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SEPSIS SCREEN AS A DIAGNOSTIC TOOL IN NEONATAL SEPTICAEMIA

Pathology

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ABSTRACT

INTRODUCTION: Neonatal sepsis is the commonest cause of neonatal mortality. Blood culture is gold standard in diagnosis, but it is time consuming and hence sepsis screen using haematological parameters are used. **OBJECTIVES:** To study and analyse sepsis screen of neonates suspicious of sepsis and correlate sepsis screen with blood culture. **METHODOLOGY:** It is a 6 months prospective study in which 106 neonates with history of sepsis were included and were scored according to Rodwell's sepsis score. Blood culture was performed. Sepsis screen results were correlated with blood culture. **RESULTS:** Blood culture was positive in 30.3% and Klebsiella was most common organism. Sepsis screen showed high sensitivity of 93.15% and specificity of 70%. **CONCLUSION:** The sepsis screen is simpler, cost effective and readily available tool in the early diagnosis of neonatal sepsis and provides guidelines for antibiotic therapy.

KEYWORDS

Sepsis Screen, Neonatal Septicaemia, Blood Culture

INTRODUCTION

Neonatal septicaemia can be defined as generalised bacterial infection in infants during first month of life. But clinical features of sepsis are nonspecific in neonates. So high index of suspicion is required for early diagnosis (Ahirao et al & Zawar et al).[1,2] Neonatal Sepsis is the most important cause of morbidity and mortality especially among low birth weight and preterm babies in developing countries. The incidence of neonatal sepsis is around 30 per 1000 live births. (Pramana et al & Singh et al).[3,4]

Paediatricians desire a screening blood test that predicts the presence or absence of bacterial infection causing sepsis with a high degree of accuracy and confidence, but currently no single test fulfils the criteria of an ideal diagnostic test(s). Blood culture considered as gold standard for diagnosis of septicaemia is time consuming and demands a well equipped laboratory. According to various studies the haematological parameters are simple, quick and cost effective tool in early diagnosis of neonatal sepsis and documented that when studied in combination has high sensitivity and specificity.

Makkar et al, concluded in his study that sepsis screen helps clinician to reach a probable diagnosis, and help in a rational approach towards the patient medication.[5]

Rodwell et al developed haematological scoring system based on the WBC count, total and immature neutrophil counts and ratios, degenerative changes in neutrophils and thrombocytopenia, which appears to be useful with 96% sensitivity and 99% negative predictive value.[6]

Neonatal sepsis and its early diagnosis based on clinical features is still a big challenge. This study is undertaken to validate sepsis screen using haematological parameters in the early diagnosis of neonatal septicemia which includes simple laboratory tests such as total WBC count, Absolute neutrophil count (ANC), Immature neutrophill count (INC), Immature to Total neutrophil count ratio (I/T), Immature to Mature neutrophil count ratio (I/M), Degenerative changes in neutrophils (toxic granules, cytoplasmic vacuoles etc), and platelet count.

MATERIALS AND METHODS

This was 6 months prospective study conducted in our department. A total number of 106 neonates clinically suspected to have sepsis were included in this study. The blood samples were collected aseptically in EDTA vacutainers and blood culture bottles by peripheral venipuncture and received in the Pathology and Microbiology departments. Relevant clinical history was noted. Haematological values were obtained from Sysmex XP-100, three part automated cell counter. Leishman stained peripheral smears were examined under oil immersion at a magnification of ×1000, for nucleated RBCs and thereby corrected WBC count, differential counts, absolute neutrophil count, immature neutrophil count, toxic granulations **[Fig 1 and 2]** and degenerative changes in neutrophils **[Fig 3]**. The peripheral smears of all newborns from birth up to 28 days were analysed. Blood culture reports of same samples were collected from Microbiology department. Culture positivity was considered gold standard for definitive diagnosis. Each parameter was studied in both culture positive as well as in culture negative cases and evaluated statistically based on standard reference values **[Table 1]**.

Sensitivity, specificity, positive and negative predictive values (NPV & PPV) were calculated for each parameter and for sepsis screen. *P* value was also calculated. Data was statistically analyzed by using SPSS software.

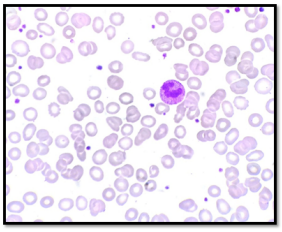

Fig1: Peripheral Smear Showing Toxic Granules In Neutrophil (leishman Stain, 1000x)

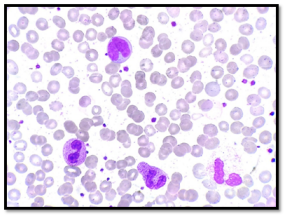

Fig 2: Peripheral Smear Showing Toxic Granules In Band/stab Forms (leishman Stain, 1000x)

