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Original Research Article

Diagnostic Accuracy of Thrombocytopenia in Neonatal Sepsis: Keeping Blood Culture as Definitive Diagnostic Test

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Name of Author:
Romesa Akram[1], Amir Muhammad[2], Ghazala[3], Fatima[4], Saima Zakia[5], Muhammad Khan[6]

Affiliation:
[1,2,4,6]Lady Reading Hospital Peshawar, Pakistan.
[3]Bacha Khan Medical Complex, Swabi, Pakistan.
[5]Khyber Teaching Hospital, Peshawar, Pakistan.

Corresponding Author:
Romesa Akram
Email: khanrumesa38@gmail.com

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Abstract: **Objective:** To determine diagnostic accuracy of thrombocytopenia in neonatal sepsis while keeping blood culture as gold standard. **Study Design:** Cross sectional validation study. **Place and Duration of Study:** Conducted from 05 July 2025 to 05 November 2025 at Department of Paediatrics, Lady Reading Hospital, Peshawar. **Methodology:** A total of 126 neonates aged 1–28 days with clinical neonatal sepsis were included by using WHO sensitivity and specificity calculator. Platelet count was measured by automated haematology analyser and thrombocytopenia was labelled when platelet count <150,000/mm^3. Blood culture was performed as gold standard. Data was analysed on SPSS version 26. Continuous variables was presented as mean ± standard deviation and categorical variables as n (%). Diagnostic accuracy including sensitivity, specificity, positive predictive value and negative predictive value was calculated by 2×2 contingency table. **Results:** Mean age was 7.62 ± 6.61 days, mean weight was 2.77 ± 0.61 kg and mean duration of illness was 38.02 ± 21.93 hours. Male neonates were 79 (62.7%) and females 47 (37.3%). Thrombocytopenia was positive in 74 (58.7%) while blood culture was positive in 38 (30.2%) cases. True positive cases were 30, false positive 44, false negative 8 and true negative 44. Sensitivity was 78.90%, specificity 50%, positive predictive value 40.5%, negative predictive value 84.60% and overall diagnostic accuracy 58.70%. **Conclusion:** Thrombocytopenia shows moderate diagnostic accuracy with good sensitivity but low specificity, so it is more useful to exclude neonatal sepsis rather than confirm it.

Keywords: Blood Platelets, Infant Newborn, Neonatal Sepsis, Sensitivity and Specificity, Thrombocytopenia

Running title: Diagnostic accuracy of thrombocytopenia in neonatal sepsis

INTRODUCTION

Neonatal sepsis is a severe disease with a systemic inflammatory response to infection, posing a difficult condition in the neonate [1]. A primary cause of newborn illness and death, particularly among the preterm infant, the disease results from the invasion of the bloodstream by pathogens, which leads to an exaggerated immune response that causes failure of organs [1]. Early diagnosis and treatment are the most important factors to achieve better results, but the diagnosis of neonatal sepsis is difficult due to the nonspecific nature of its clinical presentation [1]. Fever, lethargy, poor feeding, and respiratory distress are typical symptoms that overlap with other conditions in the neonate, making it difficult to diagnose sepsis as compared to a non-infected etiology of illness [2]. Clinicians therefore have to rely on a mix of clinical suspicion, laboratory findings, and microbiological tests to detect and manage the life-threatening disease [2].

Thrombocytopenia, or a low count of platelets, is a common finding in neonates with sepsis and has been proposed as a potential diagnostic marker [3]. Platelets play a vital role in hemostasis and inflammation, and loss of them in sepsis could result either from consumption due to disseminated intravascular coagulation or impaired marrow production [3]. Thrombocytopenia is more frequently found in neonates with severe sepsis or septic shock than with mild infection [4]. While its presence alone is not a sign of sepsis, the severity and duration of thrombocytopenia relate to the severity of illness as well as the prognosis.4 Variability of the count of platelets among normal neonates and the impact of other conditions like prematurity or asphyxia need careful interpretation [4]. Thrombocytopenia is thus a useful adjuvant in the diagnosis of neonatal sepsis but cannot serve as an exclusive diagnostic criterion.

