Section: Miscellaneous

Original Research Article

STUDY ON CLINICO-BACTERIOLOGICAL PROFILE OF NEONATAL SEPSIS IN A TERTIARY CARE CENTRE IN GARHWAL REGION OF UTTARAKHAND

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ABSTRACT

Background: Neonatal mortality rate (NMR) in India is 20 per 1000 live births (23 in rural areas and 12 in urban areas). Neonatal mortality rate of Uttarakhand is 17 per 1000 live births which is almost same in both rural and urban regions (17 and 18 respectively). According to the partnership of maternal, newborn and child health 2021 while significant reductions have been achieved in under-5 mortality rates, progress on newborn mortality and stillbirths has fallen behind. It was estimated that almost half of under-5 deaths occurred during the neonatal period, and that only half of small and sick newborns have access to high-quality care. Globally, there were 6.31 million incident cases of neonatal sepsis and 0.23 million deaths due to neonatal sepsis. Neonatal sepsis still remains a major cause of morbidity and mortality in this age group. The clinical signs and symptoms of neonatal sepsis are indistinct and non- specific. This study was conducted to determine the risk factors and clinical features associated with neonatal sepsis. The secondary objective was to determine the organisms causing neonatal sepsis and their antibiotic sensitivity pattern.

Materials and Methods: It was an observational study carried out on newborns admitted to a tertiary care hospital in Garhwal region of Uttarakhand as a case of sepsis during study period of January 2023 to December 2023 after getting ethical clearance from Institutional Review Committee and informed consent from patient relatives. Statistical testing has been conducted using SSPS version 20.

Results: Preterm and low birth weight babies have higher blood culture positivity which is also statistically significant. Prolonged leaking per vagina (20.5%) followed by perinatal asphyxia (15%) were the most common antenatal risk factors present in the patients admitted with sepsis. Culture positivity rate in this study was 38.5%. Common causative organisms for EONS included MRCONS (35.5), Staphylococcus aureus (5%), enterococcus (13.3%), Klebsiella (12.2%) while E. coli (2.2%) and Enterobacter (2.2%) were also involved in late onset sepsis.

Conclusion: Preterms and low birth weight babies have a statistically significant risk of culture positive sepsis. Multidrug resistance is a serious issue contributing to neonatal morbidity and mortality. Antibiotic stewardship, infection control practices and development of new antibiotics can be done to address the issue.

Keywords: Neonate, sepsis, morbidity, mortality.

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. According to UNICEF some of the major causes of newborn deaths among babies less than 29 days old are—prematurity and low birth weight (48%), birth asphyxia and birth trauma (13%), neonatal pneumonia (12%) and non-communicable diseases (7%).[1,2]

MATERIALS AND METHODS

This was a hospital based Observational study, carried out on all newborn patients till 28 days of life and fulfilling the inclusion criteria, admitted in the Neonatal Intensive Care Unit (NICU) at a tertiary care center in Garhwal region of Uttarakhand from January 2023 to December 2023.

Evaluation of patients was based on their demographic parameters and presenting clinical features. Detailed clinical examination was done and routine investigations sent. Sepsis screen and blood cultures were sent. Blood culture and sensitivity is the gold standard for diagnosis of sepsis. Blood samples were taken before administering the first dose of antibiotics and sent to the microbiology department for culture and sensitivity testing. Sepsis screen components include- Total leucocyte count (TLC), absolute neutrophil count (ANC), micro- Erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), immature to total count (I/T) ratio. Investigations were reviewed for relevant findings and clinical courses were monitored. Patients were treated based on standard treatment protocols and the associated comorbidities. Appropriate duration of treatment was provided and the final outcome was recorded.

Patient's attendants were counselled about the objectives of the study, and written consent obtained. Structured interviews were conducted at first contact with the patient's attendants. During hospital stay and at discharge the nature of the patient's condition was explained and counselling regarding further follow up was done.

