

PREVALENCE OF URINARY TRACT INFECTION IN NEONATES ADMITTED IN NEONATAL INTENSIVE CARE UNIT WITH SEPSIS

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ABSTRACT

Background: Urinary tract infection (UTI) is an important but potentially underrecognized source of infection in neonates presenting with clinical sepsis. Because neonatal UTI often presents with nonspecific clinical manifestations, microbiological confirmation is essential for accurate diagnosis and appropriate management.

Objective: To determine the prevalence of culture-confirmed urinary tract infection among neonates admitted to the neonatal intensive care unit with sepsis.

Methods: This cross-sectional study was conducted among 58 neonates aged 0–28 days admitted to the neonatal intensive care unit with clinical suspicion of sepsis. Consecutive sampling was used. Urine samples were collected by sterile transurethral catheterization before initiation of antibiotics and submitted for culture. UTI was defined as growth of $>10^3$ CFU/mL of a single pathogenic organism. Demographic, neonatal, maternal, clinical, and laboratory variables were recorded and analyzed using SPSS version 29.

Results: Among the 58 neonates evaluated, 5 (8.6%) had positive urine cultures fulfilling the predefined criterion for UTI, while 53 (91.4%) had negative cultures. Among culture-positive cases, *Escherichia coli* and *Klebsiella pneumoniae* each accounted for 40% of isolates, while *Enterococcus* species accounted for 20%. UTI was observed more frequently among neonates with prematurity, low birth weight, late-onset sepsis, maternal UTI, and urinary catheterization; however, these associations did not reach statistical significance.

Conclusion: Culture-confirmed UTI was identified among neonates admitted with clinical sepsis, highlighting the importance of considering urinary infection during neonatal sepsis evaluation. Standardized urine collection before antibiotic administration and appropriate urine culture can facilitate accurate diagnosis and support targeted antimicrobial management.

KEYWORDS: Neonates; urinary tract infection; neonatal sepsis; neonatal intensive care unit; urine culture; *Escherichia coli*; *Klebsiella pneumoniae*.

INTRODUCTION

Urinary tract infection (UTI) is an important but potentially under-recognized bacterial infection in neonates, particularly among those requiring neonatal intensive care. Neonatal sepsis remains a major contributor to morbidity and mortality worldwide; recent global analyses continue to demonstrate a substantial burden of neonatal sepsis and other neonatal infections, with marked disparities affecting low- and middle-income regions. {1} A 2024 Lancet review reported that neonatal sepsis, together with preterm birth, contributes to almost half of deaths among children younger than five years globally, emphasizing the clinical importance of early recognition and appropriate antimicrobial treatment. {2}

UTI may coexist with systemic infection and can be difficult to recognize because neonatal manifestations are frequently nonspecific. Fever or hypothermia, poor feeding, lethargy, respiratory distress and other signs of sepsis may occur without distinctive urinary symptoms. Recent NICU data demonstrate considerable variation in the occurrence of neonatal UTI according to population and clinical setting. In a multicenter United States cohort of 86,492 very-low-birth-weight infants, 5,988 (7.0%) developed UTI, while a Brazilian NICU study involving 1,474 neonates reported UTI in 3.9% of infants. {3,4} More recent neonatal data from Kuwait identified significant bacteriuria in 282 of 3,996 urine samples (7.1%), with *Klebsiella pneumoniae* and *Escherichia coli* among the leading pathogens. {5}

The clinical importance of detecting UTI in septic neonates extends beyond immediate infection management because delayed recognition may contribute to inappropriate antimicrobial therapy, persistent infection and renal complications. Prematurity, low birth weight, catheterization and prolonged hospitalization have been associated with

increased neonatal UTI risk. {3,6} However, contemporary evidence specifically addressing the frequency of culture-confirmed UTI among neonates admitted with clinical sepsis remains limited, particularly in resource-constrained settings. The present study therefore aims to determine the prevalence of culture-confirmed UTI and evaluate associated clinical and neonatal risk factors among neonates admitted with sepsis to the NICU at Patel Hospital, Karachi. The study is intended to provide locally relevant evidence for improving urinary screening and timely management of septic neonates.

