Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

ANALYSING THE BLOOD CULTURE IN NEONATAL SEPSIS BY EXAMINING THE PREDICTORS OF POSITIVE BLOOD CULTURE – AN OBSERVATIONAL STUDY

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How to cite: Bhattacharya A, Chatterjee N. Analysing the blood culture in neonatal sepsis by examining the predictors of positive blood culture – an observational study. International Research Journal of Pharmacy; 2023,14:6:35-41.

Doi:10.56802/2230-8407.1303602

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ABSTRACT

Background: Due to non-specific clinical presentation and a lack of trustworthy diagnostic markers, diagnosing neonatal sepsis is extremely difficult. Therefore, it is necessary to find clinical predictors that can aid in the early detection of neonatal sepsis, particularly through the use of blood culture.

Aim: The goal of the current study was to determine clinical and laboratory factors that can aid medical professionals in the early detection and diagnosis of sepsis by examining the predictors of positive blood culture in neonatal sepsis. Healthcare providers can improve outcomes for impacted infants by initiating timely and focused treatment by knowing these predictors.

Methods: After adhering to the inclusion and exclusion criteria, 270 neonates with a confirmed diagnosis of neonatal sepsis were included in the study. CRP (C-reactive protein), CBC (complete blood count), and blood culture aftereffects were among the laboratory data collected. The mortality rate, length of hospital stay, and need for support in the intensive care unit (ICU) were among the follow-up data collected from research participants. Maternal risk factors, clinical signs and symptoms, and laboratory parameters were among the independent variables evaluated in the study as clinical and laboratory predictors. The results of positive blood cultures, which demonstrated the presence of confirmed neonatal sepsis, were also evaluated.

Results: Maternal factors like PROM, chorioamnionitis, and fever during labor were found to be significantly associated with positive blood cultures in neonatal sepsis. Low birth weight and premature babies were found to have a higher risk of positive blood cultures. Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus, and Streptococcus pneumoniae are blood culture species. complex, Citrobacter species, Enterococcus species, and Serratia marcescens demonstrated 100% sensitivity and true positive values in 45, 7, 6, 5, 4, 3, 8, and 6 cases. With a sensitivity of 100%, true positive and true negative values for Burkholderia cepacian were observed in five and two subjects, respectively.

Conclusion: The current study concludes that delayed crying, low birth weight, very low birth weight, extremely low birth weight, male gender, LSCS delivery, and gestational age less than 34 weeks are important clinical predictors of positive blood cultures in neonatal sepsis. The correlation analysis revealed a strong relationship 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), septicemia is a common cause of infant mortality and morbidity. Approximately 5 million neonatal deaths are reported annually, with almost all of these deaths occurring in developing countries like India. The WHO has established criteria for the initial diagnosis of neonatal sepsis; however, the clinical

diagnosis's specificity and sensitivity differ. In order to avoid complications and septicemia-related death, early diagnosis and timely treatment are essential. Neonates have a blood culture-positive rate of 25–54 percent. While a number of rapid immunological techniques, such as the CRP (C-reactive proteins) assay, can aid in the diagnosis of septicemia, many centers in developing countries lack the ability to assess particular pathogens.[1]

The gold standard for a definitive and confirmed diagnosis of septicemia is blood culture for isolation of offending pathogens; however, results from blood culture may not be reported for hours or days, so empirical therapy must be started in suspected cases. Understanding common pathogens' antimicrobial susceptibility patterns and predictors of positive blood cultures is essential for directing local empirical antibiotic selection.[2]

Respiratory distress, poor feeding, fatigue, temperature instability, and many other clinical factors are favorable to sepsis. Nevertheless, the signs and symptoms are not unique to sepsis. Congenital heart conditions, inborn metabolic errors, and hypoglycemia also exhibit similar patterns. However, when sepsis is suspected, complete blood counts, ESR, CRP, CSF culture, and blood culture must be evaluated.[3]

