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**ORIGINAL ARTICLE**

# Frequency and Antimicrobial Sensitivity Pattern of Urinary Tract Infections in Late Onset Sepsis among Neonates at Children's Hospital Lahore

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## ABSTRACT

**Objective**: This research was conducted to determine the frequency and antimicrobial sensitivity patterns of urinary tract infections (UTIs) among neonates with late-onset sepsis in order to guide clinical decision-making and develop effective strategies for prevention and management of UTIs.

**Study Design**: A cross-sectional, observational study employing non-probability consecutive sampling. It included neonates aged 7-28 days diagnosed with late onset sepsis.

**Place and Duration of Study:** Carried out at Neonatal unit of the Children's Hospital, Lahore over six months, i.e., September 2022 to March 2023.

**Material and Methods:** Sample size of 100 neonates was estimated. Data including demographic information, urine samples, and antibiotic sensitivity patterns were collected and analyzed using SPSS v. 25.0. The analysis utilized the Chi-square test, with significance set at a p-value of ≤ 0.05.

**Results:** A mean age of 27.25 ± 4.45 days among neonates, with a male predominance of 77% was found. E. coli was the most common organism causing UTIs (64.7%), followed by klebsiella (17.64%) and staphylococci (11.76%). Pseudomonas was least commonly isolated (5.88%). Antibiotic sensitivity patterns varied among organisms, with amikacin and cefotaxime showing high sensitivity rates against E. coli. There was no significant difference between female and male neonates in the frequency of different organisms.

**Conclusion:** E. coli is the most frequently isolated organism in neonatal UTIs, with varying resistance and sensitivity patterns to different antibiotics. Understanding these patterns is crucial for guiding treatment decisions for the prevention and management of UTIs in neonates with LOS.

**Key Words:** *E. coli, Neonatal sepsis, UTIs, Antimicrobial pattern*

## INTRODUCTION

Neonatal sepsis is a substantial cause of illness and neonatal deaths in developing nations, accounting for nearly 30-50% of neonatal deaths in Pakistan.[1] Urinary tract infection (UTI) is a

prevalent illness in newborns and is often associated with neonatal sepsis. UTI may be the primary cause of bacteremia or a consequence of it in newborns.[2] In either case, it is critical to identify UTI early, as they can lead to prolonged hospital stays, death, or long-term health problems if not properly managed.[2,3] Hypertension and chronic renal failure are among the complications that may result from progressive renal damage in infancy or early childhood. UTIs were present in 9% of cases of late-onset sepsis among newborns, according to reports.

Symptoms of UTIs in newborns are non-specific and may present with systemic symptoms like temperature instability, refusal to eat, vomiting, jaundice, lethargy, abdominal distension or poor weight gain.[3] As a result, a urine examination could be a part of the investigation plan of late-onset sepsis in newborns but is not recommended as a routine.

When neonatal sepsis or UTIs are suspected, empirical antibiotic therapy is started immediately based upon the clinician's knowledge / experience about the probable bacterial pathogen.[4] Considering above mentioned facts, the study was conducted to collect local data on the frequency of UTI and its antimicrobial culture and sensitivity patterns in late-onset sepsis (LOS) among newborns to identify the most appropriate antibiotics that will aid in reducing the emergence of multi-drug-resistant organisms, hence reduce morbidity and mortality. Furthermore, this will curtail the likelihood of readmission and increase the length of the newborn's hospital stay.

## MATERIALS AND METHOD

**Study Design:** A cross-sectional, observational study.

**Setting:** Study was carried out at the Neonatal unit of the Children's Hospital, Lahore.

**Study Duration:** 26th September 2022 to 26th March 2023.

**Sample Size:** The sample size of 100 neonates was estimated with 95% confidence level and 7% margin of error and frequency of UTI 14.9% [5] in the newborns with late onset sepsis. Non-probability consecutive sampling was applied for selection of cases.

**Operational Definitions:** Late Onset Sepsis (LOS): It was taken as sepsis occurring in neonates after 7 days of life.

Sepsis: Defined as presence of suspected infection (consolidation on chest x-ray, positive blood culture, positive urine culture) with any ≥ 2 systemic inflammatory response syndrome criteria: i) fever (>38.3°C) or hypothermia (core temperature <36°C), ii) tachycardia (>160 per minute) or bradycardia (<60 per minutes), iii) tachypnea (respiratory rate >60/min), iv) irritability or lethargy, v) abnormal white blood cell count or >10% immature bands.[6] UTI was labeled if there was growth of 10,000 CFU/ml of a single urinary tract organism in catheterized sample.[7]

Antibiotic sensitivity pattern: It was identified as the response of the most frequently isolated organisms i.e. E. coli, klebsiella, staphylococci and pseudomonas to the antibiotics i.e., ampicillin, amikacin, gentamicin, cefotaxime and ceftriaxone using CLSI criteria. (ampicillin: MIC- 16 µg/ml, zone diameter <13 mm resistant and >17 mm sensitive, cefotaxime: MIC- 4 ug/ml, zone diameter 22 mm resistant and >26 mm as sensitive, gentamicin: MIC- 2 µg/mL, zone diameter 12 mm resistant and ≥15 mm sensitive, ceftriaxone: MIC- 64 µg/ml, zone diameter 13 mm resistant and ≥ 18 mm sensitive and amikacin: MIC- 32 µg/ml., zone diameter 14 mm resistant and ≥17 mm as sensitive.

