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Clinical Profile of Urinary Tract Infections in Neonates with Suspected Sepsis: A Prospective Observational Study

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Abstract

Background: Neonatal urinary tract infections (UTIs) frequently present with nonspecific signs overlapping sepsis, leading to diagnostic delays and risk of renal injury. Data on prevalence, microbiology, and risk factors in Indian neonatal intensive care units are limited.

Objectives: To determine the prevalence, clinical presentation, microbiological profile, and perinatal risk factors for culture-confirmed UTIs among neonates evaluated for suspected sepsis.

Methods: In this prospective observational cohort study (January–December 2024) at the Level III NICU of Sree Mookambika Institute of Medical Sciences, 106 neonates (≤28 days old) with suspected sepsis underwent standardized catheterized urine sampling alongside blood cultures. Significant bacteriuria was defined as ≥10^5 CFU/mL. Clinical data, perinatal history, and laboratory results were recorded. Categorical comparisons utilized chi-square or Fisher's exact tests; continuous variables were analysed by t-tests or Mann–Whitney U tests. Multivariate logistic regression identified independent predictors of UTI, with significance at $p < 0.05$.

Results: UTI prevalence was 15.1%. Preterm neonates exhibited higher UTI rates than term infants (23.7% vs. 10.3%; $p = 0.044$). PROM > 12 hours was also associated with UTI (20.6% vs. 12.5%; $p = 0.043$). *Escherichia coli* predominated (62.5%), of which 80% were ESBL-producers. UTI-positive neonates had longer hospital stays (12.5 ± 4.1 vs. 10.2 ± 3.6 days; $p = 0.003$).

Conclusion: Routine catheterized urine culture in neonatal sepsis evaluations identifies a substantial UTI burden, particularly among preterm infants and those with prolonged membrane rupture. High ESBL rates underscore the need for local antibiogram–guided empirical therapy. Incorporating standardized urine screening into sepsis protocols may enable timely, targeted treatment and reduce renal sequelae.

KEYWORDS: UTI, Neonatal sepsis, Escherichia coli , ESBL.

INTRODUCTION

Urinary tract infections (UTIs) in neonates often masquerade as generalized sepsis, owing to the absence of pathognomonic signs in this age group; instead, they present with systemic manifestations that overlap significantly with sepsis: temperature instability (fever >38 °C or hypothermia <36 °C), respiratory distress (tachypnea, grunting, chest retractions), feeding intolerance characterized by poor feeding, frequent vomiting or gastric residuals, neurological signs such as lethargy, irritability, or seizures, and cardiovascular changes including tachycardia (>180 beats/min) or prolonged capillary refill (>3 seconds)[1]. These nonspecific symptoms underscore the challenge of early UTI detection and the risk of missed or delayed diagnoses with potential for irreversible renal damage.

The pathophysiology of neonatal UTI involves ascending bacterial colonization from the perineum: uropathogens such as Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis, and Proteus mirabilis adhere to immature neonatal urothelium through adhesins and fimbriae. Neonatal bladder physiology—characterized by low capacity, high compliance, and incomplete voiding—facilitates bacterial retention and proliferation. Preterm neonates face additional risks: underdeveloped detrusor innervation, higher intravesical pressures during filling, and vesicoureteral reflux, which allows retrograde flow of bacteria into renal parenchyma[1,5]. Renal cortical invasion triggers inflammatory cascades

involving interleukin-6, tumor necrosis factor-alpha, and other cytokines, leading to oxidative stress, tubular epithelial apoptosis, and interstitial fibrosis. Over time, these processes predispose to renal scarring, hypertension, and chronic kidney disease in survivors.

Epidemiological studies from high-income countries report neonatal UTI in 5–10% of infants undergoing sepsis evaluations[2]. However, emerging data from India indicate a higher prevalence, 8–12% overall and up to 15% among preterm neonates in tertiary NICUs. This is driven by variations in clinical practices, sampling techniques (catheterized urine vs. suprapubic aspirate), and differing thresholds for significant bacteriuria (≥10^4 vs. ≥10^5 CFU/mL) (3,4). Key perinatal risk factors include prolonged rupture of membranes (>12 hours in Indian setup), clinical chorioamnionitis or the newer Triple I criteria, maternal intrapartum fever, and maternal urinary tract infection in the third trimester[7].

Acute morbidity from neonatal UTI encompasses acute kidney injury (5–7% incidence), electrolyte derangements, and need for invasive interventions such as catheter drainage or surgical correction of congenital anomalies when detected[5]. Hospitalization durations are prolonged by 2–4 days compared to non-UTI sepsis, augmenting costs and parental stress. Follow-up renal ultrasonography and radionuclide scans demonstrate scarring in 3–5% of affected neonates, with potential long-term sequelae including hypertension and impaired renal growth[5,11].

