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Original Research Paper

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EVALUATION OF CORD BLOOD CULTURE AS AN EARLY PREDICTOR FOR THE DETECTION OF EARLY ONSET NEONATAL SEPSIS IN TERTIARY CENTRE OF CENTRAL INDIA.

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ABSTRACT

BACKGROUND : Neonatal sepsis is one of the major causes of neonatal morbidity and mortality. Peripheral venous blood culture and sensitivity is gold standard for the diagnosis of neonatal sepsis. Low sensitivity of blood culture in newborn is due to small volume of blood sample collected from neonates & antibiotics given before sampling.

AIM : To evaluate the utility & compare the Umblical cord blood culture(UCBC) with Peripheral venous blood culture(PVBC) for detection of Early Onset Neonatal Sepsis(EONS)

METHOD : 100 inborn neonates with two or more risk factors for EONS, chosen by sequential sampling method were included in this prospective analytical study. Blood samples were collected from umbilical cord and peripheral vein for culture. Sepsis screen was done to corroborate the diagnosis of neonatal sepsis.

RESULT : Out of 100 neonates, 21 belongs to sepsis; 14 to probable sepsis; 65 to no sepsis. UCBC had Sensitivity-65.71% , Specificity-93.84%, PPV-85.18% , NPV-83.56% & PVBC had Sensitivity-60% , Specificity-95.38% , PPV-87.5% , NPV-81.57%.

CONCLUSION : UCBC is simple and convenient method for the diagnosis of EONS compared to PVBC. Organisms grown are comparable to PVBC sample.

KEYWORDS : Neonatal sepsis, Umbilical cord blood culture, Peripheral vein blood culture.

INTRODUCTION :

Neonatal sepsis is the most common cause of neonatal mortality. Incidence of neonatal sepsis in India is 30 per 1000 live births(NNPD database).[8] Early onset Neonatal sepsis can have wide spectrum of clinical presentation. Aggressive approach to diagnosis and management is the principle determinant of the prognosis. Early diagnosis of neonatal sepsis is important to reduce the case fatality rate.[1]

Early onset neonatal sepsis(EONS) usually occurs in the first 72 hours of life, with 80 to 90% of cases presenting upto 48 hours after birth. Early onset sepsis typically manifests as fulminant, multisystem illness usually acquired by vertical transmission from the mother with high case fatality rate.[1]

Blood culture to identify the organism is the gold standard for the diagnosis of EONS. However, the yield is low due to - low inoculum in the sample, inability of the laboratory to identify all the organisms, prior antibiotic usage. Added to this is the delay in obtaining the results as it takes 48 hours of incubation of blood sample. This period could be too late for the clinician to initiate any useful treatment.

Umbilical cord blood(UCB) can be collected for blood culture for diagnosing EONS, as it is-painless and ensures adequate volume of blood for culture .

METHOD :

This prospective analytical study was carried out in nursery of tertiary care centre of central india over a period of one year from May 2019 to May 2020 after getting clearance from Ethics & Scientific Review Committee (registration no.- EC/ MGM/ March-19/08) in which 100 inborn neonates delivered with presence of 2 or more of the following risk factors (Inclusion Criteria[1]) were included in the study by sequential sampling method:

a) Prematurity (< 37 weeks)
b) Preterm Premature rupture of membranes
c) More than 3 vaginal examinations after rupture membranes / 1 unclean vaginal examination
d) History of maternal fever
e) Foul – smelling liqour
f) Chorioamniotis
g) prolonged rupture of membrane (>18hrs)
h) prolonged labour > 24 hours
i) Perinatal asphyxia (apgar score of <4 in 1 minute)
j) Meconium stained liquor

- Neonates born with lethal congenital anomalies & outborns were excluded.

UCB is collected(4-6 ml) at birth under asepsis from the placental end of umbilical artery or vein and send for CBC, peripheral smear, sepsis screen & blood culture. Similarly peripheral venous blood(PVB) sample is also taken within 6 hours of birth for above investigations before starting antibiotics according to NICU protocols.

