e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(7); 1468-1474

Original Research Article

Evaluation of Screening Parameters in the Assessment of Neonatal Sepsis

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Received: 18-05-2023 / Revised: 14-06-2023 / Accepted: 25-07-2023

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Conflict of interest: Nil

Abstract:

Introduction: Early-onset neonatal sepsis and late-onset neonatal sepsis are both types of the same infection that occurs in infants and are classified differently. EOS is caused by infections that occur in the genitourinary system of the mother, whereas LOS is acquired after birth. Premature infants are fragile. Blood cultures, a cerebrospinal fluid check, and biomarker testing are all parts of the diagnostic process. Rapid approaches aid in pathogen identification.

Aims and Objectives: The purpose of this research was to determine the best ways to screen for and diagnose newborn sepsis.

Methods: This prospective study, conducted over a year, included 100 newborn infant suspected of having septicemia who was admitted to the Neonatal Intensive Care Unit. The purpose of these studies was to investigate the clinical presentation, diagnostic techniques, and outcomes of septicemia in this population, in addition to studying its incidence and features. The study gave useful information for gaining a better knowledge of septicemia in neonates who are particularly sensitive.

Results: The bacterial culture results, age of onset, gender, and birth weight of each patient are listed in Table 1. Table 2 shows the cultural findings broken down by age range. In Table 3, we can see the sensitivity, specificity, PPV, and NPV values for each test combination. The results provide insight into test combination efficacy in predicting septicemia and the prevalence of different cultures, as well as age-related patterns.

Conclusion: Neonatal sepsis is a leading cause of death in preterm, low-birth-weight infants, especially males, especially in the early-onset and Gram-negative forms.

Keywords: Neonatal sepsis, infants, Intensive Care Unit, PPV, and NPV.

Introduction

The medical name describing a bloodstream infection in newborn babies fewer than 28 days old is "neonatal sepsis." It still plays a significant role in neonatal morbidity and death, particularly in nations with middle and low incomes. Early-onset sepsis (EOS) & late-onset sepsis (LOS) are two categories of neonatal sepsis defined when symptoms appear after birth. Some doctors claim that infant sepsis that manifests during the first 7 days of existence is referred to as EOS, while sepsis that occurs throughout the initial 72 hours of a person's existence is LOS [1].

Female genitourinary systems frequently cause early-onset sepsis (EOS) by transmitting pathogens to the child or foetus. These viruses have the ability to infiltrate the amniotic fluid in addition to the uterus, cervix, & vagina. Newborns may also get an infection while they traverse the uterine artery after delivery or even while they are still in the womb. The usual bacterial infections that cause. EOS includes Listeria monocytogenes, Haemophilus influenza, Coagulase-negative Staphylococcus, Group B streptococcus (GBS), and Escherichia coli. Chorioamnionitis, GBS colonisation, delivering birth before 37 weeks, and a protracted membrane rupture lasting over eighteen hours are all risk factors for neonatal sepsis in women [2].

After birth, infections are typically transmitted via the immediate surroundings, including any contact with carers or hospital staff, leading to late-onset sepsis (LOS). A portion of LOS could additionally be brought on by a horizontally transmitted disease's tardy symptom. Infants are more susceptible to developing LOS if they need the Insertion of an intravascular catheter or other intrusive practices that cause mucosal disruption [3].

Preterm infants are more susceptible to sepsis and an infection than mature births. Preterm infants are more susceptible to illnesses, which are often brought by:

- Immune system deficit, mostly caused by reduced IgG antibodies and ineffective opsonization & complement activation
- caused mostly by the juvenile epithelial barrier, which was composed inherent immune system.
- because of the severe diseases that go along with them, there is a greater requirement for intrusive devices including urinary tract catheters, endotracheal tubes, tubes for feeding, and vascular access.

More than LOS is brought on by coagulase-negative bacteria in 50% of cases in developed countries' staphylococcal species, particularly Staphylococcus epidermis. But other more Infections caused by bacteria and viruses may contribute to LOS [4].

