

Original Research Article

EFFECT ON PLATELET INDICES AND THEIR PROGNOSTIC SIGNIFICANCE IN NEONATAL SEPSIS IN CORRELATION WITH C-REACTIVE PROTEIN

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ABSTRACT

Background: Aim: To study the effect on Platelet count and their Indices and their prognostic significance in Neonatal Sepsis in correlation with C- Reactive Protein.

Materials and Methods: It was a prospective - Observational study. This research was conducted in the Neonatal Intensive Care Unit (NICU) at the Department of Pediatrics, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Madhurawada, Visakhapatnam, from May 2022 to May 2024. The study involved 100 neonates who displayed clinical signs indicative of sepsis and tested positive for C-reactive protein (CRP).

Results: 100cases which were satisfying the inclusion criteria were included the study. Out of 100 cases 48 (48%) cases were male and 52 (52%) were females. 56 (56%) cases were having birth weight less than 2500 gms and 44 (44%) cases are equal or more than 2500 gms. Out of 100 cases, 22 (22%) cases had Culture Positive Sepsis and 78 (78%) cases were Culture Negative Sepsis. Out of 100 cases, 82 cases improved, 15 worsened requiring additional antibiotics or hike of antibiotics etc., and 3 babies died. Out of 100 cases, 67 (67%) had thrombocytopenia. Thrombocytopenia was observed in all 22 (100%) culture-positive sepsis cases and in 45 (57.69%) of the 78 culture-negative sepsis cases. Out of 100 cases, 67 (67%) had high MPV. Out of 100 cases, 57 (57%) had high PDW. On Day 1, the mean CRP value was 26.8800 µg/ml with a standard deviation of 12.89059 µg/ml, ranging from 12.0 µg/ml to 48.0 µg/ml. CRP for culture-positive sepsis: 25.6364 ± 13.50325 µg/ml. CRP for culture-negative sepsis: 27.2308 ± 12.78079 µg/ml. CRP and Platelet Count: Spearman correlation coefficient -0.246, p-value = 0.014 - significant correlation. CRP and MPV: Spearman correlation coefficient = 0.017, p-value = 0.867 - no significant correlation. CRP and PDW: Spearman correlation coefficient = 0.215, p-value = 0.031- significant correlation.

Conclusion: The present study concluded that, Platelet indices, particularly thrombocytopenia, MPV, and PDW, can serve as early markers for neonatal sepsis and provide valuable information about disease progression and treatment response.

Keywords: Neonatal sepsis, Platelet count, C-Reactive protein, MPV, PDW.

INTRODUCTION

Neonatal sepsis, characterized by systemic infection occurring within the first 28 days of life, remains a

critical concern in perinatal healthcare. Globally, it contributes significantly to neonatal morbidity and mortality, posing challenges for healthcare providers in timely diagnosis and intervention. Despite advances in medical science, neonatal sepsis

diagnosis remains a complex task, often hindered by the nonspecific nature of clinical symptoms and the limitations of current diagnostic methods such as blood culture and clinical parameters.^[1]

Early and accurate diagnosis of neonatal sepsis is paramount for initiating prompt and targeted interventions, thereby improving clinical outcomes.^[2] Traditional diagnostic approaches, though valuable, suffer from limitations such as prolonged turnaround times for blood culture results and a lack of specificity in clinical signs and symptoms.^[3] As a result, there is a growing interest in exploring novel biomarkers that can enhance the diagnostic precision of neonatal sepsis.

Platelets, small cellular fragments with crucial roles in hemostasis and immune response, have gained attention as potential indicators of sepsis severity.^[4] Platelet indices, including mean platelet volume (MPV) and platelet distribution width (PDW), represent measurable parameters derived from routine complete blood counts (CBC).^[5] Alterations in platelet indices have been observed in various infectious diseases and inflammatory conditions, reflecting the dynamic response of platelets to physiological stressors.^[6]

to serve as readily available and cost-effective biomarkers. However, a comprehensive understanding of how platelet indices change in neonatal sepsis and their prognostic implications is still evolving. Moreover, exploring the correlation of these indices with established inflammatory markers, such as C-reactive protein (CRP), may provide a more enhanced understanding of the underlying pathophysiology and enhance diagnostic accuracy.^[7] C-reactive protein, an acute-phase reactant produced by the liver in response to inflammation, has long been utilized as a marker of infection and inflammatory processes.^[8] Despite its widespread use, the correlation between CRP levels and platelet indices in neonatal sepsis remains an area of interest, with potential implications for refining diagnostic algorithms and prognostication.^[9]

This study seeks to address these gaps in knowledge by conducting a comprehensive investigation into the impact of neonatal sepsis on platelet count, MPV, and PDW. Additionally, the study aims to assess the prognostic significance of these platelet indices and explore their correlation with CRP levels. By shedding light on the intricate interplay between platelet dynamics and inflammatory markers, this research endeavors to contribute valuable insights that may shape the future landscape of neonatal sepsis management.

Aims and Objectives

Aim of the study:

- To study the effect on Platelet count and their Indices and their prognostic significance in Neonatal Sepsis in correlation with C- Reactive Protein.

Objectives

• Primary Objective

To evaluate the prognostic significance of Platelet Indices in Neonatal Sepsis and their changes.