Demographic, birth & clinical details of all the subjects is recorded & tabulated. The data was expressed in terms of rates, ratio and percentages. Chi-square test was used to compare or associate nominal data. A probability value (p value) of less than 0.05 was considered statistically significant. After admission baby is assessed for the clinical signs of sepsis & the haematological parameters and culture reports once arrived was recorded. Using the above data diagnostic parameters – sensitivity, specificity, positive predictive value(ppv), negative predictive value(npv) of UCBC & PVBC is calculated and compared.

In our study true positive are those which are culture +ve with clinical signs of sepsis present (sepsis screen can be +/-) ; false positive are those which are culture +ve with no clinical signs of sepsis (sepsis screen –ve; contaminants) ; false negative are those which are culture –ve with clinical signs of sepsis present (sepsis screen can be +/-) ; true negative are those which are culture –ve with no clinical signs of sepsis (sepsis screen –ve). So

sensitivity=true positive / (true positive + false negative)
specificity=true negative / (true negative +false positive)
ppv=true positive / (true positive + false positive)
npv=true negative / (true negative + false negative)

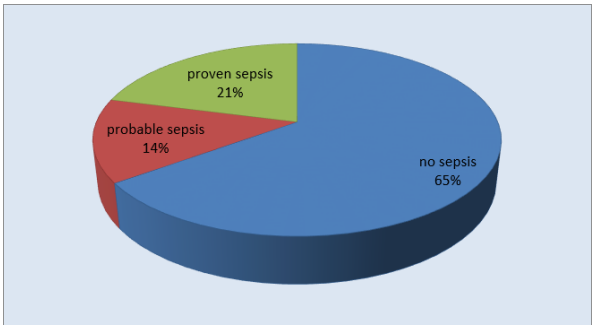
Diagnostic outcome of all subjects were divided into three categories –

- - Neonates with no signs of sepsis in next 72 hrs with PVBC

sterile will be considered normal or no sepsis group
- Neonates with clinical signs of sepsis with sepsis screen+/- with PVBC sterile, were diagnosed as probable /clinical sepsis
- Neonates with clinical signs of sepsis & PVBC showing growth were grouped as proven sepsis.[4]

RESULTS :

Figure 1 : Diagnostic distribution for EONS



Distribution of diagnostic outcome of all 100 neonates-

No sepsis - 65% (**PVBC sterile cases with no clinical signs of sepsis**)
Probable sepsis - 14% (**PVBC sterile cases with signs of sepsis present and sepsis screen can be +ve/-ve**)
Proven sepsis - 21% (**PVBC +ve cases with signs of sepsis present and sepsis screen can be +ve/-ve**).

