Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

CLINICAL INDICATORS OF POSITIVE BLOOD CULTURE IN NEONATAL SEPSIS IN NEWBORNS

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How to cite: Gupta Y. Clinical indicators of positive blood culture in neonatal sepsis in newborns. International Research Journal of Pharmacy. 2020;11:3:54-60.
Doi: 10.7897/2230-8407.110330

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ABSTRACT

Background: Neonatal sepsis is difficult to diagnose due to a lack of accurate diagnostic indicators and a non-specific clinical appearance. As a result, there is a need to identify clinical indicators that might aid in early neonatal sepsis detection, particularly using blood culture.

Aim: The current study sought to investigate the predictors of positive blood cultures in newborn sepsis in order to find clinical and laboratory characteristics that might assist healthcare practitioners in the early detection and diagnosis of sepsis**.**

Methods: The study eventually comprised 270 neonates having a confirmed diagnosis of neonatal sepsis. Laboratory data collected comprised CRP (C-reactive protein), CBC (complete blood count), and blood culture aftereffects. The study's variables comprised a variety of independent clinical and laboratory predictors, such as laboratory measurements, clinical signs and symptoms, and maternal risk factors. The study also looked at the outcomes of positive blood cultures, which showed newborn sepsis present.

Results: There was a strong link between positive blood culture in newborn sepsis and maternal variables such PROM, chorioamnionitis, and fever during birth. Premature newborns and those with low birth weight were more likely to have a positive blood culture. Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii complex, Citrobacter species, Enterococcus species, and Serratia marcescens were true positive in 45, 7, 6, 5, 4, 3, 8, and 6 cases, respectively, with a sensitivity of 100%. In Burkholderia cepacian, genuine positive and true negative readings were found in 5 and 2 participants respectively, with a sensitivity of 100%.

Conclusion: delayed cry, low birth weight, very low birth weight, very low birth weight, male gender, LSCS delivery, and gestational age less than 34 weeks were significant clinical predictors of positive blood cultures in neonatal sepsis. The correlation study revealed a substantial association between these clinical features and a positive blood culture.

Keywords: Blood culture, clinical predictors, Neonatal ICU, neonatal sepsis.

INTRODUCTION

According to the World Health Organization (WHO), approximately 5 million newborn fatalities occur each year, with nearly all of them occurring in poor countries such as India, and septicemia is a leading cause of child mortality and morbidity. WHO has established criteria for diagnosing newborn sepsis; nevertheless, the specificity and sensitivity of clinical diagnosis differ.

Early identification and treatment are critical in avoiding complications and mortality from septicemia. The positive blood culture rate in newborns ranges from 25 to 54. Various tools, such as quick immunological tests and the CRP (C-reactive proteins) testing, can aid in the diagnosis of septicemia; however, the ability to diagnose particular pathogens is absent at many hospitals in underdeveloped countries.1

Blood culture for the isolation of offending microorganisms is the gold standard for conclusive and proven diagnosis of septicemia; however, findings from blood cultures might take hours to days to be reported, hence empirical therapy should be initiated in suspected instances. Knowledge about determinants of positive blood cultures and antimicrobial susceptibility patterns of prevalent infections is critical for guiding local empirical antibiotic selection.2

Respiratory distress, poor eating, fatigue, temperature instability, and a variety of other clinical conditions all contribute to sepsis risk. However, the symptoms and indications are not limited to sepsis. Similar trends have been documented for congenital cardiac disease, inborn metabolic abnormalities, and hypoglycemia. However, when sepsis is suspected, CSF culture, blood culture, ESR, CRP, and full blood counts should be performed as needed.3

Sepsis can occur early or late. Early-onset sepsis was caused by bacterial contamination from female genitourinary structure newborns within 72 hours of delivery, whereas late-onset sepsis was caused by bacterial pathogen transmission from the surrounding environment in the Neonatal Intensive Care Unit (NICU) after 72 hours and up to 90-120 days.

