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# FREQUENCY OF THROMBOCYTOPENIA IN PREMATURE NEONATES WITH BACTERIAL SEPSIS

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## ABSTRACT

**Objective:** To determine the frequency of thrombocytopenia in preterm babies affected with neonatal sepsis.

**Methodology:** This cross-sectional study was conducted at the department of pediatrics, Lady Reading Hospital Peshawar from March 2021 to June 2021 by non-probability consecutive sampling technique. A total of 385 premature infants with clinical sepsis of Pakistani origin were included. Neonates with congenital malformations were excluded. Age, gender, blood culture, clinical features of neonatal sepsis, thrombocytopenia, and bacterial pattern in blood cultures were recorded. Data analysis was done in SPSS 22. A Chi-square test was applied to stratify thrombocytopenia among age and gender.  $P \leq 0.05$  was considered significant.

**Results:** The mean age of the participants was  $5.32 \pm 6.4$  days. Males were 192(49.9%) and females were 193(50.1%). Thrombocytopenia was present in 168(43.6%) in premature babies suffering from sepsis. Blood culture was positive in 97(25.2%) cases. In 272(70.6%) infant the C-reactive protein level was less than 5. The common clinical feature were respiratory distress ( $n=246$ , 63.9%), reluctant to feed ( $n=243$ , 63.1%), tachypnea ( $n=189$ , 49.1%), vomiting ( $n=182$ , 47.3%), cyanosis ( $n=45.2\%$ ) and diarrhea ( $n=171$ , 44.4%). Most common type of bacteria were Staph. Aureus ( $n=78$ , 22.3%) followed by E.coli ( $n=66$ , 18.9%) and Klebsiella Pneumoniae ( $n=48$ , 13.7%). Frequency of thrombocytopenia was higher in 1-10 days infants ( $n=149$ , 88.7%) than 21-28 days ( $n=19$ , 11.3%) and was statistically significant ( $P=.024$ ).

**Conclusion:** The frequency of thrombocytopenia is quite higher in neonates suffering from sepsis so the clinicians should be vigilant in the management of thrombocytopenia to prevent serious complications.

**Keywords:** Neonates; Neonatal Sepsis; Thrombocytopenia; Blood Platelets

## INTRODUCTION

Neonatal sepsis is a systemic infection and is one of the most common health conditions around the world affecting newborn children in the first month.<sup>1,2</sup> The mortality and morbidity rate is still high even in this advanced era where technology made everything possible in the world of medical sciences.<sup>3</sup> In literature there are 29.5% of neonatal sepsis cases a reported in Pakistan.<sup>4</sup> The prevalence of neonatal sepsis is higher in bacterial susceptible infants.<sup>5</sup> Low birth weight and premature delivery are risk factors for this condition. This condition is associated with neutropenia, abnormal chemotaxis (functional abnormalities) of leukocytes, less amount of cytokines secretion, and a decrease in antibody level.<sup>6</sup>

Thrombocytopenia is a condition in which platelet count is below  $150 \times 10^9/L$  and is commonly found in infants having sepsis.<sup>7</sup> The pathogenesis though not clear but commonly attributed to damage of endothelium resulting in aggregation, death, and ultimately

decrease in platelet production.<sup>8,9</sup> In low birth weight child births there is a strong relation has been reported between thrombocytopenia with neonatal sepsis.<sup>10,11</sup> In neonatal intensive care units the rate of preterm infants who develops thrombocytopenia is about 8%.<sup>12</sup> An Indian study reported that 82.6% prevalence of thrombocytopenia in less than 4 weeks of infant suffering from neonatal sepsis.<sup>13</sup> The frequency of thrombocytopenia in neonatal sepsis was 68.24% in Islamabad.<sup>14</sup>

There is a dearth of local literature on the frequency of thrombocytopenia in neonatal sepsis in preterm infants. Neonatal thrombocytopenia can be used as a rapid screening tool along with other markers. Thrombocytopenia is a treatable condition that can be helpful in the prevention of premature birth. This study will help in the rapid diagnosis and management of neonatal sepsis. This investigation can aid the clinicians to be more vigilant about the diagnosis and management of thrombocytopenia. The objective of this study was to determine the frequency of thrombocytopenia in preterm babies suffering from neonatal sepsis and

common pathogens that are involved in bacterial sepsis.

