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FREUENCY OF EARLY-ONSET NEONATAL SEPSIS IN NEONATES BORN TO MOTHERS WITH PREMATURE RUPTURE OF MEMBRANES (≥18 HOURS) - A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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Abstract

Background: *Early-onset neonatal sepsis (EONS) is a significant cause of morbidity and mortality in neonates, particularly in those born to mothers with premature rupture of membranes (PROM). The frequency and risk factors associated with EONS in this population are not well established in Pakistan.*

Study setting and Duration*: This study was conducted at NICU of Combined Military Hospital Lahore, Pakistan, from 4th Jan 2025 to 4th April 2025.*

Study design: *The study employed a cross-sectional design to investigate the frequency and risk factors associated with EONS in neonates born to mothers with PROM ≥18 hours.*

Methodology: *The study included 150 neonates born to mothers with PROM of ≥18 hours, with a gestational age of more than 28 weeks. Neonates with congenital anomalies, those receiving empiric antibiotics before septic workup, and pregnancies complicated by maternal comorbidities were excluded. Data were collected using a structured proforma, and statistical analysis was performed using SPSS version 26.*

Results: *The frequency of EONS in the study population was 12%. Preterm birth ($p = 0.02$) and birth weight < 2000 grams ($p < 0.05$) were identified as significant risk factors for developing EONS. The most common pathogens isolated from blood cultures were Escherichia coli, Staphylococcus aureus, and Klebsiella pneumoniae.*

Conclusion*: This study highlights the importance of early recognition and treatment of EONS in neonates born to mothers with PROM, with preterm birth and low birth weight being significant risk factors for developing EONS in these neonates.*

INTRODUCTION

Amniotic membranes are protective to the fetus because of their anti-inflammatory, anti-bacterial, and anti-viral properties.(1) Premature rupture of membranes (PROM) is defined as the rupture of chorioamniotic membranes before the onset of labour.(2) The most common causes of amniotic membranes rupture are short cervical length (less than 25mm at 28 weeks of gestation), cervical colonization, hypertension during pregnancy, history of abortion, Caesarean section in the last pregnancy and premature rupture of membranes in a previous pregnancy as well .(3) The incidence of PROM is 8% to 10% of all pregnancies.(4)

Globally about 1.6 million neonates die because of neonatal sepsis accounting for 30-50% overall neonatal mortality annually. Pakistan has a neonatal mortality rate (NMR) of 42/1000 which is highest in the world, far more than the NMR in the neighbouring countries, for example India has NMR of 23/1000, Bangladesh has 17/1000, and Sri Lanka has NMR of 5/1000.(5) Early-onset neonatal sepsis remains one of the most common causes of neonatal morbidity and mortality worldwide.(6) it is defined as sepsis occurring within 72 hours of life. The occurrence of early-onset neonatal sepsis is estimated to affect around 0.1% of newborns accounting for about 0.9% of neonatal admissions. Neonates born to mothers with premature rupture of membranes (PROM) are particularly at higher risk for developing early-onset neonatal sepsis with an incidence ranging from 1% to 5%. Therefore, PROM, as a cause of early-onset neonatal sepsis, remains a critical concern in the care of neonates. It is because of the potential challenges posed by the timely diagnosis and management of neonatal sepsis and its long term effects on the neonate.(7)

Due to the marked heterogeneity of results of various studies, the true incidence of neonatal sepsis remains unknown in most countries of the world.(8) it indicates the need to increase the number of epidemiological studies and improve the quality of research in this field to know the true incidence of early-onset neonatal sepsis in our country. This will help to formulate and implement specific and targeted interventions to improve the outcomes and mortality posed by the neonatal sepsis. Therefore, we conducted this hospital-based cross-sectional study to determine the current frequency of EONS in neonates born to mothers with PROM. Our objective was to determine the frequency of early-onset neonatal sepsis (EONS) following premature rupture of membranes (PROM) of ≥18 hours.