Depending on local antibiotic-resistant patterns, empirical care with suitable antibiotics should begin while findings are anticipated, including aminoglycosides and ampicillin in early-onset sepsis patients and aminoglycosides and ampicillin in late-onset sepsis.4

Clinical factors like as physical signs and symptoms can be useful predictors of positive blood cultures, although their specificity and sensitivity are limited. Neonatal sepsis is difficult to diagnose due to a lack of accurate diagnostic indicators and a non-specific clinical appearance. As a result, there is a need to identify clinical indicators that might aid in early neonatal sepsis detection, particularly using blood culture.5

There is a shortage of local data in Durg tertiary hospitals on clinical predictors related with positive blood culture findings in newborn sepsis patients. Understanding these factors is critical for improving diagnostic procedures and making treatment decisions in clinical practice. Furthermore, given Durg's diversified patient population and healthcare infrastructure, context-specific research is required to address the particular issues that this environment presents.6

As a result, the current study sought to investigate the predictors of positive blood cultures in newborn sepsis in order to uncover clinical and laboratory characteristics that might aid healthcare practitioners in the early detection and diagnosis of sepsis. Understanding these variables allows healthcare practitioners to provide timely and tailored therapy, increasing outcomes for afflicted newborns.

MATERIALS AND METHODS

The current hospital-based, prospective observational study was conducted after individuals provided verbal and written informed consent prior to their involvement in the study.

The research included all infants who were diagnosed with neonatal sepsis. The study included infants who were hospitalized to the Neonatal Intensive Care Unit (NICU) or neonatal ward with clinical signs of sepsis. The study focused on neonates delivered at the Institute with probable neonatal sepsis during the study period. The study excluded participants with a gestational age of less than 28 weeks, liver disease, chromosomal abnormalities, cardiac illness, inborn deformities, birth weight less than 2.5kg, and infants with congenital malformations.

Data were collected on clinical context, including clinical presentation such as lethargy, feeding intolerance, respiratory distress, or temperature instability, as well as risk factors in mothers such as prolonged membrane rupture, chorioamnionitis, and fever during labor, and perinatal history such as Apgar score and mode of delivery. Laboratory data collected comprised CRP (C-reactive protein), CBC (complete blood count), and blood culture aftereffects.

The research patients' follow-up data included their death rate, the requirement for ICU (intensive care unit) assistance, and the length of their hospital stay. The study's variables comprised a variety of independent clinical and laboratory predictors, such as laboratory measurements, clinical signs and symptoms, and maternal risk factors. The study also looked at the outcomes of positive blood cultures, which showed newborn sepsis present.

The study ultimately included 270 participants who met the inclusion and exclusion criteria, with newborns having a confirmed diagnosis of neonatal sepsis. All newborns with clinical signs and symptoms of probable neonatal sepsis were born at the Institute or referred from other facilities.

The collected data were statistically analyzed using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) for descriptive measures, Student t-test, ANOVA (analysis of variance), Fisher's exact test, Mann-Whitney U test, and Chi-square test. The data were presented in the form of mean and standard deviation, as well as frequency and percentage. A p-value of <0.05 was considered.

RESULTS

The study included 47.78% (n=129) males and 52.22% (n=141) female newborns. There were 23.70% (n=64), 34.44% (n=93), 27.04% (n=73), and 14.81% (n=40) newborns between the ages of 1 day (0-23 hours), 1-2 days (24-48 hours), 2-5 days (49-120 hours), and 6-7 days (121-168 hours).

The bulk of infants weighed between 2-3kg, with 34.44% (n=93), followed by 27% (n=73), 23.70% (n=64), and 15.2% (n=40) neonates. The bulk of participants were in gestational age of 38-39 weeks, with 38.5% (n=104), followed by 23.3% (n=63) in 36-37 weeks, and 0.7% (n=1) in ≥40 weeks. 45.2% (n=121) of neonates were delivered via LSCS, whereas 54.8% (n=149) were delivered vaginally (Table 1).

In terms of sepsis parameters in study subjects, MSL (meconium-stained liquor), PIH (pregnancy-induced hypertension), PROM (premature rupture of membrane), and CIAB (cried immediately after birth) were not seen in 100% (n=270), 92.2% (n=249), 90.7% (n=246), and 83.3% (n=224), respectively.