## METHODOLOGY

This cross-sectional study was conducted at the department of pediatrics, Lady Reading Hospital, Peshawar from March 2021 to June 2021 by non-probability consecutive sampling technique. With a population of 50%, WHO software produced a sample size of 385 people with a 95% confidence interval and a 5% margin of error. The hospital ethical committee provided an ethical approval letter. After a thorough discussion, the parents of newborns gave their verbal informed permission. The parents were told that their information would be kept private and that their children would not be harmed.

In this study Pakistani nationals were included, Preterm newborns born before the 37<sup>th</sup> week of pregnancy with clinical sepsis. Neonates with congenital abnormalities were not allowed to participate. Neonates were newborns with a lifespan of fewer than 28 days. Reduced spontaneous activity, less forceful sucking, reluctance to feed, apnea, bradycardia, hypothermia/hyperthermia, unexplained abdominal distention, peri-umbilical erythema, discharge, coma, convulsions, and respiratory distress were all used to identify sepsis. Thrombocytopenia was diagnosed in babies with platelet counts of fewer than 150,000/mm<sup>3</sup> using an automatic blood analyzer. A detailed history and medical examination of all participants was done by a consultant. All investigations including complete blood count, C-reactive protein, and blood culture were done from the hospital lab. Age, gender, clinical feature, and pattern of bacteria in the culture were recorded. SPSS 22 was used for data analysis. Quantitative variable like age was expressed as mean and standard deviation. Gender, clinical feature, and thrombocytopenia were expressed as frequency and percentages. A Chi-square test will be applied

to stratify thrombocytopenia among age and gender.  $p < 0.05$  was a significant level.

## RESULTS

Table 1 shows the mean age of the participants was  $5.32 \pm 6.4$  days with a range from 1 to 28 days. Males were 192 (49.9%) and females were 193 (50.1%). Thrombocytopenia was present in 168 (43.6%) premature babies suffering from sepsis. Blood culture was positive in 97 (25.2%) cases. Most of the infants had a CRP level of less than 5 ( $n=272$ , 70.6%). Most common type of bacteria in neonatal sepsis in preterm babies was *S. aureus* ( $n=78$ , 22.3%) followed by *E. coli* ( $n=66$ , 18.9%) and *Klebsiella pneumoniae* ( $n=48$ , 13.7%).

Table 2 shows the frequency of thrombo-

cytopenia in neonatal sepsis between genders was not different statistically ( $P=0.567$ ). Frequency of thrombocytopenia was higher in age group 1-10 days ( $n=149$ , 88.7%) than 21-28 days ( $n=19$ , 11.3%). These results were statistically significant ( $P=.024$ ).

The clinical feature of preterm babies suffering sepsis were respiratory distress ( $n=246$ , 63.9%), reluctant to feed ( $n=243$ , 63.1%), tachypnea ( $n=189$ , 49.1%), vomiting ( $n=182$ , 47.3%), cyanosis ( $n=45.2\%$ ), diarrhea ( $n=171$ , 44.4%), diminished spontaneous activity ( $n=151$ , 39.2%), lethargic reflexes ( $n=130$ , 34.3%), tachycardia ( $n=103$ , 26.8%), hypothermia ( $n=129$ , 33.5%), seizure ( $n=101$ , 26.2%), bulging anterior fontanel ( $n=92$ , 23.9%) and abdominal distension ( $n=62$ , 16.1%).

Table 1: Frequency of gender, thrombocytopenia, blood culture, and crp level and distribution of bacteria in culture

Variables		Frequency (%)
Gender of Patient	Male	192 (49.9%)
	Female	193 (50.1%)
Thrombocytopenia	Yes	168 (43.6%)
	No	217 (56.4%)
Blood Culture	Positive	97 (25.2%)
	Negative	288 (74.8%)
CRP level	Less than 5	272 (70.6%)
	More than 5	113 (29.4%)
Type of Bacteria	<i>Candida</i> spp.	32 (9.1%)
	<i>Citrobacter</i> spp.	24 (6.9%)
	<i>E. coli</i>	66 (18.9%)
	<i>Enterococcus</i>	39 (11.1%)
	<i>Klebsiella pneumoniae</i>	48 (13.7%)
	<i>Proteus</i>	33 (9.4%)
	<i>Pseudomonas</i> spp.	30 (8.6%)
	<i>S. aureus</i>	78 (22.3%)

