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Neonatal Sepsis and its Bacteriological Profile in a Tertiary Care Hospital: A Cross-Sectional Study

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ABSTRACT

Introduction: A condition in which bacteria, viruses or fungi causes hemodynamic changes in the neonates and results in morbidity and mortality is called Neonatal sepsis. The symptoms of neonatal sepsis are nonspecific but some of them are respiratory distress convulsions and temperature dysregulation.

Aim: To determine the Neonatal Sepsis and its Bacteriological Profile in a tertiary care hospital:

Methodology: All neonates who were suspected of having neonatal sepsis were included in the study. Sepsis was diagnosed through clinical examination. Some clinical features were observed such as fever, lethargy, respiratory distress, jaundice and umbilical infections. Under aseptic conditions, sepsis cultures and screens were sent. Analyzation of data was done using STATA version 11. Chi-square test was used to analyze clinical features. Descriptive statistics was helpful in analyzing bacteriological profile.

Results: A total of 2325 neonates were admitted to the hospital. Out of these admissions, 312 were eligible for clinical sepsis. The blood culture positivity rate was 12%. Early onset sepsis was present in 52.2% cases. Culture positive rate in late onset sepsis was increased due to low birth weight, prematurity and parenteral nutrition. Positive screen had sensitivity of 80.1% and negative value of 85.6%. Isolation of gram-negative organisms was more common. *Klebsiella pneumoniae* and *Acinetobacter* were the commonly isolates.

Conclusion: Neonatal sepsis was associated with low birth weight, low APGAR score, preterm and parenteral nutrition. *Klebsiella pneumoniae, Acinetobacter* and *Staphylococci* are the main causative organisms. Gram-negative bacteria were resistant to a wide range of medications.

Key Words: Neonatal sepsis, Neonates, Prevalence, Bacterial profile, *Klebsiella pneumoniae*, *Acinetobacter*

INTRODUCTION

A condition in which bacteria, viruses or fungi causes hemodynamic changes in the neonates and results in morbidity and mortality is called Neonatal sepsis.[1] The symptoms of neonatal sepsis are nonspecific but some of them are respiratory distress convulsions and temperature dysregulation.[2] Early onset sepsis (EOS) occurs within 72 hours of birth, while late onset sepsis (LOS) occurs after 72 hours. EOS is usually transferred from maternal genital tract to the child. Its risk factors can be increased due to maternal urinary tract infection prior to delivery, multiple gestations and peripartum fever. Postnatal nosocomial infections are the cause of late onset sepsis. Prolonged invasive interventions, failure of early enteral nutrition and underlying respiratory and cardiovascular disorders are all risk factors for late onset sepsis.[3] The rate of occurrence of neonatal sepsis differs in developing countries than developed countries because of presence of gram-negative organisms in resource poor areas.[4] In southern Asia and Saharan Africa, the rate of neonatal sepsis is 1.4 million infants each year.[5] So, neonatal sepsis is the main cause of neonatal mortality. The causes of neonatal mortality are neonatal infection, prematurity and congenital malformations.[6] This study mainly focuses to determine the

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Neonatal Sepsis and its Bacteriological Profile in a tertiary care hospital.

Study design: A cross-sectional study

Place and Duration: This study was conducted at Shaheed Nawab Ghos Bakhash Raisani Memorial hospital Mastung Pakistan from March 2019 to March 2021.

METHODOLOGY

Permission was taken from the ethical review committee of the institute. The inclusion criteria were to include patients suspected to have neonatal sepsis. Sepsis was diagnosed through clinical examination. Some clinical features were observed such as fever, lethargy, respiratory distress, jaundice and umbilical infections. Those neonates were excluded whose parents did not agree to give consent. Attendants gave their informed and willing signed consents. The objective of study was also explained to the parents.

Sepsis includes a leukocyte count of <4800 or >19000.[7] It includes neutrophil count, I: T of >0.3, an erythrocyte sedimentation rate (ESR) >14mm and C-reactive protein(CRP) > 1 mg/L.[8]Brain Heart Infusion (BHI) agar was used to draw 1.5 CC blood which was contained in aerobic BacT/ALERT microbial detection system. The sample was incubated at 37°C and was observed for 4 days for bacterial growth. Some specimens were considered sterile because they did not show any bacterial growth after 4 days. The specimens which showed bacterial growth were considered a gold standard of diagnosis of neonatal sepsis.[9] Resistance and antibiotic susceptibility tests were carried according to clinical standard guidelines and intermediate susceptibility was taken as resistance. (as shown in Table 3)

From mother's obstetric records and a questionnaire, data was collected. Questionnaire was based on the previous research studies. When neonates were admitted to the center, interview of mothers was taken and, on that basis, data was collected and daily assessment of neonates was made to obtain clinical data. Data was kept under the supervision of an investigator. Entering of data was made through EpiData for quality control. Some inconsistencies in data were also removed. Backup of data was also made. Analysis and processing were made through STATA/SE version 11. Comparison and analysis of clinical sepsis and culture positive sepsis was also done. Culture positive sepsis and culture negative cases were compared for statistical analysis. P value was determined using Chi-square method. All factors with $p<0.05$ were considered significant. Descriptive statistics was used for the analyzation of microbiological data.