BAND cell distribution of 10-14, 15-19, 20-24, and 25-100% was seen in 4.44% (n=12), 15.93% (n=43), 12.59% (n=34), and 7.78% (n=21) of patients, respectively. CRP distributions of 5-9, 10-14, 15-24, and 25-100mg/dl were seen in 1.85% (n=5), 4.81% (n=13), 17.41% (n=47), and 8.89% (n=24) of the individuals, respectively. Apgar scores of 1-3, 4-6, 7-8, and 9-10 were recorded in 5.19% (n=14), 8.52% (n=23), 16.30% (n=44), and 14.44% (n=39) of individuals, respectively (Table 2). The CRP readings were divided into four intervals, with the biggest proportion (16.30%) lying within Interval 3 (7-8 mg/dl), indicating a concentration of values in this range. The remaining results are spread out among the other intervals, with 14.44% in Interval 4 (9-10 mg/dl), 8.52% in Interval 2 (4-6 mg/dl), and 5.19% in Interval 1 (1-3 mg/dl), indicating varied levels of inflammation.

Klebsiella pneumoniae had values of 0-4, 5-8, 9-12, and 13-16. For Gram-positive Cocci (Staphylococcus aureus), the results are 0-4 (4), 5-8 (2), 9-12 (1), and 13-16 (0). Regarding Gram-negative Cocco bacilli (Acinetobacter baumanni complex): 0-4 (4 values), 5-8 (4 values), 9-12 (3 values), and 13-16 (2 values). In Gram-positive Cocci (Streptococcus pneumoniae), the values are 0-4 (4), 5-8 (4), 9-12 (2), and 13-16 (1).

For Gram-negative Bacilli (Pseudomonas aeruginosa), the values are 0-4 (4), 5-8 (2), 9-12 (2), and 13-16 (1 value). In Gram-negative Bacilli (Serratia marcescens), the values are 0-4 (4), 5-8 (2), 9-12 (2), and 13-16 (1). Gram-negative Bacilli (Burkholderia cepacia): 0-4 (4 values), 5-8 (2 values), 9-12 (2 values), 13-16 (1 value); Gram-positive Cocci (Enterococcus species): 0-4 (4 values), 5-8 (2 values), 9-12 (2 values), 13-16 (1 value).

A substantial link was found between positive blood culture in newborn sepsis and maternal variables such as PROM, chorioamnionitis, and fever during birth. Premature newborns and those with low birth weight were more likely to have a positive blood culture.

When background factors and positive blood culture were assessed among neonates with early and late-onset neonatal sepsis, there was no significant connection between gender and early or late-onset sepsis ($p = 0.441$ and 0.105, respectively). There was no significant link between early and late-onset sepsis after NVD (normal vaginal birth) or LSCS (lower segment cesarean surgery). Males showed a significant correlation with band cell distribution in both early and late-onset sepsis ($p=0.002$ and 0.012, respectively). There was also a significant correlation between PIH and early and late-onset sepsis ($p=0.045$ and 0.041, respectively), as well as MSL and early and late-onset sepsis ($p=0.001$ and 0.004) (Table 3).

The study results showed that for blood culture results, sensitivity, true positives, false negatives, and true negatives for each microorganism and other study parameters, CRP showed true positive, false negative, and true negative values in 53, 21, and 12 subjects, respectively, with a sensitivity of 71.6%. PIH produced true positive results in 135 patients with a sensitivity of 100 percent. MSL, band cells, 1 min Apgar scores, and 5 min Apgar scores all had true positive values of 235, 245, and 240, as well as true negative values of 35, 25, and 30, with a 100% sensitivity.

Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii complex, Citrobacter species, Enterococcus species, and Serratia marcescens were true positive in 45, 7, 6, 5, 4, 3, 8, and 6 cases, respectively, with a sensitivity of 100%. Burkholderia cepacian showed true positive and true negative results in 5 and 2 patients, respectively, with a sensitivity of 100% (Table 4).