METHODOLOGY

A cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU), Patel Hospital, Karachi, over a period of six months following approval of the synopsis by the College of Physicians and Surgeons Pakistan (CPSP) and the Institutional Ethical Review Committee. The study population comprised neonates aged 0–28 days admitted to the NICU with clinical suspicion of sepsis. Neonates of either sex and of any gestational age, including preterm and term neonates, were eligible for inclusion. Written informed consent was obtained from the parents or legal guardians before enrollment.

The sample size was calculated using the WHO sample size calculator for estimation of a single population proportion using the formula $n = Z^2 \times P \times (1-P) / d^2$. A 95% confidence level was used with a Z value of 1.96, an anticipated frequency of urinary tract infection of 8% ($P=0.08$), and an absolute precision of 7% ($d=0.07$). The calculated sample size was 57.55, which was rounded up to 58 neonates. Participants were recruited using a non-probability consecutive sampling technique.

Neonates who had received systemic antibiotics before collection of the urine specimen were excluded because prior antimicrobial therapy could result in false-negative urine cultures. Neonates with major congenital anomalies of the urinary tract, such as posterior urethral valves, hydronephrosis, or antenatally diagnosed vesicoureteral reflux, were excluded because these conditions independently increased the risk of urinary tract infection. Neonates with known chromosomal or major congenital anomalies incompatible with survival or requiring palliative care were also excluded. In addition, neonates with incomplete clinical or laboratory records relevant to the study variables were excluded.

After approval of the study by the Institutional Ethical Review Committee of Patel Hospital and CPSP, eligible neonates were enrolled consecutively. Demographic and clinical information was collected using a pre-structured data collection proforma. Age was calculated in days from the date of birth to the date of admission. Sex was recorded according to physical examination and hospital registration records. Gestational age was determined from the maternal last menstrual period and confirmed, where available, by first-trimester or early second-trimester obstetric ultrasound findings. Birth weight was recorded in grams from the neonatal record and was measured using a calibrated digital neonatal weighing scale within the first hour of life.

Urine samples were collected from all enrolled neonates before initiation of antibiotic therapy using sterile transurethral catheterization under strict aseptic conditions to minimize contamination. The specimens were immediately transported to the microbiology laboratory for culture and sensitivity testing. Urinary tract infection was confirmed by growth of more than 10^3 colony-forming units (CFU)/mL of a single pathogenic organism. Blood culture results, C-reactive protein, complete blood count, and other relevant laboratory parameters were obtained from the patients' medical records. Maternal history, including urinary tract infection during pregnancy and relevant perinatal risk factors, was obtained through parental interview and review of medical records. A standardized urine collection technique and uniform data collection proforma were used for all participants. Laboratory personnel processing the urine cultures were blinded to the clinical details of the neonates, while consecutive sampling was used to reduce selection bias.

The study variables included demographic variables such as age, sex, gestational age, and birth weight, while clinical variables included type of neonatal sepsis, categorized as early-onset or late-onset, prematurity, low birth weight, maternal history of urinary tract infection, history of catheterization, and clinical features of sepsis including fever, hypothermia, poor feeding, lethargy, and respiratory distress. The primary outcome variable was the presence or absence of urinary tract infection confirmed by urine culture.

Data were entered and analyzed using SPSS version 29.0. The normality of continuous variables, including age, gestational age, and birth weight, was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were presented as mean $\pm$ standard deviation, whereas non-normally distributed variables were presented as median with interquartile range. Categorical variables were summarized as frequencies and percentages. The frequency of urinary tract infection was calculated as the proportion of culture-positive neonates among the total enrolled neonates with clinical sepsis. Associations between urinary tract infection and independent variables, including sex, gestational age, birth weight, prematurity, type of sepsis, maternal urinary tract infection, and history of catheterization, were assessed using the chi-square test or Fisher's exact test, as appropriate. Stratification was performed for potential confounders, particularly gestational age and birth weight, followed by post-stratification analysis. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant.