A critical concern is the proliferation of antimicrobial resistance in neonatal uropathogens. Extended-spectrum β-lactamase (ESBL)–producing E. coli are increasingly documented, with reported rates of 40–60% in some Indian NICUs, complicating empirical therapy and emphasizing the importance of updated local antibiograms and stewardship interventions[6,10]. Despite these significant impacts, neonatal UTIs remain underrecognized in many resource-constrained settings. Urine culture is often omitted from initial sepsis workups due to perceived procedural risks of catheterization, competing diagnostic priorities, or limited laboratory capacity.

This study addresses these gaps by employing rigorous operational definitions from Nelson's Textbook of Pediatrics and international consensus on intrauterine infection, coupled with a standardized prospective protocol, to delineate the clinical, microbiological, and perinatal risk factor profile of neonatal UTIs in suspected sepsis cases. The findings aim to inform evidence-based diagnostic workflows and antibiotic selection algorithms tailored to neonatal care in tertiary-level Indian hospitals.

METHODOLOGY & STATISTICAL ANALYSIS

Objective:

To determine the prevalence, clinical presentation, microbiological spectrum, and perinatal risk factors associated with urinary tract infections in neonates (0–28 days) with suspected sepsis.

Study Design & Setting:

A prospective, observational cohort study conducted over 12 months (January–December 2024) in the Level III neonatal intensive care unit of Sree Mookambika Institute of Medical Sciences, a tertiary care referral center in southern India.

Inclusion criteria:

Neonates aged ≤28 days admitted with suspected sepsis, defined by at least one perinatal risk factor (PROM >12 hours, maternal fever ≥38 °C, clinical chorioamnionitis or Triple I) plus two or more clinical signs (thermoregulatory instability, respiratory distress, cardiovascular changes, neurologic signs, feeding intolerance, or hematologic abnormalities) [7].

Exclusion criteria:

Known major congenital uropathy or urinary tract malformations
Antibiotic exposure within 72 hours prior to urine sampling
Inability to obtain adequate catheterized urine specimen.

Recruitment & Consent:

Eligible neonates were identified by on-duty pediatrician and parents or guardians received detailed verbal and written information in the local language, outlining study procedures, risks, and benefits. Written informed consent was obtained prior to catheterization and data collection.

Data Collection:

A total of 106 neonates were enrolled. Demographic information (age in days, sex, birth weight, gestational age) and perinatal risk factors (mode of delivery, PROM duration, maternal fever, antenatal UTIs) were recorded. Clinical

signs at presentation were documented using standardized case report forms. Urine samples were collected aseptically via sterile catheterization, simultaneously with blood cultures. Diagnostic evaluations included:
- Urine dipstick analysis (leukocyte esterase, nitrite);
- Urine microscopy (pyuria defined as ≥5 WBCs/hpf);
- Quantitative urine culture (≥10^5 CFU/mL significant for catheterized specimens).

Isolates were species-identified using automated systems and conventional biochemical tests; antibiotic susceptibility (including ESBL detection) followed Clinical and Laboratory Standards Institute guidelines.

Statistical Analysis:

Data was entered into an excel sheet (MS Excel 2021), with discrepancies resolved by review of source documents. Analysis was performed using SPSS version 25.0. Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile range (IQR), and categorical variables as counts and percentages. The chi-square or Fisher's exact test compared categorical variables (e.g., UTI status vs. PROM, prematurity, sex). Independent-samples t-tests or Mann–Whitney U tests assessed differences in continuous variables (e.g., age at presentation, length of stay). Variables with $p < 0.10$ in univariate analysis entered into multivariate logistic regression to identify independent UTI predictors, reporting adjusted odds ratios (OR) with 95% confidence intervals (CI). Prevalence and subgroup proportions included exact binomial 95% CI. Statistical significance was set at $p < 0.05$ (two-tailed).

RESULTS

Table 1. Demographic and Clinical Characteristics

Variable	UTI-positive (n = 16)	UTI-negative (n = 90)	Total (n = 106)	p-value
Mean age (days)	4.6 ± 2.2	3.8 ± 1.9	4.0 ± 2.0	0.07
Length of stay (days)	12.5 ± 4.8	10.2 ± 3.9	10.8 ± 4.2	0.003*
Male sex, n (%)	9 (56.3%)	51 (56.7%)	60 (56.6%)	0.98
Preterm (< 37 wk), n (%)	9 (56.3%)	29 (32.2%)	38 (35.8%)	0.044*
PROM > 12 h, n (%)	7 (43.8%)	27 (30.0%)	34 (32.1%)	0.043*
Mode of delivery – C-section, n (%)	10 (62.5%)	45 (50.0%)	55 (51.9%)	0.40
Mode of delivery – Vaginal, n (%)	6 (37.5%)	45 (50.0%)	51 (48.1%)	0.40
History of maternal fever in 3rd trimester, n (%)	3 (18.8%)	10 (11.1%)	13 (12.3%)	0.46
Mean birth weight (g)	2700 ± 450	2900 ± 410	2800 ± 430	0.12

***p value < 0.05**

Of all the factors studied only preterm birth, PROM had significant association with UTI.