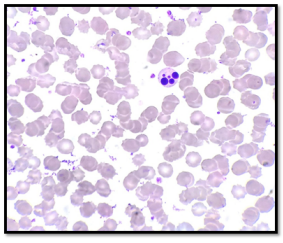

Fig 3: Peripheral Smear Showing Degenerated Neutrophil (leishman Stain, 1000x)

Table1 Showing Cut Of Values For The Tests According To Rodwell Haematological Scoring System[6]

PARAMETERS	ABNORMALITY	SCORE
Total WBC Count	↓ or ↑ (< 5,000/mm^3 or > 25,000, 30,000, and 21,000/mm^3 at birth, 12-24 hrs, and day 2 onward, respectively)	1
Absolute Neutrophil Count	↓ or ↑ [7,800 – 14,500 /mm^3 (<72 hours),	1

	1,750 – 4500 / mm^3 (>72 hours)]	
Immature Neutrophil Count	↑ [>1450/mm^3 (<72 hrs), > 500/mm^3 (>72 hrs)]	1
I/M ratio	≥ 0.3	1
I/T ratio	≥ 0.2	1
Platelet Count	< 150000	1
Toxic Granulation/ Degenerated Neutrophil	Present	1

RESULTS

In our study 106 neonates were studied, among which 32 cases were culture positive and 74 cases were culture negative. Sepsis screen was done for both culture positive and culture negative cases. Among culture positive cases commonest organisms isolated was Klebsiella in 13 neonates, followed by E Coli in 06 and CONS in 05 neonates. Out of 106 neonates 75 (70.7%) were in early neonatal period (≤ 72 hrs or <3 days) and 31 (29.3%) were in late neonatal period (> 72 hrs or 4 to 28 days), 55 neonates (51.8%) were males and 51 neonates (48.2%) were females, M:F ratio was 1.08:1. Among 106 neonates, 57 (54%) had LBW, 56 (53%) were preterm. Among 106 suspected cases of neonatal sepsis, 43(40.5%) had clinical history of PROM followed by maternal fever in 29(27.3%) and delayed cry in 10(9.4%), other medical history being prolonged labour in 08 (7.5%), excessive cry in 08(7.5%), respiratory distress in 06(6%) and convulsions in 2(1.9%) **[Table 2]**

Table 2 Showing Distribution Of Neonatal Profile

		NO OF NEONATES	PERCENTAGE (%)
AGE OF ONSET	Early neonatal period (<72hr)	75	70.7
	Late neonatal period (>72 hrs)	31	29.3
SEX	Male	55	51.8
	Female	51	48.2
BIRTH WEIGHT	Low birth weight (2.5KG)	57	54
	Normal weight (≥2.5KG)	49	46
MATURITY	Preterm	56	53
	Term	50	47
CLINICAL HISTORY	PROM	43	40.5
	Maternal fever	29	27.3
	Delayed cry	10	9.4
	Prolonged labor	08	7.5
	Excessive cry	08	7.5
	Respiratory distress	06	6
	Convulsions	2	1.8

In our study when individual parameters of sepsis screen were considered five of seven were statistically significant (P value <0.001) except ANC and INC (P value >0.05). Among individual parameters, platelet count was most sensitive (92.2%) and showed highest NPV (91.4%), whereas I/M ratio was most specific (79.6%). I/T ratio comparatively showed higher PPV (60.2%) and better diagnostic accuracy (77.7%) **[Table 3]**

Table 3 Showing Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value And Diagnostic Accuracy Of Individual Parameters

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)	P Value
Total wbc count	67.2	66.7	46.7	82.4	66.8	<0.001
Absolute neutrophil count	85.9	21.1	32.2	77.5	40.8	0.258
Immature neutrophil count	50	42.2	27.4	66	44.6	0.297
I/M ratio	65.6	79.6	58.3	84.2	75.4	<0.001
I/T ratio	78.1	77.6	60.2	89.1	77.7	<0.001
Platelet count	92.2	36.1	38.6	91.4	53.1	<0.001
DN/TG	84.4	58.5	47	89.6	66.4	<0.001

Sepsis score is given to all neonates using above 7 criteria. Upon doing sepsis screen, it showed high sensitivity of 93.15%, specificity of 70%, PPV of 62% and NPV of 95.05% **[Table 4]**. Sepsis screen was found to be statistically significant (P value <0.001).