The study was conducted after approval by the Institutional Ethical Review Committee of Patel Hospital, Karachi, and the College of Physicians and Surgeons Pakistan (CPSP). Written informed consent was obtained from the parents or legal guardians of all participating neonates before enrollment. The institutional ethics committee had approved the submitted study protocol and required that any subsequent modification to the protocol be submitted for prior approval.

RESULT

A total of 58 neonates were included in the analysis. The mean age was 12.1 ± 7.4 days, and the mean gestational age was 35.8 ± 3.1 weeks. Thirty-four (58.6%) neonates were male and 24 (41.4%) were female. Twenty-nine (50.0%) neonates were preterm and 29 (50.0%) were born at term. The mean birth weight was 2185 ± 610 g, while low birth weight was recorded in 39 (67.2%) neonates. Early-onset sepsis was present in 22 (37.9%) neonates and late-onset sepsis in 36 (62.1%). The demographic and clinical characteristics of the study population are presented in Table 1. Culture-confirmed urinary tract infection was identified in 5 (8.6%) of the 58 neonates, whereas 53 (91.4%) had negative urine cultures. Among culture-positive specimens, *Escherichia coli* was isolated in 2 (40.0%) cases, *Klebsiella pneumoniae* in 2 (40.0%), and *Enterococcus* species in 1 (20.0%). The urine culture findings are summarized in Table 2.

The association between culture-confirmed UTI and selected demographic and clinical characteristics is shown in Table 3. UTI was identified in 3 (8.8%) male and 2 (8.3%) female neonates ($p=1.000$). Among preterm neonates, 4 (13.8%) had UTI compared with 1 (3.4%) among term neonates ($p=0.353$). UTI occurred in 5 (12.8%) neonates with low birth weight and in none of those without low birth weight ($p=0.165$). Among neonates with late-onset sepsis, 4 (11.1%) had UTI compared with 1 (4.5%) among those with early-onset sepsis ($p=0.639$). UTI was present in 2 (25.0%) neonates with a maternal history of UTI and 3 (6.0%) without such history ($p=0.153$). Among neonates with a history of catheterization, 3 (16.7%) had UTI compared with 2 (5.0%) among those without catheterization ($p=0.321$).

Table 1. Demographic and clinical characteristics of the study population (N=58)

Variable	Frequency / Summary
Age (days), mean $\pm$ SD	12.1 ± 7.4
Male sex	34 (58.6%)
Female sex	24 (41.4%)
Gestational age (weeks), mean $\pm$ SD	35.8 ± 3.1
Preterm	29 (50.0%)
Term	29 (50.0%)
Birth weight (g), mean $\pm$ SD	2185 ± 610
Low birth weight (<2500 g)	39 (67.2%)
Early-onset sepsis	22 (37.9%)
Late-onset sepsis	36 (62.1%)
Fever	14 (24.1%)
Hypothermia	17 (29.3%)
Poor feeding	31 (53.4%)
Lethargy	27 (46.6%)
Respiratory distress	33 (56.9%)
History of catheterization	18 (31.0%)
Maternal UTI during pregnancy	8 (13.8%)
PROM	16 (27.6%)
Intrapartum fever	7 (12.1%)

Table 2. Urine culture and microbiological findings (N=58)

Finding	Frequency, n (%)
Urine culture positive	5 (8.6%)
Urine culture negative	53 (91.4%)
Culture-confirmed UTI	5 (8.6%)
No culture-confirmed UTI	53 (91.4%)
<i>Escherichia coli</i>	2 (40.0%)*
<i>Klebsiella pneumoniae</i>	2 (40.0%)*
<i>Enterococcus</i> species	1 (20.0%)*

Table 3. Association of selected characteristics with culture-confirmed UTI

Variable	UTI present	UTI absent	p-value
Male sex	3/34 (8.8%)	2/24 (8.3%)	1.000
Preterm	4/29 (13.8%)	1/29 (3.4%)	0.353
Low birth weight	5/39 (12.8%)	0/19 (0.0%)	0.165
Late-onset sepsis	4/36 (11.1%)	1/22 (4.5%)	0.639
Maternal UTI	2/8 (25.0%)	3/50 (6.0%)	0.153
History of catheterization	3/18 (16.7%)	2/40 (5.0%)	0.321

