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Original Research Article

To Study the Hematological Indices and CRP in the Screening of Neonatal Sepsis

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Abstract

Introduction: To study the haematological indices and serum CRP levels for the early diagnosis of neonatal septicaemia.

Purpose of study: Establishment of a modified sepsis screen score which is easy, cost effective and less time consuming for the early diagnosis of neonatal septicaemia.

Results: Total 80 newborns were studied; consecutive 3 days sepsis screen score is established considering blood culture as a gold standard. Overall sensitivity and specificity of septic screen was 94.5% and 80% respectively while PPV and NPV was 91.2% and 87%. Overall diagnostic accuracy of septic screen was 90%.

Conclusion: Sepsis screening methods using CRP and haematological indices are easily available, rapid, cost-effective screening method and effect rapid diagnosis of neonatal sepsis and save lives due to timely detection and interventions.

Keywords: PPV and NPV, serum CRP

Introduction

Neonatal sepsis is a systemic inflammatory response to infection by pathogenic organisms and/or isolation of these organisms from the blood stream in the neonatal period (first 28 days) of life. When these pathogenic organisms enter into the blood-stream, they can cause an overwhelming infection which leads to development of septicaemia. When these organisms predominantly restricted to the lung, they may cause pneumonia or if restricted to the meninges then meningitis, respectively [1].

Systemic inflammatory response explains a clinical syndrome in which there are two or more of the following symptoms: fever, hypothermia, tachycardia, Rapid breathing or tachypnoea and increased or decreased white blood cells. [1].

Sepsis is one of the most common causes of neonatal hospitalisations in recent times[2–4] and causes about 26% of all neonatal deaths worldwide [5]. It contributes to 30 to 50% of neonatal deaths (first 28 days of life) in the developing countries [6]. In India, 8.5 per 1,000 live births was the incidence of blood culture proven sepsis reported to be for the year 2002–2003 as per the National Neonatal Perinatal Database (NNPD report 2002-03) [7].

Neonatal sepsis is classified as early onset sepsis if it occurs within the first 72 hours of life and late onset sepsis if it occurs after 72 hours of life [8,9]. Early onset sepsis is caused by the pathogenic organisms present in the maternal genital tract, labour room or operation theatre [10, 11] whereas late onset sepsis usually results from nosocomial (Hospital acquired)or community-acquired infection [3, 11.]

Aims and Objectives

1. To learn the haematological indices and serum C-Reactive Protein in the early diagnosis of neonatal sepsis by using blood culture as a gold standard investigation
2. To study a modified sepsis screen score for the early diagnosis of neonatal sepsis

Materials and Methods

A) Study Type / design:

Study of a diagnostic or screening test

B) Study settings:

N.I.C.U. of a tertiary health care institute.

C)Study duration:

August 2016 to December 2018.

D)Study population:

Neonates delivered in our institute as well as referred from other centres.

1) Sampling technique and Sample size

The prevalence of neonatal sepsis in neonates admitted in NICU is approx. 20.0% [51]. So, by taking this prevalence and using formulae given below, the sample size is calculated:

$$n \geq \frac{Z^2 1-\alpha/2\ Sensitivity\ [1-Sensitivity]}{d^2 \times prevalence}$$

d = Estimation Error [0.05]

Testing Sensitivity = 0.99

Prevalence = Prevalence of the disease [0.20]

Z = 1.96

α =0.05

Using the above formula, Sample size = 80

Thus, a total of 80 consecutive patients of suspected sepsis, fulfilling the eligibility criteria were taken up for the study after informed consent from parents.

2) Eligibility criteria:

Inclusion criteria - Neonates with high risk of developing neonatal sepsis.

Exclusion criteria – Neonates admitted from other centres having positive blood culture.

3) Methodology:

Present study was conducted in Level 3 N.I.C.U. of a tertiary care hospital

Our N.I.C.U. setup is divided into 2 Parts. One is inside that is newborns delivered in our institute and the other is outside that is newborns referred from other centres.

Recruitment- Based on detailed history, clinical examination and risk factors

Investigations: 1st day of admission haematological investigations and CRP was sent for consecutive 3 days and for

each day sepsis screen score was established.

Blood culture: It was sent on 1st day of admission before starting antibiotics.

Culture report was be considered as the gold standard

Modified Sepsis Screen

CRITERIA	TESTING VALUES	SCORE
TOTAL WBC COUNT	<5000/μ*l*	1
	>25000 at birth	1
	>30000-12 to 24 hrs	1
	> 21000 day 2 onwards	1
PLATELET COUNTS	1 lac to 1.5 lacs	1
	< 1 lac	2
C-REACTIVE PROTEIN	>0.6 mg/dl	2
ABSOLUTE NEUTROPHIL COUNT	<2700/mm^3	1
	>13000/mm^3	1

Score zero is considered for normal ranges

1.Total WBC count:
- 5000-25000 At birth
- 5000-30000 12 to 24 hours
- 5000-21000 day 2 onward

2.Platelet count: >1.5 lacs

3.CRP:≤ 0.6

4. ANC: 2700-13000/mm^3

RESULTS:

Table 1: Distribution of cases as per Septic screen results

Septic Screen	N	%
Positive	57	71.3%
Negative	23	28.8%
Total	80	100.0%

Sepsis screen was positive in 71.3% cases while negative results were seen in only one 28.8% cases. (Table 1)

Table 2: Distribution of Culture and screen result cases as per type of sepsis

Type of Sepsis	N	%
Culture & Screen -ve	20	25.0%
Culture & Screen +ve	52	65.0%
Culture -ve/ Screen +ve	5	6.3%
Culture +ve/ Screen -ve	3	3.8%
Total	80	100.0%

