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REVIEW OF SEPSIS IN NEONATES BY HEMATOLOGICAL PARAMETERS ALONGWITH C-REACTIVE PROTEIN AS A BIOMARKER

Pathology

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ABSTRACT

Background- Sepsis is the leading cause of Mortality and Morbidity among neonates. Definitive diagnosis of bacterial sepsis is made by blood culture results, which require a lengthy time. Hematological scoring system by Rodwell et al and C-reactive protein levels are rapid tests that may be useful for diagnosing neonatal sepsis earlier.

Method- This prospective observational study is conducted for 1 year on neonates admitted to neonatal intensive care unit [NICU], Kamla Raja Hospital, J.A. Group of Hospitals, Gwalior Madhyapradesh India.Seven hematological parameters alongwith creactive protein has been assesed in this study over 200 clinically suspected neonates.

Results-Out of 200 cases studied 123 cases required sepsis work up, Senstivity(88%) and negative predictive value(78%) are highest for immature Pmn count while specificity(100%) and positive predictive value(100%) are highest for Crp (quantitative).

Conclusion-This study findings conclude that CRP in combination with Hematological scoring system(HSS) demonstrated a better screening output in neonatal sepsis evaluation for timely management decision.

KEYWORDS

Hematological Scoring System, Neonatal Sepsis, C- Reactive Protein, Immature Polymorphonuclear Count.

INTRODUCTION

Neonatal sepsis is an infection in the bloodstream that poses severe health risks to newborns characterized by clinical syndromes within the first month of life[1]. Despite major advances in neonatology within the past few decades, bacterial sepsis remains one of the foremost important causes of morbidity and mortality during this age group worldwide, especially in developing countries[2] . Annually five million neonates die in Asia and Africa, out of which 1.6 million (20%) attain mortality due to neonatal sepsis[3] . In India, the incidence of neonatal sepsis varies from 11-24.5/1000 live births[4] . Rapid diagnosis and therapeutic intervention of the sepsis is of great importance for a far better outcome of patients[5]. However it still remains a challenge to diagnose neonatal sepsis at earliest because the clinical symptoms aren't reliable, although blood culture has been the gold standard method for diagnosis[6], the result's available late, usually within 24- 72 hours. An intensive look for a spread of hematological and biological markers has been administered by many investigators for the evaluation of clinical sepsis. there's an increasing battery of laboratory tests available for diagnosis of sepsis but most have did not reach the extent of accuracy and consistency[7]

MATERIAL AND METHOD

This study is conducted for 1 year on neonates admitted to neonatal intensive care unit [NICU], Kamla Raja Hospital, J.A. Group of Hospitals, Gwalior. Informed consent is obtained from theparents. The blood is obtained under aseptic conditions from neonates prior to the initiation of antibiotics.

Hematological scoring has been done by using fully automated 5part cell analyser[MINDRAY-BC5380] for complete blood count and detail microscopy examination from peripheral smear.

We have performed C-reactive protein test –Qualitatively by latex agglutination test and Quantitatively in few cases by semi-automatic analyser. This is a prospective observational study which includes neonates(<28days of age] admitted in neonatal intensive care unit of Gajraraja Medical College, Gwalior.

PROCEDURE: Assesment of Hematological parameters were done using RODWELL et al standard values. (Table-1).[8]

Immature neutrophils include promyelocytes, myelocytes, metamyelocytes and band forms.

Absolute polymorphonuclear neutrophilcount, immature to total PMN (I:T) ratio and immature to mature PMN (I:M)ratio were calculated from the observed values. that is;

Score of ≤ 2: sepsis unlikely
Score 3-4: sepsis possible
Score ≥ 5: sepsis very likely
Minimum score- 0
Maximum score- 8

The scores were compared with clinical parameters and the most predictive factor was identified.