There are two types of sepsis: early and late onset. Late-onset sepsis was brought on by bacterial pathogens from the surrounding environment in the Neonatal Intensive Care Unit (NICU) after 72 hours and up to 90-120 days, while early-onset sepsis was caused by bacterial contamination from female genitourinary framework infants within 72 hours of birth. Using aminoglycosides and ampicillin in cases of early-onset sepsis and aminoglycosides and ampicillin in cases of late-onset sepsis, empirical management with the appropriate antibiotics must be started until results are obtained, depending on local antibiotic-resistant patterns.4

Though their specificity and sensitivity are still low, clinical traits like physical signs and symptoms can be trustworthy indicators of a positive blood culture. Due to non-specific clinical presentation and a lack of trustworthy diagnostic markers, diagnosing neonatal sepsis is extremely difficult. Therefore, it is necessary to find clinical predictors that can aid in the early detection of neonatal sepsis, particularly through the use of blood culture.5

In order to find clinical and laboratory factors that can aid medical professionals in the early detection and diagnosis of sepsis, the current study set out to investigate the predictors of positive blood culture in neonatal sepsis. By understanding these predictors, healthcare professionals can initiate prompt and targeted treatment, improving outcomes for affected infants.

MATERIALS AND METHODS

The present hospital-based, prospective observational study was done in the Department of Microbiology of the institute. Verbal and written informed consent were taken from all the subjects before participation in the study. Healthcare providers can improve the outcomes for impacted infants by starting timely and focused treatment by knowing these predictors.

Every newborn with a diagnosis of neonatal sepsis was included in the study. Neonates admitted to the Neonatal Intensive Care Unit (NICU) or neonatal ward with suspected sepsis based on clinical presentation met the study's inclusion criteria. Neonates born at the Institute who were suspected of having neonatal sepsis during the study period were specifically included in the study. Subjects with gestational age less than 28 weeks, liver disease, chromosomal abnormalities, coronary disease, inborn deformities, birth weight less than 2.5 kg, and neonates with congenital anomalies were all excluded from the study.

Clinical context information was collected, including information on clinical presentation such as lethargy, feeding intolerance, respiratory distress, or temperature instability; risk factors in mothers, such as prolonged membrane rupture, chorioamnionitis, and fever during labor; and perinatal history, such as Apgar score and delivery method. CRP (C-reactive protein), CBC (complete blood count), and blood culture aftereffects were among the laboratory data collected. The mortality rate, length of hospital stay, and need for support in the intensive care unit (ICU) were among the follow-up data collected from research participants. Laboratory parameters, clinical signs and symptoms, and maternal risk factors were among the independent variables evaluated in the study as clinical and laboratory predictors. The results of positive blood cultures, which demonstrated the presence of confirmed neonatal sepsis, were also evaluated.

Following the inclusion and exclusion criteria, 270 neonates with a confirmed diagnosis of neonatal sepsis were included in the study. Every newborn exhibiting clinical signs and symptoms of suspected neonatal sepsis was either born at the Institute or was referred from another facility.

Using SPSS (Statistical Package for the Social Sciences) software, the collected data was statistically analyzed using the Student t-test, ANOVA (analysis of variance), Fisher's exact test, Mann-Whitney U test, Chi-square test, and assessment

of descriptive measures. The mean, standard deviation, frequency, and percentages were used to express the results. A p-value of less than 0.05 was taken into account.

RESULTS

There were 47.78% (n=129) male neonates and 52.22% (n=141) female neonates in the study. Neonates aged 1 day (0-23 hours), 1-2 days (24-48 hours), 2-5 days (49-120 hours), and 6-7 days (121-168) comprised 23.70% (n=64), 34.44% (n=93), 27.04% (n=73), and 14.81% (n=40). 34.44% (n=93) of the neonates were in the 2-3 kg weight range, followed by 27% (n=73), 23.70% (n=64), and 15.2% (n=40), in that order. 38.5% (n=104) of the subjects were in the 38–39 week gestational age range, followed by 23.3% (n=63) in the 36–37 week range and 0.7% (n=1) in the ≥40 week range. 54.8% (n=149) of newborns were delivered vaginally, while 45.2% (n=121) were delivered via LSCS (Table 1).

