

Diagnostic accuracy of combination of abnormal total leukocyte count, platelet count and C-reactive protein for diagnosis of neonatal sepsis taking blood culture as gold standard

Hasan Sardar Sadiq, Shoaib Ali, Habib Ullah, Sahira Aaraj, Aleena Khan, Malik Muhammad Atif

Departments of Medicine, Allama Iqbal Medical College, Childrens Hospital and Institute of Child Health, Lahore, Shifa Tameer-e-Millat University, Islamabad and King Edward Medical University, Lahore, Pakistan

Objective: To determine the diagnostic accuracy of combination of abnormal total leukocyte count, platelet count and C-reactive protein (CRP) for diagnosis of neonatal sepsis taking blood culture test as gold standard.

Methodology: This cross sectional study was conducted at Children Hospital, Lahore from 15-11-2019 to 15-6-2020 and included 201 neonates. Blood sample was collected for total leukocyte count, platelet count and CRP. Total leukocyte count $>30000/\text{mm}^3$, $<5000/\text{mm}^3$, platelet count $<100000/\text{mm}^3$ and CRP $>10\text{mg/L}$ were

considered diagnostic for neonatal sepsis.

Results: The mean age of neonates was 14.57 ± 7.88 days; male to female ratio was 1.2:1. The sensitivity, specificity, & diagnostic accuracy of combination test were 77.59%, 92.94% & 84.08%, respectively taking blood culture as gold standard.

Conclusion: The combination of abnormal total leukocyte count, platelet count and CRP for diagnosis of neonatal sepsis is a reliable method. (Rawal Med J 202;46:8862-865).

Keywords: C-reactive protein, leukocyte count, neonatal sepsis, platelet count.

INTRODUCTION

Sepsis is a syndrome of systemic manifestations and amplified host immune responses, due to an infectious agent that has gained widespread access to blood circulation.¹ If this process occurs during the initial twenty eight days of life, it is termed "Neonatal sepsis". This is classified as early-onset and late-onset sepsis, depending upon the time of onset of symptoms from birth i.e. before and after 72 hours. The cause of each of these varies.^{2,3}

Onset of sepsis is most rapid in premature or low birth weight neonates.⁴ Of all the newborn, up to 20% develop sepsis, and those who survive this ordeal may be afflicted with life-long disabilities and derangements.⁵ A local study from Rawalpindi showed that out of 2,480 neonates, incidence of neonatal sepsis was 29.5% and mortality from culture-confirmed sepsis was 25.9%.⁶

For diagnosis, blood culture is considered as gold standard.³ Cultures for both aerobic and anaerobic pathogens are used because it involves both types of bacteria as 16% are anaerobic organisms.⁷ Blood cultures typically reveal the causative pathogen within 2 days, and may be obtained from

venipuncture or umbilical cord sampling. Sometimes urine cultures are also required, especially for investigating late-onset sepsis.⁸ However the culture is onerous, as it needs days to give results, and requires laboratories with extensive equipment. Therefore, quicker and cheaper alternative tests must be sought. Complete Blood Count (CBC) with C-reactive protein (CRP) were shown to have sensitivity and negative predictive value of more than 90%.^{5,9}

Thus a better approach may be to combine Platelet Count (PC), TLC and CRP together for increased diagnostic accuracy. A study by Sherazi and Ashfaq from Sargodha, Pakistan showed the prevalence of neonatal sepsis to be 63.8% keeping blood culture as the gold standard for diagnosing neonatal sepsis.¹⁰ A combination of PC, TLC & CRP was found to have specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) as 92.5%, 75.3%, 94.6% and 67.9%, respectively.¹⁰ Sepsis if not diagnosed timely can cause significant mortality (up to 50%) and morbidity in affected neonates.^{1,6,11} The aim of this study was to determine the accuracy of combination of TLC, PC and CRP

for diagnosis of neonatal sepsis taking blood culture test as gold standard.

METHODOLOGY

It was an observational cross sectional study conducted at Department of Neonatology, Children Hospital Lahore from 15-11-2019 to 15-5-2020 after approval by ethical review board of the institution. An Informed consent was taken from parent or legal guardian. A sample size of 201 was calculated considering expected prevalence of neonatal sepsis to be 63.8% with 92.5% specificity and 75.3% sensitivity. Non-probability Purposive sampling technique was used. Newborns of both genders of age less than 29 days having two out of these three features were included in this study: 1) Hypothermia (<36°C) or Hyperthermia (>38.5°C), 2) Respiratory rate >60/min and 3) Heart Rate of >190 beats/min at rest. All premature neonates of <32 weeks gestation (on antenatal record), birth Weight less than 1000 grams and those full term neonates who had already received

antibiotics were excluded from the study.

A blood sample was collected in EDTA for estimation of PC and TLC and was collected in plain bulb for measuring CRP. Demographic features like age, gender and weight were noted. If any of these tests was not positive, it was taken as negative hematological profile for neonatal sepsis.

Statistical Analysis: The data were analyzed by using SPSS version 23. Specificity and sensitivity was calculated using a 2X2 model along with Positive predictive value (PPV) and Negative predictive value (NPV).

RESULTS

Out of 201 neonates, 109(54.23%) were male and 92(45.77%) females (Male-Female Ratio 1.2:1). Mean age was 14.57±7.88 days and mean weight was 3.20±0.4 kg. Sensitivity, specificity, PPV, NPV & diagnostic accuracy of combination of abnormal TLC, PC & CRP was 77.59%, 92.94%, 93.75%, 75.24% and 84.08%, respectively taking blood culture as the diagnostic gold standard (Table 1).

