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CORRELATION BETWEEN UMBILICAL CORD BLOOD CULTURE AND PERIPHERAL VENOUS BLOOD CULTURE IN DIAGNOSING EARLY ONSET NEONATAL SEPSIS.

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INTRODUCTION:

The most common cause of neonatal mortality worldwide is neonatal sepsis.[1] It is responsible for around 3 million neonatal deaths annually, with a neonatal mortality rate of roughly 23.9 per 1000 live births.[2] National Neonatal-Perinatal Database 2002– 2003 showed that 2219 out of 145623 (67%) neonates had EONS. Early onset neonatal sepsis (EONS) appears 72 hours or earlier in life and usually presents as pneumonia and respiratory distress.[3] The mother's vaginal tract is typically the source of this infection, implying a vertical transmission of pathogens during the intrapartum period.[4] To decrease the rates of neonatal morbidity and mortality, early detection of sepsis is necessary for the timely administration of antibiotics.[5] Even though peripheral venous blood culture (PVBC) is considered the gold standard for diagnosing neonatal sepsis, it is a painful and challenging procedure that involves expertise. Additionally, peripheral blood culture sensitivity varies, primarily as a result of insufficient volume of blood collected, intrapartum antibiotics and giving antibiotics to the neonate before sample collection.[6,7] Repeated phlebotomies might also increase the chances of neonatal anaemia, especially in preterm neonates. Blood collection from heel prick, umbilical vein, central venous lines as well as arterial lines are alternative sites for blood collection.[8] Umbilical cord blood provides an appropriate volume of blood for culture, is a painless procedure, and can be obtained as early as possible, facilitating the timely initiation of antibiotics.[9,10]
Although some previous studies have suggested umbilical cord blood culture (UCBC) to be safe and reliable for universal screening of newborns with risk factors for EONS, [9-21] there is insufficient data providing guidelines for the use of the same in the diagnosing EONS.

MATERIALS AND METHODS

The study was an observational, cross-sectional study, conducted in the NICU and post-natal ward of the Paediatric department of Tata Motors Hospital, Jamshedpur, Jharkhand from June 2022 to April 2024, on the newborns delivered at Tata Motors Hospital, fulfilling 2 or more inclusion criteria.

Ethical committee clearance was taken. Written informed consent was obtained from the parents. Following the Helsinki Declaration on research bioethics, the parents were given an option not to participate in the study if they wished.

INCLUSION CRITERIA: Presence of ≥ 2 of the following criteria-

- Prematurity (<37 completed weeks of gestation)
- Premature rupture of membranes (rupture 1 hour before the onset of labour)
- Prolonged rupture of membranes (rupture >18 hours before delivery).
- Single, unclean or, >3 sterile vaginal examinations during labour.
- Prolonged labour (Duration of the first and second stages of labour is >24 hours)
- Perinatal asphyxia with APGAR <7 at 1 minute.
- Low birth weight (<2500 grams)
- Maternal fever [single measurement of ≥39°C or ≥100.2°F oral temperature or a repeated measurement of oral temperature being ≥38ººC or ≥100.4°F if the first measurement of oral temperature was between 38ºC (100.4°F) and 39ºC (102.2°F)]
- Maternal leucocytosis (TLC >15,000/mm³).
- Foetal tachycardia (>160beats/min for ≥10 minutes)
- Foul-smelling liquor

EXCLUSION CRITERIA:

- Neonates without any risk factor or <2 risk factors.
- Congenital anomaly.
- Birth trauma.
- Still-birth
- Out-borns.
- Neonate whose parents did not give consent.

Procedure- A detailed antenatal history was recorded in all cases fulfilling the inclusion criteria to look for the following risk factors-Maternal factors like gestational age, fever, leucocytosis, or foul-smelling liquor; foetal tachycardia on antenatal scans, number of sterile and unsterile P/V examinations, History of prolonged rupture of membranes (>18 hours), premature rupture of membranes (rupture one hour before the onset of labour) and prolonged labour (sum of first and second stage labour >24 hours). Immediately post-delivery, the umbilical cord was clamped on both the placental and umbilical ends maintaining strict asepsis and was cut between the clamps. The placenta with the attached umbilical cord was then kept in a sterile container and under sterile technique, the umbilical cord was wiped thrice with 70% isopropyl alcohol and povidone-iodine alternatively. Around 1 ml of blood was withdrawn from the placental end of the umbilical vein using a 5 ml sterile syringe and injected into an aerobic culture bottle containing Brain Heart Infusion (BHI) broth for further processing. The ratio of blood to broth was 1:10.

