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Diagonostic Accuracy of Umbilical Cord Blood Culture Versus Peripheral Venous Blood Culture in Newborn Babies with High Risk Factors for Neonatal Sepsis - A Cross-Sectional Study

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KEYWORDS

Neonatal Sepsis, PVBC, and UCBC

ABSTRACT:

Introduction: The gold standard investigation for diagnosing NS is the culture of peripheral venous blood. Though not used routinely blood samples collected from the umbilical cord are a non-invasive and painless technique not require any special skill.

Aim: To compare the diagnostic accuracy of umbilical cord blood culture and peripheral venous blood culture in newborn babies with high-risk factors for neonatal sepsis. Objective -To assess the diagnostic accuracy of umbilical cord blood culture versus peripheral venous blood culture concerning specificity, sensitivity, negative predictive value, and positive predictive value.

Materials and Method- It was a Cross-sectional study, done in a Tertiary Care Hospital of Central India from January 2021 to December 2023. 100 newborn babies with high risk factors for neonatal sepsis were included and babies with life-threatening congenital anomalies and those born outside the study setting were excluded. Under all aseptic precautions, umbilical cord blood and peripheral venous blood were collected and it was sent to the laboratory immediately for culture and detection of micro-organisms. Appropriate statistical tests were applied.

Results: Of the 100 neonates included in our study, UCBC showed growth in 24% of cases, whereas PVBC showed high positivity with growth in 67% of the cases. The positive predictive value for UCBC was 58.33%, compared to 40.30% for PVBC. PVBC had a negative predictive value of 87.88%, compared to 77.63 % in UCBC. Accuracy was better in UCBC (76%) than in PVBC (56%).

Conclusion: PVBC had high sensitivity, in contrast to UCBC, which had a sensitivity. On the other hand, UCBC had high specificity compared to PVBC. UCBC had a better positive predictive value compared to PVBC, while the latter had a better negative predictive value. Accuracy was better in UCBC compared to PVBC.

1. INTRODUCTION

Neonatal mortality is a pertinent public health plight throughout the globe and more so in the developing nations. (1) Though the rate at which neonatal sepsis (NS) occurs has decreased in the past few years, it still remains the notable reason of morbidity and mortality among new-born particularly in resource limited countries like India. (2) As per a study, incidence of NS was found to be 19 /1000 live births in India in 2016 to 2019. (3)

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The clinical picture of NS may range from mild and self-limiting subclinical infection to life threatening severe focal/systemic disease. (5) Neonatal sepsis based on latency of time of presentation after childbirth is categorized as either early or late onset sepsis. Early onset sepsis (EOS) includes cases presenting as sepsis within 72 hours after birth and the infecting pathogen may originate from intrauterine/vaginal maternal floras ally due to vertical transmission of pathogen from the vaginal environment after rupture of membranes. Infection can also be due to transplacental transmission. Late onset sepsis (LOS) refers to sepsis occurring 3 days after the childbirth of and source in this case is usually the environmental exposure to pathogen in hospital setting (Horizontal transmission). (2,4,6,7)

Clinical features of neonatal sepsis can have a wide range from very general and nonspecific symptoms to hemodynamic collapse. Symptoms like irritability, excessive crying, lethargy and poor feeding or refusal to feed can appear first in some neonates while others may rapidly land up into respiratory distress or develop fever, hypothermia, decrease in blood pressure with poor perfusion and shock like state. (2,4,5)

The diagnosis of NS depends upon clinical as well as lab parameters. History-taking helps evaluating the high-risk factors for sepsis in the new- born and in the mother. There is a strong correlation between occurrence of sepsis and factors like prematurity and low birthweight. High degree of suspicion is necessary for diagnosis of sepsis based on history and Some laboratory findings like hyperglycemia or hypoglycemia, acidosis, or hyperbilirubinemia. (2,4) Laboratory testing therefore plays a crucial role in early diagnosis of sepsis and for the favorable outcome of the neonate. If sepsis is suspected in neonate, blood culture should be drawn on immediate basis. Recommendation is to draw a minimum 1 ml of blood sample as small sample volumes may miss low level of bacteremia. (2,8)