Blood culture remains the gold standard for the definitive diagnosis of neonatal sepsis, with direct proof of bacterial or fungal pathogens in the blood.5 Despite the progress that the field of molecular diagnostics has achieved, blood culture still maintains the highest specificity and the ability to guide directed antimicrobial treatment with antibiotic susceptibility tests [5]. Its use is, however, restricted by a variety of factors including low sensitivity, delayed results, and the need for an appropriate volume of sample, which is challenging to achieve in the neonate [6]. Collection of the specimen also runs the risk of contamination, leading to false-positive results.6 As such, though invaluable for the diagnosis of sepsis, the restrictions of its use underscore the need to complement it with other clinical and laboratory parameters to aid diagnosis and the institution of treatment. Thrombocytopenia generally precedes positive blood culture results and may serve as an initial warning sign that prompts empirical antibiotic treatment and more rigorous surveillance [7]. Its dynamic nature also allows repeated assessment, as the disease process or resolution is followed by the clinician [7]. The use of thrombocytopenia alone, however, risks over diagnosis and inappropriate intervention due to its association with non-infectious etiologies.8 Thrombocytopenia therefore needs to be viewed as an adjunct, but not a substitute, for blood culture. Using these methods in combination allows clinicians to enhance diagnostic accuracy, optimize the use of resources, and ultimately benefit vulnerable neonates with sepsis [8].

In a study by Yadav BB, et al. has shown that sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of thrombocytopenia in diagnosis of neonatal sepsis were 85.60%, 28.2%, 80.4% and 30.1 % respectively with the prevalence of neonatal sepsis by 38% [9].

Neonatal sepsis constitutes a significant health problem in developing countries. Early diagnosis is a problem, particularly in areas that do not have sufficient facilities for diagnosis. Although blood culture is deemed the best diagnostic tool for this purpose, it is a time-consuming procedure and is not always available. Thrombocytopenia is a known feature among septic newborns and serves as a useful predictor of sepsis, but its sensitivity and specificity as a diagnostic tool remain to be proven among our community. This research is being carried out to establish the sensitivity and specificity of thrombocytopenia in neonatal sepsis.

METHODOLOGY

This cross sectional validation study was carried out in the Department of Pediatrics at Lady Reading Hospital from 05 July 2025 to 05 November 2025. Ethical approval was obtained from the institutional ethical committee with reference number No. 191/LRH/MTI dated 14/05/2025. The sample size was calculated by using WHO sensitivity and specificity calculator by taking sensitivity 85.60%,9 specificity 28.2%9 and prevalence 38%9 with 95% confidence interval and 10% precision. A total of 126 neonates were included in the study.

Inclusion criteria: Neonates of age 1–28 days of both gender admitted in neonatal intensive care unit and having clinical diagnosis of neonatal sepsis were considered eligible. Clinical neonatal sepsis was taken when neonate had two or more findings including abnormal temperature either less than 36.0°C or more than 38.0°C, respiratory distress such as respiratory rate more than 60/min, retractions, grunting or increased oxygen requirement, cardiovascular instability like heart rate more than 160/min or less than 100/min or hypotension with mean arterial pressure less than 30 mmHg in term and less than 25 mmHg in preterm and feeding intolerance including abdominal distension, vomiting, increased gastric residuals or poor feeding.

Exclusion criteria: Neonates having history of congenital thrombocytopenia or platelet disorders, major congenital anomalies, hypersplenism, birth asphyxia with Apgar score less than 5 at 5 minutes, prematurity, low birth weight and those who received prophylactic antibiotics before blood culture sampling were excluded from the study.

After taking informed consent from parents or caregivers, baseline demographic details including age, gender, weight, duration of symptoms, residential status and family socioeconomic status was recorded on a predesigned proforma. Confidentiality was ensured and it was explained that study had no additional risk to patient.

