

**SENSITIVITY AND SPECIFICITY OF MICRO ESR VERSUS DEFINITIVE BLOOD MARKERS
FOR NEONATAL SEPSIS AS SCREENING TEST IN TERTIARY CARE HOSPITAL, NAVI
MUMBAI**

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Abstract

Background: Neonatal sepsis significantly contributes to neonatal mortality and morbidity in developing countries. The delay in diagnosis due to the time-consuming gold standard blood culture necessitates rapid, accessible, and cost-effective diagnostic markers.

Aims: This study aimed to evaluate the sensitivity and specificity of Micro-ESR for early neonatal sepsis diagnosis and compare its effectiveness with other standard markers.

Methodology: Conducted at D.Y. Patil Hospital's Department of Pediatrics in Navi Mumbai, this prospective observational study included 200 neonates suspected of sepsis. Blood samples were analyzed for CBC, CRP, Micro-ESR, and bacterial culture before antibiotic initiation. Micro-ESR's diagnostic performance was assessed against other markers based on confirmed sepsis cases via blood culture.

Results: Among 200 neonates, 16 had a positive blood culture. Micro-ESR showed a sensitivity of 87.5% and specificity of 28.80%. In comparison, Total Leucocyte Count (TLC) and Absolute Neutrophil Count (ANC) demonstrated higher specificity (91.25% and 70% respectively) but lower sensitivity. Platelet count and CRP indicated high specificity (94.56%) and sensitivity (100%) respectively, albeit with low predictive values.

Conclusions: While CRP exhibited the highest sensitivity, TLC and platelet count showed superior specificity. Despite its lower specificity, Micro-ESR's high sensitivity suggests its utility as a supportive early diagnostic marker alongside CBC, CRP, and ANC. Blood culture remains the definitive diagnostic standard.

INTRODUCTION

Neonatal sepsis, presenting with or without bacteremia in the first 28 days of life, encompasses a range of systemic infections including septicemia, pneumonia, and meningitis, among others.^{1,2} It is a leading cause of neonatal mortality in developing countries, accounting for 30-50% of neonatal deaths annually, with an

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estimated 20% of neonates developing sepsis.^{3,4}

The risk factors for neonatal sepsis are multifaceted, involving maternal, fetal, and environmental elements. Maternal factors include conditions like premature rupture of membranes and maternal fever, while fetal factors involve birth weight and gestational age. Environmental factors include invasive procedures and nursing care.^{5,6,7}

Neonatal sepsis is classified into Early Onset Sepsis (within 72 hours of birth) and Late-Onset Sepsis (after 72 hours). The clinical signs are diverse and non-specific, making early detection challenging yet crucial for reducing mortality through timely antimicrobial therapy.^{8,9}

Blood culture is the definitive diagnostic standard for neonatal sepsis but is hindered by its requirement for sophisticated labs and trained staff, and its delayed results. Alternative diagnostic tests like CBC, CRP, and procalcitonin offer confirmation but are often costly and not readily available in remote regions.¹⁰

Given these challenges, there's a critical need for accessible, cost-effective diagnostic markers with high sensitivity and specificity. Micro-ESR stands out as a promising option, offering simplicity, affordability, and requiring minimal training or equipment, making it suitable for use in remote settings. Its ability to be repeatedly conducted offers additional benefits in monitoring disease progression or treatment response.¹¹

This study aims to assess the sensitivity and specificity of Micro-ESR in early neonatal sepsis detection, comparing it with other blood markers such as total leucocyte count, absolute neutrophil count, platelet count, C-reactive protein, and procalcitonin, to establish its efficacy and potential as a routine diagnostic tool in resource-limited settings.

AIM AND OBJECTIVES

Primary objective: - To determine the sensitivity and specificity of Micro-ESR in early diagnosing neonatal sepsis.

Secondary objective:-To correlate the usefulness (sensitivity and specificity) of Micro Erythrocyte Sedimentation rate (Micro-ESR) and other standard markers for early detection of neonatal septicemia.

MATERIAL AND METHODS

This prospective observational study was carried out in the NICU and post-natal wards of the Department of Pediatrics at D.Y. Patil Hospital, Nerul, Navi Mumbai, from June 2019 to June 2021. The study included neonates suspected of sepsis, adhering to inclusion criteria such as a hemoglobin level between 10gm/dl and 20gm/dl, excluding those with genetic disorders, pre-existing sepsis treatment, a weight below 1000gm, or congenital anomalies.

