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Frequency of Urinary Tract Infection in the Late Neonatal Sepsis in a Tertiary Care Hospital

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ABSTRACT

Background: Late neonatal sepsis is a serious condition that develops during the second through fourth week of life and is a remarkably important disease and death causative condition among newborns. Urinary tract infection is among the prominent yet underrated disease and death causative conditions of late neonatal sepsis. Diagnosis of urinary tract infection among this patient group is important in guiding therapy, averts complications, and promotes survival. Statistics regarding the prevalence of urinary tract infection in this regard are scanty, particularly among local communities. **Objective:** To determine the frequency of urinary tract infection in neonates presenting with late neonatal sepsis at a tertiary care hospital. **Study Design:** Cross-sectional study. **Duration and Place of Study:** The study was carried out from January 2025 to May 2025 in the Department of Pediatrics, Lady Reading Hospital, Peshawar. **Methodology:** Eighty-one neonates aged between eight and twenty-eight days who fulfilled the diagnostic criteria for late neonatal sepsis were included. Patients with congenital abnormalities of the urinary system, neural tube defects, or congenital heart disease were excluded. Detailed demographic information was recorded, followed by clinical evaluation and relevant laboratory investigations. Urinary tract infection was diagnosed when urine examination revealed ten or more white blood cells per milliliter or five or more white blood cells per high power field along with a positive nitrite test. **Results:** The mean age of neonates was 17.2 ± 6.1 days, with a predominance of males. Urinary tract infection was observed in 14.8 percent of cases, more commonly in male neonates and in those younger than fifteen days, although no demographic factor showed a significant association. **Conclusion:** Infection of the urinary tract represents an important contributor to late neonatal sepsis, present in approximately one out of seven affected neonates.

INTRODUCTION

Late neonatal sepsis is a systemic infectious condition that arises after 72 hours of life until 28 days of life and is commonly acquired from the environment, caretakers, or hospital.[1,2] Although early-onset sepsis is classically associated with maternal transmission, late-presenting infections are more often seen in association with nosocomial or community acquisition.[3] The symptoms of the condition are nonspecific and clinical and therefore hard to appreciate early.[4] Due to the immaturity of the neonates' immune system, late neonatal sepsis adds much more weight to morbidity and mortality, more so in low- and middle-income countries.[5]

Causative etiologies of late neonatal sepsis are multicausal and geographical location-, hospital practice-, and environmental-dependent.[6] Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Candida species are common causative organisms.[7] Multidrug-resistant organisms are more commonly implicated, especially in hospital acquisitions, and this makes therapy difficult.[8] Gram-negative organisms more commonly have high mortality, while Gram-positive organisms, such as coagulase-negative staphylococci, more commonly occur in association with indwelling medical devices.[9] Identification of organisms by culture of the blood, urine, and cerebrospinal fluid is needed for focused therapy and enhanced survival.[10]

Urinary tract infection (UTI) is a common and not infrequently undiagnosed origin of late neonatal sepsis.[11] Neonates infected by UTI may have minimal or atypical symptoms, e.g., fever that cannot be explained, jaundice, or failure to thrive, rather than classic urinary symptoms.[12] Escherichia coli is still the most common organism, followed by Klebsiella and other Gram-negative bacilli.[13] Male infants are at higher risk, especially those that have structural uropathies.[6] Early detection and treatment of UTI in late neonatal sepsis are critical for the prevention of complications such as renal scar formation, septicemia,

and prolonged renal failure.[7] Thus, urine culture should be included in the evaluation for sepsis in neonates with late-onset disease.[8] According to a study, frequency of urinary tract infection in late neonatal sepsis was observed to be (21.6%).[14]

This research was urgently needed for Peshawar because the region has a high rate of neonatal infection due to limited resources, crowded hospitals, and unequal infection control practice. National statistics for the prevalence and offending organisms of urinary tract infection for late neonatal sepsis are not available, and it is difficult to establish guidelines from evidence. The generation of region-specific evidence will not only help in early treatment and diagnosis but also guide antibiotic guidelines, reduce morbidity and mortality, and improve outcomes for this population of neonates.

METHODOLOGY

This research was carried out in the Department of Pediatrics at Lady Reading Hospital, Peshawar, between January and May 2025, adopting a cross-sectional study design. Approval to conduct the study was obtained from the hospital's ethical review committee as well as the research department of the College of Physicians and Surgeons Pakistan. The required number of participants was estimated through the WHO calculator, assuming a prevalence of urinary tract infection of 21.6% among neonates with late sepsis,[14] with a 95% confidence level and an absolute precision of 9%. This resulted in a minimum of 81 cases.