MSL (meconium-stained liquor), PIH (pregnancy-induced hypertension), PROM (premature rupture of membrane), and CIAB (cried immediately after birth) were not observed in 100% (n=270), 92.2% (n=249), 90.7% (n=246), and 83.3% (n=224) of the study participants, respectively. 4.44% (n=12), 15.93% (n=43), 12.59% (n=34), and 7.78% (n=21) of the subjects had BAND cell distributions of 10-14, 15-19, 20-24, and 25-100%, respectively. 1.85% (n=5), 4.81% (n=13), 17.41% (n=47), and 8.89% (n=24) of the subjects had CRP levels in the ranges of 5-9, 10-14, 15-24, and 25-100 mg/dl, respectively. 5.19% (n=14), 8.52% (n=23), 16.30% (n=44), and 14.44% (n=39) of the subjects had an Apgar score of 1-3, 4-6, 7-8, and 9-10, respectively (Table 2). The highest percentage of CRP values (16.30%) fell within Interval 3 (7-8 mg/dl), suggesting a concentration of values in this range. CRP values were distributed across four intervals.

The remaining values, which indicate varying degrees of inflammation, are dispersed throughout the other intervals: 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). The gram-negative bacteria Klebsiella pneumoniae, 0–4, 5–8, 9–12, and 13–16 were found in 4, 7, 6, and 5 values, respectively. 0–4 (4 values), 5–8 (2 values), 9–12 (1 value), and 13–16 (0 values) for Gram-positive cocci (Staphylococcus aureus). Gram-negative Cocco bacilli (Acinetobacter baumanni complex): 0–4 (4 values), 5–8 (4 values), 9–12 (3 values), and 13–16 (2 values). 0–4 (4 values), 5–8 (4 values), 9–12 (2 values), and 13–16 (1 value) in Gram-positive Cocci (Streptococcus pneumoniae).

0-4 (4 values), 5-8 (2 values), 9-12 (2 values), and 13-16 (1 value) for Gram-negative Bacilli (Pseudomonas aeruginosa). 0–4 (4 values), 5–8 (2 values), 9–12 (2 values), and 13–16 (1 value) in Gram-negative Bacilli (Serratia marcescens). There were 0-4 (4 values), 5-8 (2 values), 9-12 (2 values), and 13-16 (1 value) for Gram-negative Bacilli (Burkholderia cepacia) and 0-4 (4 values), 5-8 (2 values), 9-12 (2 values), and 13-16 (1 value) for Gram-positive Cocci (Enterococcus species).

Maternal characteristics like PROM, chorioamnionitis, and fever during labor were found to be significantly correlated with positive blood cultures in neonatal sepsis. Low birth weight and premature babies were found to have a higher risk of positive blood cultures.

Gender did not significantly correlate with either early-onset or late-onset neonatal sepsis (p=0.441 and 0.105, respectively) when background characteristics and positive blood cultures were evaluated. Early and late-onset sepsis did not significantly correlate with NVD (normal vaginal delivery) or LSCS (lower segment cesarean section). Males with early-onset sepsis and late-onset sepsis showed a significant correlation with band cell distribution (p=0.002 and 0.012, respectively). Additionally, there was a significant correlation between MSL and early and late-onset sepsis (p=0.001 and 0.004, respectively) and PIH and early and late-onset sepsis (p=0.045 and 0.041) (Table 3).

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

With a sensitivity of 100%, the blood culture species Klebsiella pneumoniae, Staphylococcus aureus, streptococcus pneumoniae, Citrobacter species, Enterococcus species, and Serratia marcescens demonstrated true positive values in 45, 7, 6, 5, 4, 3, 8, and 6. With a sensitivity of 100%, true positive and true negative values in Burkholderia cepacian were observed in five and two subjects, respectively (Table 4).