• Secondary Objective

To know the correlation of C- Reactive Protein with Platelet Count and their Indices in Neonatal Sepsis.

MATERIALS AND METHODS

This research was conducted in the Neonatal Intensive Care Unit (NICU) at the Department of Pediatrics, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Madhurawada, Visakhapatnam, from May 2022 to May 2024.

Study Design: Prospective - Observational study.

Sample Size: The study involved 100 neonates who displayed clinical signs indicative of sepsis and tested positive for C-reactive protein (CRP).

Clinical suspicion of sepsis was based on symptoms and signs such as:

- Diminished activity and reduced feeding
- Signs of respiratory distress including retractions, nasal flaring, apnea, and cyanosis
- Seizures, lethargy, and bulging of the anterior fontanel
- Presence of fever or hypothermia
- Abdominal swelling, vomiting, jaundice
- Prolonged capillary refill time
- Weak pulses
- Other associated signs

Inclusion Criteria

- Neonates with signs suggestive of Sepsis.
- Asymptomatic neonates presenting with two or more risk factors of neonatal sepsis.
- Outborn cases of neonatal sepsis who did not receive antibiotics prior to NICU admission.

Exclusion Criteria

- Outborn cases who received antibiotics prior to admission.
- Asymptomatic neonates presenting with one risk factor for neonatal sepsis.
- Newborn with any other causes of Thrombocytopenia.
- Newborn with congenital abnormalities.
- Newborn with bleeding disorders.
- Newborn suspected to have inborn errors of metabolism.

The following diagnostic tests were conducted on the infants:

Before initiating the study, the institutional ethics committee of Gayatri Vidya Parishad Institute of Health Care and Medical Technology granted its approval. Written informed consent was obtained from one of the parents prior to starting the study. Each baby involved in the study underwent thorough maternal and neonatal history collection and clinical examination. The gestational age of the neonates was determined using the New Ballard's Score chart, with results documented in a pre-structured proforma.

- a) A complete blood count, platelet count, mean platelet volume (MPV), and platelet distribution width (PDW).
- b) Assessments of platelet count, MPV, and PDW were carried out on the 1st, 3rd, and 7th days following the diagnosis of sepsis.
- c) Blood culture and sensitivity.
- d) Measurement of C-Reactive Protein levels.

Complete blood picture, platelet count was done by the automated cell counter method. CRP done by using serum and it is qualitative and semi quantitative latex agglutination kit.

Collection of Sample:

Blood samples were collected under strict aseptic conditions. Sterile gloves were used during the procedure. The skin at the venepuncture site was cleaned with 70% alcohol, creating a cleaned area with a diameter of 5 cm. This area was allowed to air-dry. Subsequently, 2% tincture of iodine was applied in expanding circles starting from the center to the periphery, which was then allowed to air-dry for a minute. The needle was then inserted into a peripheral vein to draw blood. Once the needle was removed, the site was cleaned again with 70% alcohol. A total of 1.5 ml of blood was drawn: 0.5ml was used for blood culture and sensitivity, 0.5 ml was used for a Complete Blood Count (CBC) in an automated analyzer, and 0.5 ml for C-Reactive Protein (CRP) measurement.

C-Reactive protein (CRP): CRP is an acute phase reactant. In our setup, the measurement of CRP levels is carried out using a semi-quantitative method that leverages the principles of turbidity and latex agglutination. This method is efficient, relatively simple, and cost-effective, suitable for routine use in a neonatal intensive care unit (NICU) setting.

The results are categorized as:

Negative: CRP levels less than or equal to 6 µg/mL, indicated by the absence of noticeable turbidity or agglutination.

Positive: CRP levels at 12, 24, or 48 µg/mL, indicated by increasing levels of turbidity and agglutination intensity

Normal Platelet Counts: Typically range from 150,000/mm³ to 400,000/mm³.

Thrombocytopenia: Defined as a platelet count less than 150,000/mm³.

Mild thrombocytopenia is indicated by a platelet count between 100,000/mm³ and less than 150,000/mm³.

Moderate thrombocytopenia is indicated by a platelet count between 50,000/mm³ and 100,000/mm³.

Severe thrombocytopenia occurs when platelet counts are less than 50,000/mm³.

Analysis of data:

All the Data related to history, clinical findings and investigations was entered in prestructured proforma. The data was entered managed and assessed using SPSS software version 21. Different variables are compared with Kruskal - Wallis test for determination of significance between two parameters and p value <0.05 is considered positive.

RESULTS

This research was conducted during time period from May 2022 to May 2024 in NICU, Department of Pediatrics, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Visakhapatnam which is a tertiary care center.

Total number of cases admitted in NICU during the study period was 462. Out of these,334 cases were excluded from the study, since these babies were not showing symptoms or signs of sepsis and were admitted for other reasons.

Out of the remaining 128 cases admitted with clinical suspicion of sepsis, 28 cases were excluded from the study because had received medication before admission and the remaining 100 cases with clinically suspected neonatal sepsis with CRP positive were taken up for the study.