Newborns of either sex, aged between 8 and 28 days, who satisfied the diagnostic criteria for late neonatal sepsis were included. Cases were not enrolled if there was evidence of neural tube anomalies, congenital cardiac malformations, or pre-existing abnormalities of the urinary tract. Participation in the study was voluntary and written consent was obtained from the parents or legal guardians after providing full information regarding the objectives of the research and ensuring that no harm would result from involvement.

Baseline information such as the infant's age, sex, anthropometric measurements, maternal occupation and educational background, socioeconomic class, and area of residence was recorded on a pre-designed proforma. A comprehensive clinical evaluation was performed in neonates satisfying the inclusion criteria, and necessary laboratory investigations were done under the supervision of a pediatric consultant with over five years of post-fellowship experience.

To operationalize late neonatal sepsis, cases were classified when at least two clinical characteristics—like instability of body temperature (fever >38.5 °C or hypothermia <35 °C), respiratory distress with a rate >60/min, hypoxemia, heart failure including tachycardia >160/min, capillary refill delay, hypotension, or weak pulses, and perfusion abnormalities like altered consciousness level, metabolic acidosis with a pH of artery <7.25, or oliguria <0.5 ml/kg/hr were seen along with two laboratory findings, including a leukocyte count <5000/mm^3 or >30,000/mm^3, platelet count <150,000/µL, or elevated C-reactive protein more than thrice the normal limit. Urinary tract infection was identified in neonates that, in the context of sepsis, exhibited urine microscopy by ≥10 white cells per ml or ≥5 per high power field and positive nitrite test.

Data were analyzed using IBM SPSS version 25. Distribution of continuous variables was assessed for normality using the Shapiro–Wilk test, with results presented as mean and standard deviation or as median with interquartile range. Categorical variables were expressed in frequencies and percentages. Effect modifiers were addressed by stratification, and group comparisons were performed using chi-square or Fisher's exact test where appropriate. A p-value of ≤0.05 was considered statistically significant.

RESULTS

The mean age of the study cohort was 17.22±6.18 days, indicating a late neonatal period presentation (Table-I). Gender distribution revealed a male predominance with 52 patients (64.2%) being male and 29 patients (35.8%) being female, showing a male-to-female ratio of approximately 1.8:1 (Table-I). Socioeconomic stratification demonstrated equal representation between lower class and middle class populations, with each group comprising exactly 37 patients (45.7%), while upper class patients represented a small minority of 7 patients (8.6%) of the total study population (Table-I). Maternal educational status showed that 46 mothers (56.8%) were educated, representing a slight majority, while 35 mothers (43.2%) were uneducated, indicating educational disparities within the study population (Table-I). Employment patterns among mothers revealed a significant unemployment rate, with 64 mothers (79.0%) being unemployed compared to only 17 mothers (21.0%) who were employed, reflecting an approximately 4:1 unemployment-to-employment ratio (Table-I). Geographical distribution indicated rural predominance, with 50 patients (61.7%) residing in rural areas compared to 31 patients (38.3%) in urban areas, demonstrating a rural-to-urban ratio of approximately 1.6:1 (Table-I).

Table 1
Patient Demographics

Demographics		Mean ± SD
Age (days)		17.22±6.18
Gender	Male n (%)	52 (64.2%)
	Female n (%)	29 (35.8%)
Socioeconomic Status	Lower Class n (%)	37 (45.7%)
	Middle Class n (%)	37 (45.7%)
	Upper Class n (%)	7 (8.6%)
Mother Education	Educated n (%)	46 (56.8%)
	Uneducated n (%)	35 (43.2%)
Mother Occupation	Employed n (%)	17 (21.0%)
	Unemployed n (%)	64 (79.0%)
Residence	Urban n (%)	31 (38.3%)
	Rural n (%)	50 (61.7%)

The primary outcome analysis revealed that urinary tract infection occurred in 12 patients (14.8%) of the total cohort with late neonatal sepsis, while the majority of 69 patients (85.2%) did not develop UTI, indicating that approximately 1 in 7 patients with late neonatal sepsis developed concurrent UTI (Table 2).