DISCUSSION

The majority of band cells (15.93 percent) fell within the 15–19% percentile (43 values) of distribution, according to discussion study results. The 34 values in the 20–24 percentile represented 12.59 percent, whereas the 12 values in the 10–14 percentile represented 4.44 percent. Remarkably, 21 qualities (7.78%) had band cell levels higher than 25%, suggesting the presence of juvenile neutrophils. Different levels of inflammation were evident in the CRP distribution,

with 47 values (17.41 percent) falling between 15 and 24 mg/dl. 1.85% of values (5 values) and 4.81 percent of values (13 values) were attributed to the lower ranges of 5-9 mg/dl and 10-14 mg/dl, respectively.

Interestingly, 24 values (8.89 percent) with CRP levels greater than 25 mg/dl indicated severe inflammation. The majority, 16.30 percent, were in the 7–8 mg/dl range (44 values), while 14.44 percent (39 values) were in the 9–10 mg/dl range. This was comparable to the findings of Guleria S et al.7 in 2020 and Sankar MJ et al.8 in 2016, who found that the distribution of band cell and CRP levels in neonatal sepsis subjects was similar.

Maternal characteristics like PROM, chorioamnionitis, and fever during labor were found to be significantly correlated with positive blood cultures in neonatal sepsis. Low birth weight and premature babies were found to have a higher risk of positive blood cultures.

Gender did not significantly correlate with either early-onset or late-onset neonatal sepsis (p=0.441 and 0.105, respectively) when background characteristics and positive blood cultures were evaluated in neonates with early and late-onset neonatal sepsis. These results were in line with research by Misallati A et al. (2000) and Kayange N et al. (2010), which found a similar correlation between maternal factors and positive blood culture. The study's findings also revealed that prolonged labor, instrumental delivery, and premature membrane rupture (PROM) lasting longer than eighteen hours were all clinical indicators of positive blood cultures in neonatal sepsis.

Additionally, a positive blood culture was more common in neonates with a 5-minute Apgar score of 7 and a gestational age of 37 weeks or less. Additionally, prior antibiotic use and the use of invasive devices such as urinary catheters and central lines were associated with an increased risk of positive blood cultures. These results imply that by combining clinical and obstetric factors to predict the probability of a positive blood culture in neonatal sepsis, early intervention and targeted antibiotic therapy can be guided. These results were consistent with the findings of Fadero FF et al.11 in 2007 and Eman M et al.12 in 2015, where the authors also reported factors that contributed to an increase in positive blood cultures.

Our study's findings are consistent with those of a related study conducted by Guleria S et al.12, which also identified instrumental conveyance, delayed work, and premature layer break as significant clinical markers of positive blood culture in neonatal sepsis. However, our focus also revealed a significant correlation between low birth weight, gestational age, and 5-minute Apgar score with positive blood culture, highlighting the vulnerability of children at high risk.

Our review revealed a slightly higher percentage of female children (52.22%) with positive blood cultures than Guleria S et al.'s study, which found a higher percentage of male children with positive blood cultures. This suggests that there are expected differences between male and female children in terms of resistant reactions and weakness to contamination. When anticipating and managing neonatal sepsis, Together, these results show how important it is to consider both obstetric and neonatal factors.

Additionally, it was observed that CRP demonstrated true positive, false negative, and true negative values in 53, 21, and 12 subjects, respectively, with a sensitivity of 71.6%, with regard to blood culture results, sensitivity, true positives, false negatives, and true negatives for each microorganism and other study parameters. With a 100% sensitivity, PIH produced true positive results in 135 subjects. With sensitivity of 100%, MSL, band cells, 1 minute Apgar scores, and 5 minute Apgar scores had true positive values of 235, 245, and 240 and true negative values of 35, 25, and 30, respectively.

Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus, and Streptococcus pneumoniae are blood culture species. complex, Citrobacter species, Enterococcus species, and Serratia marcescens demonstrated 100% sensitivity and true positive values in 45, 7, 6, 5, 4, 3, 8, and 6 cases. With a sensitivity of 100%, true positive and true negative values in Burkholderia cepacian were observed in five and two subjects, respectively. These findings were consistent with those of Bulkowstein S et al. (2016) and Ojukwu JU et al. (2006), who reported blood culture results, sensitivity, true positives, false negatives, and true negatives.

CONCLUSION

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 are important clinical predictors of positive blood cultures in neonatal sepsis. The correlation analysis revealed a strong relationship between these clinical features and a positive blood culture. Because they highlight the importance of considering these clinical predictors and correlations when diagnosing and treating neonatal sepsis, the study's findings are instructive for medical professionals and will ultimately improve outcomes for these susceptible patients.

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S. No	Characteristics	Number (n)	Percentage (%)
1.	**Gender**		
a)	Males	129	47.78
b)	Females	141	52.22
2.	**Age range (hours)**		
a)	1 day (0-23 hours)	64	23.70
b)	1-2 days (24-48 hours)	93	34.44
c)	2-5 days (49-120 hours)	73	27.04
d)	6-7 days (121-168)	40	14.81
3.	**Birth weight (kg)**		
a)	1-2	64	23.70
b)	2-3	93	34.44
c)	3-4	73	27
d)	4-6	40	15.2
4.	**Gestational age (weeks)**		
a)	25-29	4	1.5
b)	30-31	23	8.5

c)	32-33	24	8.9
d)	34-35	33	12.2
e)	36-37	63	23.3
f)	38-39	104	38.5
g)	40-41	33	12.2
h)	42 or above	1	0.7
5.	**Delivery mode**		
a)	LSCS	121	45.2
b)	Normal vaginal delivery	149	54.8

Table 1: Demographic and disease data in study neonates

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

Table 2: Sepsis parameters in study subjects

S. No	**Parameter**	**Number (n)**	**Early onset sepsis ≤72 hours**		**p-value**	**Number (n)**	**Late-onset sepsis >72 hours**		**p-value**
			n	**%**			**n**	**%**	
1.	**Gender**								
a)	Male		41	30.74	0.441		71	30.06	0.105
b)	Female		42	30.45			77	44.1	
2.	**Delivery mode**								
a)	LSCS (n=248)								
i.	Male								
ii.	Female	72	22	19.5		64	10	8.9	
b)	NVD (n=194)								
i.	Male				0.312				0.329
ii.	Female	40	45	50		48	68	50	
3.	**Band cell**								
a)	Male	136	54	37.60	**0.002**		43		**0.012**
b)	Female	134							
4.	**MSL**								
a)	Male	136	64	35.01	**0.001**		43	26.45	**0.004**
b)	Female	134	63	34.89			40	23.02	
5.	**PIH**								
a)	Male	136	54	29.56	**0.045**		47	22.15	**0.041**
b)	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

S. No	Parameter	True positives (n)	False negatives (n)	True negatives (n)	Sensitivity (%)
1.	**CRP**	53	21	12	71.6
2.	**PIH**	135	0	0	100
3.	**MSL**	136	0	134	100
4.	**Band cells**	235	0	35	100
5.	**1 min Apgar score**	245	0	25	100
6.	**5 min Apgar score**	240	0	30	100
7.	**Blood culture species**				
a)	Klebsiella pneumoniae	45	0		100
b)	Staphylococcus aureus	7	0		100
c)	Streptococcus pneumoniae	6	0		100
d)	Pseudomonas aeruginosa	5	0		100
e)	Acinetobacter baumannii complex	4	0		100
f)	Citrobacter species	3	0		100
g)	Enterococcus species	8	0		100
h)	Serratia marcescens	6	0		100
i)	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