

A PROSPECTIVE COMPARATIVE STUDY OF UMBILICAL CORD BLOOD CULTURE VERSUS PERIPHERAL VENOUS BLOOD CULTURE IN DIAGNOSIS OF EARLY ONSET NEONATAL SEPSIS IN PRETERM NEONATES IN NEONATAL INTENSIVE CARE UNIT OF TERTIARY CARE HOSPITAL

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Abstract

Background

Neonatal sepsis is major cause of neonatal morbidity and mortality. Blood culture and sensitivity is gold standard for the diagnosis of neonatal sepsis. Low sensitivity of blood culture especially in newborn is due to small volume of blood sample collected from neonates and antibiotics given before sampling.

Study Methodology

A prospective, analytical, cross sectional study where comparison of umbilical cord blood culture and peripheral venous blood culture was done in 100 inborn neonates . Sensitivity and specificity, positive and negative predictive values were calculated. P value was calculated, Chi Square test was applied and association was quantified.

Results

Higher sensitivity(81.0%) and accuracy(87%) for predicting disease outcome of patients by UCBC method against PVBC method conclude that UCBC can be used as reliable and alternate tool to predict final outcome.

Conclusion

- UCBC can be useful diagnostic test for EONS. Adequate amount of blood is obtained by umbilical cord method which can be difficult to obtain in a low birth weight new born. Inadequate samples of PVBC can lead to a false negative report.
- Umbilical cord blood is obtained from placental end of umbilical cord, there are less chances of introducing iatrogenic infection unlike routine culture technique where chances of false positive and risk of introducing iatrogenic infection is high.
- If umbilical cord blood is taken at birth, normal appearing newborn could be followed up in postnatal wards and discharged if reports are normal. If umbilical cord blood is collected at birth and culture report comes positive, we can prevent sequelae of sepsis by providing antibiotics for fixed duration and for units practising empirical antibiotics, antibiotics can be discontinued if report is negative.

Keywords: Umbilical Cord Blood Culture, sepsis, Peripheral Venous blood culture.

Introduction:

Neonatal period is considered most important age group at all times as newborns are most susceptible to diseases and death. Neonatal sepsis is most common cause of neonatal mortality. It accounts for nearly 3 million neonatal deaths per year and an estimated neonatal mortality rate of 23.9 per 1000 live births globally. *Klebsiella pneumoniae* was most frequently isolated pathogen (32.5%), followed by *Staphylococcus aureus* (13.6%). Among extramural neonates (referred from community/other hospitals), *Klebsiella pneumoniae* was again commonest organism (27%), followed by *Staphylococcus aureus* (15%) and *Pseudomonas* (13%). Neonatal sepsis is defined as blood stream infection which develops within 28 days after birth. Early onset neonatal sepsis is defined as infection within the 1st three days of life and is associated with transmission of organism from birth canal. Gold standard for diagnosis of neonatal sepsis is blood culture collected from peripheral veins. Recovery of pathogen is advantageous, as it confirms the diagnosis of bacteremia and allows for

identification and susceptibility testing on the organism to optimize antimicrobial therapy and duration. A negative blood culture is just as important, as it rules out cases of bacteremia and prompts continued investigation of other infectious or noninfectious etiologies or cessation of unnecessary empirical antimicrobial therapy. Umbilical cord (placental end) is less commonly

used site for collection of blood culture. Umbilical cord blood collection procedure for culture is painless and it ensures adequate volume of blood for culture with less contamination. Serum proteins like C-reactive protein (CRP), haptoglobin and fibrinogen, can be used as nonspecific indicators of bacterial sepsis. The early identification of septic neonates is difficult because subtle initial signs are not seen or not present.

Methods:

Materials & Methods

• A prospective, analytical, study was conducted in Neonatal Intensive Care Unit, Sir T. Hospital, Bhavnagar for a period of 12 months from 1st August 2019 to 31st July 2020

• Participants of the study were newborns who were attended at birth by pediatric resident at the time of delivery in Labor room and Obstetric Operation theatre, Sir T. Hospital, Bhavnagar.

Those newborns were included who were at risk of developing sepsis based on presence of two or more risk factors.

Inclusion Criteria

1. Prematurity (≥ 28 weeks - < 38 completed weeks)
2. Premature rupture of membrane (1 hour before onset of labour)
3. Prolonged rupture of membrane (> 18 h of membrane rupture)
4. Foul smelling liquor
5. Maternal fever ($> 100.4^\circ\text{F}$)
6. Birth asphyxia
7. Low Birth Weight (≤ 3 examination)

Exclusion Criteria

1. Congenital Anomaly
2. Birth Trauma
3. Full term infant
4. Still Birth

Those newborns being admitted in other NICU's after birth, Still births, Failed to resuscitate after birth were excluded. There were many instances where sample couldn't be acquired in a proper method and time - these also were excluded from the study.