Culture and septic screen positive sepsis was seen in 65% cases while culture positive and septic screen negative sepsis was seen in 3.8% cases. Culture and septic screen negative i.e., clinical sepsis was seen in 25% cases. (Table2)

Table 3: Diagnostic accuracy of septic screen for culture positive sepsis

Septic Screen	Blood Culture		Total
	Negative	Positive	
Negative	20	3	23
Positive	5	52	57
Total	25	55	80

Table 4: sensitivity and specificity of septic screen

Parameters	%
Sensitivity	94.5%
Specificity	80.0%
PPV	91.2%
NPV	87.0%
Accuracy	90.0%

Overall sensitivity and specificity of septic screen was 94.5% and 80% respectively while PPV and NPV was 91.2% and 87%. Overall diagnostic accuracy of septic screen was 90%. (Table 4)

Discussion:

Neonatal sepsis is one of the most important and common cause of deaths in neonatal period especially in the developing countries like our country. It is a life-threatening emergency and causes death if there is any delay in prompt treatment. Neonatologists often face a great challenge to diagnosis of sepsis. Clinical diagnosis is many times difficult due to non-specific signs and symptoms. In addition, Blood culture which is the gold standard for definitive diagnosis is costly, time consuming, demands a proper laboratory setup and is positive only in nearly 40% cases [12].

Haematological scoring system (HSS) which was first proposed by Rodwell et al. [13,] includes a complete blood picture which includes white blood cell count, absolute neutrophil count and platelet count and C-reactive protein. Early treatment is possible with the support of these indirect markers which are collectively known as the sepsis screen. The advantage of sepsis screen is that it is easy to perform and applicable to all infants, including those who have received antibiotics.

Present research was thus conducted to study the screening efficacy of haematological indices and C - reactive protein in the screening of neonatal sepsis.

A total of 80 consecutive neonates fulfilling the eligibility criteria were taken for study after taking informed consent. The neonates were enrolled on the basis of signs and symptoms of clinical sepsis as per the NNF guidelines with thorough clinical examination and history taking. Also, any predisposing factors for septicemia presumed early onset sepsis was considered while inclusion of cases along with the relevant laboratory investigations.

Demography

As per the study conducted of Vaidya et al., 1.6:1 was the Male: Female ratio.[14] ·Anitha Sharma et al., also reported with 37 males out of 50 cases (74% male predominance)[15]· In the study conducted by Anuradha De et al.[16]. out of 200 suspected cases of neonatal septicaemia 114 (57%) were males and 86 (43%) were females [16]. Male predominance in neonatal septicaemia has suggested sex linked factor in the host susceptibility. Other authors also made Similar observations as well. [17-22]

Obstetric History

In this study, about 46.3% cases were the pre-term births out of the suspected accounting for almost half of the cases. Mean gestation age of delivery was 36.27 weeks.

Other workers also have made similar reports. K.K. Anand et al. reported 62.1% of neonates as preterm [23] whereas K. Chug et al., reported much higher percentage of 73.3% of cases as preterm. [24]. However, Galhotra et al. [25] observed about 55% of suspected septicaemia cases as pretern newborns. Basu R et al. and Sonawane SB et al also observed similar results. [26]. According to Barbara. J. Stoll et al., decreasing gestational age increases incidence of septicaemia[27].

In our study, Overall sensitivity and specificity of septic screen was 94.5% and 80% respectively while PPV and NPV was 91.2% and 87%. Overall diagnostic accuracy of septic screen was 90%.

Among the parameters of septic screen, highest sensitivity was seen with CRP (92.7%) while highest specificity was seen with absolute neutrophil count (80%) and TLC levels (72%). Highest diagnostic accuracy was seen with CRP (81.3%) followed by platelet count (77.5%).

Conclusion:

Neonatal sepsis is a life-threatening emergency and any delay in treatment may cause death. Blood culture is considered as the gold standard investigation for diagnosis of neonatal sepsis, but its culture positivity rates are relatively low. Initial signs of neonatal sepsis are slight and nonspecific. Therefore, in suspected sepsis, two or three days empirical antibiotic therapy should begin immediately after cultures have been obtained without awaiting the results. Modified Sepsis screening parameters using CRP and other haematological parameters are easily accessible, rapid, cost-effective screening method and offers early detection. The presence of two or more abnormal parameters (septic screen positive) yielded better correlation with blood culture status than individual tests. Positive septic screen has a good negative predictive value but has a very high sensitivity and so that the antibiotic can be started in culture negative and asymptomatic cases too which helps to reduce the delay in instituting antibiotic therapy. it will curtail the sepsis mortality by timely intervention. Moreover, establishing early diagnosis will extensively reduce antibiotic abuse and help in rationalising a unit policy for the judicious use of antibiotics, thus preventing the emergence of multidrug-resistant micro-organisms

Though ample new markers have been explored, much of the population in developing countries may not be able to afford them, because they require sophisticated technology. In such situations, modified sepsis screen would be an apt marker, especially in Early Onset Septicaemia, thus aiding in timely intervention and reducing the mortality. This is extremely crucial in developing countries where Early Onset Septicaemia is fulminant and is caused by gram-negative micro-organisms leading to early mortality. Despite being costly, the governing bodies of developing nations should reconsider the

need of including these modern biomarkers in the septic screen of these fragile neonates, as they are more specific and help in prompt diagnosis. This, in turn, would reduce the overall burden on the healthcare system and would therefore prove to be more cost effective in the long run due to curtailing the cost of prolonged hospital stays, mortality, and morbidity burden. In conclusion, despite of an array of biomarkers being available, it is crucial to select the appropriate combination of these markers that allows only minimal blood loss in the neonate for a timely, precise diagnosis of sepsis.

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