TABLE NO 1 : Hematological scoring system

PARAMETERS	ABNORMALITY	SCORE
Total WBC Count	≤5000µl	1
	≥25000 at birth	1
	≥30000 at 12-24hrs	
	≥21000 day 2 onwards	
Total PMN count	1800-5400	0
	No mature PMN	2
	Increased or Decreased count	1
Immature PMN count	600	0
	Increased	1
I:T PMN ratio	0.12	0
	Increased	1
I:M PMN ratio	≤0.3	0
	≥0.3	1
Degenerative changes in PMN	Toxic granules or cytoplasmic vacuolations	1
Platelet count	≤1.5 lakhs/µl	1
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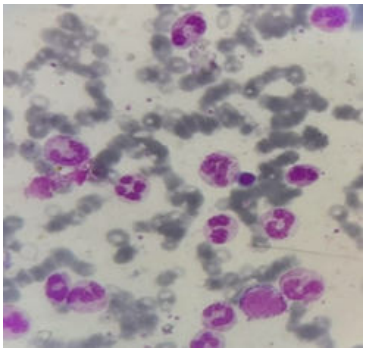
C-REACTIVE PROTEIN ESTIMATION

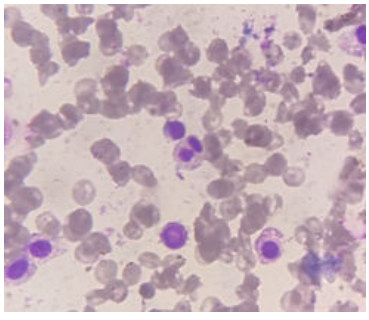
QUALITATIVE METHOD -Estimation of serum CRP- CRP is estimated by slide latex agglutination method.

QUANTITATIVE METHOD- Turbilatex is a quantitative turbidimetric test for the measurement of C-Reactive protein done in few cases.

IMAGES:



1-PICTURE SHOWING NEUTROPHILIC LEUKOCYTOSIS AND TOXIC GRANULES IN NEUTROPHILS.



2-PICTURE SHOWING DEGENERATIVE CHANGES IN THE NEUTROPHILS.

RESULTS/STATISTICAL ANALYSIS

The statistical analysis was done using the results of present study.

Table 2: Distribution of the Participants in Terms of Sepsis Score (n = 200)

Sepsis Score	
Mean (SD)	3.05 (1.76)
Median (IQR)	3 (2-4)
Range	0 – 7

The variable Sepsis Score was not normally distributed (Shapiro-Wilk Test: p = <0.001).

The mean (SD) of Sepsis Score was 3.05 (1.76). The median (IQR) of Sepsis Score 3.00(2-4), Sepsis Score ranged from (0-7) .

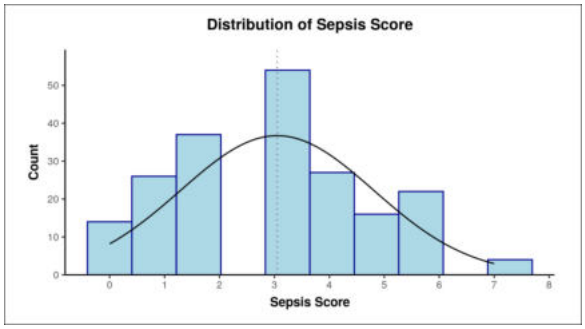
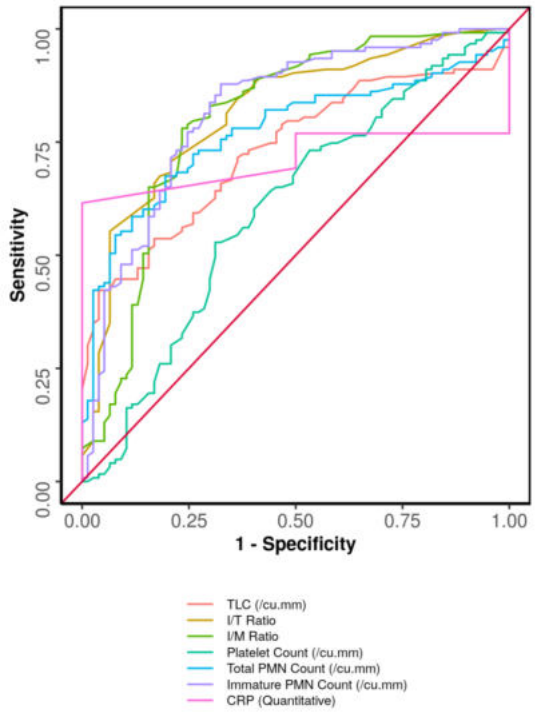


