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RISK FACTORS FOR EARLY-ONSET NEONATAL SEPSIS: A RETROSPECTIVE ANALYSIS IN ISLAMABAD, PAKISTAN

Samrina Hassan[*1], Shaista Gul Tareen[2], Tamseela Gul Tareen[3], Syed Furqan Ali Sherazi[4], Asma Azhar[5], Haseeb Ur Rehman[6]

*[*1]MS Obs and Gynae Sandeman Civil Hospital Quetta*
[2]MBBS, MCPS Sen.Medical Officer Sandeman Provincial Hospital Quetta
[3]Medical officer, Cantonment General Hospital Cantonment Board Quetta
[4]House Officer at P.O.F Hospital, Wah Cantt
[5,6] MBBS at Wah Medical College, Wah Cantt

[*1]drsamreenbaloch@gmail.com

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Corresponding Author: *
Samrina Hassan

Abstract

Background:
Early-onset neonatal sepsis (EOS) continues to be a significant contributor to neonatal morbidity and mortality globally, especially in low- and middle-income nations like Pakistan. Pakistan still has a high rate of neonatal sepsis, even though there are efforts around the world to stop it. This is because there isn't enough prenatal screening, infection control isn't good enough, and antibiotics aren't being used properly. The goal of this study was to find maternal, perinatal, and clinical risk factors linked to EOS so that targeted prevention strategies could be developed.

Methods:
From January 2024 to January 2025, a retrospective observational study took place at the Neonatal Intensive Care Unit (NICU) of POF Hospital in Wah Cantt, Islamabad. There were a total of 160 newborns who were clinically suspected of having sepsis. Neonates were classified as having early-onset sepsis (EOS) if they were ≤72 hours old or late-onset sepsis (LOS) if they were >72 hours old. Information about demographics, maternal health, and clinical factors was taken from medical records. Microbiological confirmation was based on blood culture results. The Chi-square test was used to look at the relationships between categorical variables and sepsis type, with a significance level of $p < 0.05$.

Results:
Of 160 neonates, 88 (55.0%) had EOS and 72 (45.0%) had LOS. Late preterm birth (79.5% vs. 47.2%; $p = 0.000$) and low birth weight (79.5% vs. 16.7%; $p = 0.000$) were significantly associated with EOS. Maternal Group B Streptococcus (GBS) colonization, chorioamnionitis, and prolonged rupture of membranes (PROM) were exclusively linked to EOS ($p = 0.000$ for all). Blood culture positivity was observed only in EOS (100%), predominantly with Group B Streptococcus, whereas Klebsiella pneumoniae was isolated in LOS. Clinical symptoms such as fever, hypothermia, lethargy, poor feeding, and respiratory distress were universally present in EOS and absent in LOS ($p = 0.000$).

Conclusion:
Early-onset neonatal sepsis in Islamabad is significantly linked to maternal risk factors, including GBS positivity, chorioamnionitis, and PROM, as well as neonatal attributes such as prematurity and low birth weight. EOS and LOS show different microbial and clinical profiles, which shows how important it is to screen mothers, improve infection prevention, and tailor neonatal surveillance.

INTRODUCTION

Worldwide, early-onset neonatal sepsis (EOS) continues to be a leading cause of illness and mortality among infants, particularly in low- and middle-income nations like Pakistan.[1] The most common cause of EOS, which often manifests during the first 72 hours of life, is bacteria that is transferred from the mother to the infant during labour or delivery.[2] Between one and two incidences of EOS occur for every 1000 live births worldwide.[3] According to research from Pakistan, the prevalence among newborns admitted to neonatal intensive care units (NICUs) is 12.3%, which is much higher. Group B Streptococcus (GBS) and Escherichia coli (E. coli) are the most prevalent bacteria that cause early newborn infections worldwide.[4,5] Finding and comprehending the risk factors for EOS is crucial to reducing the number of preventable newborn fatalities because the burden is so great and the organisms that cause it can change.