The key element making newborns more susceptible to severe sepsis is a still-evolving immune system. Polymorphonuclear neutrophils, macrophages, & T lymphocytes are unable to adequately carry out an inflammatory response in due to their immature function in infants. Additionally, infants are born with insufficient immunoglobulins and thus are unable to establish a sufficient immune response, either quantitatively or qualitatively, to pathogenic microorganisms. The little time premature infants spend inside Immune globulins is less likely to be transmitted to the body through the uterus. growing foetus. Because of this immunoglobulin deficiency, babies born preterm have a considerably greater risk of acquiring sepsis than term neonates [5].

Babies with bacteremia could not exhibit any symptoms and undergo a regular examination. Laboratory testing is therefore essential for diagnosis. In a blood culture Blood should be obtained right soon from a newborn who appears to have sepsis. The minimum amount of blood to draw is 1 ml. since smaller aliquots might not be able to detect low-level bacteremia. Cultures should be collected from the location of the catheter if one is present. For EOS assessment, urine cultures are frequently not indicated, but they ought to be taken into account for LOS evaluation. A lumbar puncture, cerebrospinal fluid (CSF) examination [6]. Any newborn with positive blood cultures or a child whose clinical symptoms suggest an infection should have their cerebrospinal fluid (CSF) examined and cultured. the presentation suggests neurological involvement. Another To ensure the CSF is sterile, lumbar puncture ought to be performed no later than 48 hours following treatment. Research is now being done using polymerase chain reaction (PCR) technologies to diagnose sepsis and the etiological agent more quickly than blood cultures [7].

A CSF analysis might reveal:

- Elevated amount of protein
- Cultures with higher WBC positivity
- Less glucose in the blood
- Successful PCR

Additionally important to get are the laboratory tests C-reactive protein (CRP) as well as a full blood count (CBC) with differential, which are typically conducted in succession. Given their limited ability to detect newborn sepsis, these markers perform more effectively when employed to rule it out. Neutropenia is a more focused indicator of newborn sepsis than neutrophilia. As it may be increased in as many as 50% of babies who are not sick, an elevated immaturity a ratio of total neutrophil (I/T) exceeding 0.27 an insufficient positive predictive value (25%) but an extremely high negative accuracy for prediction (99%). These counts could be exaggerated, particularly after delivery. It is preferable to do CBC 6–12 hours after birth to prevent the physiological alterations to CBC values that are often noticed at that time [8].

Neonatal CRP levels rise during an infectious incident in 6 to 8 hours and peak 24 to 48 hours later. Consistently Strong evidence for bacterial sepsis is provided by normal CRP levels. It is possible to leverage this strong link to assist the clinician's choice to stop antibiotic treatment for an infant who is otherwise healthy. Procalcitonin, haptoglobin, & cytokines are some other inflammatory indicators that may be measured to confirm the diagnosis or assess the effectiveness of treatment. A chest radiograph might be performed on a baby exhibiting respiratory symptoms or signs to look for any pulmonary abnormalities [9].

Microbiological culture methods

The "gold standard" for confirming neonatal sepsis continued to be diagnosed as conventional culture methods. The period of time it takes to find an organism has been cut in half to 24-48 hours thanks to the development of automated methods that look for growth caused by bacterial CO2 generation [10].

Blood volume acquired, collection time, and sample count are all variables that might affect the pathogen recovery from the blood. Blood culture sensitivity in newborns may be lowered by maternal intrapartum antibiotic treatment and the occurrence of low-grade or sporadic bacteremia. The prolonged time between pathogen detection to

Increasing exposure to broad-spectrum medicines through antibiotic susceptibility testing might lead to bacterial drug resistance and prolong the time between focused antimicrobial therapy and its initiation [11].

Rapid testing techniques for blood cultures that are positive

When compared to conventional techniques, a number of diagnostic technologies have been created for quick species identification in blood culture specimens that are positive.