Table 1: Distribution of cases according to the gender N=100

Gender	Number of Babies N (%)
Male	48 (48.0)
Female	52 (52.0)
Total	100 (100)

In this research, out of the 100 neonates admitted in the Neonatal Intensive Care Unit with possible sepsis and proven sepsis, 48 (48.0%) of the babies were males and 52 (52.0%) were female babies, indicating that female babies constituted a majority.

Table 2: Distribution of cases based on birth weight N=100

BIRTH WEIGHT	NUMBER OF BABIES N(%)
<2500gms	56 (56.0)
≥2500gms	44 (44.0)
Total	100(100)

In this research, out of the 100 newborns studied, 56 (56.0%) babies weighed less than 2500gms and 44 (44.0%) babies weighed > 2500gms, indicating that there is a predominance of low birth weight babies weighing <2500gms.

Table 3: Distribution of cases based on type of delivery (N = 100)

Type of Delivery	Number of cases
Normal Vaginal Delivery	46
Elective Cesarean Section	28
Emergency Cesarean Section	24
Forceps Assisted Delivery	02

In the study, 46 deliveries were Normal vaginal deliveries. 28 were Elective Cesarean Sections, 24 were Emergency Cesarean Sections and 02 were forceps assisted deliveries.

Table 4: Distribution of cases based on bacterial growth N=100

Bacterial Growth	Number of babies N(%)
Culture Positive	22 (22.0)
Culture Negative	78 (78.0)
Total	100 (100)

Table 5: Distribution of cases based on severity of thrombocytopenia on day1 N = 67

GRADING OF THROMBOCYTOPENIA	NO. OF CASES (%)
Mild (1.5lakhs-1 lakhs)	29 (43.28%)
Moderate (1 lakh-50,000)	29 (43.28%)
Severe (<50000)	9 (13.44%)
Total	67 (100%)

In this research out of 100 cases, 67 (67%) cases had thrombocytopenia. Out of 67 cases 29 (43.28%) cases had mild thrombocytopenia, 29 (43.28%) cases had moderate- thrombocytopenia and 9 (13.44%) cases had severe thrombocytopenia.

Table 6: Distribution of cases based on severity of thrombocytopenia on day 3 N = 55

GRADING OF THROMBOCYTOPENIA	NO. OF CASES (%)
Mild(1.5lakhs-1 lakhs)	30 (54.54%)
Moderate(1 lakh-50,000)	19 (34.54%)
Severe(<50000)	6 (10.92%)
Total	55 (100%)

In this research out of 100 cases, 55 (55%) cases had thrombocytopenia on Day 3. Out of 67 cases 30 (54.54%) cases had mild thrombocytopenia, 19 (34.54%) cases had moderate- thrombocytopenia and 6 (10.92%) cases had severe thrombocytopenia.

Table 7: Distribution of cases based on severity of thrombocytopenia on day 7 [N = 37]

GRADING OF THROMBOCYTOPENIA	NO. OF CASES (%)
Mild(1.5 lakhs -1 lakhs)	21 (56.75%)
Moderate(1 lakh-50,000)	11 (29.72%)
Severe(<50000)	5 (13.53%)
Total	37 (100%)

In this research out of 100 cases, 37 (55%) cases had thrombocytopenia on Day 7. Out of 37 cases 21 (56.75%) cases had mild thrombocytopenia, 11 (29.72%) cases had moderate- thrombocytopenia and 5 (13.53%) cases had severe thrombocytopenia.

Table 8: Distribution of cases with thrombocytopenia based on type of sepsis on day 1

TYPE OF SEPSIS	NO. OF CASES (%)
Culture Positive Sepsis (n=22)	22 (100%)
Culture Negative Sepsis (n=78)	45 (57.69%)
Total	67

In this research study of 100 cases, 67 (67%) cases had thrombocytopenia, i.e. less than 1.5 lakh/mm³ on day 1 of sepsis. Out of 22 cases of proven sepsis i.e culture positive sepsis 22 (100%) cases have thrombocytopenia and out of 78 cases of possible sepsis i.e culture negative cases 45 (57.69%) cases have thrombocytopenia. More number of culture positive cases had thrombocytopenia compared to possible sepsis.

Table 9: Distribution of cases with thrombocytopenia based on type of sepsis on day 3 [N = 55]

TYPE OF SEPSIS	NO. OF CASES (%)
Culture Positive Sepsis (n=22)	20 (90.90%)
Culture Negative Sepsis (n=78)	35 (44.87%)
Total	55

In this research study of 100 cases, 55 (55%) cases had thrombocytopenia, i.e. less than 1.5 lakh/mm³ on day 3 of sepsis. Out of 22 cases of proven sepsis i.e culture positive sepsis 20 (90.90%) cases have thrombocytopenia and out of 78 cases of possible sepsis i.e culture negative cases 35 (44.87%) cases have thrombocytopenia. More number of culture positive cases had thrombocytopenia compared to possible sepsis.