Detailed history and clinical examination was done in all cases. For laboratory assessment, about 2 mL venous blood was taken under aseptic conditions in EDTA tube for complete blood count. Platelet count was measured by automated haematology analyser

and in cases of very low count, peripheral smear was also reviewed manually. For confirmation of sepsis, another 2 mL venous blood sample was collected aseptically and inoculated into aerobic paediatric blood culture bottle and incubated at 37°C in automated system. Bacterial growth was observed within 24–48 hours and fungal growth within 3–7 days. Thrombocytopenia was considered where the patient had a platelet count below 150,000 cells per cubic mm as tested in laboratory analysis. Positive sepsis with blood culture was considered when a known pathogen such as Group B Streptococcus, E. coli, Klebsiella spp., Staphylococcus aureus, Enterococcus spp., Pseudomonas aeruginosa or Candida spp. was cultured within the specified period of incubation. The diagnosis of thrombocytopenia was confirmed against blood cultures. All data was entered and analysed by using SPSS version 26. Continuous variables like age and weight was presented as mean ± standard deviation. Categorical variables including gender, duration of symptoms, residential status, family socioeconomic status, thrombocytopenia results and blood culture results was presented as frequency and percentages. Diagnostic accuracy measures including sensitivity, specificity, positive predictive value and negative predictive value was calculated by using 2×2 contingency table.

RESULTS

A total of 126 neonates were enrolled in this study. The mean age of the patients were 7.62 ± 6.61 days, mean weight were 2.77 ± 0.61 kg, and mean duration of illness were 38.02 ± 21.93 hours. Regarding gender distribution, majority of the neonates were male 79 (62.7%) whilst female neonates account for 47 (37.3%). Most of the patients were from urban areas 73 (57.9%) as compared to rural areas 53 (42.1%). In terms of socioeconomic status, low income group comprised 47 (37.3%) of the patients, middle income group comprised 46 (36.5%), and high income group comprised 33 (26.2%) of the total study population (Table 1).

Table 1. Patient Demographics

Demographics	Mean ± SD
Age (days)	7.62 ± 6.61
Weight (kg)	2.77 ± 0.61
Duration (hours)	38.02 ± 21.93
Gender	
Male n (%)	79 (62.7%)
Female n (%)	47 (37.3%)
Residence	
Rural n (%)	53 (42.1%)
Urban n (%)	73 (57.9%)
Socioeconomic Status	
Low n (%)	47 (37.3%)
Middle n (%)	46 (36.5%)
High n (%)	33 (26.2%)

With regards to the overall diagnostic findings, thrombocytopenia were found positive in 74 (58.7%) neonates and negative in 52 (41.3%) neonates. Blood culture, which were kept as the definitive diagnostic test, were positive in 38 (30.2%) and negative in 88 (69.8%) of the total 126 neonates (Table 2).

Table 2. Overall Results of Thrombocytopenia and Blood Culture in Diagnosis of Neonatal

Neonatal Sepsis	Thrombocytopenia	Blood Culture
Positive	74 (58.7%)	38 (30.2%)
Negative	52 (41.3%)	88 (69.8%)
Total	126 (100%)	126 (100%)

On comparison of thrombocytopenia against blood culture, there were 30 true positive cases where both thrombocytopenia and blood culture were positive simultaneously (Table 3).

Table 3. Comparison of Thrombocytopenia versus Blood Culture in Diagnosis of Neonatal Sepsis

Thrombocytopenia	Blood Culture	Total
	Positive	Negative
Positive	30 (TP)	44 (FP)
Negative	8 (FN)	44 (TN)
Total	38	88

Key: ***TP*** *= True positive,* ***FP*** *= False positive,* ***FN*** *= False negative,* ***TN*** *= True negative*

The diagnostic accuracy parameters of thrombocytopenia in diagnosing neonatal sepsis were also evaluated. The sensitivity of thrombocytopenia were found to be 78.90% and specificity were 50.00%. The overall diagnostic accuracy were calculated as 58.70%. The positive predictive value (PPV) were 40.50% whereas the negative predictive value (NPV) were 84.60%, suggesting that thrombocytopenia may performs better in ruling out neonatal sepsis rather than confirming it (Table 4).