The prevalence and microbiological features of EOS vary by population, reflecting differences in maternal screening programs, antibiotic prophylactic measures, and hospital infrastructure. The use of intrapartum antibiotic prophylaxis has significantly reduced the incidence of GBS-related EOS in developed countries.[6,7] On the other hand, E. Coli has emerged as the primary cause of illness in underdeveloped nations and frequently exhibits medication resistance. GBS and E. coli are the most common pathogens identified in neonatal blood cultures, according to studies from Pakistan, underscoring the need of local surveillance in directing empirical treatment and infection control measures.[8] The persistently high prevalence of EOS in these settings emphasises the need for specialised care and prevention measures.

A higher risk of EOS has been linked to a number of maternal and neonatal variables. Premature rupture of membranes (PROM), chorioamnionitis, intrapartum fever, and GBS colonisation are examples of maternal risk factors.[9] Prematurity, low birth weight, and male gender have all been repeatedly identified as important indicators of infection in newborns. The likelihood of early-onset infections is further increased by perinatal problems such meconium-stained amniotic fluid, perinatal hypoxia, and repeated vaginal inspections during labour.[10] For prompt diagnosis and the avoidance of sepsis in newborns, it is essential to identify and control these risk factors.

Research on the incidence and aetiology of EOS in Pakistan is largely lacking, despite increased awareness. Comprehensive local data on bacterial isolates, antibiotic resistance patterns, and maternal and neonatal risk factors are scarce. Standardised risk assessment instruments are also desperately needed in order to reduce the overuse of antibiotics and identify issues early. These kinds of tools can improve the utilisation of healthcare resources and aid in improved antibiotic stewardship. In order to improve neonatal outcomes and empirical antibiotic treatments, future research should focus on clarifying the dynamics of bacterial resistance trends.

Maternal infections and inadequate prenatal care continue to be major contributors to the high prevalence of EOS in Pakistan. Pregnancy monitoring and infection prevention remain challenges, as evidenced by the high prevalence of maternal diseases such as chorioamnionitis and PROM. Despite their proven effectiveness in reducing neonatal infections, routine prenatal GBS screening and timely prophylactic antibiotic therapy are rarely used. Therefore, any approach to eradicate EOS must include enhancing neonatal care facilities, raising knowledge about infection prevention, and improving maternal health services. In order to supplement the current local evidence needed for the development of focused interventions, this study aims to identify and assess the maternal and neonatal risk factors associated with early-onset newborn sepsis in Islamabad.

Objectives

1. To determine the association between maternal and perinatal factors (such as gestational age, birth weight, gender, Group B Streptococcus positivity, and chorioamnionitis) and the development of early-onset neonatal sepsis (EOS).
2. To evaluate the clinical characteristics (including fever, hyperthermia, lethargy, poor feeding, respiratory distress) in neonates with suspected or confirmed EOS.

METHODOLOGY

Study Design and Setting

This retrospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of POF Hospital, Wah Cantt, Islamabad, Pakistan, from January 2024 to January 2025. The study aimed to identify maternal, perinatal, and clinical factors

associated with the development of early-onset neonatal sepsis (EOS).

Study Population
A total of 160 neonates admitted to the NICU with a clinical suspicion of sepsis were included. Neonates were classified into two groups based on the timing of symptom onset: early-onset sepsis (EOS) (≤72 hours of life) and late-onset sepsis (LOS) (>72 hours of life). Inclusion criteria comprised all neonates with clinical or laboratory evidence suggestive of sepsis. Neonates with congenital anomalies or incomplete medical records were excluded.

Data Collection
Patient data were retrieved from hospital medical records using a structured data collection form. The variables recorded included demographic and perinatal factors (gestational age, birth weight, gender, maternal Group B *Streptococcus* [GBS] positivity, chorioamnionitis, and prolonged rupture of membranes [PROM]) and clinical findings (fever, hypothermia, lethargy, poor feeding, respiratory distress,).Microbiological confirmation of sepsis was based on blood culture positivity, and pathogens were identified through standard microbiological techniques.