Data collection tool was pre-coded which was also translated in the local dialect. All the patient's details were followed till they were discharged/expired. Data was analysed using R Studio. Chi square test was used to check the association between the variables. P value <0.05 was considered statistically significant.

Selection Criteria

Inclusion Criteria

All newborns suspected of neonatal sepsis admitted in NICU were included in the study. Symptoms of sepsis included lethargy, poor feeding, mother/nurse reports that the baby is not well, fever, hypothermia, vomiting, diarrhoea, abdominal distension, seizures, encephalopathy, poor perfusion and shock. Rarely-bleeding, sclerema and shock.

Exclusion Criteria

- Healthy newborns
- Newborns with diagnosis other than neonatal sepsis
- Congenital defect

RESULTS

In this study, 327 newborns fulfilled the criteria of probable sepsis. Blood culture was done in 234 patients, out of which 90 (%) were positive and 144 (%) were negative.

Table 1: Baseline characteristics.

Variable	Culture positive sepsis	Culture negative sepsis	p value
Sex			
Male	61	87	0.3
Female	29	57	
Place of delivery			
Inborn	40	70	0.6
Outborn	50	74	
Gestational age			
Preterm	43	46	0.023
Term	47	98	
Birth weight			
<2.5kg	57	64	0.007
≥2.5 kg	33	80	
Onset of sepsis			
EONS	77	118	0.5
LONS	13	26	
Mode of delivery			
NVD	73	107	0.2
LSCS	17	37	
Antenatal Risk factors			
Y	32	60	0.4
N	58	84	
Resuscitation required			
Yes	12	22	0.8
No	78	122	
Leaking pv			
Yes	15	33	0.3

No	75	111	
Foul smelling discharge			
Yes	9	22	0.33
N	81	122	
Maternal fever			
Yes	3	3	1
No	87	114	
Inotrope use			
Yes	30	18	0.0002
No	60	126	

Table 2: Antenatal Risk Factors.

Antenatal Risk Factors	Frequency (Percentage)
Foul smelling discharge	31 (13)
Prolonged leaking per vagina	48 (20.5)
Fever	6 (2.6)
Perinatal asphyxia	35 (15)

Table 3: Clinical symptoms and signs at presentation

Clinical feature	Frequency (Percentage)
Respiratory distress	73
Yellowish discoloration of skin	29
Refusal to feed	27
Temperature instability	20
Lethargy	10
Neonatal seizures	3
Vomiting	3
Abdominal distension	2
Cyanosis	2
Hypoglycemia	2
Loose stools	2
Irritability	1
Abscess	1

Table 4: Etiological profile of EONS and LONS cases

Microorganism	EONS	LONS
MRCONS	28	4
Staphylococcus aureus	3	2
Enterococcus	10	1
Klebsiella	9	2
Acinetobacter	10	-
Pseudomonas	3	-
Burkholderia	3	-
E coli	-	2
Enterobacter	-	2
Sphingomonas	1	-
Morganella	1	-
Stenotrophomonas	1	-
Citrobacter	1	-