The gold standard investigation for diagnosing NS is the culture report of peripheral venous blood but still there is variability in sensitivity for the diagnosis of neonatal EOS owing to the imprecise volume of collected venous blood sample, use of intrapartum antibiotics, and use of antibiotics in neonates before the sample is withdrawn. (8,9,10)

Though being not used routinely blood sample collected from the umbilical cord is non-invasive and painless technique not requiring any special skill. The entire evaluation of EOS can then be performed in the delivery or labor room and the culture results can be procured and interpreted before any clinical signs and symptoms of EOS develop, thus allowing timely initiation of treatment. (9,11)

This objective of the study was to evaluate diagnostic accuracy of umbilical cord blood culture and compare it with that of peripheral venous blood culture in newborn babies with high risk factors for NS.

2. AIM- To compare the diagnostic accuracy of umbilical cord blood culture and peripheral venous blood culture in newborn babies with high risk factors for neonatal-sepsis.

Objective- To assess the diagnostic accuracy of umbilical cord blood culture

versus peripheral venous blood culture in newborn babies with high risk factors for neonatal sepsis with respect to specificity, sensitivity, negative predictive value and positive predictive value.

Materials and Method

It was a cross-sectional study carried out in a tertiary care hospital of Central India from January 2021 to December 2023. A total of 100 neonates with high risk factors for neonatal sepsis were selected by convenient sampling method. The study was carried out after approval from institutional ethics committee and informed consent from parents

Inclusion criteria: All newborn babies with high risk factors for neonatal sepsis

Exclusion Criteria: Newborn babies with life-threatening congenital anomalies, Neonates born outside the study setting

Sample size Calculation was done from a previous study by CD Aundhakar et a. (17) The sample size was 100.

Under all aseptic precautions, the umbilical cord clamped and was cut, wiped with 70% isopropyl alcohol and with a 22-gauge syringe 4 ml blood sample was collected in a BACT/ALERT PF Plus blood culture bottle and sent to laboratory immediately for culture and detection of micro-organisms.

Under all aseptic precautions, peripheral venous blood, 1ml blood sample was collected in a BACT/ALERT PF Plus blood culture bottle and it was sent to laboratory

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immediately for culture and detection of micro-organisms.

Statistical Analysis

Data was entered in excel, coded and analyzed in statistical software GraphPad prism version 8

For qualitative data frequency and percentage were calculated. Specificity, sensitivity, Positive predictive value, Negative predictive value and accuracy was calculated for UCBC and PVBC.

3. RESULTS

A total of 100 neonates born in our study center with high risk for early onset neonatal sepsis who met the eligibility criteria were included. Of them 58% of the neonates were male. Lower segment caesarean section was the mode of delivery in 58% of the subjects.

Table 1: Risk factor distribution

Risk factor	Sepsis screen positive	Sepsis screen negative	Total
Preterm labor	12	26	38
PROM	7	16	23
MSL	8	12	20
Maternal fever	2	5	7
Prolonged labor	1	5	6
Maternal UTI	0	4	4
Birth Asphyxia	1	1	2
Total	**31**	**69**	**100**

MSL- Meconium-stained liquor, PROM- Premature rupture of membranes

Table 1 shows the risk factors associated with early onset neonatal sepsis in both sepsis screen positive and negative patients. Preterm labour (38%), Meconium-stained liquor (20%) and premature rupture of membranes (23%), Birth asphxia in 2%, and maternal h/o fever, prolonged labour & UTI in 7%, 6% & 4% respectively were the most common risk factors seen in our study. Similar distribution of risk factors was seen in sepsis screen positive cases, which is depicted in figure 1 below.