RESULTS

A total of 2325 neonates were admitted to the hospital during the study period. Out of these admissions, 312 were eligible for clinical sepsis. Many of them were early onset, culture negative sepsis. Culture-positive cases were 46. Majority of patients were male (As shown in Table 1). Up to 7 antenatal visits were made by mothers whose babies had confirmed culture positive sepsis to receive intra-partum antibiotics (As shown in Table 2).

Neonates had clinical features like fever, jaundice and respiratory distress. When culture positive sepsis was compared with culture-negative-sepsis some clinical features like bulging fontanels, hypothermia and jaundice were observed. Factors associated with positive early onset sepsis were prematurity, low APGAR score and intrapartum antibiotic use. When early onset sepsis culture negative babies were compared with early onset sepsis positive babies it was found that majority of babies with negative early onset sepsis have low birth weight with high significant difference. Late onset culture positive sepsis was due to birth weight, parenteral nutrition and gestational age. Increased risk factors for culture positive late onset sepsis were low birth weight, prematurity and administration of total parenteral nutrition (TPN). Out of 312 sepsis screens, 294 screens were complete. Positive septic screen has features like specificity of 21.4%, sensitivity of 80.7%, positive and negative predictive value of 14.5% and 86.6% respectively. For 312 neonates blood cultures were done. Isolation of 47 organisms from 42 culture positive neonates was made. Late onset sepsis and early onset sepsis had 23.3% and 9.20% blood culture positivity respectively. Blood culture positivity rate in this was 12%. There was more isolation of gram-negative organisms than gram positive organisms. In inborn neonates' blood culture positivity rate was higher than out born neonates. There were no cerebrospinal fluid cultures isolated any organisms.

Coagulase negative staphylococcus (CONS) was considered a contaminant so there was no antibiotic sensitivity testing done for CONS. There were more than 85% *Klebsiella pneumoniae* isolates that had resistance to third generation cephalosporins.

There were 28 deaths in the cohort of 312. Out of these 64.4 % deaths were culture-negative neonates. Culture negative sepsis had low mortality rate than culture positive sepsis.

Culture proven early onset sepsis has also low mortality rate than culture proven late onset sepsis. Out of 28 deaths, 7 deaths were due to gram negative sepsis. *Acinetobacter* had low mortality rate than *Klebsiella pneumoniae*.

Table 1: Comparison of clinical sepsis and culture-positive sepsis based on their neonatal characteristics

Variables	Clinical sepsis		Culture positive sepsis		P- value
Gender	n	%	n	%	
Male	185	56.4	25	53.4	0.527
Female	138	43.6	22	48.8	
Onset of sepsis					
Early onset sepsis	240	75.2	25	55.6	0.008
Late onset sepsis	85	26.8	23	46.7	
Place of delivery					
Inborn	285	89.3	40	87.5	0.733
Out born	40	12.7	7	14.5	
Birth weight					
<2.6KG	88	28.2	27	60.2	<0.002
>2.6KG	235	73.8	20	42.8	
Gestational age					
Preterm	72	22.2	25	53.3	<0.002
Term	252	78.8	23	46.8	
Mode of delivery					
Normal vaginal delivery	220	70.1	22	46.7	0.012
Assisted	12	4.2	3	5.5	
LSCS	94	30.5	23	52	
APGAR score 1 min					
<6	56	18.2	15	32.7	0.020
>6	268	83.8	32	70.1	
APGAR score 5 min					
<6	20	6.8	8	15.5	0.058
>6	303	95.2	40	88.5	
Mechanical ventilation					
No	270	285.6	30	66.8	0.006
Yes	55	18.6	16	35.2	
Parental nutrition					
No	285	89.6	35	77	0.015
Yes	38	12.6	12	26	

Table 2: Comparison of clinical sepsis and culture-positive sepsis based on their maternal characteristics

Variables	Clinical sepsis		Culture proven sepsis		P- value
Maternal age	n	%	n	%	
<22 years	12	3.5	3	5.5	0.708
>22 years	312	95.5	44	96.6	
Education					
Illiterate	65	20.8	15	30.7	0.508
Up to secondary	185	58	25	53.4	
Higher education	64	20.2	8	16.6	
Nonformal education	13	4.5	2	2.5	
PROM >18 hours					
No	232	73	37	80.4	0.348

Table 2: *(Continued)*

Variables	Clinical sepsis		Culture proven sepsis		P- value
Yes	88	28.2	9	20.2	
Unknown	5	0.8	2	2.5	
Antenatal visits					
>8 visits	298	93.6	38	80.9	0.020
<8 visits	25	8.5	9	20.1	
Foul smelling liquor					
No	313	96.3	45	98.9	0.608
Yes	10	3.7	1	1	
Maternal fever					
No	299	94.7	40	95.4	0.935
Yes	25	8.3	5	7.7	
Chorioamnionitis					
No	320	98.9	45	99	1.001
Yes	5	0.8	1	1	
Maternal UTI					
No	316	99.0	45	99	1.001
Yes	7	1.8	1	1	
Multiple PV examination					
> 5 times	105	33.2	10	20.6	0.118
<5 times	220	66.8	37	80.6	
Intrapartum IV antibiotics					
No	172	55	16	35.2	0.020
Yes	150	46	30	66.8	