DISCUSSION

The present study evaluated culture-confirmed urinary tract infection (UTI) among neonates admitted to the neonatal intensive care unit with clinical sepsis. The frequency observed in the study was comparable to that reported in contemporary neonatal populations, although estimates vary according to gestational age, clinical setting, urine-collection technique, and diagnostic criteria. In a large multicenter cohort of 86,492 very-low-birth-weight infants, UTI was diagnosed in 5,988 (7%) infants. {7} A Brazilian NICU study involving 1,474 neonates reported UTI in 3.9% of patients and demonstrated considerable variation in incidence over the study period. {8} More recent neonatal data have also reported increasing UTI incidence over time, indicating that the epidemiology of neonatal UTI may differ substantially between institutions and populations. {9}

The identification of UTI among septic neonates is clinically relevant because neonatal urinary infection commonly presents with nonspecific systemic manifestations. Fever, poor feeding, lethargy, respiratory abnormalities and temperature instability may occur with UTI as well as with other neonatal infections, making clinical differentiation difficult. Recent neonatal research reported fever and poor feeding among the common clinical manifestations of neonatal UTI. {9} The large multicenter VLBW cohort also demonstrated that only a minority of neonates with UTI had a concordant positive blood culture, indicating that a urinary source may not always be identified through blood-culture evaluation alone. {7} These findings support consideration of urine culture as part of the diagnostic evaluation of appropriately selected neonates with suspected infection.

Prematurity and low birth weight are important biological considerations in neonatal UTI. Immaturity of innate and adaptive immune responses, reduced integrity of epithelial barriers, prolonged hospitalization and greater exposure to invasive procedures may increase susceptibility to bacterial infection in premature and low-birth-weight infants. Recent evidence identified low birth weight as an independent risk factor for neonatal UTI, with an odds ratio of 2.831, while lower gestational age has also been associated with UTI in very-low-birth-weight populations. {7,9} These mechanisms provide a plausible explanation for the increased vulnerability of immature neonates and support the inclusion of gestational age and birth weight among the variables evaluated in the present study.

Urinary catheterization represents another potential mechanism for neonatal UTI. Catheter insertion can facilitate bacterial access to the urinary tract and may disrupt normal protective mechanisms. Recent neonatal evidence identified an indwelling urinary catheter as an independent risk factor for UTI, with an odds ratio of 3.452. {9} In the NICU environment, however, catheterization may also be associated with greater illness severity and prolonged hospitalization, making it difficult to separate the direct effect of catheterization from the clinical characteristics of infants requiring invasive care. The present study therefore evaluated catheterization as an associated clinical factor rather than assuming a causal relationship.

Maternal infection during pregnancy may represent an additional pathway for neonatal infection. Recent research identified maternal infection during pregnancy as an independent risk factor for neonatal UTI, with an odds ratio of 2.154. {9} Possible mechanisms include perinatal exposure to pathogenic organisms and transmission of maternal bacterial colonization. Nevertheless, the cross-sectional nature of the present study did not permit determination of whether maternal infection directly caused neonatal urinary infection. Maternal UTI was therefore appropriately evaluated as an associated variable rather than interpreted as a causal factor.

The microbiological findings were consistent with contemporary evidence demonstrating the importance of Gram-negative organisms in neonatal UTI. In the Brazilian NICU study, 74.6% of isolated uropathogens were Gram-negative bacteria, while *Escherichia coli* and *Klebsiella* species were among the principal organisms. {8} Similarly, the large multicenter VLBW cohort identified *Enterococcus* species, *E. coli*, and *Klebsiella* species among the leading organisms. {7} More recent data have suggested changes in pathogen distribution over time, with a decline in the proportion of Gram-negative organisms and a corresponding increase in Gram-positive organisms. {9} Such institutional and temporal variation emphasizes the importance of local microbiological surveillance when developing empirical treatment strategies.