Table 2: Thrombocytopenia in neonatal sepsis stratified by gender and age group

Variables		n (%)	n (%)	p-Value
		Yes	No	
Thrombocytopenia	Male	81 (42.2%)	87 (45.1%)	.567
	Female	111 (57.8%)	106 (54.9%)	
Age Group (days)	1-10	149 (88.7%)	174 (80.2%)	.024
	21-28	19 (11.3%)	43 (19.8%)	

## DISCUSSION

This study aimed to determine the frequency of thrombocytopenia in preterm babies suffering from neonatal sepsis. Our findings showed that thrombocytopenia was present in 43.6% of infants, blood culture was positive in 25.2%, most common type of bacteria was *Staph. Aureus* (22.3%) followed by *E.coli* (18.9%) and *Klebsiella Pneumoniae* (13.7%). Thrombocytopenia is the commonest blood dyscrasia in ill neonates, preterm babies, and those admitted to intensive care units.<sup>15</sup> The rate of mortality in thrombocytopenia associated with neonatal sepsis is from 20-40%. Almost any pathogenic bacteria involved in sepsis can induce thrombocytopenia.<sup>16</sup> Neonatal Sepsis and necrotizing enterocolitis are usually associated with thrombocytopenia. It is yet to be elucidated that what are the exact mechanisms underlying the thrombocytopenia in neonatal sepsis.<sup>15</sup>

Our findings showed that thrombocytopenia was present in 43.6% of the children. Previous studies showed that the frequency of thrombocytopenia can vary from 49% to 82.6%.<sup>13,14,17</sup> An Indian study reported the 82.6% prevalence of thrombocytopenia in less than 4 weeks of infants suffering from neonatal sepsis.<sup>13</sup> The frequency of thrombocytopenia in neonatal sepsis was 68.24% in a study conducted in Islamabad.<sup>14</sup> The variability in results can be due to variations in sample size, and genetic and environmental factors.

In this study, it was reported that only 25% of neonates with sepsis have positive blood culture. Previous studies showed that many neonates diagnosed with possible sepsis but no bacterial cause recognized” and this condition referred to as culture-negative sepsis.<sup>18</sup> The possible reason for negative blood culture in neonatal sepsis can be attributed to less number of bacteria, less amount of blood obtained from sick neonates, and ma-

ternal use of antibiotics during delivery.<sup>19</sup>

C-reactive protein is an acute-phase reactant found in neonates. Its determination is fast, simple, and economical. Literature showed premature infants have less CRP levels than term infants.<sup>20</sup> Our results showed that 29% of cases have high CRP levels. This shows that the CRP level is not an accurate method of diagnosis of neonatal sepsis. A Cochrane review conducted in 2019 included 20 studies and found that CRP levels cannot be used with efficiency to diagnose neonatal sepsis.<sup>21</sup> Our results showed that the most common type of bacteria in neonatal sepsis in preterm babies was *S. aureus* followed by *E.coli* and *Klebsiella pneumoniae*, *S. aureus* is a normal commensal of skin so it can cause neonatal sepsis easily. Infants admitted to ICUs can acquire *Klebsiella* infection. Another cause of common occurrence of *Klebsiella* in blood culture can be its ability to form colonies and acquire resistance to antibiotics.<sup>22</sup> An investigation in Peshawar on neonatal sepsis found that *S. aureus*, *E.coli* and *Klebsiella* were common pathogens in culture.<sup>23</sup> Similarly another study in Abbottabad found that the most numerous bacterial colonies in blood culture from neonates had *Staph. Aureus* and *E.coli*.<sup>24</sup> Other studies also found that *S. aureus* is the most common pathogen in neonatal sepsis.<sup>16,25</sup> These findings support our study. This study has some limitations like it is the single center and cross-sectional descriptive study. A case-control study can provide the real association in a quantifiable term like odds ratio and help in establishing cause-effect relationship.

## CONCLUSION

This study concludes that the frequency of thrombocytopenia is quite higher in neonates suffering from sepsis so the clinicians should give due importance to the management of thrombocytopenia to prevent serious complications. Most pathogens in blood cul-

ture-positive neonatal sepsis are *staph. aureus*, *E.coli* and *Klebsiella Pneumoniae*.

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### Author's Contribution

KKW conceived the idea and reviewed the manuscript. AM collected the data, the manuscript writing, and revisions. UM Analyzed data and compilation of the manuscript. NS Reviewed the data analysis and provided final approval. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

### Conflict of Interest

Authors declared no conflict of interest

### Grant Support and Financial Disclosure

None

### Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.