Table 1. Accuracy of combined blood component in diagnosing neonatal sepsis, taking blood culture as gold standard.

		Blood Culture		Total		
		Positive	Negative			
Combination of blood component: Total leukocyte count, platelets & C reactive protein	Positive	90	6	96	Sensitivity	77.59%
	Negative	26	79	105	Specificity	92.94
Total		116	85	201	PPV	93.75%
					NPV	75.24%
					Diagnostic Accuracy	84.08%

Table 2. Analysis of diagnostic accuracy by age, weight and gender.

Stratification by Age								
Combination of blood components		Blood Culture		Total				
		Positive	Negative					
Age (days)	≤15	Positive	52	2	54	≤15	≥15	
		Negative	20	44	64	Sensitivity	72.22%	86.36%
	>15	Positive	38	4	42	Specificity	95.65%	89.74%
		Negative	6	35	41	PPV	96.3%	90.48%
					NPV	68.75%	85.37%	
					Diagnostic Accuracy	81.36%	87.95%	
Stratification by weight								
Combination of blood components		Blood Culture		Total				
		Positive	Negative					
Weight (kg)	≤3.5	Positive	59	4	63	≤3.5	>3.5	
		Negative	23	53	76	Sensitivity	71.95%	91.18%
	>3.5	Positive	31	2	33	Specificity	92.98%	92.86%
		Negative	3	26	29	PPV	93.65%	93.94%
					NPV	69.74%	89.66%	
					Diagnostic Accuracy	80.58%	91.94%	
Stratification by gender								
Combination of blood components		Blood Culture		Total		Male	Female	
		Positive	Negative					
	Male	Positive	45	3	48	Sensitivity	80.36%	75.00%
		Negative	11	50	61	Specificity	94.34%	90.63%
	Female	Positive	16	32	48	PPV	93.75%	93.75%
		Negative	15	29	44	NPV	81.97%	65.91%
					Diagnostic Accuracy	87.16%	80.43%	

Diagnostic accuracy was 81.36 % in neonates with age ≤ 15 days and 87.95% in neonates with age > 15 days. In neonates weighing ≤ 3.5 kg, it was 80.58% whereas it was 91.94% in neonates weighing > 3.5 kg. Diagnostic accuracy in male neonates was 87.16%, whereas in female neonates it was 80.43 % (Table 2).

DISCUSSION

The incidence of neonatal sepsis in developing countries like Pakistan is higher than in developed countries. A study from Lady Reading Hospital, Peshawar, 115 blood culture-proven cases of neonatal sepsis were found over a period of 10 months, of which early-onset sepsis were 29.57% and late-onset sepsis were 70.43%¹³ The sensitivity and specificity of CRP for diagnosis of neonatal sepsis has been found to be 84% and 65%, respectively.¹⁴ A meta-analysis done for diagnostic value of CRP reported 69% sensitivity & 77% specificity.¹⁵ Whereas sensitivity and specificity for PC was 48% and 96%, respectively in another study.¹⁶

On the other hand, some studies used different tests (including TLC, absolute neutrophil count, immature to total neutrophil (I:T) ratio, PC, serum ferritin and CRP) in several different combinations to investigate infants with possible sepsis, and reported that those combinations increased accuracy than any of these individual tests.^{5,9,10,17,18} A study by Anwer and Mustafa concluded that five tests, namely TLC, absolute neutrophil count, immature to total neutrophil (I:T) ratio, PC and CRP, when used together had 100% specificity & 100% PPV for diagnosing neonatal sepsis within hours.¹⁷ Another study reported that Immature to Total Neutrophil ratio plus Absolute Neutrophil count plus CRP was one of the best and quickest combinations which gave 88% sensitivity, 84% specificity, 86% PPV and 85% NPV.¹⁹ Another study by Ayub et al showed that the combination of absolute neutrophil count (ANC), immature/total leukocytes ratio (I:T), PC, CRP and serum ferritin was a reliable method for diagnosis with 90.9% and 76.8% sensitivity and specificity respectively.²⁰ A local study from Sargodha, Pakistan by Sherazi and Ashfaq showed that combination of TLC, PC &

CRP had sensitivity, specificity, PPV & NPV of 75.3%, 92.5%, 94.6% and 67.9%, respectively.¹⁰ Beltempo et al concluded that both CBC and CRP should be done to increase sensitivity and this combination allowed a high negative predictive value to be reached, rather than the use of an individual test²¹

CONCLUSION

Results our study showed that three commonly available investigations TLC, Platelet Count & CRP when used in combination, had significant validity & reliability for early diagnosis of neonatal sepsis.

Author Contributions:

Conception and design: Shoaib Ali, Sahira Aaraj
Collection and assembly of data: Habib Ullah, Shoaib Ali
Analysis and interpretation of data: Shoaib Ali, Sahira Aaraj
Drafting of the article: Hasan Sardar Sadiq, Habib Ullah, Aleena Khan
Critical revision of article for important intellectual content: Habib Ullah, Sahira, Aleena Khan
Statistical expertise: Hasan Sardar Sadiq, Sahira Aaraj
Final approval and guarantor of the article: Hasan Sardar, Muhammad Atif

Corresponding author email: Muhammad Atif:

mmatif236@gmail.com

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