A 3ml peripheral venous blood sample was immediately withdrawn from a peripheral vein under asepsis using a 5ml sterile syringe, of which, 1ml was injected into the aerobic culture bottle containing BHI broth, for PVBC testing and the remaining blood was used to study CBC, Platelets, ANC, CRP, ESR and ITR.

After collection of both umbilical cord blood and peripheral venous blood, the samples were kept in an incubator at 37ºC for 24 hours after which they were sub-cultured in blood agar and MacConkey agar and kept in an incubator for another 24 hours. Readings of both UCBC and PVBC were time taken at 48-72 hours. Data had been entered into an Excel spreadsheet and was analysed using SPSS Package 20.0 by importing the Excel spreadsheet into SPSS. The qualitative variables have been described in the form of proportions and the quantitative variables have been described in terms of mean. Data was checked for normality before applying appropriate tests of significance. All the

qualitative data wes analysed by cross-tabulation using Chi-Square. The significance of p-value was taken as $p< 0.05$. A comparison between PVBC and UCBC was done by estimating sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the tests.

RESULTS-

PREVALENCE OF CONFIRMED EONS-

Considering PVBC to be the gold standard test, all neonates with positive PVBC outcome were taken as confirmed EONS. Out of 132 neonates with suspected EONS, **15 (11.40%)** had confirmed EONS whereas **117 (88.60%)** did not have EONS.

TABLE 1: CORRELATION BETWEEN UCBC AND PVBC-

UCBC	**PVBC**		**Total**
	Positive	**Negative**	
Positive	**11**	**6**	**17**
Negative	**4**	**111**	**115**
Total	**15**	**117**	**132**

Considering PVBC to be the gold standard diagnostic test, UCBC had a **sensitivity of 73.3%, specificity of 94.9%, PPV of 64.7% and NPV of 96.5%.**

TABLE 2: CORRELATION OF UCBC WITH SEPSIS SCREEN-

UCBC	**Sepsis Screen**		**Total**
	Positive	**Negative**	
Positive	**12**	**5**	**17**
Negative	**4**	**111**	**115**
Total	**16**	**116**	**132**

Statistics $x^2 = 62.621$; df=1; **p<0.001**

Correlation of UCBC with sepsis screen showed a highly significant statistical correlation between UCBC positivity and sepsis screen positivity**. (p<0.001).**

RATE OF FALSE POSITIVITY OR FALSE NEGATIVITY OF UCBC- Out of 21 neonates with PVBC and/or UCBC positivity, **6 (28.6%)** were false positive cases (positive UCBC outcome but negative PVBC outcome) and **4 (19%)** were false negative cases (negative UCBC outcome but positive PVBC outcome).

DISCUSSION-

In our study, out of 132 neonates suspected to have EONS, **17 (12.9%)** were UCBC positive and **15 (11.4%)** were PVBC positive. This was similar to the results of the study by **Ojha M et al.[12],** which showed a UCBC positivity rate of 9% and PVBC positivity rate of 7%. Similarly, the UCBC positivity rate in the study by **Porval NP et al.[17]** was 17.3%. The study by **Jain P. et al[11]** showed that 26% neonates were UCBC positive and 21 neonates were PVBC positive. These were higher than the UCBC and PVBC positivity rates in our study probably because only LBW neonates were included in their study. In the study by **Meena R et al.[16]**, around 21.2% (17 out of 80) neonates had positive UCBC outcome and 18.7% (15 out of 80) had positive PVBC outcome. In the study by **Kalathia MB et al.[20],** the incidence of UCBC positivity was 24.4% whereas that of PVBC positivity was 17.8%. The study by **Mulay S et al**.[15] showed that 35.3% neonates were UCBC positive.