Figure 1: Risk factor distribution in sepsis screen positive cases

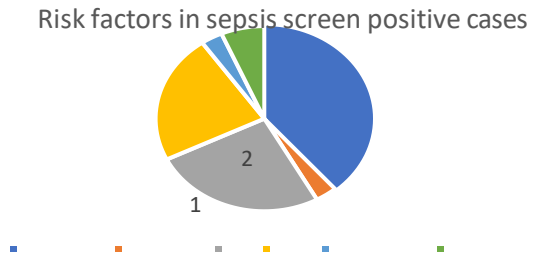

Table 2: Comparison of True positive reports in Umbilical Cord Blood Culture and Peripheral Venous Blood Culture

Result	Umbilical Cord Blood Culture	Peripheral Venous Blood Culture	Common in both
Positive Culture	24	67	17
True positive (Sepsis Screen positive)	14	27	10
Percentage of true positives	58.33%	40.30%	58.82%

Table 3: Comparison of True negative reports in Umbilical Cord Blood Culture and Peripheral Venous Blood Culture

Result	Umbilical Cord Blood Culture	Peripheral Venous Blood Culture	Common in both
Negative Culture	76	33	26
True Negative (Sepsis Screen negative)	59	29	26
Percentage of true negatives	77.63%	87.88%	100%

Table 2 and 3 shows the culture reports by UCBC and PVBC. UCBC showed growth in 24% of cases whereas

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PVBC showed high positivity with growth in 67% of the cases. Among the positive culture reports, 58.33% cultures of UCBC and 40.30% cultures of PVBC turned positive for EOS on sepsis screening. 17 cases showed growth both on UCBC and PVBC in which 10 (58.82%) cases turned positive for EOS on sepsis screening. Among the negative culture reports, 77.63% cultures of UCBC and 87.88% cultures of PVBC turned out to be true negatives for EOS. All the 26 cases which showed negative culture in both UCBC and PVBC proved to be negative for EOS on sepsis screen.

Table 4: Organisms isolated in UMBILICAL CORD BLOOD CULTURE and PERIPHERAL VENOUS BLOOD CULTURE

Organism	Umbilica Cord Blood Culture	Peripheral Venous Blood Culture	Both
Candida albicans	5	31	4
E. coli	7	5	2
Pseudomonas	6	5	1
Klebsiella	5	9	3
Coagulase negative S. aureus	0	8	0
Burkholderia Cepacia	0	7	0
MRSA	0	1	0
Non-fermenter	0	1	0
Contaminant growth	1	0	0

The organisms isolated on UCBC were E. coli (7%), Pseudomonas aeruginosa (6%), Klebsiella (5%) and Candida albicans (5%). PVBC showed Candida growth in 31% of the cases. Other organisms seen in PVBC were Klebsiella (9%), Coagulase negative staphylococcus aureus (8%), Burkholderia Cepacia (7%), E. coli (5%), Pseudomonas (5%), MRSA and Non-fermenter in 1 case each.

Table 5 : Diagnostic Accuracy of Umbilical Cord Blood Culture and Peripheral Venous Blood Culture

Parameter	Umbilical Cord Blood Culture	Peripheral Venous Blood Culture
Sensitivity	45.16%	87.09%
Specificity	85.50%	42.02%
Positive predictive value	58.33%	40.30%
Negative predictive value	77.63%	87.88%
Accuracy	73%	56%

Table 5 shows comparison of diagnostic accuracy of early onset neonatal sepsis between UCBC and PVBC. PVBC had high sensitivity of 87.09% in contrast to UCBC which had a sensitivity of 45.16%. On the other hand UCBC had high specificity of 85.50% in contrast to PVBC which showed 42.02% specificity. UCBC had better positive predictive value compared to PVBC while the latter had better negative predictive value. Accuracy was better in UCBC (76%) compared to PVBC (56%).