Table 5: Antibiotic sensitivity and resistance profile of isolated organisms

Antibiotic (S-sensitive) (R-Resistant)	Ampicillin n (%)	Cefotaxim n (%)	Amikacin n (%)	Gentamicin	Piperacillin-Tazobactum	Linezolid	Imipenam	Levofloxacin	Teicoplanin
Klebsiella-S	0	0	6 (54.5)	3 (27.3)	3 (27.3)	2 (18.2)	3 (27.3)	-	-
R	11 (100)	11 (100)	5 (45.5)	8 (72.7)	8 (72.7)	9 (81.8)	8 (72.7)	-	-
Acinetobacter-S	1 (10)	0	6 (60)	7 (70)	3 (30)	1 (10)	2 (20)	0	-
R	9 (90)	10 (100)	4 (40)	3 (30)	7 (70)	9 (90)	8 (80)	10 (100)	-
Pseudomonas-S	0	0	0	0	3 (100)	0	1 (33.3)	-	-
R	3 (100)	3 (100)	3 (100)	3 (100)	0	3 (100)	2 (66.7)	-	-
Burkholderia- S	0	0	0	1 (33.3)	3 (100)	0	0	-	-
R	3 (100)	3 (100)	3 (100)	2 (66.7)	0	3 (100)	3 (100)	-	-
E. coli- S	0	0	0	1 (50)	1 (50)	1 (50)	0	-	-
R	2 (100)	2 (100)	2 (100)	1 (50)	1 (50)	1 (50)	2 (100)	-	-
Enterobacter- S	0	0	2 (100)	2 (100)	0	0	1 (50)	0	0
R	2 (100)	2 (100)	0	0	2 (100)	2 (100)	1 (50)	2 (100)	2 (100)
Sphingomonas-S	0	0	0	0	0	0	0	0	0

R	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Morganella- S	0	0	1 (100)	0	0	0	0	0	-
R	1 (100)	1 (100)	0	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	-
Stenotrophomonas- S	0	0	1 (100)	0	0	0	0	-	-
R	1 (100)	1 (100)	0	1 (100)	1 (100)	1 (100)	1 (100)	-	-
Citrobacter- S	0	0	1 (100)	1 (100)	0	1 (100)	0	0	-
R	1 (100)	1 (100)	0	0	1 (100)	0	1 (100)	1 (100)	-
Enterococcus fecalis-S	1 (8.3)	0	2 (16.7)	3 (25)	1 (8.3)	4 (33.3)	3 (25)	2 (16.7)	-
R	11 (91.7)	12 (100)	10 (83.3)	9 (75)	11 (91.7)	8 (66.7)	9 (75)	10 (83.3)	-
MRCONS- S	0	1 (3.1)	4 (12.5)	6 (18.7)	1 (3.1)	28 (87.5)	-	-	-
R	32 (100)	31 (96.9)	28 (87.5)	26 (81.3)	31 (96.9)	4 (12.5)	-	-	-
Staphylococcus aureus- S	0	1 (20)	1 (20)	2 (40)	0	5 (100)	0	-	-
R	5 (100)	4 (80)	4 (80)	3 (60)	5 (100)	0	5 (100)		--

DISCUSSION

The incidence of neonatal sepsis with a positive blood culture was 38% (85/234) in our study.

Male neonates were more compared to females in both culture positive and negative groups but the difference was not statistically significant. Similarly males were involved more commonly than females in studies done by Jatso et al,[3] Salama B et al,[4] and Sethi K et al.[5] Reason for this trend might be the fact that synthesis of gamma globulins is regulated by elements on the x chromosome, leading to reduced immune protection in male infants compared to their female counterparts due to their single x chromosome.[6]

36% of inborn patients and 40% of outborn patients admitted with sepsis had culture positive sepsis. Maternal administration of antibiotics and the low blood volume obtained for blood culture could explain the low rate of positive blood cultures. In the study done by Salama B et al and Bhakri et al,[7] inborn patients were much higher than outborn patients. Being the first tertiary level government referral centre of this region, might be the reason for more outborn patients in our study.

The culture positive group is associated with a higher proportion of neonates with birth weight <2.5kg (p value- 0.007) and preterms (p value-0.023) and the culture negative group has a higher proportion of neonates with birth weights >2.5kg and the difference is statistically significant. This indicates that culture positivity in low birthweight babies admitted with sepsis was more. Similar results were seen in study done by Jatso et al, Salama B et al, Verma P et al.[8,9]

Onset of sepsis, mode of delivery, antenatal risk factors and resuscitation requirement showed no statistically significant difference between the 2 groups, similar results were found by Manandhar S et al.[10] Inotrope use showed statistically significant difference between the 2 groups (pvalue-0.0002) with more use in culture positive group.