Blood-based indicators

Neutrophils: Neonatal sepsis is often diagnosed by Absolute neutrophil count (1000 - 5000/mm3), A peripheral blood smears (toxic granulation, vacuolization, and Dohle bodies) and immature/total neutrophil count (>0.2) are all indicators of infection [12].

At lower gestational ages (GA), the amount of neutrophils in the white blood cells (WBC) seems to be lower and peaks 6–8 hours after birth. The number of neutrophils is impacted by medical circumstances such In addition to intraventricular haemorrhage, hemolysis, pneumothorax, convulsions, maternal fever & hypertension, perinatal hypoxia, meconium aspiration syndrome, birth technique, and even weeping are all possible symptoms.

Compared to neutrophilia, absolute neutrophil count (ANC) neutropenia (ANC 1,000/mm3 is believed to be more specific to early neonatal sepsis (at 4 h).

The most sensitive sign of newborn sepsis among other haematological indicators may be whereas that Immature: Complete Neutrophil (I: T) Proportion GA & postnatal age both affect this parameter. The I: T ratio in healthy neonates peaks at 0.16 on day one and then steadily drops over the following days [13].

Red blood cell: Inflammatory and infectious diseases cause increased red blood cell production. disorders, as seen by red cell distribution width (RDW). It has been demonstrated that elevated RDW is linked to an increase in sepsis-related mortality in both adults and newborns.

Thrombocytopenia: Neonatal sepsis and thrombocytopenia are related. In addition to becoming more active and linked to cytokines and inflammatory mediators, platelet volume rises.

Biomarkers of inflammation

Acute phase reactants—The liver produces acute phase reactants in reaction to cytokines, which are brought on by damage to tissue and infection. Neonatal sepsis has been studied in relation to TNF, Pro-adrenomedullin (pro-ADM), fibronectin, haptoglobin, PCT, CRP, and SAA [14].

Methods

Research design

This prospective study was conducted between December 2008 and September 2010 at the Department of Pathology of a tertiary care hospital. The study lasted for an entire year. Participants in the study were one hundred newborns diagnosed with a clinical suspicion of septicemia and admitted to the Neonatal Intensive Care Unit. This study included neonates ranging in age from the day they were born to 28 days after birth. The study aimed to investigate and analyse the occurrence of septicemia in this particular group of newborns and the features of those who had it. The researchers wanted insights into the clinical presentation, diagnostic procedures, and consequences of septicemia in newborns. Thus, they prospectively examined these cases with the hopes of learning more. Because of how the study was designed, we obtained important data that will contribute to our comprehension of septicemia in these susceptible individuals.

Inclusion and exclusion criteria

Inclusion

- This study included newborns with clinical suspicion of septicemia hospitalised in the Neonatal Intensive Care Unit between birth and 28 days.
- Temperature instability, respiratory symptoms, cardiovascular symptoms, neurologic abnormalities, and gastrointestinal symptoms were required.

Exclusion

- Congenital abnormalities, fungal infections, and antibiotic-treated neonates were excluded.
- Parents or guardians gave informed consent, and a patient proforma was used to collect the mother and baby's clinical history.

Statistical analysis

Statistical analysis was used to analyse the data collected. For each important variable, the mean, standard deviation, and frequency distribution were determined to provide a better understanding of the data. Chi-square and Fisher's exact tests are examples of inferential statistics used to establish statistical significance between groups. To be statistically significant, the p-value has to be under 0.05. In order to draw valid conclusions from the data, we ran all analyses through statistical software (SPSS).

Ethical approval: The ethics committee's approval of this study ensured that all procedures followed all necessary rules and regulations for conducting ethical research.