4. DISCUSSION

In our study, we compared the diagnostic accuracies of UC and PV for newborn sepsis using blood samples from 100 neonates with a high risk of acquiring EOS. When compared to PVBC (56%), UCBC's accuracy rate

was higher (76%) In investigations by Hansen et al. and Arya et al., where the sample size ranged from 100 to 113, the sample size was similar to that in the current study. (13,16)

58% of births were through lower segment caesarean section, whereas 42% were delivered naturally vaginally. 60% of the newborns in a study by Arya et al. underwent NVD delivery, compared to 52.4% in a study by Jain et al., while a lower percentage of 47.6% underwent LSCS delivery. The conclusions of these investigations concur with those of our study,

which likewise revealed a higher rate of LSCS delivery. (13,15) Infants born by caesarean section frequently experience respiratory morbidity, which is a morbidity linked to neonatal infection and the inability to remove foetal lung fluid. (18)

In our study, preterm labour (38%), meconium-stained amniotic fluid (20%), and premature rupture of membranes (PROM) (23%) were evaluated as risk factors for early onset neonatal sepsis. In cases where a sepsis screen was positive, same risk factor distribution was seen. Other danger signs were maternal fever, protracted labour, maternal UTI, and hypoxia during birth.

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In a study by Arya et al., 2021, the risk factors included prematurity (37 weeks gestational age), maternal fever, PROM (>18 hours), 3 or more vaginal examinations after membrane rupture, MSL, birth asphyxia, prolonged labour (>24 hours), and chorioamnionitis. (13)

Resuscitation techniques used after birth asphyxia often expose neonates to harmful microorganisms because hypoxia creates an immune injury. Due to the stress of birth, newborns with low Apgar scores frequently have poor adaptability to extra uterine life and are hence more vulnerable to infection. Jain et al., 2021, found 27% of participants who tested positive for UCBC had an Apgar score of 7 or lower at birth, compared to 14.3% of

subjects who tested positive for PVBC.(66) In a research by Adatara et al., neonates with an Apgar score of less than 7 had a 2.69-fold higher risk of developing early-onset neonatal sepsis than those with an Apgar score of 7 or higher. (19)

In a study by Hansen et al, 2005, the risk factors associated were maternal colonization (59%), maternal fever (56%), PROM (6%). (16) These were in accordance with our study in having similar risk factors of preterm labor, meconium-stained liquor, PROM, maternal fever, etc.

In our study, UCBC showed growth in 24% of cases whereas PVBC showed high positivity with growth in 67% of the cases.

The study by Mutalik et al, 2017, was one of the first published study where diagnostic accuracy measures of UCBC and PVBC were compared taking suspected clinical EOS as the standard. Of the 25 neonates with suspected EOS, 21 (84%) neonates were UCBC positive, while 16 (64%) neonates were PVBC positive and all developed clinical EOS, eventually.

(11) This discrepancy in the findings with higher percentages in their study maybe due to the fact that preterm neonates with birth weight <2000 grams were included.

A total of 17 articles were included in Dierikx et almeta-analysis .'s from 2022, which discovered that the incidences of positive PVBC and UCBC were low across all investigations. The consistency between favourable PVBC and UCBC results was thus revealed to have a significant amount of heterogeneity. (14)

In our study, the organisms isolated on UCBC were E. coli (29.2%), Pseudomonas aeruginosa (25%) Klebsiella (20.8%) and Candida albicans (20.8%). PVBC showed Candida growth in 46.27% of the cases. Other organisms seen in PVBC were Klebsiella (9%), Coagulase negative staphylococcus aureus (11.9%), Burkholderia Cepacia (10.4%), E. coli (7.5%), Pseudomonas (7.5%), MRSA and non-fermenter in 1.5% cases.

In the study by Jain et al., 2021, Klebsiella (57.6%), Staphylococcus aureus (23%), and Escherichia coli (15.3%) were the most frequently identified organisms among newborns who tested positive for UCBC. Similar to this, Klebsiella (52.3%) was the most frequently isolated bacterium in infants with PVBC positivity. Escherichia coli (14.2%) was the second most prevalent, followed by Staphylococcus (23.8%). (15)

Results of bacterial isolation in the study by Mutalik et al, 2017, showed that gram-negative bacteria were predominant (91.4%) with the commonest pathogen being Acinetobacter Baumannii complex (18.75%) followed by Klebsiella pneumoniae (26%), Escherichia coli (21.7%), and Pseudomonas aeruginosa (13%). (11)

Findings in every study might be somewhat unique because of the differences in epidemiological factors and the geographical variability in culture and sensitivity pattern.

