Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.443

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Frequency of Urinary Tract Infection in Neonates Presenting with Neonatal Sepsis

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ARTICLE INFO

Keywords

Neonatal Sepsis, Urinary Tract Infection, Term & Preterm.

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Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History

Received: 02-01-2025, Revised: 18-03-2025
Accepted: 05-04-2025, Published: 21-04-2025

ABSTRACT

Background: Neonatal sepsis, a life-threatening condition, continues to be a major cause of morbidity and mortality in neonates, despite advances in treatment. Urinary tract infections (UTIs) are a significant concern in neonates, as they can either occur independently or as part of sepsis. This study aims to explore the prevalence of neonatal sepsis and its association with UTI in neonates at a hospital in Faisalabad, Pakistan. **Methods:** A cross-sectional study was conducted from July to December 2018 at the Allied Hospital, Faisalabad, enrolling 105 neonates aged 1-28 days who exhibited clinical signs of either early- or late-onset sepsis. Demographic details, clinical features, and laboratory investigations, including urine cultures, were recorded. Data analysis was performed using SPSS version 20, with categorical variables analyzed using the Chi-square test. **Results:** Among the 105 neonates, 10.48% (n=11) were diagnosed with UTI. A significant gender difference was observed, with more females (8/11) affected compared to males (3/11). The incidence of UTI was higher in neonates with late-onset sepsis (LOS) compared to early-onset sepsis (EOS). No significant difference in UTI occurrence was found based on age or gestational age (P>0.05). The study observed a significant association between gender and UTI in neonatal sepsis (P=0.02). **Conclusion:** Neonatal sepsis is commonly associated with UTIs, with a higher prevalence in female neonates. Early identification and management of UTIs in neonates with sepsis are crucial for improving clinical outcomes. Further research with larger sample sizes is needed to confirm these findings and establish effective management protocols for neonatal sepsis and UTI.

INTRODUCTION

Sepsis is defined as the body's extreme response to an infection and is considered a life-threatening medical emergency. It occurs when an infection spreads and triggers a chain reaction throughout the body. Generally, sepsis begins before a patient is brought to a medical facility. Neonatal sepsis is a clinical disorder in infants under 28 days of age, characterized by general signs of infection and the isolation of a bacterial pathogen from the bloodstream[1]. Despite advancements in antibiotic therapy, neonatal sepsis remains a major cause of morbidity and mortality in neonates, necessitating the development of effective treatment protocols to address this critical issue.

Neonatal sepsis is categorized based on the age of the infant at the onset of symptoms. When symptoms appear within the first seven days of life, it is referred to as early-onset sepsis (EOS). However, some researchers define EOS more narrowly as symptoms appearing within the first three days of life.[1] Similarly, late-onset sepsis (LOS) has been variably defined, with some experts classifying it as the onset of symptoms occurring after 72 hours of life, up to seven days[2,3]. The occurrence of neonatal sepsis is inversely related to gestational age. Among full-term infants, the incidence of neonatal sepsis is generally low. With the introduction of intrapartum antibiotic prophylaxis (IAP), the incidence of early-onset sepsis in the United States has decreased, primarily by reducing Group B Streptococcal (GBS) infections[4].

The colonization of pathogens in the urinary tract—including the kidneys, ureters, bladder, and urethra—is termed a urinary tract infection (UTI). The prevalence of UTI among the pediatric population varies based on age, sex, race, and circumcision status[5]. UTI is a common bacterial infection in children, affecting 3–5% of girls and 1% of boys in the Indo-Pak region[6]. The prevalence of UTI is highest during the first year of life, affecting both sexes equally at early ages, but becoming more common in girls thereafter. Preterm neonates are

particularly susceptible to UTI, with a prevalence of 3%, compared to 1% in term neonates[6].

An underdeveloped immune system is a major risk factor for the development of UTI in neonates. Although fever, vomiting, irritability, and poor feeding are the most common clinical findings, the manifestations of neonatal UTI are nonspecific and closely resemble those of neonatal sepsis[7]. Neonatal UTI may result from bacteremia or begin as a primary infection that subsequently leads to bacteremia[8].

Neonates with sepsis are at risk of concurrently developing UTI, which may present with asymptomatic or nonspecific symptoms[9]. The risk of UTI in neonates with symptoms of sepsis is inversely related to gestational age, birth weight, and postnatal age greater than 72 hours. Therefore, obtaining a urine culture is of paramount importance, especially when late-onset sepsis (LOS) is suspected[10].

Urine culture is the gold standard for diagnosing UTI, although results typically require 24 to 48 hours to become available[11,12]. Rapid screening tests such as urinalysis and dipstick testing have long been employed to identify potential UTI cases. Rapid detection is crucial in preventing renal involvement[13]. Suprapubic aspiration and bladder catheterization are considered the most reliable methods for obtaining urine samples for culture in neonates[14].