Table 3: Comparison of the Diagnostic Performance of Various Predictors in Predicting Sepsis Likelihood: Possible/Very Likely vs Sepsis Likelihood: Unlikely (Full Sample)

Predictor	AUROC	95% CI	P	Sn	Sp	PPV	NPV	DA
TLC (/cu.mm)	0.730	0.661-0.799	<0.001	42%	96%	94%	51%	63%
I/T Ratio	0.816	0.755-0.877	<0.001	71%	79%	84%	63%	74%
I/M Ratio	0.801	0.732-0.869	<0.001	78%	77%	84%	69%	78%
Platelet Count (/cu.mm)	0.601	0.518-0.684	0.016	53%	69%	73%	48%	59%
Total PMN Count (/cu.mm)	0.771	0.705-0.836	<0.001	68%	80%	85%	61%	72%
Immature PMN Count (/cu.mm)	0.819	0.757-0.882	<0.001	88%	68%	81%	78%	80%
CRP (Quantitative)	0.712	0.514-0.909	0.348	62%	100%	100%	17%	64%

AUROC: Area under ROC curve; CI: Confidence interval; P: P value; Sn: Sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; DA: Diagnostic Accuracy.



Immature PMN Count (/cu.mm), I/T Ratio, I/M Ratio, Total PMN Count (/cu.mm), TLC (/cu.mm), Platelet Count (/cu.mm) significantly predicted Sepsis Likelihood: Possible/Very Likely

DISCUSSION

Blood culture is the gold standard to diagnose the sepsis. But there is a significant delay in getting the final report and sensitivity of the organisms to various antibiotics. To overcome this problem there are various clinical and hematological parameters suggested to predict the neonatal sepsis in advance.

The present study also evaluated the seven parameters of Rodwell's Hematological Scoring System, and the results revealed that the score of more than five when compared to the score of more than four has higher likelihood of sepsis and is well correlated with Rodwells study[9]. In present study Immature polymorphonuclear(pmn) count is highly sensitive 87.8%, followed by immature to total (i:m) ratio 78% and total immature to mature (i:t) count 70.7%. total leucocyte count 96.1%, degenerative changes 93.5% and platelet count were highly specific tests for diagnosing sepsis. the positive predictive value(ppv) was highest with total leucocyte count 94.5%whereas negative predictive value(npv) was highest with immature polymorphonuclear count (pmn)77.6%.

TABLE4.Comparison of different studies for studying immature polymorphonuclear count in present study

	Sensitivity%	Specificity%	PPV%	NPV%
MAKKARetal[10] 2013	96.87	91.68	91	97.05
MAKADIAetal[11] 2020	55.44	97.97	96.55	68.30
NARSIMHAetal[12]2011	78.94	8.3	73	11.11
PRESENT STUDY	88	68	81	78

In present study immature polymorphonuclear count is found to be the most reliable indicator in terms of higher sensitivity,negative predictive value and diagnostic accuracy as compare to other parameters .The values in the present study is found to be very similar to the study done by Makkar etal 2013.

CONCLUSION

Sepsis screen parameters using CRP and ,hematological parameters are easily available ,cost effective,rapid screening tests with good sensitivity and good diagnostic accuracy .

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