Outcome Measures
The primary outcome was the diagnosis of early-onset versus late-onset sepsis, to determine the association between maternal and perinatal factors (such as gestational age, birth weight, gender, Group B Streptococcus positivity, and chorioamnionitis) and the development of early-onset neonatal sepsis (EOS) and to evaluate the clinical characteristics (including fever, hyperthermia, lethargy, poor feeding, respiratory distress) in neonates with suspected or confirmed EOS.

Statistical Analysis
All data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Descriptive statistics were presented as frequencies and percentages for categorical variables. Associations between categorical variables and sepsis type (EOS vs. LOS) were evaluated using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations
The study was approved by the Institutional Review Board (IRB) of POF Hospital, Wah Cantt. As this was a retrospective review of anonymized medical records, individual informed consent was waived. Confidentiality and data privacy were maintained throughout the study.

RESULTS

Table 1. Demographic Characteristics of Neonates (n = 160)

Variable	Category	n (%)
Gestational Age (weeks)	Late preterm	104 (65.0)
	Term	56 (35.0)
Gender	Male	66 (41.3)
	Female	94 (58.8)
Birth Weight (grams)	Low birth weight	82 (51.2)
	Normal birth weight	78 (48.8)
Age at Sepsis Suspicion (days)	Early-onset sepsis	88 (55.0)
	Late-onset sepsis	72 (45.0)

Table 1 shows that this study included 160 newborns, 104 (65.0%) of whom were late preterm and 56 (35.0%) of whom were born at term. More than half of the newborns were girls (94; 58.8%), and boys made up 66 (41.3%) of the study group. Low birth weight (<2500 g) was noted in 82 (51.2%) neonates, while 78 (48.8%) exhibited normal birth weight. In terms of the timing of sepsis onset, 88 (55.0%) neonates had early-onset neonatal sepsis (EOS), and 72 (45.0%) had late-onset sepsis (LOS).

Table 2. Association of Demographic and Maternal Factors with Type of Sepsis (n = 160)

Variable	Category	EOS n (%)	LOS n (%)	Total n (%)	p-value
Gestational Age (weeks)	Late preterm	70 (79.5)	34 (47.2)	104 (65.0)	0.000
	Term	18 (20.5)	38 (52.8)	56 (35.0)	
Birth Weight (grams)	Low birth weight	70 (79.5)	12 (16.7)	82 (51.2)	0.000
	Normal birth weight	18 (20.5)	60 (83.3)	78 (48.8)	
Age at Sepsis Suspicion (days)	Early-onset	72 (81.8)	16 (22.2)	88 (55.0)	0.000
	Late-onset	16 (18.2)	56 (77.8)	72 (45.0)	
Maternal GBS Positive	Yes	88 (100.0)	24 (33.3)	112 (70.0)	0.000
	No	0 (0.0)	48 (66.7)	48 (30.0)	
Chorioamnionitis	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	
PROM (Prolonged Rupture of Membranes)	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	

There were significant association between neonatal and maternal factors and the type of sepsis (Table 2). Late preterm neonates exhibited a higher propensity for early-onset sepsis (EOS) in comparison to term neonates (79.5% vs. 47.2%; p = 0.000). In the same way, low birth weight was closely linked to EOS (79.5%) compared to late-onset sepsis (LOS) (16.7%; p = 0.000). Maternal factors exhibited significant correlations: Group B Streptococcus (GBS) positivity, chorioamnionitis, and prolonged rupture of membranes (PROM) were exclusively linked to EOS (p = 0.000 for each). Conversely, LOS was more common in neonates lacking these maternal risk factors.