**Sample Selection:**

**Inclusion Criteria**

1. Neonates (age 7-28 days), of both gender, diagnosed with LOS (according to definition).
2. Patients in whom informed consent was given by parents.

**Exclusion Criteria**

1. Neonates with gross congenital anomalies involving genitourinary track and anorectal abnormalities (on clinical examination).
2. Newborns who received antibiotics prior to hospital admission (on medical record and history from parents).
3. Neonates who expired within 24 hours of hospital admission.

Neonates fulfilling selection criteria (after taking ethical approval from research evaluation unit of the College of Physicians and Surgeons Pakistan (CPSP) - Ref No. CPSP/REU/PED-2020-075-5794) were enrolled for the study. Demographic information (age, gender, gestational age at birth, current weight and weight at birth) was noted. Catheterized urine samples were taken by a nurse under aseptic measures and sent to laboratory of Children's Hospital Lahore for urine culture. Reports were assessed and if culture was found to be positive with organism, then urinary tract infection was labeled and the organism isolated from urine sample was noted. Sensitivity pattern of causative organism was also noted. All this information was recorded in proforma.

**Data Analysis Procedure:** The data was input and analyzed with SPSS version 25. Frequency and percentage were expressed for qualitative variables like gender, UTI, organism isolated and its antimicrobial sensitivity. Quantitative variables like age, gestational age at delivery, current weight and birth weight were expressed by mean and standard deviation. Data stratification was done for gender, age, gestational age at delivery, birth and current weight to deal with effect modifiers. Chi-square test was employed to compare UTI, isolated organisms, and their sensitivity patterns across stratified groups. A significance level of p-value ≤ 0.05 was utilized.

## RESULTS

The neonates in present study had mean age of 27.25 ± 4.45 days. Overall there was male predominance where 77% (n=77)**.** The mean weight of all patients was 1.90 ± 0.37 kg. Overall, there were 17% (n=17) cases of sepsis reported due to UTI out of 100 neonates. E. coli was the major organism causing UTI (64.7%, n=11), followed by klebsiella (17.64%, n=3) and staphylococci (11.76%, n=2). Pseudomonas (5.88%, n=1) was least commonly isolated organism in neonatal urinary sepsis.

**TABLE 1*:* Distribution of organisms isolated from urine culture**

| Organism | Frequency | Percentage |
|---|---|---|
| E. coli | 11 | 64.70 |
| Klebsiella | 03 | 17.64 |
| Staphylococci | 02 | 11.76 |
| Pseudomonas | 01 | 5.88 |
| **Total** | **17** | **100.0** |

In case of E. coli, the highest sensitivity rates were for amikacin (47.16%) and cefotaxime (64.71%), while the lowest sensitivity rate was to ampicillin (11.77%). The highest resistance rates were to ampicillin (88.23%) and gentamycin (58.8%). The distribution of antibiotic resistance and sensitivity frequencies for klebsiella revealed some interesting patterns. Among the tested antibiotics, amikacin, cefotaxime and gentamicin had a resistance frequency of 66.66%, while there was a sensitivity frequency of 33.33%. Ampicillin and ceftriaxone, on the other hand, exhibited a 100% resistance frequency, indicating its ineffectiveness against klebsiella (table 2A). In case of staphylococci (table 2B), organism was 100% sensitive to amikacin, whereas ampicillin and ceftriaxone had a 100% resistance. Similarly, cefotaxime and gentamycin displayed a resistance frequency of 1 (50% relative frequency) and a sensitivity frequency of 1 (50% relative frequency.

The single case of UTI caused by pseudomonas in this study was found to be sensitive to amikacin and cefotaxime (100%) and resistant to ampicillin, ceftriaxone and gentamycin (100%) (table 2B)

**TABLE 2 A: Distribution of antibiotic resistance and sensitivity for E. coli and Klebsiella**

| Distribution of antibiotic resistance and sensitivity for E. coli | | | | |
|---|---|---|---|---|
| **Antibiotic** | **Resistance frequency** | **Resistance relative frequency (%)** | **sensitivity frequency** | **Sensitivity relative frequency (%)** |
| Amikacin | 6 | 52.94 | 5 | 47.16 |
| Ampicillin | 10 | 88.23 | 1 | 11.77 |
| Cefotaxime | 4 | 35.29 | 7 | 64.71 |
| Ceftriaxone | 6 | 52.94 | 5 | 47.06 |
| Gentamicin | 7 | 58.82 | 4 | 41.18 |

| Distribution of antibiotic resistance and sensitivity for Klebsiella | | | | |
|---|---|---|---|---|
| **Antibiotic** | **Resistance frequency** | **Resistance relative frequency (%)** | **Sensitivity frequency** | **Sensitivity relative frequency (%)** |
| Amikacin | 2 | 66.66 | 1 | 33.33 |
| Ampicillin | 3 | 100.0 | 0 | 0 |
| Cefotaxime | 2 | 66.66 | 1 | 33.33 |
| Ceftriaxone | 3 | 100.0 | 0 | 0 |
| Gentamicin | 2 | 66.66 | 1 | 33.33 |