Out of 15 PVBC positive neonates, **11 (73.3%)** had positive UCBC results too while the remaining 4 (26.7%) had negative UCBC results. Out of 117 neonates with negative PVBC outcome, **111 (94.9%)** had negative results by UCBC while the remaining 6 (5.1%) had positive UCBC results. Considering

PVBC to be the gold standard diagnostic test, UCBC had a **sensitivity of 73.3%, specificity of 94.9%, PPV of 64.7% and NPV of 96.5%,** thus proving that UCBC could be a **reliable diagnostic alternate to PVBC.** The study done by **Jain P et al.[11]** had similar results where UCBC had a sensitivity of 81.0%, specificity of 88.6%, PPV of 65.38% and NPV of 94.59% with a diagnostic accuracy of 87% for predicting disease outcome. The study done by **Meena R et al.[16]** also showed results similar to our study where if PVBC was considered the gold standard, the sensitivity, specificity, PPV and NPV for UCBC were 66.7%, 89.2%, 58.8% and 92.1% respectively. In the study done by **Ojha M et al**.[12], the diagnostic parameters of both PVBC and UCBC were compared to sepsis screen positivity (taken as confirmed EONS) and showed that UCBC had a sensitivity of 100%, specificity of 74.4%, PPV of 28.1% and NPV of 100% whereas PVBC had a sensitivity and specificity of 77.7% and 72.5%, respectively, and PPV and NPV of 21.8% and 97%, respectively. Similarly, the study by **Meena J et al.[21]** showed that on correlating UCBC with PVBC, UCBC had a sensitivity of 100%, specificity of 94.9%, PPV of 33.3% and NPV of 100%. The specificity and NPV of UCBC were comparable to our study.

The study by **Kalathia MB et al.[20]** showed that UCBC had a sensitivity of 80%, specificity of 91.43%, PPV of 72.73% and NPV of 94.12% which was similar to the diagnostic parameters of our study.

Out of 132 neonates suspected to have EONS, **16 (12.1%)** had sepsis screen results positive and the remaining 116 (87.8%), had sepsis screen results negative. Out of the 16 neonates having sepsis screen positive results, **12 (75%)** were UCBC positive while the remaining **4 (25%)** were UCBC negative. On correlating UCBC with sepsis screen showed a highly significant statistical correlation between UCBC positivity and sepsis screen positivity**. (p<0.001).** The study by **Jain P et al**.[11] also showed a statistically significant ($p<0.05$) association between positive UCBC and positive sepsis screen results. The study by **Mandot S et al.[18]** showed that out of 23 neonates with sepsis screen positive results, 6 (26.1%) had UCBC results positive too. This was lesser than the incidence of UCBC positivity among sepsis screen positive neonates in our study. The study by **Meena J et al.[21]** showed that all 3 UCBC positive neonates (100%) had sepsis screen positivity. However, of 11 sepsis screen positive neonates, only 3 (27.3%) had UCBC positive results which was much lesser than the prevalence of UCBC positive neonates among the sepsis screen positive neonates in our study.

Considering proven sepsis to be PVBC positive neonates, out of 21 neonates with PVBC and/or UCBC positivity, **6 (28.6%)** were false positive cases (positive UCBC outcome but negative PVBC outcome) and **4 (19%)** were false negative cases (negative UCBC outcome but positive PVBC outcome). The false positivity of UCBC could be attributed to the presence of contaminants. Out of 132 neonates with suspected EONS, **6 (4.5%)** had false positive results by UCBC and **4 (3%)** had false negative results by UCBC. This was similar to the study by **Meena R et al.[16]** in which out of 80 neonates suspected of EONS, 3 (3.7%) showed false negative UCBC results which was comparable to the 3% false negative cases out of the total sample in our study.

CONCLUSION: The findings in our study thus conclude that UCBC could be used as a reliable alternative to PVBC in diagnosing EONS for early detection and timely initiation of antibiotics to reduce the neonatal mortality owing to EONS. It could also be used as a reliable alternate to sepsis screen for corroborating the diagnosis of EONS.

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