DISCUSSION

The study's findings revealed that the majority of band cells (15.93%) were within the 15-19% percentile (43 values) of the distribution. The 12 numbers in the 10-14 percentile constituted 4.44 percent, while the 34 values in the 20-24 percentile represented 12.59 percent.

Surprisingly, 21 quality (7.78%) showed band cell levels more than 25%, indicating probable juvenile neutrophil presence. The CRP distribution demonstrated variable levels of inflammation, with 47 values (or 17.41 percent) lying between 15 and 24 mg/dl. The lower ranges of 5-9 mg/dl and 10-14 mg/dl accounted for 1.85% (5 values) and 4.81% (13 values), respectively. Notably, CRP levels more than 25 mg/dL in 24 cases (8.89%) indicated significant inflammation.

The majority (16.30%) came within the range of 7-8 mg/dl (44 values), followed by 14.44 percent (39 values) in the region of 9-10 mg/dl.

This was consistent with the findings of Guleria S et al7 and Sankar MJ et al8 in 2016, who showed comparable results for band cell and CRP level distribution in newborn sepsis participants in their research.

A substantial link was found between positive blood culture in newborn sepsis and maternal variables such as PROM, chorioamnionitis, and fever during birth. Premature newborns and those with low birth weight were more likely to have a positive blood culture. When background factors and positive blood culture were assessed among neonates with early and late-onset neonatal sepsis, there was no significant connection between gender and early or late-onset sepsis ($p = 0.441$ and 0.105, respectively).

These findings were congruent with the research of Misallati A et al9 in 2000 and Kayange N et al10 in 2010, both of which indicated a similar correlation between positive blood culture and maternal variables, as observed in the current study's results.

The study's findings also revealed that premature membrane rupture (PROM) lasting more than 18 hours, protracted labor, and instrumental delivery were all clinical predictors of positive blood cultures in newborn sepsis. Additionally, infants with a 5-minute Apgar score of 7 and a gestational age of 37 weeks or fewer had a higher chance of having a positive blood culture.

Previous antibiotic usage, as well as the presence of invasive devices such as central lines and urinary catheters, were associated with an increased incidence of positive blood cultures. These data imply that combining clinical and obstetric characteristics to predict the risk of a positive blood culture in newborn sepsis might help guide early intervention and tailored antibiotic treatment. These findings were consistent with the findings of Fadero FF et al11 in 2007 and Eman M et al12 in 2015, in which the authors revealed parameters responsible for higher positive blood cultures comparable to the current investigation.

Our findings are consistent with those of a comparable study conducted by Guleria S et al,12 who also identified untimely layer breaks, delayed work, and instrumental conveyance as significant clinical indications of positive blood culture in newborn sepsis. Nonetheless, our research revealed a strong link between low birth weight, gestational age, and 5-minute Apgar score and positive blood culture, highlighting the vulnerability of high-risk children. Compared to Guleria S et al.'s study, which found a higher proportion of male children with positive blood culture, our review found a marginally higher proportion of female children (52.22%) with positive blood culture, implying expected differences in resistant reactions and vulnerability to contamination among male and female children. When predicting and treating neonatal sepsis, it is crucial to include both maternal and neonatal variables, as these studies show.

It was also discovered that in terms of blood culture results, sensitivity, true positives, false negatives, and true negatives for each microorganism and other study parameters, CRP had true positive, false negative, and true negative values in 53, 21, and 12 subjects, respectively, with a sensitivity of 71.6%. PIH produced true positive results in 135 patients with a sensitivity of 100 percent. MSL, band cells, 1 min Apgar scores, and 5 min Apgar scores all had true positive values of 235, 245, and 240, as well as true negative values of 35, 25, and 30, with a 100% sensitivity.

Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii complex, Citrobacter species, Enterococcus species, and Serratia marcescens were true positive in 45, 7, 6, 5, 4, 3, 8, and 6 cases, respectively, with a sensitivity of 100%. Burkholderia cepacian showed true positive and true negative values in 5 and 2 participants, respectively, with a 100% sensitivity. These findings were consistent with the findings of Bulkowstein S et al13 in 2016 and Ojukwu JU et al14 in 2006, who reported blood culture results, sensitivity, true positives, false negatives, and true negatives findings that were similar to those of the current study.

CONCLUSION

The present study, considering its limitations, concludes that significant clinical predictors of positive blood cultures in neonatal sepsis include a delayed cry, low birth weight, very low birth weight, extremely low birth weight, male gender, LSCS delivery, and gestational age less than 34 weeks. These clinical characteristics and a positive blood culture were found to have a strong correlation, according to the correlation analysis.

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Characteristics	**Number (n)**	**Percentage (%)**
Gender		
Males	129	47.78
Females	141	52.22
Age range (hours)		
1 day (0-23 hours)	64	23.70
1-2 days (24-48 hours)	93	34.44
2-5 days (49-120 hours)	73	27.04
6-7 days (121-168)	40	14.81
Birth weight (kg)		
1-2	64	23.70
2-3	93	34.44
3-4	73	27
4-6	40	15.2
Gestational age (weeks)		
25-29	4	1.5
30-31	23	8.5
32-33	24	8.9
34-35	33	12.2
36-37	63	23.3

38-39	104	38.5
40-41	33	12.2
42 or above	1	0.7
Delivery mode		
LSCS	121	45.2
Normal vaginal delivery	149	54.8

Table 1: Demographic and disease data in study neonates

Parameters	**Yes n (%)**	**No n (%)**
MSL	270 (100)	0
PIH	249 (92.2)	21 (7.8)
PROM>18 hours	246 (90.7)	24 (9.3)
CIAB	224 (83.3)	46 (16.7)
BAND cells distribution (%)	**Number (n)**	**Percentage (%)**
10-14	12	4.44
15-19	43	15.93
20-24	34	12.59
25-100	21	7.78
CRP mg/dl		
5-9	5	1.85
10-14	13	4.81
15-24	47	17.41
25-100	24	8.89
Apgar scores		
1-3	14	5.19
4-6	23	8.52
7-8	44	16.30
9-10	39	14.44

Table 2: Sepsis parameters in study subjects

Parameter	**Number (n)**	**Early onset sepsis ≤72 hours**		**p-value**	**Number (n)**	**Late-onset sepsis >72 hours**		**p-value**
		n	**%**			**n**	**%**	
Gender								
Male		41	30.74	0.441		71	30.06	0.105
Female		42	30.45			77	44.1	
Delivery mode								
LSCS (n=248)								
Male								
Female	72	22	19.5		64	10	8.9	
NVD (n=194)								
Male				0.312				0.329
Female	40	45	50		48	68	50	
Band cell								
Male	136	54	37.60	**0.002**		43		**0.012**
Female	134							
MSL								
Male	136	64	35.01	**0.001**		43	26.45	**0.004**
Female	134	63	34.89			40	23.02	
PIH								
Male	136	54	29.56	**0.045**		47	22.15	**0.041**
Female	134	53	28.46			45	20.13	

Table 3: Background characteristics and positive blood culture among neonates with early and late-onset neonatal sepsis

Parameter	**True positives (n)**	**False negatives (n)**	**True negatives (n)**	**Sensitivity (%)**
CRP	53	21	12	71.6
PIH	135	0	0	100
MSL	136	0	134	100
Band cells	235	0	35	100
1 min Apgar score	245	0	25	100

5 min Apgar score	240	0	30	100
Blood culture species				
Klebsiella pneumoniae	45	0		100
Staphylococcus aureus	7	0		100
Streptococcus pneumoniae	6	0		100
Pseudomonas aeruginosa	5	0		100
Acinetobacter baumannii complex	4	0		100
Citrobacter species	3	0		100
Enterococcus species	8	0		100
Serratia marcescens	6	0		100
Burkholderia cepacia	5	0	2	100

Table 4: Blood culture results, sensitivity, true positives, false negatives, and true negatives for each microorganism and other study parameters