Procedure-

Predelivery parents were explained about purpose of study and procedure in detail. Written consent was taken beforehand. Those neonates fulfilling criteria were given appropriate care after birth and before cutting the umbilical cord, blood was collected.

Postdelivery umbilical cord was clamped on both placental & umbilical end & was cut between each pair of clamps. The placental end was wiped with isopropyl alcohol & with a 22 gauge syringe, 2 to 3ml blood was collected from the placental end of

umbilical vein. Blood was immediately transferred to blood culture bottle. Blood culture vials containing 25 ml of brain heart infusion, yeast extract, SPS & other stabilisers were used.

Principle of test is that each type of organism needs a certain time to grow and multiply. Plating on Agar medium and subsequent antibiotic susceptibility testing was done according to microbiology laboratory protocol of the hospital.

Neonate was at risk of sepsis, patient was admitted in Neonatal intensive Care unit (NICU) for further care.

After Admission in NICU, similarly peripheral venous blood culture and test for sepsis (CBC, CRP, ESR, Blood culture) were done. Study involved preterms with less blood volume, amount of blood in culture was approximately 0.5 ml to 1 ml.

Empirical Antibiotics were started according to NICU protocol till culture sensitivity reports came. Specific Antibiotics were started after sensitivity reports came for the organism isolated. Newborns were routinely monitored, vitals were charted in case sheet and case record forms. (temperature, respiratory rate, heart rate, Capillary refill time, Oxygen saturation).

Patients were routinely reviewed for any signs of septicemia - feed intolerance, vomiting, abdominal distension, temperature instability, jaundice, sclerema, bleeding etc. Appropriate steps were taken if any of these were noted.

Patient was followed up till the stay in NICU. The entire process was done with full aseptic precautions to avoid any inadvertent error. Equipments needed for the study - Cord Clamp Scissor Syringe with needle Isopropyl alcohol, Cotton swabs 26 G Intracatheter EDTA & Plain Vacutainers Blood Culture Bottles. This study has no role of controls. Statistical Analysis Comparison of both methods were done together and in comparison with septic screen. Frequency and type of organisms isolated from both the techniques were charted. Sensitivity and specificity, positive and negative predictive values were calculated. Statistical tests in form of Chi Square tests were applied and results were generated.

Results:

Majority of neonates in study(25%) were asymptomatic,14% had Feed Intolerance, 13% had Vomiting, 12% had Jaundice&Abdominal Distension followed by 10% of neonates who had Respiratory distress, 6% hadHypoglycemia and Hypothermia,1% had Bleeding and Sclerema.

74% were having negative, 26% were having positive UCBC ,21 % had positive PVBC culture reports.

9 females were PVBC positive, while 12 out of 21 positive were male neonates in PVBC group. 12 out of 26 positive UCBC neonates were female, rest were male.

18 out of 21 pvbc positive neonates belonged to 1-2kg weight group. None of the patients less than 1 kg came pvbc positive, while 1 out of 26 in UCBC positive group was less than 1 kg.

Patients having Positive PVBC Outcome show the higher percentage 52.4% for NVD mode while,lower percentage 47.6% had LSCS mode of delivery.

Patients having Negative PVBC Outcome show the higher percentage 86.1% for >7 score while, the lower percentage 13.9% had<=7 Apgar score. Similarly, patients having Positive PVBC Outcome show the higher percentage 85.7% for>7 score while, the lower percentage 14.3% had<=7 Apgar score.

Association between PVBC Outcome and Frequent Vaginal Examination Status of the respondents was found to be nonsignificant .

Association between PVBC Outcome and Maternal Fever Status of the neonates was found to be non-significant .

Association between PVBC Outcome and Symptoms of respondents which found to be significant.

Maximum neonates with Negative UCBC & Negative PVBC reports were Asymptomatic. Most neonates with Positive PVBC Outcome had respiratory distress(28.6%) followed by 23.8% having abdominal distension while none had sclerema,bleeding and hypoglycemia. Bleeding, Feed intolerance, hypothermia, jaundice

and vomiting do not show any major difference in positive and negative patients.

Association between PVBC Outcome and Septic Screen which was found to be significant.

68.4 % PVBC Negatives had Negative Septic Screen,while only 31.6% had positive septic screen. 95.2% had positive septic screen, while4.8% of positive neonates had Negative Septic Screen Results. High sensitivity of 95.2% shows that septic screen method is a quite reliable tool for predicting the positive patients as per the final outcome of gold standard PVBC method.