Table 10: Distribution of cases with thrombocytopenia based on type of sepsis on day 7

TYPE OF SEPSIS	NO. OF CASES (%)
Culture Positive Sepsis (n=22)	16 (72.72%)
Culture Negative Sepsis (n=78)	21 (26.92%)
Total	37

In this research study of 100 cases, 37 (37%) cases had thrombocytopenia, i.e. less than 1.5 lakh/mm³ on day 7 of sepsis. Out of 22 cases of proven sepsis i.e culture positive sepsis 16 (72.72%) cases have thrombocytopenia and out of 78 cases of possible sepsis i.e culture negative cases 21 (26.92%) cases have thrombocytopenia. More number of culture positive cases had thrombocytopenia compared to possible sepsis.

Table 11. Platelets counts/cumm3 on day 1, day 3, day 7 among culture positive sepsis and culture negative sepsis (N = 100) Table 5.11

Day	Type of sepsis	Number of cases	Minimum	Maximum	Mean	Standard Deviation
Day 1	Culture Positive Sepsis	22	23000	120000	75500.00	29318.855
	Culture Negative Sepsis	78	14000	431000	160782.05	85173.566
Day 3	Culture Positive Sepsis	22	26000	180000	89000.00	40617.847
	Culture Negative Sepsis	78	23000	462000	174846.15	82319.788
Day 7	Culture Positive Sepsis	22	12000	240000	109272.74	61179.036
	Culture Negative Sepsis	78	21000	491000	205679.49	82738.595

- In the present study, Platelet values were compared on Day 1, Day 3, Day 7 of sepsis in between Culture Positive Sepsis and Culture Negative Sepsis.
- Platelet mean value on Day 1 of Culture Positive Sepsis was 75500.00/mm³ and Culture Negative Sepsis 160782.05/mm³.
- On Day 3 sepsis mean value of platelets in Culture Positive Sepsis was 89000.00/mm³ and in Culture Negative Sepsis was 174846.15/mm³,
- On Day 7 of sepsis, mean value of platelets Culture Positive Sepsis was 109272.74/mm³ and in Culture Negative Sepsis was 205679.49/mm³.
- On Day 1 mean value is lower in both Culture Positive and Culture Negative Sepsis compared to day 3 and day 7 in both groups.

Table 12: distribution of cases with increase in mean platelet volume based on type of sepsis on day 1 [N = 67]

TYPE OF SEPSIS	NO. OF CASES(%)
Culture Positive Sepsis (n = 22)	17 (77.27%)
Culture Negative Sepsis (n = 78)	50 (64.10%)
Total	67

- In this research of 100 cases, 67 (67%) cases had Mean Platelet Volume more than mean value i.e 11.3 fl on Day 1 of sepsis.
- Out of 22 cases of Culture Positive Sepsis, 17 (77.27%) cases had Mean Platelet Volume more than 11.3fL.
- Out of 78 cases of Culture Negative Sepsis, 50 (64.10%) cases had high MPV more than 11.3fL.
- High mean platelet volume cases seen more in Culture Positive Sepsis compared to Culture Negative Sepsis.

The majority of Culture Positive Sepsis patients had a high Mean Platelet Volume on Day 1, implying a correlation.

Table 13: Distribution of cases with increase in mean platelet volume based on type of sepsis on day 3 [N = 52]

TYPE OF SEPSIS	NO. OF CASES (%)
Culture Positive Sepsis (n = 22)	18 (81.81%)
Culture Negative Sepsis (n = 78)	43 (55.12%)
Total	61

- In this research of 100 cases, 61 (61%) cases had Mean Platelet Volume more than mean value i.e., 11.0 fL on Day 3 of sepsis.
- Out of 22 cases of Culture Positive Sepsis, 18 (81.81%) cases had Mean Platelet Volume more than 11.0fL.
- Out of 78 cases of Culture Negative Sepsis, 43 (55.12%) cases had high MPV more than 11.0fL.
- High mean platelet volume cases seen more in Culture Positive Sepsis compared to Culture Negative Sepsis.
- The majority of Culture Positive Sepsis patients had a high Mean Platelet Volume on Day 3, implying a correlation.

Table 14: Mean platelet volume on day 1, day 3, day 7 among culture positive sepsis and culture negative sepsis

Day	Type of sepsis	Number of cases	Minimum	Maximum	Mean	Standard Deviation
Day 1	Culture Positive Sepsis	22	8.8	14.7	11.986	1.4136
	Culture Negative Sepsis	78	7.1	12.7	11.121	1.910
Day 3	Culture Positive Sepsis	22	9.1	13.0	11.677	1.0447
	Culture Negative Sepsis	78	8.8	12.8	10.891	1.0746
Day 7	Culture Positive Sepsis	22	9.1	13.4	11.577	1.0510
	Culture Negative Sepsis	78	9.1	12.1	10.742	1.0255

- In the present study, Mean Platelet Volume values were compared on Day 1, Day 3, Day 7 of sepsis in between Culture Positive Sepsis and Culture Negative Sepsis.
 - MPV mean value on Day 1 of Culture Positive Sepsis was 11.986 fL and Culture Negative Sepsis 11.121 fL.
 - On Day 3 sepsis mean value of MPV in Culture Positive Sepsis was 11.677 fL and in Culture Negative Sepsis was 10.891 fL.
 - On Day 7 of sepsis, mean value of platelets Culture Positive Sepsis was 11.577 fL and in Culture Negative Sepsis was 10.742 fL.
- On Day 1 mean value is Higher in both Culture Positive and Culture Negative Sepsis compared to day 3 and day 7 in both groups.