Methodology

After approval from the hospital ethical committee, this cross-sectional study was conducted conducted at the Neonatal Intensive Care Unit of a tertiary care government hospital in Pakistan over a period of 3 months from 4th Jan - 4th April 2025. Informed consent was taken from the parents of the patients. The sample size was calculated to be 150 by using WHO sample size calculator (4). A non-probability consecutive sampling technique was employed to collect the data.

Inclusion and Exclusion Criteria

The inclusion criteria were

- All the babies of both sexes with gestational age more than 28 weeks on ultrasound scan and age up to 7 days after birth
- Born to mothers with PROM of ≥18 hours, with mothers aged 18-38 years
- Singleton pregnancies

The exclusion criteria were

- Neonates with congenital anomalies
- Neonates getting empiric antibiotics before septic workup
- Pregnancies with maternal co morbidities: eclampsia, pre-eclampsia, gestational diabetes, pregnancy induced hypertension, ante partum hemorrhage
- Neonates who were discharged home before 48 hours of life

Data Collection and analysis

PROM was defined as premature rupture of membranes ≥ 18 hours before the onset of labor which was confirmed by history of per vaginal leaking and pooling on vaginal speculum examination.(2) Moderate preterm was defined for the neonates born at 32-33+6 weeks while the late preterm was defined as neonates born at 34-35+6 weeks. EONS was defined by the presence of clinical features (fever,

tachycardia, tachypnea, poor perfusion), laboratory characteristics (abnormal TLC count, platelet count & CRP levels and metabolic acidosis) and a positive culture from blood sample drawn within 72 hours of birth.(9) Data were collected through the use of a structured proforma, which recorded demographic features, signs of sepsis, blood culture results, and and laboratory results, including blood cultures and biomarkers of sepsis (e.g., C-reactive protein, total leukocyte count, and platelet count). Subsequent data were analyzed by using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY)., with frequency and percentages computed for categorical variables and mean and standard deviation calculated for continuous variables. The primary outcome variable, early-onset neonatal sepsis (EONS), was calculated and expressed as a percentage of the total study population. Stratified analysis was performed to examine the association between EONS and various risk factors, including gestational age, birth weight, gender, mode of delivery, and duration of premature rupture of membranes (PROM ≥18 hours). The chi-square test was used to compare categorical variables, and a p-value of <0.05 was considered statistically significant.

Results

A total of 150 neonates were included in the study, with 90 male neonates (60%) and 60 female neonates (40%). Among all neonates, 55 were moderate preterm (36.7%) and 95 were late preterm (63.3%) with a mean gestational age of 34±1.3 weeks. The mean birth weight was 2200 ± 420 grams.

Table 1: Neonatal Demographic Characteristics

Variable	Frequency	Perentage
Mode of Delivery		
SVD	45	30
Elective LSCS	3	2
Emergency LSCS	102	68
Gender of the Neonate		
Male	90	60
Female	60	40
Gestational age (weeks)		
Moderate Preterm (32 - 33+6)	55	36.70
Late preterm (34 - 35+6)	95	63.30
Birth Weight (Grams)		
<2000	65	43.30
≥2000	85	56.70
Mothers receiving antibiotics	130	86.70

Table 2: Quantitative Variable Descriptive Statistics

Variable	Mean ± SD
Birth weight (grams)	2200 ± 420
Gestational age (weeks)	34 ± 1.3
Total leukocyte count (x10^9/L)	28.87 ± 7.32
Platelet count (x10^9/L)	100.15 ± 71.21
C-reactive protein level (mg/dL)	20 ± 7.25

Early-onset neonatal sepsis (EONS) occurred in 18 neonates (12%), and culture-positive results were seen in 13 neonates (8.7%).