Prolonged leaking per vagina (pv) (20.5%) was the most common antenatal risk factor associated with sepsis followed by perinatal asphyxia (15%), foul smelling discharge (13%) and maternal fever (6%). The fetal membranes play a critical role during gestation providing mechanical and immunologic protection for the developing fetus. Breach in this protective mechanism can result in neonatal sepsis from ascending genital infections. Intensive care needed in a patient with perinatal asphyxia including frequent peripheral intravenous access, central line, supplemental oxygen/mechanical ventilation also increases risk of neonatal sepsis.

Culture positivity rate in this study was found to be 38.5%, similar result was found by Sethi K et al. Common causative organisms for EONS included MRCONS (35.5), Staphylococcus aureus (5%), enterococcus (13.3%), Klebsiella (12.2%) while E. coli (2.2%) and Enterobacter (2.2%) were involved in late onset sepsis. Previously, Cons were considered contaminant and non-pathogenic but in recent years their role as important human pathogens is recognized. A study done by Ansari F et al reported 41.77% Staphylococcus aureus and 13.83% as CONS. In a study done by Rath S et al,[12] Klebsiella was the predominant organism in EOS and Acinetobacter was the leading cause of LOS. In this study, 54% gram positive and 39% gram negative organisms were isolated. The most common organism was MRCONS (35.5%) followed by Enterococcus (13.3%) and Klebsiella pneumoniae (12.2%). Similar bacteriological profile was reported by a study done by Sethi K et al, Jin Z et al,[13] Wuni FK et al.[14] This was in contrast to a study done by Bhargava A et al,[15] and DeNIS collaboration,[16] where gram negative organisms were a more common cause of sepsis compared to gram positive organisms. Among the gram-negative organisms Klebsiella showed 100% resistance to ampicillin and cefotaxime. Amikacin was the most potent drug against Klebsiella with sensitivity of 54.5%. Sensitivity to gentamycin, piperacillin- tazobactum and imipenem was 27.3% and to linezolid was 18.2%. In the study done by Panigrahi P et al,[17] majority of Klebsiella isolates tested were sensitive to amikacin (84%), gentamicin (86%), ciprofloxacin (73%), imipenem (100%). Three of six isolates tested (50%) were sensitive to Cefotaxim and most Klebsiella isolates were resistant or intermediate to ampicillin (30/36 tested, 83%). In the study done in South India, majority of the Klebsiella pneumoniae

isolates were resistant to all the antibiotics tested except amikacin and meropenem.[18] It can be seen that resistant strains of Klebsiella are now emerging to broad spectrum antibiotics like carbapenems and sensitivity to amikacin and gentamicin has also declined. The increased identification of isolates of hypervirulent klebsiella pneumonia sequence type (ST) 23 carrying resistant genes to the carbapenem antibiotics is becoming a major issue in recent years as per a WHO report.[19] Similar antibiotic sensitivity pattern was seen with Acinetobacter except that maximum organisms were sensitive to gentamicin (70%) which was in contrast to the study done by Jatso et al. In our study also carbapenem resistance was 80% which was similar to studies done by Jatso et al. This may signify that injudicious use of high level antibiotics has resulted in resistance to them and contrary to this, antibiotics that were ineffective in the past are now becoming sensitive. Pseudomonas showed multidrug resistance to most of the antibiotic groups but was 100% sensitive to piperacillin tazobactum. The single isolates of the rest of the gram negative organisms were resistant to most of the antibiotics. Lineolid along with vancomycin remains the drug of choice in MRCONS with 87.5% isolates being sensitive to linezolid.

CONCLUSION

Preterms and low birth weight babies have a statistically significant risk of sepsis. Multidrug resistance is a serious issue contributing to neonatal morbidity and mortality. Antibiotic stewardship, infection control practices and development of new antibiotics can be done to address the issue.

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