Table 1 : Association of neonatal profile with EONS

Patient's Profile	No Sepsis (n=65) No. (%)	Probable Sepsis (n=14) No. (%)	Proven Sepsis (n=21) No. (%)	Total No.(%)	p value
Gender:					
Male	30 (46.1)	**5 (35.7)**	**6 (28.6)**	41 (41.0)	
Female	35 (53.8)	**9 (64.3)**	**15 (71.4)**	59 (59)	
Gestational age:					
Preterm(<37 weeks)	40 (61.5)	**9 (64.2)**	**13 (61.9)**	62 (62.0)	
Term(≥37 weeks)	25 (38.5)	**5 (35.8)**	**8 (38.1)**	38 (38.0)	
Birth Weight:					
BW (<2.5 kg)	38 (58.4)	**9 (64.2)**	**15 (71.4)**	62(62.0)	
BW (≥ 2.5 kg)	27 (41.5)	**5 (35.7)**	**6 (28.6)**	38(38.0)	
Mode of delivery:					
LSCS	28 (43)	**5 (35.7)**	**7 (33.3)**	40 (40.0)	
NVD	37 (57)	**9 (64.3)**	**14 (66.7)**	60 (60.0)	
Risk factors distribution:					
Prematurity (<37 weeks)	40 (62.0)	6 (42.8)	13 (61.9)	**59**	**0.0009**
Maternal Fever	19 (30.4)	8 (57.1)	14 (66.7)	**41**	**0.002**
Prolonged Rupture of Membrane (>18 hours)	23 (35.4)	5 (35.7)	9 (42.8)	**37**	**0.03**
Preterm Premature Rupture of Membrane	20 (31.6)	4 (28.5)	7 (33.3)	**31**	**0.04**
3 or more Vaginal Examination After Rupture of Membrane	20 (30.4)	4 (28.5)	6 (28.5)	30	0.34
Meconium Stained Liquor	18 (27.8)	1 (7.1)	3 (14.3)	22	0.20
Birth Asphyxia (apgar score of <4 in 1 minute)	12 (19.0)	4 (28.5)	2 (9.5)	18	0.30
Prolong Labour (>24 hours)	13 (19.0)	3 (21.4)	1 (4.7)	17	0.55
Foul Smelling Liquor	0 (0.0)	1 (7.1)	8 (38.1)	9	**0.001**
Chorioamniotis	0 (0.0)	1 (7.1)	8 (38.1)	9	**0.001**

Baseline characteristics of subjects was studied. **Mean gestational age was 34 weeks & mean birth weight was 2.2kg**. The risk factor found to be **statistically significant (pvalue <0.05) associated with sepsis are maternal fever, prematurity, prolong rupture of membrane, preterm premature of rupture of membrane, chorioamniotis, foul smelling liquor.**

Table 2 : Distribution Of Clinical Features Of Eons

Clinical Features	Sepsis (proven+probable) (n=35)	
	No.	%
Respiratory distress (tachypnoea, grunting, chest retraction)	24	68.57
Shock	20	57
Lethargy	16	45.7
Abdominal distension	13	37
Feeding difficulty/intolerance	11	31
Bleeding/altered orogastric aspirate	11	31
Seizure	10	28.6
Hypoglycemia	8	22.8
Jaundice	7	20
Fever	5	14
Others	14	40

Out of 35 sepsis cases which presented with clinical features of EONS, the **commonest clinical manifestation was respiratory distress(69%).**

Table 3 : Umbilical cord & Peripheral venous blood culture distribution

	DIAGNOSIS		Total (N=100)
	Sepsis (proven+probable) (n=35)	No Sepsis (n=65)	
UCBC :			
POSITIVE	23	4	27
NEGATIVE	12	61	73
PVBC :			
POSITIVE	21	3	24
NEGATIVE	14	62	76
TOTAL	35	65	100

Table 4 : Diagnostic parameters of UCBC & PVBC

	Sensitivity	Specificity	PPV	NPV
Umbilical cord blood culture	**65.71%**	**93.84%**	**85.18%**	**83.56%**
Peripheral vein blood culture	**60%**	**95.38%**	**87.5%**	**81.57%**

Diagnostic parameters values of UCBC is comparable to PVBC with higher sensitivity for UCBC to detect EONS.

DISCUSSION :

Over past two decades neonatal morbidity associated with sepsis has increased due to changing microbial spectrum. To establish early diagnosis of EONS is a challenge because of varied clinical presentations. For definite diagnosis of EONS peripheral blood culture results are gold standard which are

time consuming & cumbersome. Therefore there is always a need for test which helps in early detection of EONS that could be easily performed .In this study we have evaluated the effectiveness & importance of UCBC in the detection of the EONS & its comparison with PVBC.

