births, and certain maternal conditions. The average age of participants was 9.87 days, and 68.9% exhibited thrombocytopenia, with a higher prevalence in males (59.7%) and infants weighing less than 2 kg (50.4%). The most common pathogens identified were Staphylococcus aureus, E. coli, and Klebsiella pneumoniae. No statistically significant associations were found between thrombocytopenia and age, weight, or gender (P>0.05). The findings highlight the need for vigilance in diagnosing and managing thrombocytopenia in neonatal sepsis to prevent complications(18). Another study by Sharma et al., aimed to evaluate the incidence of thrombocytopenia in neonatal sepsis and its potential as a screening tool. It included 220 neonates under 28 days old with suspected sepsis. Results showed that 40.45% of the infants had thrombocytopenia, with varying severity levels. Blood cultures were positive in 25.4% of cases, predominantly identifying Klebsiella species and coagulase-negative Staphylococci. Thrombocytopenia was significantly linked to blood culture positivity, cesarean delivery, small for gestational age, and positive CRP



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results. The findings suggest that thrombocytopenia can serve as an early predictor of neonatal sepsis, aiding in prompt diagnosis and treatment(19). A study by I. Ahmed et al aimed to evaluate the prevalence of thrombocytopenia and its impact on mortality in neonates with sepsis, it involved 190 neonates under 28 days with positive blood cultures. Results indicated a significant prevalence of thrombocytopenia in 67.89% of cases, with 18.4% classified as severe. The study found that neonates with thrombocytopenia had a fourfold higher mortality rate, highlighting the correlation between age, low birth weight, platelet count, and the severity of thrombocytopenia with neonatal sepsis outcomes. Overall, thrombocytopenia is common in neonatal sepsis and is associated with increased mortality, particularly in severe cases(20).

Conclusion

Overall, the results from our study indicate a predominance of term births and a higher number of males in the sample. While conditions like respiratory distress, poor feeding, lethargy, poor capillary refill, and vomiting were relatively uncommon, the high prevalence of seizures and severe thrombocytopenia highlights critical health concerns that warrant attention in this population. The mean age indicates that the study focuses newborns from first day of life till 29 days old. Most participants are within the normal birthweight range, although variability exists. The total leukocyte count and CRP levels indicate a range of immune responses and inflammatory statuses, highlighting the need for further investigation into the health conditions affecting this population. The variability in TLC and CRP levels may suggest underlying infections or inflammatory processes that could be relevant for clinical management. The Chi-square tests reveal significant associations between thrombocytopenia status and respiratory distress as well as seizures, suggesting that these conditions may be related to lower platelet counts. In contrast, no significant associations were found with pregnancy term, gender, poor feeding, fever, lethargy, poor capillary refill, or vomiting. These findings highlight the importance of monitoring respiratory and neurological symptoms in patients with thrombocytopenia. Further research may be warranted to explore the underlying mechanisms linking these associations.

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