Results

Table 1 shows the breakdown of cases based on bacterial culture results, age at onset, gender, and birth weight. Of the cases, 63 tested positive for culture, and 37 tested negative. Most culture-positive cases (74.6%) were defined as having an early onset (within three days). In contrast, the remaining 25.4% (16 instances) were classified as having a late onset (between four and twenty-eight days). Regarding gender, 46 out of the 73.02% of culture-positive cases were male, while just 17 out of the 73.02% were female. Regarding birth weight, 71.43 per cent (45 cases) of the culture-positive cases were below 2500 g, whereas 28.57 per cent (18 cases) were above 2500 g. Further data analysis differentiates between EOS and LOS depending on birth weight, revealing the distribution of culture results across several subcategories.

Table 1 Distribution of cases according to bacterial culture

Bacterial Culture	**Culture positive**	**Culture Negative**	**Total**		
No. of Cases	63	37	100		
Age of onset	Culture Positive	Culture Negative	Total		
0 -3 days (early onset)	47 (74.6%)	19	66		
4-28days (late onset)	16 (25.4%)	18	34		
Total	63	37	100		
Sex	Culture Positive	Culture negative	Total		
Male	46 (73.02%)	18 (48.65%)	64		
Female	17 (26.98%)	19 (51.35%)	36		
Total	63	37	100		
Birth weight	Culture Positive	Culture Negative	Total		
≤ 2500gms	45 (71.43%)	18	63		
> 2500gms	18 (28.57%)	19	37		
Total	63	37	100		
Birth Weight	**Culture positive**		**Culture Negative**		**Total**
	EOS	**LOS**	**EOS**	**LOS**	
≤ 2500gms	34 (72.34%)	11 (68.75%)	15	3	63
> 2500gms	13 (27.66%)	5 (31.25%)	4	15	37
Total	47	16	19	18	100

Table 2 displays the breakdown of cases by age and culture results, separated into positive and negative groups. Sixty-seven per cent (42 cases) of the preterm newborns were culture positive, whereas thirty-three per cent (21 cases) were culture negative. Third (33.33%; 21 cases) were culture positive in the full-term group, whereas nearly half (48.18%; 20 cases) were culture negative. Culture positivity for EOS was found in 74.47% (35 cases) of the preterm newborns, whereas LOS positivity was found in 43.75% (7 instances) of the neonates. Of the full-term cases, 25.53% (12) tested positive for EOS, and 56.25% (9) tested positive for LOS in culture. The results provide light on the age-dependent distribution of culture results and the differentiation between EOS and LOS in septic newborns.

Table 2 Distribution of cases according to Maturity

Maturity	**Culture Positive**	**Culture Negative**	**Total**		
Preterm	42 (66.67%)	17	59		
Full-term	21 (33.33%)	20	41		
Total	63	37	100		
Maturity	**Culture positive**		**Culture Negative**		**Total**
	EOS	**LOS**	**EOS**	**LOS**	
Preterm	35 (74.47%)	7 (43.75%)	15	2	59
Full-term	12 (25.53%)	9 (56.25%)	4	16	41
Total	47	16	19	18	100

Table 3 shows the results of the various test combinations utilised in the study, broken down by their sensitivity, specificity, "positive predictive value (PPV)", and negative predictive value (NPV). High PPV (97.43%) and moderate NPV (59.02%) were found for the combination of C-RP (C-

reactive protein) and I/T ratio (immature to total neutrophil ratio), with a sensitivity of 60.32% and specificity of 97.29%. C-reactive protein and micro erythrocyte sedimentation rate (m-ESR), C-reactive protein and toxic granules, and C-reactive protein and total leukocyte count followed the same patterns. C-reactive protein, international normalised ratio, and platelet count all together showed 100% specificity and PPV but only 38.10% sensitivity. These results demonstrate the heterogeneity of diagnostic performance among test combinations in predicting septicemia.