Accurate microbiological diagnosis is particularly important in neonates because inappropriate classification of contaminated cultures as true UTI may result in unnecessary antimicrobial exposure. A 2024 NICU quality-improvement study demonstrated that implementation of standardized diagnostic criteria improved consistency in UTI diagnosis and showed that most true UTIs were caused by Gram-negative organisms, particularly *E. coli*. {10} The

authors also noted that *Enterococcus* was frequently considered a contaminant, illustrating the importance of interpreting culture results in conjunction with standardized diagnostic criteria. The present study used a predefined urine-culture criterion and standardized catheterized urine collection to reduce contamination and improve diagnostic consistency.

Antimicrobial resistance represents an increasing challenge in neonatal UTI. A 2025 study of 51 neonatal UTIs reported substantial resistance among *E. coli*, *Klebsiella pneumoniae*, *Enterobacter* species and *Enterococcus* species, with multidrug-resistant organisms identified among several major neonatal uropathogens. {11} The Brazilian NICU study likewise reported multidrug-resistant organisms among both Gram-negative and Gram-positive isolates. {8} These findings emphasize the importance of obtaining urine cultures before antimicrobial treatment whenever clinically feasible and subsequently tailoring therapy according to organism identification and antimicrobial susceptibility.

Standardized diagnosis also has implications for antimicrobial stewardship. Neonates admitted to NICUs are frequently exposed to empiric antimicrobial therapy because of the high clinical consequences of untreated sepsis. However, treatment of contaminated or incorrectly classified urine cultures may result in avoidable antibiotic exposure. A recent NICU study demonstrated that implementation of a standardized UTI diagnostic guideline improved uniformity in diagnosis and was designed specifically to reduce unnecessary antibiotic exposure. {10} Contemporary expert consensus has similarly emphasized timely recognition, appropriate diagnostic evaluation and early treatment of neonatal UTI while seeking to reduce missed diagnoses. {12} These considerations support the use of structured clinical and microbiological criteria in neonatal practice.

The study had several strengths. Consecutive sampling was used, eligibility criteria were predefined, urine specimens were collected using a standardized aseptic technique before antibiotic administration, and UTI was determined using a prespecified microbiological criterion. Laboratory personnel processing urine cultures were blinded to the clinical information of participants, reducing the possibility of observer-related bias. The study also assessed multiple demographic, neonatal and maternal variables that were clinically relevant to neonatal UTI.

Several limitations should be considered. The study was conducted in a single tertiary-care NICU, which may limit generalizability to other institutions and neonatal populations. The sample size was relatively small, limiting the precision of prevalence estimates and the ability to detect smaller associations between UTI and potential risk factors. The cross-sectional design allowed assessment of associations but did not establish temporal or causal relationships. Some maternal and clinical information was obtained from medical records or parental reporting and could therefore have been affected by information bias. In addition, the study did not assess long-term renal outcomes or provide a detailed analysis of antimicrobial-resistance patterns.

The findings have clinical implications for the evaluation of septic neonates in NICU settings. Culture-confirmed UTI should remain an important diagnostic consideration, particularly in neonates with recognized risk factors or clinical features compatible with infection. Standardized urine collection and culture-based diagnosis may assist in distinguishing urinary infection from other causes of neonatal sepsis and may support more appropriate antimicrobial use. Future multicenter prospective studies with larger sample sizes should evaluate standardized neonatal UTI definitions, pathogen-specific antimicrobial susceptibility, risk-factor profiles and long-term renal outcomes. Such evidence could strengthen locally appropriate screening strategies and antimicrobial-stewardship practices for neonatal UTI

CONCLUSION

Urinary tract infection represents an important component of infectious morbidity among neonates admitted to the neonatal intensive care unit with clinical sepsis. The findings highlight the importance of considering UTI during evaluation of septic neonates, particularly when clinical manifestations are nonspecific and other sources of infection are not clearly identified. Standardized urine collection before antimicrobial administration and appropriate culture-based diagnosis can improve identification of urinary infection and facilitate targeted treatment. Recognition of relevant neonatal and maternal risk factors may further support clinical assessment. Multicenter studies with larger populations are warranted to strengthen the evidence regarding neonatal UTI epidemiology, associated risk factors, microbiological patterns, and optimal diagnostic and therapeutic strategies.

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