Among neonates, the reported incidence of UTI varies from 7% to 15%, with most infections involving the upper urinary tract. Delayed treatment can result in permanent renal scarring and eventual kidney failure.[15] Selecting the most appropriate first-line antibiotics for treating UTI in neonates is essential to improving clinical outcomes, and understanding the susceptibility patterns of uropathogens in neonates can aid this process[16].

Studies have reported variations in the incidence of UTI in neonates with sepsis, ranging from 6% to 15.4% in different regions[15,18,19]. A recent study conducted in Egypt in 2022 found a higher incidence rate (11%) of concurrent UTI in neonates with sepsis. The incidence was significantly higher in LOS (16.36%) compared to EOS (4.44%)[20].

To date, no study has been conducted to determine the extent of the problem in the local population. Therefore, this study was planned to explore the prevalence of neonatal sepsis and its association with UTI among neonates in Faisalabad, Pakistan. The findings aim to guide the development of effective management plans to reduce adverse outcomes and mortality in neonates.

MATERIALS AND METHODS

Study Design, Setting and Duration

This cross-sectional study was conducted in the Department of Pediatric Medicine Unit I, Allied Hospital, Faisalabad for a duration of 06 months from July 2018 to December 2018. One hundred and five (n=105) neonates of either gender from birth to the age of 28 days with clinical signs of either early- or late-onset sepsis were enrolled in this study. The sample size (105) was calculated with confidence interval of 9, 7% margin of error and taking expected percentage of UTI, 15.4%[4] in neonates with neonatal sepsis. A non-probability, consecutive sampling technique was used for sampling.

Sample Selection

The study included neonates aged 1-28 days of either gender who presented with two or more of the following clinical features: temperature instability (either < 35°C or > 38°C), poor skin perfusion (with a capillary refill time greater than 3 seconds), tachypnea (defined as a respiratory rate exceeding 60 breaths per minute), tachycardia (heart rate > 150 beats per minute at rest), and oliguria (urine output < 0.5 ml/kg/hr).

Neonates who met any of the following exclusion criteria were excluded from the study: those with a history of recurrent infections, those who had acquired hospital-associated sepsis (as documented in their medical records), or those who had already received an antibiotic course prior to inclusion in the study (as noted in their medical records).

Data Collection

One hundred and five (105) neonates fulfilling the inclusion criteria were recruited from Pediatric Emergency, Department of Pediatrics, Allied Hospital, Faisalabad. Demographic details like name, age, sex, gestational age at birth was also recorded. All patients were subjected to complete history from parents, physical examination and laboratory investigations including complete blood count, C-reactive protein and urine culture. Reports were assessed and if bacterium present in urine sample and showed antibiotic sensitivity, then UTI was labeled (as per operational definition). Neonates, positive for UTI were managed as per hospital protocol. All this information was recorded on proforma (attached).

Statistical Analysis

The data collected / recorded were statistically using SPSS version 20.0. Mean ± SD were presented for quantitative variables like age and gestational age at birth. Frequency and percentages were calculated for categorical variables like gender and UTI. The effects of gender, age and gestational age were determined on neonatal sepsis occurrence. The Chi square test ($P \leq 0.05$) was used to compare UTI in stratified groups.

Ethical Considerations

The study protocol was approved by the Research Ethics Committee, Allied hospital Faisalabad. Informed consent from the parents of the neonates was obtained informing them the objectives and procedures of the

study. The confidentiality of participants' information and their right not to participate in the study was respected.

RESULTS

The age distribution of the patients revealed that 60% (n=63) were between 1-15 days of life whereas 40% (n=42) were between 16-28 days of life, with mean age as 15.11±8.13 days. It was further noted that 58.10% (n=61) of the patients were male whereas 41.90% (n=44) were females. According to gestational age categorization, it was found that 47.62 % (n=50) of the patients had <37 weeks and 52.38%(n=55) had ≥37 weeks of gestation. (Table No. 1)

Frequency of urinary tract infection in neonates presenting with neonatal sepsis was recorded as 10.48% (n=11) whereas 89.52%(n=94) had no findings of the morbidity. (Table No. 2)

Out of 11 cases of UTI, 4 were between 1-15 days of life and 7 were between 16-28 days of life and the difference was non-significant (P >0.05). (Table No. 3)

There was significant difference in occurrence of UTI between males (3) and female (8) out of 11 patients. (Table No. 4)

The patients with UTI were 4 having <37 weeks of gestational age and 7 had ≥37 weeks of gestation P≥0.05) (Table No. 5)

Table 1

Demographic Characters Among the Study Group

Variables	N	%age	Mean+SD
Age at admission(days)			
1-15	63	60	15.11±8.13
16-28	42	40	
Gender			
Male	61	58.10	
Female	44	41.90	
Gestational age			
Term	50	47.62	
Pre-term	55	52.38	

Table 2

Frequency of Urinary Tract Infection in Neonates Presenting with Neonatal Sepsis (n=105)