Using literature-based estimates for sensitivity and specificity and applying the formula from Buderer (1996), a sample size of approximately 200 neonates was determined to ensure statistical validity, factoring in a 5% Type I error and a 32% estimated prevalence of neonatal sepsis.⁶

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Following ethical committee approval and guardian consent, neonates were divided into confirmed sepsis (positive clinical signs and blood culture) and probable sepsis (negative blood culture but positive clinical and laboratory signs) groups. Micro-ESR was measured using the capillary tube method, requiring specific equipment such as a lancet, sodium citrate, dropper, laboratory slide, micro hematocrit capillary tubes, antiseptic solution, a special rack, a ruler, and a stopwatch. The procedure involved collecting blood using a lancet and mixing it with sodium citrate on a slide, followed by capillary tube insertion and sedimentation rate measurement after one hour.^{12,13}

Sepsis indicators were set as follows: TLC below 5000 or above 25000, ANC below 1500 or above 5400, platelets below 100,000, Micro-ESR above 15 mm/hour, and CRP above 6 mg/dl.^{14,15-19}

Data collection was systematic, with information entered into a pre-formed case record form and analyzed using SPSS. Statistical analyses included descriptive statistics, t-tests for intergroup comparisons, and chi-square tests for categorical variable frequency comparisons, with $p < 0.05$ indicating statistical significance. The study's statistical power was set at 80%.

RESULTS

Table 1: Demographic details of study population

Neonate's characteristics	No of neonates (n=200)	%
Age in days		
• 0-3 days	157	78.5
• 4-28 days	43	21.5
Gender		
• Male	109	54.5
• Female	91	45.5
Gestational age		
• Term	84	42
• Preterm	116	58
Birth weight (gms)		
• <1500	27	13.5
• 1500-2500	51	25.5
• >2500	122	61
Mode of delivery		
• SVD	97	48.5
• LSCS	103	51.5

The study enrolled 200 neonates, with the majority (78.5%) being in the age group of 0-3 days and a smaller proportion (21.5%) aged 4-28 days. A slight predominance of males (54.5%) over females (45.5%) was observed. The gestational age distribution showed that 58% of the neonates were preterm, while 42% were term. Most neonates (61%) had a birth weight greater than 2500 grams. The mode of delivery was fairly evenly split between spontaneous vaginal delivery (SVD) at 48.5% and lower segment cesarean section (LSCS) at 51.5%.

Table 2: Organisms isolated from various culture samples

	BLOOD CULTURE	ET TIP CULTURE	UMBILICAL TIP CULTURE	URINE CULTURE
1. ACINETOBACTER Species	8 (4%)	7 (3.5%)	4 (2%)	0(0%)
2. CANDIDA SPECIES	3 (1.5%)	2 (1%)	2 (1%)	1 (0.5%)
3. PSEUDOMONAS AEROGINOSA	3 (1.5%)	2 (1%)	0(0%)	0(0%)
4. MRCONS	2 (1%)	0(0%)	1 (0.5%)	0(0%)
5. KLEBSIELLA PNEUMONIAE	0(0%)	4 (2%)	0(0%)	1 (0.5%)
6. NO GROWTH	184 (92%)	2 (1%)	4 (2%)	0(0%)
TOTAL SAMPLE SENT	200(100%)	17 (11.76%)	19 (9.5%)	2 (1.00%)

Blood culture identified organisms in 8% of neonates, with Acinetobacter species being the most common pathogen at 4%. The endotracheal (ET) tip and umbilical tip cultures were positive in 7.5% and 3.5% of cases, respectively, while urine culture was positive in only 0.5% of cases. No growth was reported in the majority of blood cultures (92%).

Table 3: Confirmed and Probable sepsis

Blood investigations	No.of neonates	% Of neonates	Confirmed sepsis	Probable sepsis
Micro-ESR				
>15mm/hr	145	72.5	14(9%)	131(91%)
<15mm/hr	55	27.5	2(3%)	53(97%)
TLC				
>25000/<5000	17	8.5	1(5%)	16(95%)
5000-25000	183	91.5	15(8%)	168(92%)
ANC				
<1500	60	30	5(8%)	55(92%)
>1500	140	70	11(7%)	129(93%)
Platelet				
<1,00,000	11	5	1(9%)	10(91%)
>1,00,000	189	95	15(7%)	174(93%)
CRP				
>6mm/hr	196	98	16(8%)	180(92%)
<6mm/hr	4	2	0(0%)	4(100%)
Bloodculture				
Positive	16	8	16(100%)	0(0%)
Negative	184	92	0(0%)	184(100%)
Procalcitonin				
<0.05	33	16.5	5(15%)	28(85%)
Notdone	167	83.5	11(6%)	156(94%)
ETtipculture				
Positive	15	7.5	2(15%)	13(85%)
Negative	2	1	0(0%)	2(100%)

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Notdone	183	91.5	14(7%)	169(93%)
Umbilicaltipculture				
Positive	7	3.5	0(0%)	7(100%)
Negative	12	6	2(16%)	10(84%)
Notdone	181	90.5	14(7%)	167(93%)
Urineculture				
Positive	1	0.5	1(100%)	0(0%)
Negative	1	0.5	0(0%)	1(100%)
Notsent	198	99	15(7%)	183(93%)

The Micro-ESR test showed that 72.5% of neonates had a value greater than 15mm/hr, with 9% confirmed sepsis and 91% probable sepsis within this group. White blood cell count (WBC) was above or below the normal range (25000/<5000) in 8.5% of neonates, while the majority (91.5%) fell within the normal range (5000-25000). Similarly, a low absolute neutrophil count (ANC) was observed in 30% of neonates, and thrombocytopenia (platelet count <1,00,000) was seen in 5%. Elevated C-reactive protein (CRP) levels were found in 98% of neonates, of which 8% were confirmed sepsis cases. Blood culture confirmed sepsis in 8% of neonates.