Table 4 Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of Thrombocytopenia in Diagnosis of Neonatal Sepsis

Diagnostic Parameter	Result

Sensitivity	78.90%
Specificity	50.00%
Diagnostic Accuracy	58.70%
PPV	40.50%
NPV	84.60%

DISCUSSION

In present study, majority of neonates were male 79 (62.7%), which were consistent with the known biological vulnerability of male neonates to infections, as X-linked immune regulatory genes are thought to confer relatively better immunological protection to female neonates, making males more susceptible to sepsis. Thrombocytopenia was present in 74 (58.7%) out of the neonates studied, which was significantly more compared to positive results in blood cultures at 38 (30.2%). This could be attributed to the fact that thrombocytopenia serves as a generalized response by neonates under the influence of different physiological stimuli such as birth asphyxia, breathing problems, maternal hypertension disorders, which lead to reduced platelets without the need for sepsis. The sensitivity of thrombocytopenia was found at 78.90%, implying that it was relatively good in detecting sepsis patients. Nonetheless, the specificity was at 50.00%, meaning that almost half of the neonates who did not have sepsis were misclassified as positive. This low specificity is probably due to the occurrence of platelet destruction and dysfunctional thrombopoiesis in other non-infectious diseases of newborns.

In present study, male neonates were 79 (62.7%) which were higher than females 47 (37.3%). This male predominance were similarly observed by Talat et al. 10 who reported 83 (58.5%) male neonates among sepsis cases, and were also supported by Zafar et al. 11 who found 117 (47.56%) males, though with a relatively lesser difference between genders. The biological susceptibility of male neonates to infections, possibly related to X-linked immune regulatory mechanisms, may explains this consistent pattern across studies.

Thrombocytopenia were positive in 74 (58.7%) neonates in present study, which were comparable to findings of Malik et al. 12 who reported thrombocytopenia in 75% of sepsis cases, and Talat et al. 10 who found moderate thrombocytopenia in 47 (33.1%) of their cases. However, Zafar et al. 11 reported a notably lower frequency of thrombocytopenia at 63 (25.61%), and Wajid et al. 13 reported 168 (43.6%), which were lower than present study findings. These differences may be attributable to variations in gestational age of enrolled neonates, cut-off values used to define thrombocytopenia, and differences in causative organisms, as gram-negative sepsis is more strongly associated with platelet destruction via endotoxin-mediated mechanisms.

Blood culture positivity in present study were 38 (30.2%), which were somewhat comparable to Wajid et al. 13 who reported blood culture positivity in 97 (25.2%) neonates, and Talat et al. 10 who found positivity in 58 (40.8%) cases. The relatively lower culture positivity rates across studies may reflects the inherent limitations of blood culture as a diagnostic test, including prior antibiotic use, small sample volumes, and bacteraemia of intermittent nature in neonates.

The sensitivity of thrombocytopenia in present study were 78.90% and specificity were 50.00%, which were in partial agreement with Toprak et al. 14 who reported sensitivity 81.3% and specificity 88.8% in premature neonates. Similarly, Gururaju et al. 15 reported sensitivity 73.2% and specificity 81.3% for platelet indices. The higher specificity reported by these studies as compared to present study may be explained by their inclusion of platelet indices such as mean platelet volume and platelet distribution width alongside simple platelet count, which improves discriminatory ability. In present study, only thrombocytopenia were used as a binary marker without incorporating platelet indices, which likely contributed to the lower specificity of 50.00%.

The PPV in present study were 40.50% and NPV were 84.60%, suggesting thrombocytopenia performs better in excluding rather than confirming sepsis. This pattern were consistent with Kumari et al. 16 who demonstrated that individual haematological markers including thrombocytopenia had limited positive predictive ability, and that combined markers significantly improved both sensitivity and specificity. This further supports the notion that thrombocytopenia alone may not be sufficient as a confirmatory diagnostic test for neonatal sepsis in clinical settings.17,18

Limitations

Several factors are responsible for the limitations that can be noted in the current study. First, the current research is a single-centre study conducted at one institution, and thus, the results obtained cannot be generalized for other neonates. Second, there is a relatively small sample size, which may have had an impact on the statistical strength of the findings. Third, platelet parameters, such as MPV and PDW, were not taken into account together with thrombocytopenia, which could have increased the overall specificity of the test. Lastly, the severity and time frame of thrombocytopenia relative to sepsis onset were not distinguished, which could have been useful for diagnostic purposes.

CONCLUSION

This study has found that thrombocytopenia does not have a very strong diagnostic validity for detecting

neonatal sepsis in the event that blood culture remains the criterion standard for the diagnosis of the condition. The condition presents itself with a decently high sensitivity but a low specificity and positive predictive value.

Disclaimer: none present

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Conflict of Interest:

Author declare that no conflict of interest exists in this study.

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