Table 3: Demonstrating sensitivity, specificity, and positive and negative predictive values when many tests were used

Combination of two tests	Sensitivity	Specificity	PPV	NPV
C-RP and I/T ratio	60.32%	97.29%	97.43%	59.02%
C-RP and m-ESR	63.49%	89.19%	90.90%	58.93%
C-RP and Toxic granules	61.90%	91.89%	92.86%	58.62%
C-RP and Total leukocyte count	52.38%	97.28%	97.06%	54.54%
C-RP and Platelet count	46.03%	97.29%	96.66%	51.43%
C-RP, I:T ratio and Platelet count	38.10%	100%	100%	48.68%
C-RP, m-ESR and Toxic granules	52.38%	94.59%	94.29%	53.85%
C-RP, m-ESR and I/T ratio	49.21%	100%	100%	53.62%

Discussion

As screening tests for newborn sepsis, hematologic results & published complete blood cell counts criteria was used. There was created a hematologic scoring system using the data obtained, and it gives An Atypical overall neutrophil (PMN) count, unusual total leukocyte count, high immature PMN count, high immature to general PMN ratio, and immature developing PMN proportion which is less than 0.3, an elevated platelet count for above 150,000/mm3, and obviously discernible degenerative modifications to PMNs all receive a score of 1. 298 sepsis assessments were performed (243 within the initial 24 hours of life & 55 on days 2 & 30) [15]. In comparison to 35 of 248 (14%) noninfected newborns, 26 whereas all 23 children with suspected infections had scores below 3, of 27 (96%) infants had sepsis. Sepsis was more probable to happen when the score was 3 (31% vs. 8% for preterm & term neonates under 24 hours, & 65% beyond). The postnatal and gestational ages affected this number. Sepsis was more likely to occur with a higher score. With a score of 2, sepsis was almost certainly not present (99%). The hematologic evaluation system ought to improve the total blood cell count's diagnostic precision as a sepsis screening test and might standardise and streamline its interpretation [16].

In a previous research, a haematological scoring system (HSS) was evaluated and its importance for detecting infant sepsis early was emphasised. The different screening parameters' sensitivities were shown to be adequate for detecting newborn sepsis with early onset. It is an easy-to-use and practical diagnostic tool that can help in the selection of an appropriate course of therapy [17].

India has the highest rate of newborn sepsis in the whole globe. Clinical practice and preventative tactics might be guided by the evidence on its risk factors.to examine, evaluate, and summarise the material that is currently available from India in relation to neonatal sepsis's root causes. Neonates in India are at risk for sepsis due to male neonates, outborn enrollment, the necessity for mechanical ventilation, a 37-week gestation, and an early membrane rupture. A well-planned research is essential to verify the importance of additional risk factors for newborn sepsis in India, as it has been previously reported [18].

To assess several haematological indicators both alone and together in order to create a scoring system for haematology that may be used to test babies who are clinically suspected to have an infection for sepsis.150 neonates suffering from a clinically suspected infection, ranging in age from birth to three days made up the research population. In all newborns, blood was drawn by peripheral venipuncture. The following tests were run: complete leucocyte count, undifferentiated leucocyte count, total the number of leucocytes, immature neutrophils, band-formed cells, and platelets. Juvenile total neutrophil count (I/T) & immature immature/mature neutrophil count ratios (I/M) were subsequently determined [19]. In each patient, blood cultures and tests for antibiotic sensitivity were done along with semiquantitative measurements of C-reactive protein (CRP). The HSS compared the haematological parameters separately and together. A peripheral blood analysis smears and a full blood count can yield a haematological score, allowing for an objective evaluation of the haematological alterations that take place in a newborn suspected of having sepsis. Neither as a standalone test nor in conjunction with HSS, C-reactive protein is superior [20].

Neonatal patients have a higher risk of getting sepsis, yet they frequently have vague clinical

symptoms that make it difficult to diagnose an infection. Since no biomarker has yet demonstrated sufficient diagnostic fidelity, sepsis cannot be ruled out during the time of medical suspicion. They located pre-existing cohorts of newborns with sepsis using gene expression microarray technology [21]. The Sepsis MetaScore's diagnostic efficacy was then evaluated, both on its own and in conjunction with conventional diagnostic laboratory testing. In three distinct cohorts of newborns from three different nations, the Sepsis MetaScore demonstrated outstanding diagnosis accuracy. Prior to clinical application, more prospective-focused research will be required [22].