Table 2

Frequency of Urinary Tract Infection in the Late Neonatal Sepsis

Urinary Tract Infection	Frequency	% age
Yes	12	14.80%
No	69	85.20%
Total	81	100%

Age group stratification demonstrated that patients aged ≤15 days had a UTI prevalence of 21.1% (8 out of 38 patients), while those aged >15 days showed a lower UTI rate of 9.3% (4 out of 43 patients), with a p-value of 0.210 using Fischer Exact Test, indicating no statistically significant association despite the apparent clinical difference (Table-III). Gender-based analysis revealed that male patients had a UTI prevalence of 19.2% (10 out of 52 patients), which was notably higher than the 6.9% UTI rate (2 out of 29 patients) observed in female patients, yielding a p-value of 0.196, indicating no statistically significant gender-based difference despite the apparent clinical trend (Table-III). Socioeconomic status analysis showed identical UTI rates of 16.2% in both lower class (6 out of 37 patients) and middle class (6 out of 37 patients) groups, while upper class patients showed no UTI cases (0 out of 7 patients, 0.0%), with a p-value of 0.608, demonstrating no significant association between socioeconomic status and UTI development (Table-III). Maternal education stratification revealed that children of educated mothers had a UTI prevalence of 17.4% (8 out of 46 patients), compared to 11.4% (4 out of 35 patients) in children of uneducated mothers, with a p-value of 0.539, indicating no statistically significant relationship between maternal education and UTI occurrence (Table-III). Mother's occupational status analysis demonstrated that children of employed mothers had a UTI rate of 11.8% (2 out of 17 patients), while children of unemployed mothers showed a slightly higher UTI rate of 15.6% (10 out of 64 patients), with a p-value of 0.735, indicating no significant association between maternal employment status and UTI development (Table-III). Residence-based stratification revealed that urban patients had a UTI prevalence of 9.7% (3 out of 31 patients), while rural patients demonstrated a higher UTI rate of 18.0% (9 out of 50 patients), with a p-value of 0.356, showing no statistically significant association between geographical residence and UTI occurrence despite the apparent difference in prevalence rates (Table-III). All statistical analyses were conducted using Fischer Exact Test methodology, and collectively, no demographic factor demonstrated a statistically significant association with UTI development in patients presenting with late neonatal sepsis, as evidenced by all p-values exceeding the conventional significance threshold of 0.05 (Table 3).

Table 3

Association of Urinary Tract Infection with Demographic Factors

Demographic Factors		Urinary Tract Infection		p-value
		Yes n(%)	No n(%)	
Age Group	≤15	8 (21.1%)	30 (78.9%)	0.210*
	>15	4 (9.3%)	39 (90.7%)	
Gender	Male	10 (19.2%)	42 (80.8%)	0.196*
	Female	2 (6.9%)	27 (93.1%)	
Socioeconomic Status	Lower Class	6 (16.2%)	31 (83.8%)	0.608*
	Middle Class	6 (16.2%)	31 (83.8%)	
	Upper Class	0 (0.0%)	7 (100.0%)	
Mother Education	Educated	8 (17.4%)	38 (82.6%)	0.539*
	Uneducated	4 (11.4%)	31 (88.6%)	
Mother Occupation	Employed	2 (11.8%)	15 (88.2%)	0.735*
	Unemployed	10 (15.6%)	54 (84.4%)	
Residence	Urban	3 (9.7%)	28 (90.3%)	0.356*
	Rural	9 (18.0%)	41 (82.0%)	

*Fischer Exact Test

DISCUSSION

Our findings indicated a prevalence of UTI at 14.8% among late neonatal sepsis cases, in agreement with prevailing body of knowledge that one of the common traits in neonatal sepsis is involvement of the genitourinary tract, particularly at late neonatal life when translocation and hematogenous spreading gain much prominence among modes of spreading of the infective agent. Male predominance among subjects we studied (64.2% vs 35.8%) is a faithful reflection of well-understood gender imbalance observed in neonatal sepsis, aided by the assumed immunomodulatory effect of genes that are inherited through the paternal line and bestow higher female immune competency by virtue of enhanced immune responses and by female-specific hormonal variance that delineates immune system maturation and production of antimicrobial peptides. Although not significant, increased UTI rate among male subjects (19.2% vs 6.9%) may be explained by morphological differences, that is, by smaller urethral length during early neonatal life and increased predisposition for ascending bacterial infections by virtue of incomplete maturation of urogenital tract. Increased prevalence among younger neonates (≤15 days: 21.1% vs >15 days: 9.3%) is a trend that hints at the substantial influence of immune system immaturity, as younger neonates have less differentiated adaptive immunity, depressed neutrophil efficiency, and immature complement system activation and thus are more exposed for bacterial penetration and spreading. Equal prevalence among equal classes of socioeconomic status and no significant association among mothers based on their educational or working history is an indication that UTI development in late neonatal sepsis is more a host factor- and bacterial virulence-driven phenomenon and less by environmental or by a determinant possession involving environmental and lifestyle barrier that points at the biological nature of this sequela. Elevated, although not significant, UTI rate among rural subjects (18.0% vs 9.7%)

may account for healthcare access variance, variance in practice at birth, or environmental contacting pattern variance for bacteria that would influence pattern of initiating colony and resultant pattern of ensuing infection among neonates.