Table 3. Association of Clinical Findings with Type of Sepsis (n = 160)

Variable	Category	EOS n (%)	LOS n (%)	Total n (%)	p-value
Blood Culture	Positive	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	Negative	0 (0.0)	72 (100.0)	72 (45.0)	
Pathogen Identified	Group B *Streptococcus*	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	Klebsiella pneumoniae	0 (0.0)	72 (100.0)	72 (45.0)	
Fever	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	
Hypothermia	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	
Lethargy	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	
Poor Feeding	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	
Respiratory Distress	Yes	88 (100.0)	0 (0.0)	88 (55.0)	0.000
	No	0 (0.0)	72 (100.0)	72 (45.0)	

Table 3 shows that all clinical and microbiological findings exhibited a statistically significant association with the type of neonatal sepsis (p = 0.000 for all variables). Blood culture

positivity was solely observed in early-onset sepsis (EOS) cases (100%), while all late-onset sepsis (LOS) cases were culture-negative. Group B Streptococcus was the sole pathogen detected in early-onset sepsis (EOS) cases, whereas Klebsiella pneumoniae was isolated in all late-onset sepsis (LOS) cases. Clinical manifestations, such as fever, hypothermia, lethargy, poor feeding, and respiratory distress, were present in all neonates with EOS (100%) and were not observed in those with LOS. These results show that EOS and LOS have different clinical and microbiological profiles.

DISCUSSION

This study evaluated the demographic, maternal, and clinical factors linked to early-onset neonatal sepsis (EOS) and late-onset sepsis (LOS) in neonates admitted to tertiary care centres in Islamabad, Pakistan. The results indicated that gestational age, birth weight, maternal infections, and clinical manifestations were significantly correlated with the timing and classification of neonatal sepsis as shown in other studies.[11]

A larger percentage of neonates with EOS were late preterm and had low birth weight, highlighting the susceptibility of immature neonates to early infectious exposures.[12] This finding is consistent with prior research identifying preterm birth and low birth weight as significant risk factors for EOS, attributed to impaired immune function and extended exposure to maternal and perinatal infections.[13]

In this study, maternal conditions like Group B Streptococcus (GBS) colonisation, chorioamnionitis, and prolonged rupture of membranes (PROM) were solely associated with EOS. These factors promote vertical transmission of pathogens during delivery, aligning with global evidence indicating that maternal genitourinary infections are the principal sources of early-onset neonatal infections.[14,15]

Microbiological and clinical results also showed clear differences between EOS and LOS. Group B Streptococcus was found only in EOS cases, while Klebsiella pneumoniae was more common in LOS cases. This shows that the way the disease spreads changes from vertical to nosocomial as the newborn period goes on.[16] Similar pathogen trends have been documented in regional studies from South Asia, where hospital-acquired infections are increasingly acknowledged as a cause of LOS.[17,18] Clinically, fever, hypothermia, poor feeding, lethargy, and respiratory distress were universally present in early-onset sepsis (EOS) and absent in late-onset sepsis (LOS), underscoring distinct diagnostic and pathophysiological differences between the two conditions.[19,20]

The current study was constrained by its single-center, retrospective design, potentially limiting the applicability of its findings to other populations. Furthermore, molecular identification and antimicrobial susceptibility profiling of pathogens were not conducted, which might have yielded more profound insights into resistance mechanisms. Moreover, the study failed to account for potential confounders, including antenatal antibiotic exposure and neonatal comorbidities.

CONCLUSION

This study shows that early-onset neonatal sepsis in Islamabad is closely linked to maternal risk factors, especially GBS positivity, chorioamnionitis, and PROM, as well as neonatal traits like being born too early or too small. EOS and LOS are different because they have different pathogens and clinical profiles. This shows that we need targeted prevention strategies, such as better antenatal screening, infection control, and early postnatal surveillance. Enhancing maternal health initiatives and implementing regular microbiological surveillance could significantly mitigate the incidence of neonatal sepsis in Pakistan.

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