Table 15: Distribution of cases with high platelet distribution width based on type of sepsis on day 1 [N = 57]

TYPE OF SEPSIS	NO. OF CASES (%)
Culture Positive Sepsis (n=22)	21 (95.45%)
Culture Negative Sepsis (n=78)	36 (46.15%)
Total	57

- In this research of 100 cases, 57 (57%) cases had Platelet Distribution Width more than Mean value (i.e., 16.9%) on Day 1 of sepsis.
- Out of 22 cases of Culture Positive Sepsis 21 (95.45%) cases have Platelet Distribution Width more than 16.9%.
- Out of 78 cases of Culture Negative sepsis 36 (46.15%) cases had more PDW width more than 16.9%.
- Majority of Culture Positive Sepsis cases had high PDW values and suggestive of correlation exists between PDW with Culture Positive Sepsis.

Table 16: Platelet distribution width on day 1, day 3, day 7 among culture positive sepsis and culture negative sepsis

Day	Type of sepsis	Number of cases	Minimum	Maximum	Mean	Standard Deviation
Day 1	Culture Positive Sepsis	22	16.8	18.3	17.200	0.3251
	Culture Negative Sepsis	78	14.8	18.4	16.797	0.7857
Day 3	Culture Positive Sepsis	22	16.2	17.7	16.968	0.4303
	Culture Negative Sepsis	78	14.0	18.1	16.549	0.7350
Day 7	Culture Positive Sepsis	22	15.0	17.2	16.559	0.6940
	Culture Negative Sepsis	78	13.8	18.0	16.064	0.8563

- In the present study, Platelet Distribution Width values were compared on Day 1, Day 3, Day 7 of sepsis in between Culture Positive Sepsis and Culture Negative Sepsis.
- PDW mean value on Day 1 of Culture Positive Sepsis was 17.200 fL and Culture Negative Sepsis 16.797 fL.
- On Day 3 sepsis mean value of PDW in Culture Positive Sepsis was 16.968 fL and in Culture Negative Sepsis was 16.549 fL.
- On Day 7 of sepsis, mean value of PDW in Culture Positive Sepsis was 16.559 fL and in Culture Negative Sepsis was 16.064 fL.
- On Day 1 mean value of PDW is Higher in both Culture Positive and Culture Negative Sepsis compared to day 3 and day 7 in both groups.

Variable	Diagnosis	N	Mean Rank
Platelet Distribution Width on Day 1	Culture Positive Sepsis	22	65.02
	Culture Negative Sepsis	78	46.40
	Total	100	
Platelet Distribution Width on Day 3	Culture Positive Sepsis	22	64.30
	Culture Negative Sepsis	78	46.61
	Total	100	
Platelet Distribution Width on Day 7	Culture Positive Sepsis	22	64.61
	Culture Negative Sepsis	78	46.52
	Total	100	

Test Variable	Chi - Square	df (Degree of freedom)	p - Value
PDW on Day 1	7.104	1	0.008
PDW on Day 3	6.398	1	0.011
PDW on Day 3	6.732	1	0.009

The p-value of <0.05 suggests that there is a statistically significant difference in the distributions of PDW on Day 1, Day 3 and Day 7 between Culture Positive Sepsis and Culture Negative Sepsis cases.

Table 17: C- Reactive protein on day 1, day 3 and day 7

	N	Minimum ($\mu\text{g}/\text{ml}$)	Maximum ($\mu\text{g}/\text{ml}$)	Mean ($\mu\text{g}/\text{ml}$)	Standard Deviation
CRP on Day1	100	12.00	48.00	26.8800	12.89059
CRP on Day 3	100	Negative (0.00)	48.00	18.9600	12.32057
CRP on Day 7	100	Negative (0.00)	48.00	12.2400	12.76131

- On Day 1, Mean value of CRP is 26.8800 $\mu\text{g}/\text{ml}$ with a standard deviation of 12.89059 $\mu\text{g}/\text{ml}$. Minimum being 12.0 $\mu\text{g}/\text{ml}$ and a maximum of 48.0 $\mu\text{g}/\text{ml}$.
- On Day 3, Mean value of CRP is 18.9600 $\mu\text{g}/\text{ml}$ with a standard deviation of 12.32057 $\mu\text{g}/\text{ml}$. Minimum being Negative (0 $\mu\text{g}/\text{ml}$) and a maximum of 48.0 $\mu\text{g}/\text{ml}$.
- On Day 7, Mean value of CRP is 12.2400 $\mu\text{g}/\text{ml}$ with a standard deviation of 12.76131 $\mu\text{g}/\text{ml}$. Minimum being Negative (0 $\mu\text{g}/\text{ml}$) and a maximum of 48.0 $\mu\text{g}/\text{ml}$.