Table 4 Showing Diagnostic Indices Of Sepsis Screen

SEPSIS SCREEN	ESTIMATE
Sensitivity (%)	93.15%
Specificity (%)	70%
PPV (%)	62%
NPV (%)	95.05%

DISCUSSION

Sepsis is the commonest cause of neonatal mortality (30-50% of the total neonatal deaths) in developing countries.[1,7] Biggest problem with neonatal infection is identification of the infected infant because of its nonspecific symptoms. It is current practice to start empirical antibiotic therapy in neonates showing infection-like symptoms.[3,8] This may expose newborns to adverse drug effects and lead to emergence of resistant strains. [3,9] Though blood culture remains the gold standard for diagnosis of neonatal sepsis, it is time consuming and also has low sensitivity, yields a positive result only in 30-40% of cases.[3]

In our study out of 106 neonates , 30.3% cases were culture positive, which was similar to study done by Shirazi et al[10](35%) and Mayuga et al[11] (17%). Among culture positive neonates 70.3% were in early neonatal period (≤72hrs), 56.2% were males, 72% were with low birth weight, 58% were preterm neonates. Most common clinical history being PROM in 40.3% of neonates. It shows that early onset sepsis is more common than late onset sepsis because of maternal factors and poor immune system. In developing countries like India, poor antenatal facilities as well as poverty also plays important role in early onset septicemia.[12] Buch et al observed higher incidence of neonatal sepsis in males as compared to females because of the fact that, the factors regulating the synthesis of gamma globulin are situated on X chromosome and male has only one X- chromosome.[13] Higher incidence of sepsis in low birth weight and preterm neonates is attributable to low maternal acquired IgG and inherent deficiencies of defence mechanisms.[14]

Among individual parameters of sepsis screen, platelet count showed highest sensitivity and NPV (92.2% & 91.4%). I/M ratio showed highest specificity (79.6%), I/T ratio showed highest PPV(60.2%).

Thrombocytopenia was frequently associated with sepsis and indicated poor prognosis. This is due to increased platelet destruction, failure in platelet production due to damaging effects of endotoxin on megakaryocytes.[6] In our study platelet count was the most sensitive parameter and showed highest NPV(92.2% and 91.4%), similar to study conducted by Ahlawat et al[15] (87.10 and 90.91%).

Total WBC count, ANC and INC as an individual parameter were not reliable and they were not specific. Neonatal septicemia is associated with either leucopenia or leucocytosis. In our study Total WBC count showed good sensitivity and NPV (84.4% & 89.6%) but low specificity and PPV (58.5% & ppv). Zaki et al[16] observed low sensitivity for this test (48%), Ahirrao et al[1] observed high specificity and PPV (98.5% & 98.1%).

In our study I/M ratio was the most specific single parameter (79.6%) which was comparable to studies done by Ahlawat et al[15] (100%) and Bhalodia et al[17] (94.2%). It also showed high NPV (84.2%) similar to Bhalodia et al[17] (94%). Khair et al[9] study showed 100% sensitivity and NPV whereas Ahalwat et al[15] showed 100% specificity for I/M ratio.

I/T ratio one of the most extensively studied neutrophil index showed good sensitivity (78.1%), specificity (77.6%), PPV (60.2%) and high NPV (89.1%) in our study which was similar to studies done by Buch et al[13] and Bhalodia et al.[17] Khair et al[10] observed 100% sensitivity and NPV, but very low specificity (4%) and PPV (13%).

On combining seven parameters as sepsis screen, it showed high sensitivity of 93.15% and high NPV of 95.05% where as specificity was 70% and PPV was 62%. . In our study the values of sensitivity and NPV (93.15% & 95.05%) were highest compared to other studies like Rodwell et al[6] (41% & 94%), Saleem et al[18] (90% & 93,2%),

Krishnamurthy et al[19] (80% & 88%) and Siddiqui et al[20] (90.32% & 86.96%). So sepsis screen can identify true positives very accurately. Specificity in our study was 70% which was low compared to studies done by Rodwell et al[6] (96%) and Siddiqui et al[20] (85.11%) whereas it was similar to studies done by Saleem et al[18] (74.5%) and Krishnamurthy et al[19] (70%). Also with specificity of 70%, sepsis screen can also identify true negatives quite accurately. The PPV of 62% was comparable to study done by Saleem et al[18] (65.9%).

So sepsis screen can be widely used in all basic laboratories to accurately diagnose neonatal sepsis. It is quick, cost effective and very reliable compared to blood culture. Another advantage of sepsis screen is, it can be used even after administration of antibiotics.

CONCLUSION

This study was carried out in our department to evaluate the role of sepsis screen in early diagnosis of neonatal sepsis. 106 neonates with clinical history of sepsis were studied. Out of 106 neonates, 32 cases were culture positive. Seven parameters were studied with cut off criteria.

Majority of culture positive sepsis were seen in early neonatal period. Male babies were commonly affected. Culture positive sepsis was common in preterm and very low birth weight neonates. Klebsiella was the commonest organism isolated.

Among single parameters studied, platelet count was the most sensitive (92.2%) and with high negative predictive value (91.4%). I/M ratio was most specific (79.6%) test. I/T ratio had highest positive predictive value(60.2%).

When sepsis screen was applied, it showed very high sensitivity (93.15%) and negative predictive value (95.05%) whereas specificity was 70% and positive predictive value was 62%. So sepsis screen is a quick, cost effective, reliable diagnostic tool in any basic laboratory and it will be very useful in diagnosing neonatal sepsis as early as possible and to avoid unnecessary administration of antibiotics to the neonates.

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