Our UTI prevalence of 14.8% falls within the range reported in contemporary literature, showing considerable similarity to findings from comparable settings. Tariq et al. [15] reported a lower UTI prevalence of 10.48% among 105 neonates with sepsis, which may be attributed to their inclusion of both early and late-onset sepsis cases, as early-onset sepsis typically has lower UTI association due to different pathogenic mechanisms involving maternal transmission rather than nosocomial acquisition. Similarly, Kamel et al. [16] documented an 11% overall UTI prevalence, with notably higher rates in late-onset sepsis (16.4%) versus early-onset sepsis (4.4%), supporting our focus on late neonatal sepsis and explaining the slightly higher prevalence in our exclusively late-onset cohort. In contrast, Vishwanath et al. [17] reported a substantially higher UTI prevalence of 32% among 125 septic neonates, though their urine culture positivity was only 13.6%, suggesting potential differences in diagnostic criteria or clinical definitions of UTI. The markedly higher prevalence in their study may be explained by their inclusion of lighter neonates (>1 kg weight threshold) and predominant late-onset sepsis cases (84.8%), as lower birth weight and prolonged hospitalization increase UTI risk through enhanced bacterial colonization and invasive procedures. Our findings align closely with Riaz et al. [14] who found a UTI prevalence of 21.6% among 175 neonates with late-onset sepsis, which could be attributed to their larger sample size, different geographical bacterial flora, or variations in clinical management protocols that influence UTI development rates.

The gender distribution in our study showed interesting contrasts with existing literature, as our cohort demonstrated male predominance (64.2%) with higher UTI rates in males (19.2% vs 6.9%), which differs significantly from several other studies. Tariq et al. [15] found UTI was significantly more frequent in females (72.7% vs 27.3%, P=0.02), while Vishwanath et al. [17] reported male predominance overall (54.4%) but did not specify gender-specific UTI rates. Rahman et al. [18] observed female predominance (57%) in their UTI cohort, and Amelia et al. [19] reported a male:female UTI ratio of 5:2, more closely aligning with our findings. These gender differences may be explained by varying anatomical developmental patterns in different populations, differences in catheterization practices, or distinct bacterial colonization patterns influenced by local environmental factors and healthcare protocols. Bazaid et al. [20] found males represented 66.7% of UTI cases, supporting our observation of male susceptibility, possibly due to anatomical factors including incomplete penile development and increased manipulation during clinical care in male neonates.

Age-related UTI patterns in our study showed higher prevalence in younger neonates (≤15 days: 21.1% vs >15 days: 9.3%), though not statistically significant, which aligns with the immunological hypothesis that earlier neonatal periods are associated with greater vulnerability due to immature immune responses. Tariq et al. [15] found no significant association between age and UTI, though their age stratification differed from ours, while Mohseny et al. [21] specifically studied very preterm infants and found an 11.3% UTI prevalence, suggesting that gestational age and chronological age both contribute to UTI susceptibility through different mechanisms of immune system maturation and bacterial exposure duration.

The socioeconomic and educational factors in our study showed no significant associations with UTI development, which contrasts with general pediatric infectious disease patterns where socioeconomic status typically influences infection rates. This finding suggests that in the controlled NICU environment, biological factors and clinical management protocols may override social determinants of health, as all neonates receive similar levels of medical care regardless of their family's socioeconomic background. The lack of association with maternal education and occupation further supports this hypothesis, indicating that UTI development in late neonatal sepsis is primarily mediated by host immune factors, bacterial virulence, and clinical interventions rather than social or educational determinants that typically influence community-acquired infections. Sohaib et al. [22] similarly found no gender difference in organism distribution ($P > 0.05$), reinforcing the concept that bacterial pathogenesis in NICU settings may be more influenced by nosocomial factors than demographic characteristics.

Certain limitations should be taken into account while interpreting these findings. This was a single-center trial conducted at one institution, and it may limit the generalizability of results from other healthcare settings that possess different patient populations, clinical practice, or bacterial flora. The relatively small sample size of 81 patients may have limited statistical power for identifying significant associations, particularly for those variables that had low prevalence such asrepresentation of the upper socioeconomic class. The cross-section design also precluded determining temporal relationships and causality for demographic features and UTI development. In addition, the study failed to control for certain potential confounders such as hospital stay length, performance of invasive procedures, pre-collection antibiotic use, or clinician-related clinical management protocols that influence UTI occurrence. Inclusion of microbiological characterization of UTI pathogens and resistance patterns to antimicrobials represents another limitation that would have provided useful information about treatment implications.

CONCLUSION

Our research has found that the urinary tract infection was a salient complication in late onset sepsis in neonates, more commonly seen among male cases though no statistical association was noted among demographic correlations. The failure of significant linkage between prevalence of UTI and a vast spectrum of socio-economic determinants, maternal education level, employment and residence place points towards biological and clinical parameters having a prominent influence upon the development of UTI in the controlled condition of a NICU

scenario more than by determinants of a social nature.

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