In our study, UCBC showed 14 true positives and 10 false positives out of 24 total positive cultures with 59 true negatives and 17 false negatives out of 76 total negative culture reports. PVBC showed 27 true positives and 40 false positives out of 67 total positive cultures with 29 true negatives and 4 false negatives out of 33 total negative culture reports.

Arya et al, in their study found hematological scoring system in UCBC to be true positives in 26 and 5 false positives out of 31 total positive cultures with 60 true negatives and 9 false negatives out of 69 total negative culture reports. (13)

In our study,. PVBC showed 27 true positives and 40 false positives out of 67 total positive cultures with 29 true negatives and 4 false negatives out of 33 total negative culture reports. In a study by Arya et al, PVBC showed 22 true positives and 7 false positives out of 29 total positive cultures with 58 true negatives and 13 false negatives out of 71 total negative culture reports. (13)

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In the study by Mutalik et al, 2017, 69.5% positive UCBCs also tested positive on PVBC, similarly in a study by Kalathia et al 54.4% positive UCBCs also tested positive on PVBC. (11, 12)

In our study, comparison of diagnostic accuracy of EONS between UCBC and PVBC was done. PVBC had high sensitivity of 87.09% in comparison with UCBC which had a sensitivity of 45.16%. On the other hand, UCBC had high specificity of 85.50% in contrast to PVBC which showed 42.02% specificity. UCBC had better positive predictive value compared to PVBC while the latter had better negative predictive value. Accuracy was better in UCBC (76%) compared to PVBC (56%).

According to the research by Mutalik et al. from 2017, five of sixty neonates who tested positive for UCBC but negative for PVBC went on to develop clinical EOS. This accounts for UCBC's higher sensitivity than PVBC, which is 84% versus 64%. (11) Jain et al. 2021 came to the conclusion that the UCBC method's better sensitivity (81.0%), specificity (88.6%), and accuracy (87%) for projecting patients' disease prognoses against PVBC and UCBC can be employed as a trustworthy alternative tool to forecast the ultimate result. (15)

According to the metaanalysis by Dierikx et al., 2022, PVBC had a pooled sensitivity of 20.4% (95% CI 0.0-40.9). It had specificity of 100.0%

(95% CI 100.0-100.0), compared to UCBC's 42.6% (95% CI 12.7-72.4%)

and 97.8% (95% CI 93.1-100.0) for clinical EOS, which is defined as clinical sepsis regardless of PVBC results. (15)

In our study, UCBC had high specificity of 85.50% in contrast to PVBC which showed 42.02% specificity. In the meta-analysis by Dierikx et al, 2022, it was found that PVBC had a pooled specificity of 100.0% compared to 97.8% of UCBC for clinical EOS. Jain et al,2021 found the higher specificity (88.6%) by UCBC method against PVBC. (14,15)

Despite the advantages of UCBC, a study by Polin et al reports culture contamination lacking clinical correlation. In Polin et al's study, 2 of the 6 positive UCBCs showed culture contamination and hence, the authors' suggests meticulous and fastidious sample collection to prevent contamination. High rates of contamination are reported when UCB is collected on the perineum before delivery of placenta. (9)

In our study, UCBC had better positive predictive value compared to PVBC while the latter had better negative predictive value. Accuracy was better in UCBC (76%) compared to PVBC (56%).

5. CONCLUSIONS:

PVBC had high sensitivity in contrast to UCBC which had a sensitivity. On the other hand, UCBC had high specificity in comparison to PVBC. UCBC had better positive predictive value compared to PVBC while the latter had better negative predictive value. Accuracy was better in UCBC compared to PVBC.

6. LIMITATIONS OF THE STUDY

This was a hospital-based time bound study. The sample size was small and belonged to a single center and may lack generalizability.

The hospital setup made it impossible to do more complex sepsis screening tests.

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Conflict of Interest: None

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