Mean platelet volume (MPV), which has been the subject of a growing number of research in recent years, has been found to be a reliable indicator of newborn sepsis. However, because the majority of this research concentrated on a specific location, the results are still not clear. In an investigation, they evaluated the literature using a meta-analysis & systematic review potential for MPV to serve as a biological biomarker of newborn sepsis. When contrasted with the control group, MPV was considerably greater in the newborn sepsis group. Therefore, MPV may be employed in clinical usage as an Early neonatal sepsis detection marker [23].

To provide a guideline in the diagnosis of newborn sepsis by individually and together analysing the several sepsis screen criteria. With a series of tests, 100 newborns with sepsis-like clinical characteristics and 100 healthy, asymptomatic neonates were compared. Neonatal sepsis was diagnosed using the markers Thrombocytopenia, neutrophil degeneration, gastric aspirate cytology (GAC) detecting polymorphs, total leukocyte count (TLC), absolute neutrophil count (ANC), young neutrophils relative to an overall neutrophil count ratio (I/T ratio), and C-reactive protein (CRP) are some of the other conditions that should be considered. Numerous tests, including as CRP, TLC, ANC, thrombocytopenia, cytoplasmic vacuolization in neutrophils, and GAC, are extremely sensitive to the detection of polymorphs identifying instances of newborn sepsis that do not respond to culture [24].

Sepsis is one of the main reasons why infants suffer from illness and die. newborn sepsis has a varied and non-specific clinical appearance, making early detection and diagnosis challenging. Consequently, a strategy to perform early predictive screening for newborn sepsis is required. To determine whether newborns using cord blood, are susceptible to developing newborn sepsis, and to evaluate early Early predictive screening for newborn sepsis using the Cord Blood Haematological Scoring System with an early start [25]. A number of haematological indices, including We analysed the cord blood's Total leucocyte measure, relative neutrophil measure, immature-mature proportion, immature-fully developed neutrophil proportion, neutrophil morphology, produced erythrocytes, platelet count, and microerythrocyte sedimentation rate are some of the measurements that are used. The most effective method for identifying newborn sepsis was blood cultures. It is feasible to think of the umbilical Using the cord blood haematological scoring system is a screening tool for detecting newborn sepsis with early onset. Preventing neonatal morbidity and death requires early detection of sepsis risk [26].

Before clinical deterioration takes place, Infants who are at risk for bacteremia can be identified early using clinical and laboratory signs. However, the diagnostic powers of existing prediction models are subpar. The objective of the study was to create, assess, and verify a screening method for newborn bacteremia with a late start (> 72 h post-admit), and estimate its accuracy in detecting bacteremia using standard laboratory and clinical markers. Compared to currently available techniques for screening for newborn bacteremia, the model created in the study is better. The method will be validated using historical neonatal data from our facility [27].

Conclusion

The study has concluded that premature and low birth weight newborns are more prone to neonatal sepsis. Sepsis cases are mostly male and often have predisposing characteristics. In premature and low-birth-weight neonates, early-onset sepsis is more common than late-onset. Gram-negative sepsis is more common in high-risk patients. Sepsis screening criteria such as total leukocyte count, toxic granules in neutrophils, immature to total neutrophil ratio, micro erythrocyte sedimentation rate, C-reactive protein, and thrombocytopenia are sensitive and specific for early detection. Combining these tests boosts specificity. These screening tests for early newborn sepsis identification are simple, cost-effective, fast, and may be done at the bedside without lab equipment. Early-onset and Gram-negative sepsis increase mortality. Men with low birth weight and preterm increased death risk. Pseudomonas, Citrobacter, E. coli, and Klebsiella kill most. This study's small sample size and single-centre design may restrict its generalizability. This study did not evaluate maternal variables or specific therapies, which may affect newborn sepsis outcomes. Larger, multicenter investigations are needed to confirm these findings and identify other causes of newborn sepsis and mortality.

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