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Association between UCBC Outcome and Septic Screen Results of neonates which was found to be significant.

72.97% of Neonates having negative UCBC outcome had negative Page 44 septic screen, while 27.03% had positive septic screen. 96.15% patients having Positive UCBC Outcome had positive septic screen while, 3.85% of them had Negative Septic Screen Results. High sensitivity of 96.15% shows that the septic screen method is a quite reliable tool for predicting the positive patients as per final outcome of UCBC method.

High sensitivity and specificity but moderate accuracy for predicting disease positive outcome of patients by septic screen method against UCBC Method conclude that septic screen may be used as tool to predict the same outcome as of UCBC method.

Higher sensitivity, specificity and accuracy for predicting disease outcome of patients by UCBC method against PVBC Method conclude that UCBC can be used as reliable and alternate tool to diagnose Early onset neonatal sepsis.

Discussion:

Out of the total 21 culture positive results by PVBC, 42.9%(9) were female and rest 57.1 %(12) were male . • Out of 26 culture positive results by UCBC method, 46.2%(12) were female and rest 53.8% were male . Mode of delivery and blood culture outcome was found to be nonsignificant.

85.7% peripheral vein positive cultures were in neonates between 1-2 kg birth weight, while less than 1 kg there were no positive cultures. In UCBC results, less than 1 kg there was single positive culture. 84.6% positive neonates were less than 2kg.

In PVBC positive cultures, most common symptom in septic babies was Respiratory distress(28.6%) ,followed by abdominal distension(23.8%). Around 9.5 % were asymptomatic. • In UCBC positive cultures ,most common symptom was Respiratory distress & Abdominal distension(19.2%), followed by feed intolerance and jaundice(15.4 %) each. 11.5 % subjects were asymptomatic.

27% of UCBC positive subjects were having APGAR<7 at birth, while in PVBC positive subjects 14.3% were having APGAR<7 at birth. Neonates whose APGAR<7 were 2.69 times more likely to have early onset sepsis.

In 26 UCBC positive neonates, 25 had positive septic screen. • Out of 21 PVBC positive neonates, 95%(20) had positive septic screen.

Most common isolated organism among UCBC positive neonates was Klebsiella(57.6%), followed by Staphylococcus Aureus(23%), Escherichia Coli(15.3%). • In PVBC positive neonates - Klebsiella(52.3%) was most commonly isolated organism. Staphylococcus Aureus(23.8%) was next most common followed by Escherichia Coli(14.2%).

Among 21 PVBC positive, 17 had both UCBC and PVBC positive reports and all 17 had similar organism isolated from these 2 methods.

Conclusion:

88.6% of Neonates negative by PVBC method were also negative by UCBC method, while only 11.4% PVBC negative neonates were positive by UCBC Results.

High sensitivity of 81.0% shows that the UCBC method is a reliable tool for predicting positive patients as per the final outcome of gold standard PVBC method. Also, Positive predictive value of 65.38% shows that out of patients who were diagnosed as positive, majority were finally diagnosed same as positive by PVBC method also.

Cord venous blood taken at delivery can be reliable alternative to peripheral venous culture. Without proper aseptic technique, there is higher risk of contamination from the cord blood than the peripheral venous blood.

UCBC is more accurate than PVBC as there is larger sample volume.

UCBC can be useful diagnostic test for EONS. It is especially important for neonates who were given prophylactic antibiotic before collection of blood for culture. • Adequate amount of blood is obtained by umbilical cord method which can be difficult to obtain in low birth weight newborn. • Since the Umbilical cord blood is obtained from placental end of umbilical cord, there are less chances of introducing an iatrogenic infection unlike normal routine culture technique where chances of false positive and risk of introducing iatrogenic infection is very high. • Various Centres don't admit all newborns with some risk factors for sepsis and thus there is chance of missing infection which could lead to morbidity and mortality in neonates later on because of untreated septicemia. If umbilical cord blood is taken at birth, the normal appearing newborn could thus be followed up regularly in postnatal wards and could be discharged if reports are normal and if clinically child is well. Whereas ,if umbilical cord blood is collected at birth and culture report comes positive, we can prevent sequelae of sepsis by providing antibiotics for a fixed duration, thus reducing morbidity and neonatal mortality. • If UCBC method is accepted, then units practising empirical antibiotics can start antibiotics after sending UCBC sample. Also this can be set as standard in such scenario for discontinuing antibiotics if the culture report comes out negative. However, wide multicentric research is needed with larger sample size for this practice to be accepted worldwide so that neonates at risk of sepsis, can be diagnosed of septicemia by umbilical cord blood culture technique.

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