Table 18: C-Reactive protein on day 1, day 3 and day 7 among culture positive sepsis and culture negative sepsis

Diagnosis		N	Minimum ($\mu\text{g}/\text{ml}$)	Maximum ($\mu\text{g}/\text{ml}$)	Mean ($\mu\text{g}/\text{ml}$)	Standard Deviation
Culture Positive Sepsis	CRP on Day1	22	12.0	48.0	25.6364	13.50325
	CRP on Day 3	22	12.0	48.0	25.0909	15.22814
	CRP on Day 7	22	Negative (0.0)	48.0	20.7273	17.44155
Culture Negative Sepsis	CRP on Day 1	78	12.0	48.0	27.2308	12.78079
	CRP on Day 3	78	Negative (0.0)	48.0	17.2308	10.86986
	CRP on Day 7	78	Negative (0.0)	48.0	9.8462	10.00140

- On Day 1, Mean value of CRP is 25.6364 $\mu\text{g}/\text{ml}$ with a standard deviation of 13.50325 $\mu\text{g}/\text{ml}$. Minimum being 12.0 $\mu\text{g}/\text{ml}$ and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Positive Sepsis cases.
- On Day 3, Mean value of CRP is 25.0909 $\mu\text{g}/\text{ml}$ with a standard deviation of 15.22814 $\mu\text{g}/\text{ml}$. Minimum being 12 $\mu\text{g}/\text{ml}$ and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Positive Sepsis cases.
- On Day 7, Mean value of CRP is 20.7273 $\mu\text{g}/\text{ml}$ with a standard deviation of 17.44155 $\mu\text{g}/\text{ml}$. Minimum being Negative (0 $\mu\text{g}/\text{ml}$) and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Positive Sepsis.
- On Day 1, Mean value of CRP is 27.2308 $\mu\text{g}/\text{ml}$ with a standard deviation of 12.78079 $\mu\text{g}/\text{ml}$. Minimum being 12.0 $\mu\text{g}/\text{ml}$ and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Negative Sepsis cases.
- On Day 3, Mean value of CRP is 17.2308 $\mu\text{g}/\text{ml}$ with a standard deviation of 10.86986 $\mu\text{g}/\text{ml}$. Minimum being 12 $\mu\text{g}/\text{ml}$ and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Negative Sepsis cases.
- On Day 7, Mean value of CRP is 9.8462 $\mu\text{g}/\text{ml}$ with a standard deviation of 10.00140 $\mu\text{g}/\text{ml}$. Minimum being Negative (0 $\mu\text{g}/\text{ml}$) and a maximum of 48.0 $\mu\text{g}/\text{ml}$ among Culture Negative Sepsis.

Table 19: Distribution of cases based on outcome (N = 100)

Outcome	Number of cases
Improved	82
Worsened	15
Died	03

Out of the 100 cases in the study, 82 cases improved with the initiation of treatment, 15 cases worsened needing changes in the treatment like antibiotic hike or addition if new antibiotic etc and 03 babies died in spite of all needed efforts.

Table 20: Distribution of cases based on outcome (N = 100)

Outcome	Number of cases
Improved	82
Worsened	15
Died	03

Out of the 100 cases in the study, 82 cases improved with the initiation of treatment, 15 cases worsened needing changes in the treatment like antibiotic hike or addition if new antibiotic etc and 03 babies died in spite of all needed efforts.

Table 21: Distribution of cases based on outcome in culture positive and culture negative sepsis

Diagnosis	Outcome	Number of Cases	Percentage
Culture Positive Sepsis (N = 22)	Improved	11	50.0%
	Worsened	09	40.9%
	Died	02	9.1%
Culture Negative Sepsis (N = 78)	Improved	71	91.0%
	Worsened	06	7.7%
	Died	01	1.3%

Out of 22 cases of Culture Positive Sepsis, 11 babies improved (50.0%), 09 babies worsened (40.9%) and 02 babies died (9.1%).

Table 22: Distribution of cases based on outcome in relation to platelet counts on day 1, day 3 and day 7

	Mean Rank	Chi – Square	Degree of Freedom (dF)	p – Value
Platelet Count on Day 1	Improved	53.98	8.049	0.018
	Worsened	38.37		
	Died	16.00		
Platelet Count on Day 3	Improved	56.98	22.839	<0.001
	Worsened	22.13		
	Died	15.30		
Platelet Count on Day 7	Improved	57.95	30.920	<0.001
	Worsened	19.50		
	Died	2.00		

Day 1

The mean ranks were 53.98 (improved), 38.37 (worsened), and 16.00 (death). The chi-square value was 8.049 ($p = 0.018$), indicating statistical significance.

Day 3

The mean ranks were 56.98 (improved), 22.13 (worsened), and 15.30 (death). The chi-square value was 22.839 ($p < 0.001$), indicating statistical significance.

Day 7

The mean ranks were 57.95 (improved), 19.50 (worsened), and 2.00 (death). The chi-square value was 30.920 ($p < 0.001$), indicating statistical significance.

DISCUSSION

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) at the Department of Paediatrics, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Visakhapatnam, spanning from May 2022 to May 2024.

The primary objective was to investigate the role of platelet indices in both diagnosing and predicting outcomes in neonatal sepsis. Neonatal sepsis poses a significant challenge in healthcare, particularly in developing countries, where it remains a leading cause of morbidity and mortality among newborns. Early detection and timely intervention are paramount in improving clinical outcomes for affected infants.

Platelet indices, encompassing platelet count, mean platelet volume (MPV), and platelet distribution width (PDW), have emerged as promising biomarkers in the management of neonatal sepsis. These indices reflect various aspects of platelet function and physiology, which are crucial in the immune response and inflammatory processes observed in sepsis.