Males predominantly develop sepsis in our study(Table 1), which is consistent with other studies by **Pramana et al, Makkar.M et al, Dutta NR et al**[2,3,4]. Preterm neonates predominantly develop sepsis in our study, which is consistent with other studies by **Pramana et al , Makkar.M et al , Dutta NR et al** .[2,3,4] LBW neonates predominantly develop sepsis in our study(Table 1), which is consistent with other studies **by Dutta NR et al, Pramana et al , Makkar.M. et al.**[2,3,4] There was no significant correlation of sepsis status with NVD and LSCS delivered neonates(Table 1), it is consistent with other studies by **Makkar.M et al , Pramana et al.**[2,4]

Risk factors distribution among 100 neonates(Table 1), the following risk factors shown a statistically significant correlation with EONS with pvalue <0.05, maternal fever, prematurity, prolonged rupture of membrane, premature rupture of membrane , foul smelling liquor , chorioamniotis .

While other risk factors did not show any statistically significant correlation with EONS with pvalue >0.05. Similar findings were reported in other studies by **Sanjay mandot et al, Dutta NR et al, Pramana et al.**[2,3,5]

Out of 35 sepsis (proven +probable sepsis) cases which presented with clinical features of EONS, the m/c clinical manifestation was respiratory distress(Table 2). Majority of neonates has shown > 2-3 clinical features. Similar findings were present in other studies done by **Pramana et al, Dutta NR et al**[2,3].

In this study **PVBC is considered gold standard for the diagnosis of neonatal sepsis** and it requires a minimum of 48-72 hours to yield a result. Out of 100 neonates , for the purpose of this study diagnostic accuracy and easy calculation **21 neonates (proven sepsis) and 14 neonates (probable sepsis) are included in sepsis group (n=35)** and remaining **65 neonates are included in No sepsis group**(Figure 1)**.** In UCBC out of 100 neonates, 27 were culture positive & 73 were sterile and in 27 positive 23 belong to sepsis (clinically significant with sepsis screen +ve) & 4 belong to no sepsis (probably contaminant, not clinically significant with sepsis screen -ve). And in 73 sterile UCBC , 12 belong to sepsis (clinically significant with sepsis screen can be +/-) & 61 (not clinically significant with sepsis screen -ve) belong to no sepsis(Table 3).

In PVBC out of 100 neonates(Table 3), 24 are culture positive in which 21 belong to sepsis (clinical significant with sepsis screen +ve) and 3 belong to no sepsis(probably contaminants, not clinically significant with sepsis screen -ve) . And in 76 sterile PVBC, 14 belong to sepsis (clinical significant with sepsis screen can be +/-) & 62 belong to no sepsis(not clinically significant with sepsis screen -ve).

Diagnostic parameters of UCBC(Table 4) for detecting neonatal sepsis are – **Sensitivity-65.71% , Specificity-93.84% ,PPV-85.18% , NPV-83.56%** and **diagnostic parameters of PVBC** are – **Sensitivity-60% , Specificity-95.38% , PPV-87.5% , NPV-81.57%.** These results are consistent with the study by **Ramraj meena et al.**[6]

In our study UCBC has a slightly higher sensitivity as compared to PVBC, it could be because of higher yield, due to more blood sample availability as UCB can be collected easily and effortlessly and is easily accessible without causing any pain to neonate (blood sampling by peripheral venipuncture can be difficult, painful, inadequate volume of blood & prior antibiotic exposure leading to poor yield in peripheral blood) . UCB sample is collected before instillation of antibiotics which also adds to its higher sensitivity. Other added benefit of UCB is that it prevents iatrogenic anemia and introduction of infection.

Despite the advantages of UCBC, it is also documented in the study conducted by **N.Fos et al**[7] in 2009 that UCBC results had excess of contamination lacking clinical correlation.The technique of collection of cord blood is critical to ensure meaningful results without contamination. Collection of blood from the umbilical cord on perineum before delivery of the placenta has been reported to have higher contamination.

CONCLUSION :

UCBC is a good method to have etiological diagnosis for EONS and can be good alternative to PVBC for enhanced detection of EONS in high risk neonates. However its potential in replacing peripheral venous blood culture needs to be evaluated in multicentric trials or larger sample size.

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