Table 2. Clinical Features

Feature	UTI-positive (n = 16)	UTI-negative (n = 90)	p-value
Temperature instability, n (%)	14 (87.5%)	73 (81.1%)	0.53
Respiratory distress, n (%)	9 (56.3%)	35 (38.9%)	0.05*
Feeding intolerance, n (%)	6 (37.5%)	18 (20.0%)	0.12
Neurological signs†, n (%)	8 (50.0%)	20 (22.2%)	0.01*

† Lethargy, irritability, or seizures; *p value < 0.05

Among the various clinical features, respiratory distress and neurological signs were common in neonates with UTI.

Table 3. Microbiological Profile of Isolated Pathogens

Pathogen	n (%)	ESBL positive n (%)
Escherichia coli	10 (62.5%)	8 (80.0%)
Klebsiella spp.	4 (25.0%)	2 (50.0%)
Enterococcus faecalis	1 (6.3)	–
Proteus mirabilis	1 (6.3)	–

E. coli was the most common pathogen isolated.

DISCUSSION

This prospective cohort study found a 15.1% prevalence of culture-confirmed UTIs among neonates evaluated for suspected sepsis—higher than the 5–10% reported in high-income settings[12] but consistent with Indian tertiary-centre reports[3,4]. We adhered to a catheterized sampling protocol with a $\geq 10^5$ CFU/mL cutoff, in line with CLSI standards[10] and the Indian Society of Pediatric Nephrology (ISPN) UTI guidelines[16], optimizing specificity in this age group.

Preterm neonates were at significantly greater risk (23.7% vs. 10.3% in term infants; $p = 0.044$), reflecting their immature urothelial defences and vesicoureteral reflux propensity[4]. Prolonged rupture of membranes (> 18 h) also independently predicted UTI (20.6% vs. 12.5%; $p = 0.043$), supporting the ascending infection model described in the Triple I consensus[7].

UTI-positive neonates experienced longer hospital stays (12.5 vs. 10.2 days; $p = 0.003$), increasing costs and caregiver burden. *Escherichia coli* predominated (62.5%), with an 80% ESBL-production rate—a resistance burden that underscores the need for ongoing local antibiogram surveillance and stewardship initiatives[6]. Although the follow-up for AKI and renal scarring was not done in this study, their potential for chronic kidney sequelae highlights the importance of follow-up imaging as recommended by the ISPN[16] and WHO[11].

Our findings underscore the need for integrated antimicrobial stewardship programs in NICUs, combining local antibiogram data, ISPN guidance, and rapid diagnostics to optimize empirical regimens and curb the emergence of multidrug-resistant organisms[6]. Emerging data suggest that adjunctive biomarkers—such as serum procalcitonin and neutrophil CD64 expression—may help distinguish UTI from systemic bacterial sepsis and prioritize urine testing in equivocal cases[14]. Point-of-care molecular assays for rapid pathogen identification are under investigation and could reduce time to targeted therapy and overall antibiotic exposure[15]. Cost-effectiveness analyses indicate that incorporating routine catheterized urine culture into neonatal sepsis protocols may be economically justified by shorter hospital stays and fewer complications, despite the procedural costs of catheterization[11].

CONCLUSION

In neonates with suspected sepsis, routine catheterized urine culture using a $\geq 10^5$ CFU/mL cutoff per ISPN guidelines[16] identified a 15.1% UTI prevalence, with preterm birth and prolonged membrane rupture as key risk factors. High ESBL rates among *E. coli* underscore the necessity of antibiogram-guided empirical regimens. Integrating catheterized urine culture into neonatal sepsis protocols will facilitate prompt, targeted therapy, reduce hospitalization duration, and mitigate renal sequelae.

LIMITATIONS & RECOMMENDATIONS

Strengths include prospective design, standardized ISPN/Nelson definitions, and blinded lab processing. Study limitations include its single-center nature and modest sample size, which may limit generalizability. Additionally, catheterization carries procedural risks and may not be universally feasible; future research should investigate noninvasive or minimally invasive sampling methods such as urine PCR or bag specimen analysis. Multicenter studies with larger cohorts are recommended to validate these findings and evaluate long-term renal and developmental outcomes. Follow-up imaging for renal scarring should be ideally done; comprehensive longitudinal studies assessing renal and developmental sequelae are needed. Implementation of antibiotic stewardship programs and standardized urine screening algorithms in neonatal sepsis pathways could enhance diagnostic accuracy, guide therapy, and improve clinical outcomes.

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