MPV, for instance, indicates platelet size and activation status, while PDW measures platelet size variability, both of which can provide insights into the severity and progression of sepsis.

The study aimed to correlate changes in platelet indices with clinical outcomes, including disease severity, treatment response, and patient prognosis.

By identifying specific patterns in platelet indices associated with sepsis, the research sought to enhance

diagnostic accuracy and inform targeted therapeutic strategies.

Such advancements are essential in optimizing neonatal care protocols, reducing complications, and ultimately improving survival rates among neonates affected by sepsis.

This investigation contributes to the growing body of evidence supporting the utility of platelet indices as valuable tools in the clinical management of neonatal sepsis.

The findings hold implications for healthcare practices, emphasizing the importance of integrating hematological assessments into routine neonatal care protocols, especially in resource-limited settings where early intervention can significantly impact outcomes.

COMPARATIVE STUDIES AND BROADER IMPLICATIONS OF PLATELET INDICES IN NEONATAL SEPSIS

Our study, alongside several corroborative investigations, emphasizes the diagnostic and prognostic significance of platelet indices in neonatal sepsis:

Mittal et al. (2018),^[10]: Conducted in Rajasthan with a sample size of 188 neonates, this study focused on platelet indices as diagnostic tools for neonatal sepsis.

The research highlighted the utility of Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) in identifying septic neonates, aligning closely with our findings.

Karne T.K. et al. (2017),^[11]: This study from Nashik, involving 150 neonates, examined platelet count and platelet indicators in neonatal sepsis. The findings supported the use of platelet indices as early diagnostic markers for sepsis, reinforcing the importance of these biomarkers in clinical practice.

Kumar M.K. et al. (2019),^[12]: A case-control study conducted in Kerala with 445 participants, focusing on MPV in neonatal sepsis.

Significant differences in MPV between septic and non-septic neonates were observed, consistent with our study's findings, highlighting MPV as a robust indicator of sepsis severity.

Meena et al. (2019),^[13]: Conducted in Kota with 256 neonates, this study investigated the correlation between neonatal sepsis, serum C-reactive protein (CRP), and platelet indices. Elevated MPV and PDW were identified as significant markers of sepsis in this cohort, further reinforcing the diagnostic utility of platelet indices in identifying neonates at risk.

COMPARISON OF STUDIES BASED ON GENDER

In our study, the gender distribution was balanced, with 52% females and 48% males, resulting in a male-to-female ratio of approximately 1:1.08.

This finding aligns closely with similar studies conducted by Karne T.K. et al,^[11] and Meena et al,^[13] where gender ratios of 1.2:1 and 1.1:1 were reported, respectively. The prevalence of neonatal sepsis does not show a consistent gender predilection, as evidenced by incidental distributions in various

research studies. Research suggests that male infants may exhibit a slightly higher susceptibility to infections compared to females.

COMPARISON OF PRESENT STUDY WITH OTHER STUDIES WITH CULTURE POSITIVITY IN NEONATAL SEPSIS

In our study, the culture positivity rate was 22%, a finding consistent with reported rates in existing literature. For instance, Kumar M.K. et al,^[12] documented a culture positivity rate of 17.5%, while Choudhary D.K. et al,^[14] and Okascharoen et al,^[15] reported rates of 17% and 20%, respectively. Ahmed et al,^[16] observed a higher positivity rate at 29%. These varying rates across studies highlight the influence of several factors on culture positivity outcomes in neonatal sepsis research. In contrast, late-onset sepsis cases, commonly associated with nosocomial infections, tend to have higher culture positivity rates. Further research aimed at refining diagnostic approaches and enhancing culture sensitivity in neonatal sepsis remains essential for improving patient outcomes.

COMPARISON BETWEEN PRESENT STUDY WITH OTHER STUDIES BASED ON THROMBOCYTOPENIA IN NEONATAL SEPSIS

Our study, thrombocytopenia (<1.5 lakh/mm³) was prevalent in 67% of neonates, which is notably higher compared to findings in other studies. Mittal et al,^[40] reported a thrombocytopenia prevalence of 51.3%, while Abdulla et al,^[17] found it to be 42.8%, and Choudhary D.K. et al,^[14] observed 38%. The elevated prevalence observed in our study may be attributed to factors such as the timing of sample collection and the severity of sepsis within our cohort. Thrombocytopenia was most frequently observed on day 1 of sepsis (67%) in our study, decreasing to 37% by day 7. This temporal trend is consistent with findings by Choudhary D.K. et al,^[14] who also noted a reduction in thrombocytopenia prevalence over time. The early onset and rapid decline in platelet counts underscore the acute nature of thrombocytopenia in neonatal sepsis, highlighting the critical importance of timely diagnosis and intervention.

COMPARISON BETWEEN PRESENT STUDY WITH OTHER STUDIES BASED ON SEVERITY OF THROMBOCYTOPENIA BETWEEN TYPES OF SEPSIS

In our study, the severity of thrombocytopenia varied significantly between culture-positive and culture-negative sepsis cases.