Table 3: Antibiotics susceptibility and resistance profile of isolated organisms

Antibiotics	Acinetobacter n=10%	Klebsiella pneumoniae n =14 (%)	Escherichia coli N=7 (%)	Klebsiella oxytocin n=2 (%)	Citrobacter n=3 (%)	Streptococcus pneumoniae n=2 (%)	Enterococcus n=1 (%)
AMP	-	14	7	2	3	-	1
CZO	-	14	7	2	3	-	-
CAZ	10	-	-	-	-	-	-
CRO	-	14	7	2	3	-	-
IPM	10	14	7	2	3	-	-
AMK	10	14	7	2	3	-	-
GEN	10	14	7	2	3	-	-
CIP	10	14	7	2	3	-	-
ERY	-	-	-	-	-	2	-
POL	10	-	-	-	-	-	-
PEN	-	-	-	-	-	2	1

DISCUSSIONS

In another study, higher rate of 34.4/900 admissions were reported.[10] A comparable frequency of 9.5 per 900 admissions were reported.[11] In this study it was noted that late onset sepsis positive culture was lower than early onset sepsis positive culture. Other studies also support this finding.[12] This study had higher number of males and this fact is also supported by other studies.[13] Male predominance may be due to gene located on X chromosome, disturbing the function of thymus

in male infants so providing less immunological protection than females.[14] The symptoms of neonatal sepsis found in this study are like those in other studies e.g., jaundice, respiratory distress and fever.[15] In this study, culture proven sepsis (CPS) was not found to be involved with any maternal risk factors except for the maternal intrapartum antibiotic. Because the number of early onset sepsis in this study is minimal, this finding contradicts international literature. Neonatal variables such as low birth weight and low APGAR score were linked to culture positive sepsis. According to an Indian study, preterm babies have higher CPS.[16] Infants with low birth weight have low IgG levels which make them prone to infections.[17] Sepsis is inversely related to gestation and birth weight. Poor adaptation to uterine life is found to be associated with low APGAR score which also makes the neonates more prone to infections. Late onset culture proven sepsis is found to be associated with neonatal factors like low birth weight, use of total parenteral nutrition (TPN) and preterm gestational age. These findings of this study don't match with results reported.[18]

In this study sepsis screens found to had high sensitivity, so the identification of sepsis can be done at early stage. Unnecessary use of antibiotics can hinder the detection of sepsis negative cases. Sepsis can be ruled out by a negative sepsis screen if it has high negative value. These findings are supported by results found in the study.[19] From the other studies it is concluded that isolation rate on blood cultures vary from 6.5% to 54.3%.[20] In this study blood culture positivity rate was 12%. Factors like, improper sampling and administration of antibiotics can contribute to low positivity rates. There is also a difference of results in many studies which found that isolation of gram-negative organisms is more common while another reported that isolation of gram positive is more common. Group B streptococci (GBS) is predominant pathogen in the studies of Southeast Asian countries than Western countries. There is no single growth of GBS reported in this study. The common cause of gram-negative sepsis was *Klebsiella pneumoniae*, which is similar to other studies. Similar to other studies, this study also reported that in many organisms there was resistance to most commonly used antibiotics. It was found that *Klebsiella pneumoniae* was 93% resistant to ceftriaxone. Due to the widespread usage of ciprofloxacin in its place, modest cephalosporin resistance was discovered in one investigation. Inappropriate use of antibiotics can cause 100% carbapenem resistance which is not the case in this study because it was found that *Klebsiella* isolates were carbapenem sensitive. *Acinetobacter baumannii* (CRAB) were 92% carbapenem resistant. It is reported in other studies that CRAB has been rising over the past decade. In this study CRAB caused serious therapeutic problems. It could be due to the overuse of antibiotics and poor infection control procedures. Many of the organisms showed transmission from mother to child in early onset sepsis. This result is also like results by Chakrapani et al. This study showed that among culture proven sepsis there were 19.5% deaths like Kayange et al.'s study. This study had higher mortality rate in CPS in gram negative septicemia and this fact is also supported by the study.

LIMITATIONS

Risk factor analysis was weak because there was no normal case control analysis. Blood culture positivity was limited due to anaerobic cultures and improper collection technique.

CONCLUSION

In our study late onset sepsis was less common than early onset sepsis. Increased risk of early onset sepsis was found to be associated with Preterm, low APGAR score, low birth weight and use of intrapartum antibiotics and late onset sepsis increased risk was due to total parenteral nutrition and low birth weight. True sepsis cases were detected by highly sensitive sepsis screens. Infection control measures are required to detect multidrug resistant organisms.

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None

Permission

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