UTI	No. of patients	%
Yes	11	10.48
No	94	89.52
Total	**105**	**100**

Table 3

Stratification for Frequency of Urinary Tract Infection in Neonates Presenting with Neonatal Sepsis with Regards to Age

Age (in days)	UTI		P value
	Yes	No	
1-15	4	59	0.09

Table 4

Stratification for Frequency of Urinary Tract Infection in Neonates Presenting with Neonatal Sepsis with Regards to Gender

Gender	UTI		P value
	Yes	No	
Male	3	58	0.02
Female	8	36	

Table 5

Stratification for Frequency of Urinary Tract Infection in Neonates Presenting with Neonatal Sepsis with Regards to G. Age

Gestational age	UTI		P value
	Yes	No	
<37	4	46	0.42
≥37	7	48	

DISCUSSION

Despite advancements in neonatal care, sepsis remains a major cause of mortality and morbidity. The clinical presentation of neonatal sepsis is generally nonspecific and may include fever or hypothermia, respiratory distress (including cyanosis and apnea), feeding difficulties, lethargy or irritability, hypotonia, seizures, poor perfusion, bleeding, abdominal distention, visceromegaly, jaundice, and others. In some cases, it may present with respiratory difficulties, which could be due to acidosis, pneumonia, or meconium aspiration. Neonatal sepsis is often associated with urinary tract infections (UTIs) in neonates, which may be caused by either bacteremia or urinary tract infection. Progressive renal damage in early life can result from complications related to hypertension and chronic renal failure (CRF). The consequences of UTIs in the neonatal period are nonspecific and similar to those of sepsis itself.

The results of the present study are partially supported by Madhu and colleagues, who investigated the proportion of UTIs in neonatal sepsis. They reported that among the early-onset sepsis group, 10.8% of neonates had pyuria, of which 21.4% were culture-positive. In the late-onset sepsis group, 44.2% of neonates had pyuria, of which 35.3% were culture-positive. Pyuria was more common in males (27.5%) than females (17.2%). Overall, the proportion of culture-positive UTIs in the early-onset sepsis (EOS) group was 2.3%, while in the late-onset sepsis (LOS) group, it was 15.6% (p=0.001). The overall proportion of culture-positive UTIs in the entire study group was 7.2%. The most common causative organisms were *E. coli* (53%), followed by *Klebsiella* (27%) (21). A recent study conducted in Egypt reported that the incidence of UTIs in neonates with neonatal sepsis was 11%, with a higher incidence in LOS (16.36%) than in EOS (4.44%) (20). These results are comparable to our study. A study from the United States reported a slightly higher frequency of UTIs (15.4%) in neonates with neonatal sepsis (15). However, a study conducted in Karnataka, India, in 2012

reported a lower frequency of UTIs (6%) in neonates with neonatal sepsis (18). In contrast, an older study by Riaz and colleagues in Lahore, Pakistan, in 2014 found that culture-proven UTIs in late-onset sepsis occurred in 21.6% of neonates, which is significantly higher than what was recorded in our study (22).

Some other studies have shown an incidence of UTIs as low as less than 2% (23-25), while others report it as 5-11%. A study in Taiwan by Lin et al. found a prevalence of UTIs of 13% (26). Barton et al., in a study conducted in the West Indies, found a high frequency of UTIs (38%) among neonates with serious bacterial infections (27). These variations in incidence across different studies suggest that the occurrence of UTIs varies with populations, environmental conditions, and management practices during maternity care.

In neonates with sepsis, particularly those with late-onset sepsis, it is important to consider the possibility of a urinary tract infection (UTI), as it is often overlooked. Additionally, congenital urinary tract anomalies must be explored, as they are linked to UTIs. Hypertension, end-stage renal disease, and renal scarring can result from an undetected or improperly treated UTI. This study underscores the need for routine urine analysis and culture, especially in neonates with late-onset sepsis, to ensure appropriate treatment.

CONCLUSION

In conclusion, this study highlights the prevalence and association of urinary tract infections (UTI) among neonates presenting with neonatal sepsis in Faisalabad, Pakistan. The findings reveal that approximately 10.48% of neonates with neonatal sepsis had concurrent UTIs, with a higher incidence observed in females compared to males. The study also shows that UTI occurrence did not significantly differ between preterm and full-term neonates. This aligns with prior research, which suggests varying incidence rates of UTI in neonates with sepsis across different regions. The importance of early detection and timely management of UTI in neonates with sepsis cannot be overstated, as delayed treatment can result in long-term renal complications. The results of this study contribute valuable data on neonatal sepsis and UTI in the local population, offering insights into the need for improved diagnostic and therapeutic protocols. Ultimately, this research underscores the significance of regular urine culture screening for neonates with sepsis to prevent renal damage and other complications associated with untreated UTI. Further studies with larger sample sizes are recommended to establish more robust conclusions and inform clinical guidelines for neonatal care in similar settings.

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