Among the 22 culture-positive cases

- 13.63% exhibited mild thrombocytopenia.
- 59.90% had moderate thrombocytopenia.
- 27.27% had severe thrombocytopenia.

In contrast, among the 78 culture-negative cases:

- 33.33% had mild thrombocytopenia.
- 20.51% had moderate thrombocytopenia.
- 3.84% had severe thrombocytopenia.

These findings are consistent with those reported by Karne T.K. et al,^[11] who also noted a higher prevalence of severe thrombocytopenia in culture-positive sepsis cases. The increased incidence of severe thrombocytopenia in culture-positive sepsis underscores the role of platelet indices as markers of disease severity. Severe thrombocytopenia in these cases likely reflects a more pronounced inflammatory response, contributing to heightened platelet consumption and destruction. The differential severity of thrombocytopenia based on sepsis type highlights the importance of early recognition and management strategies tailored to the underlying microbial etiology.

COMPARISON BETWEEN PRESENT STUDY AND OTHER STUDIES BASED ON MEAN PLATELET VOLUME RANGE IN TYPE OF NEONATAL SEPSIS

In our study, Mean Platelet Volume (MPV) was significantly higher in culture-positive sepsis cases compared to culture-negative cases, with values of 11.9 and 11.1, respectively ($p=0.002$). This finding aligns with similar observations by Kumar M.K. et al,^[12] who reported MPVs of 10.94 and 10.4, respectively ($p<0.001$), indicating a consistent trend across studies. Additionally, Abdelfadil AM et al,^[16] also documented elevated MPVs in culture-positive sepsis cases, reinforcing the association between MPV and sepsis severity. The observed increase in MPV in culture-positive sepsis cases likely reflects an adaptive response to increased platelet turnover and consumption during systemic inflammation. Elevated MPV is often attributed to the release of larger, more immature platelets into circulation, indicative of ongoing platelet activation and replenishment in response to inflammatory stimuli.

COMPARISON BETWEEN PRESENT STUDY WITH OTHER STUDIES BASED ON PLATELET DISTRIBUTION WIDTH

In our study, 57% of neonatal sepsis cases exhibited elevated PDW values. Specifically, 95.45% of culture-positive cases had $PDW > 16.9$, while 46.15% of culture-negative cases showed high PDW values. The mean PDW was 17.20 ± 0.3251 in culture-positive sepsis cases in our study, compared to 16.797 ± 0.7857 in culture-negative sepsis cases. Elevated PDW levels indicate increased platelet activation and heterogeneity, which are characteristic features of severe inflammatory conditions such as sepsis. Platelets undergo morphological changes and become more variable in size (anisocytosis) during inflammation, leading to higher PDW values. This biomarker serves as a useful indicator of the degree of platelet response to systemic inflammation. High PDW values have been correlated with poor clinical outcomes in various studies, suggesting its potential utility as a prognostic marker in neonatal sepsis.

COMPARISON OF PLATELET INDICES AND SEPSIS TYPES

In our study, differentiation between proven and possible sepsis based on platelet indices revealed significant differences. Culture-positive sepsis cases

exhibited higher Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) values compared to culture-negative cases. Specifically, MPV was 11.9 in culture-positive sepsis and 11.1 in culture-negative sepsis ($p=0.002$). PDW values were elevated in 95.45% of culture-positive cases compared to 46.15% in culture-negative cases. These findings indicate a more pronounced inflammatory response and increased platelet activation and consumption in culture-positive sepsis, reflecting the severity of the underlying infection.

Higher MPV and PDW values serve as valuable biomarkers for identifying neonates at higher risk of severe sepsis complications, thereby facilitating early and accurate diagnosis and timely intervention. Supporting studies by Kumar M.K. et al,^[12] and Abdelfadil AM et al,^[16] corroborate our findings, emphasizing the utility of platelet indices in neonatal sepsis management.

COMPARISON OF PRESENT STUDY WITH OTHERS STUDIES BASED ON OUTCOME

In our study, thrombocytopenia was present in 67% of neonates, and among these cases, 4.4% resulted in mortality.

This finding is consistent with studies by Charoo BA et al,^[18] and Olmez et al,^[19] which reported higher mortality rates of 26.8% and 30%, respectively, in neonates with thrombocytopenia. Variations in mortality rates across studies can be attributed to several factors, including delays in intervention, variations in the severity of sepsis presentations, and differences in patient populations such as referrals from other hospitals. The association between thrombocytopenia and increased mortality underscores its critical role as a prognostic factor in neonatal sepsis. Thrombocytopenia reflects the severity of systemic inflammation and platelet dysfunction, which contribute to adverse clinical outcomes.

CONCLUSION

In the present study, Overall, these findings suggest that while CRP levels do not correlate with platelet indices on Day 1, significant correlations emerge by Days 3 and 7. Higher CRP levels are associated with lower platelet counts and higher PDW values on Day 3, and with lower platelet counts and higher MPV values on Day 7. As sepsis progresses, CRP becomes a more reliable indicator of changes in platelet indices, which could be important for monitoring the severity and progression of sepsis in neonates. Platelet indices, particularly thrombocytopenia, MPV, and PDW, can serve as early markers for neonatal sepsis and provide valuable information about disease progression and treatment response.

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