Table 3: EONS Risk Factor Analysis

Variable	EONS	p-value
Mode of Delivery		
SVD	4	0.12
Elective LSCS	1	
Emergency LSCS	13	
Gender of the Neonate		
Male	10	0.92
Female	8	
Gestational age (weeks)		
Moderate Preterm (32 - 33+6)	14	0.02
Late preterm (34 - 35+6)	4	
Birth Weight (Grams)		
<2000	12	<0.05
≥2000	6	
Mothers receiving antibiotics		
No	15	0.18
Yes	3	

Table 4: Culture-Positive Results

Pathogen	Frequency	Percentage
Escherichia coli	6	46.20%
Staphylococcus aureus	4	30.80%
Klebsiella pneumonia	3	23.10%

Of the 18 neonates with EONS, 13 showed respiratory signs (72.2%), 7 had tachycardia (38.9%), and 2 had a fever and poor perfusion (11.1%). Ten neonates with EONS showed metabolic acidosis (55.6%), 13 had elevated CRP levels (72.2%), 7 had leukocytosis/leucopenia (38.9%), and 2 had positive findings of pneumonia on chest x-ray (11.1%).

Discussion

The present study aimed to investigate the frequency and risk factors associated with early-onset neonatal sepsis (EONS) in neonates born to mothers with premature rupture of membranes (≥18 hours) at a tertiary care hospital in Pakistan. The results of the study indicate that the frequency of EONS in this population is 12%, which is consistent with previous studies that have reported a range of 5.6-14.6% (10,11).

The most common pathogens isolated from blood cultures were Escherichia coli, Staphylococcus aureus, and Klebsiella pneumoniae, which is similar to the findings of other studies that have reported a high prevalence of these pathogens in neonatal sepsis (12,13).

The study also identified several factors associated with an increased risk of EONS, including preterm delivery (p 0.02) and birth weight < 2000 grams (p < 0.05). This finding is consistent with previous studies that have shown that preterm delivery and low-birth-weight neonates are at increased risk of developing sepsis due to their immature immune system and increased susceptibility to infection.(14,15) Similarly a study conducted in Ethiopia showed that preterm neonates are three times more susceptible to developing EONS than the term neonates.(16)

The study also found that maternal receipt of antibiotics before delivery was not significantly associated with a reduced risk of EONS (p = 0.18), which is inconsistent with previous studies that have reported a significant reduction in the risk of EONS (p 0.022) with the use of intrapartum antibiotics.(17) However, this may be due to the fact that the majority of mothers in the study received antibiotics before delivery (86.7%), which may have reduced the effectiveness of this intervention.

The results of the study also highlight the importance of early recognition and treatment of EONS in neonates born to mothers with premature rupture of membranes (≥18 hours). The study provides valuable insights into the demographic characteristics, clinical presentation, and laboratory findings of neonates with early-onset neonatal sepsis (EONS). The results show that 12% of the neonates developed EONS, with a significant proportion (72.2%) presenting with respiratory signs, 38.9% with tachycardia, and 11.1% with fever and poor perfusion.(9) The laboratory findings, particularly the levels of C-reactive protein (CRP) and total leukocyte count (TLC), are noteworthy. The mean CRP level was 20 ± 7.25 mg/dL, and the mean TLC was 28.87 ± 7.32. Elevated CRP levels are a well-established marker of infection and inflammation, and in this study, 72.2% of neonates with EONS had elevated CRP levels (1). This is consistent with previous studies, which have shown that CRP is a sensitive and specific marker for neonatal sepsis (18). Similarly, the TLC is an important indicator of infection and inflammation, and abnormal values can indicate the presence of an infection. (19) In this study, 38.9% of neonates with EONS had leukocytosis/leucopenia, which suggests that the TLC may be a useful diagnostic tool for identifying neonates at risk of EONS.

The study has several limitations, including its cross-sectional design, which limits the ability to establish causality between the risk factors and EONS. Additionally, the study was conducted at a single tertiary care hospital, which may not be representative of all hospitals in Pakistan. However, the study provides valuable insights into the frequency and risk factors associated with EONS in neonates born to

mothers with premature rupture of membranes (≥18 hours) in Pakistan, and highlights the need for further research to identify effective strategies for preventing and managing EONS in this high-risk population.

Conclusion

In conclusion, the present study provides valuable insights into the frequency and risk factors associated with early-onset neonatal sepsis in neonates born to mothers with premature rupture of membranes (≥18 hours) at a tertiary care hospital in Pakistan and highlight the need to screen every neonate for EONS born to mothers with premature rupture of membranes.

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