Table 4: Specificity, sensitivity, positive predictive value, negative predictive value, accuracy and the P-value of markers studied.

Investigations	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
Micro-ESR	87.5	28.80	9.65	96.36	33.5	0.161#
WBC>25000	6.25	91.20	5.88	91.71	84.34	0.737#
ANC<1500	31.25	70.10	8.33	92.14	67	0.909#
Platelet	6.25	94.56	9.09	92.06	87.5	0.891#
CRP(+)	100	2.17	8.16	100	10	0.551#
Procalcitonin	-	-	-	-	-	0.097#

Micro-ESR demonstrated high sensitivity (87.5%) but low specificity (28.80%) for detecting neonatal sepsis. The WBC count was highly specific (91.20%) but had low sensitivity (6.25%). ANC showed moderate sensitivity (31.25%) and specificity (70.10%). Platelet count was highly specific (94.56%) but similarly had low sensitivity (6.25%). CRP had a sensitivity of 100%, but its specificity was very low (2.17%). The Procalcitonin values were not provided.

DISCUSSION

In this comprehensive prospective observational study, we sought to evaluate the diagnostic accuracy of micro-erythrocyte sedimentation rate (Micro-ESR) in comparison to definitive blood markers, with a particular focus on its sensitivity and specificity as a screening tool for neonatal sepsis, using blood culture as the reference standard.

The demographic breakdown of our study population notably revealed a higher incidence of early-onset sepsis

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(EOS) at 78.5%, aligning with findings from Sriram R., Vinay BS et al., and Chacko B et al., who reported similar trends in EOS predominance.²⁰⁻²² The slight male preponderance observed (54.5%) is consistent with the literature, supporting theories of gender-linked immunological differences and the "male disadvantage hypothesis" that postulate higher sepsis susceptibility in male neonates.²³⁻³⁰

The Micro-ESR demonstrated high sensitivity (87.5%) but low specificity (28.80%), suggesting its potential utility as an initial screening tool. This is corroborated by the fact that out of the 72.5% positive Micro-ESR cases, 9% were confirmed for sepsis. However, the specificity was not as high as would be ideal, indicating that while Micro-ESR is effective in identifying those with sepsis, it also captures a substantial number of non-septic cases. This finding is in line with the range of sensitivity reported in other studies, though it varies widely, indicating that while Micro-ESR can be a valuable tool, it should be used in conjunction with other markers for a more accurate diagnosis.³¹⁻³⁶

Our analysis extends beyond Micro-ESR to include Total Leucocyte Count (TLC), Absolute Neutrophil Count (ANC), and Platelet count, among others. TLC's high specificity (91.20%) but low sensitivity (6.25%) reinforces its role in confirming rather than screening for sepsis. ANC's moderate sensitivity and specificity suggest its usefulness, albeit limited, in conjunction with other markers. Platelet count's high specificity (94.56%) is noteworthy, yet its low sensitivity mirrors the limitations seen with TLC.

CRP displayed a remarkable sensitivity of 100%, affirming its established role as a consistent marker for inflammation. However, its very low specificity (2.17%) in our study highlights the necessity of careful interpretation when used as a standalone test for sepsis. The absence of a full set of data for PCT precludes a comprehensive analysis within our study, though literature suggests its high sensitivity and specificity in neonatal sepsis diagnosis.³⁷⁻³⁸

CONCLUSION

Our study concludes that while micro-ESR is a sensitive screening tool for neonatal sepsis, its specificity limitations necessitate its use alongside other markers. Total Leucocyte and Platelet counts are specific but not sensitive enough for screening, whereas CRP is highly sensitive but not sufficiently specific. These findings underline the importance of a combined diagnostic approach incorporating clinical assessments, hematological markers, and culture methods, particularly in resource-limited settings where judicious use of available tests is crucial for accurate diagnosis and management of neonatal sepsis.

RECOMMENDATIONS

To optimize the early detection and management of neonatal sepsis, we advocate for enhanced maternal healthcare practices, minimizing unnecessary vaginal examinations to reduce infection risks. Utilization of blood markers such as CBC, CRP, Micro-ESR, PCT, and ANC is crucial for the timely diagnosis of sepsis. Given its simplicity, cost-effectiveness, and non-reliance on specialized equipment, Micro-ESR emerges as a valuable, albeit adjunct, tool for monitoring sepsis progression, especially beneficial in settings with limited

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resources. Nevertheless, blood culture retains its status as the definitive diagnostic standard for neonatal sepsis, underscoring the need for a balanced approach that combines rapid screening methods with confirmatory tests.

LIMITATIONS

The study is limited by its single-center design, which may not reflect broader clinical settings, and its focus on a select group of sepsis markers, excluding a wider range of potential biomarkers. Additionally, not all neonates were tested for procalcitonin due to resource constraints, and the study did not encompass viral sepsis, potentially overlooking a significant aspect of neonatal infections. The reliance on clinical suspicion for identifying sepsis cases may also introduce subjective bias into the selection process.

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