**TABLE 2 B. Distribution of antibiotic resistance and sensitivity for staphylococcus and pseudomonas**

| Distribution of antibiotic resistance and sensitivity for staphylococcus | | | | |
|---|---|---|---|---|
| **Antibiotic** | **Resistance frequency** | **Resistance relative frequency (%)** | **Sensitivity frequency** | **Sensitivity relative frequency** |
| Amikacin | 0 | 0 | 2 | 100.0 |
| Ampicillin | 2 | 100.0 | 0 | 0 |
| Cefotaxime | 1 | 50.0 | 1 | 50.0 |
| Ceftriaxone | 2 | 100.0 | 0 | 0.0 |
| Gentamicin | 1 | 50.0 | 1 | 50.0 |

| Distribution of antibiotic resistance and sensitivity for pseudomonas | | | | |
|---|---|---|---|---|
| **Antibiotic** | **Resistance frequency** | **Resistance relative frequency (%)** | **Sensitivity frequency** | **Sensitivity relative frequency** |
| Amikacin | 0 | 0.0 | 1 | 100.0 |
| Ampicillin | 1 | 100.0 | 0 | 0.0 |
| Cefotaxime | 0 | 0.0 | 1 | 100.0 |
| Ceftriaxone | 1 | 100.0 | 0 | 0.0 |
| Gentamicin | 1 | 100.0 | 0 | 0.0 |

The stratification of four types of bacteria (E. coli, Klebsiella, Staphylococcus, and Pseudomonas) in gender groups of neonates is shown in the Tables 3, which shows the percentage of each organism type in males and females, as well as the resulting p-value from a chi-square test of independence showing no significant association between the types of organisms and either gender causing UTI in present study.

**TABLE 3: Stratification for various organisms with respect to gender**

| Organism | Gender | Yes (%) | No (%) | Total (%) | p-value |
|---|---|---|---|---|---|
| E. coli | Male | 4 (44.4) | 43 (47.3) | 47 (47.0) | |
| | Female | 5 (55.5) | 48 (52.7) | 53 (53.0) | 0.421 |
| Klebsiella | Male | 1 (33.3) | 46 (47.4) | 47 (47.0) | |
| | Female | 2 (66.6) | 51 (52.6) | 53 (53.0) | 0.521 |
| Staphylococci | Male | 1 (50.0) | 46 (46.9) | 47 (47.0) | |
| | Female | 1 (50.0) | 52 (53.1) | 53 (53.0) | 0.521 |
| Pseudomonas | Male | 1 (100.0) | 46 (46.4) | 47 (47.0) | |
| | Female | 0 (0.0) | 53 (53.6) | 53 (53.0) | 0.721 |

## DISCUSSION

UTIs can be particularly dangerous in newborn babies, especially those who are premature or have other health complications. LOS is a serious condition that can result from untreated or severe UTIs in neonates. In this study, we have explored the incidence of UTIs in neonates with LOS and analyze the antimicrobial sensitivity patterns of the bacteria causing these infections. Understanding the frequency and antimicrobial sensitivity patterns of UTIs in neonates with LOS is crucial for guiding clinical decision-making and developing effective strategies for preventing and managing these infections.

The neonates in present study had mean age of 27.25 ± 4.45 days with male predominance (77%). In an Indian study, the mean age of neonates with UTIs was found to be 21.3 days, with a male

predominance of 57%.[8] Another study from Pakistan found that male neonates had a higher incidence of UTIs compared to females, and E. Coli was the most common pathogen isolated, similar to our findings.[9] In this study, among isolated organisms (17 out of 100 cases), E. Coli was the commonest pathogen (64.7%), with klebsiella (17.64%) and staphylococci (11.76%) following in frequency. Pseudomonas trailed behind with just one occurrence (5.88%). The study of neonatal UTIs in the United States revealed that the predominant pathogens were E. coli, klebsiella, and enterococcus species, aligning with our observations.[10] Another study from Nigeria reported a similar pattern of bacterial isolates, with E. Coli being commonest organism subsequent to klebsiella and staphylococcus aureus.[11]

The findings of current study are somewhat consistent with previously available literature reviews on resistance patterns of antibiotics in bacteria. For E. coli, ampicillin and gentamicin are commonly reported as antibiotics with high resistance pattren.[12,13] Cefotaxime, on the other hand, is usually reported as an effective antibiotic.

The study also found that amikacin and cefotaxime were highly effective against E. Coli, which is consistent with other studies. According to a study by Saba et al., E. Coli had high resistance rates for ampicillin and gentamicin, but low resistance rates to cefotaxime.[12] This study also found that amikacin and cefotaxime had the highest sensitivity rates against E. coli.

The study found that klebsiella had a high resistance frequency to ampicillin, cefotaxime and ceftriaxone, which is a known trend in antibiotic resistance patterns for this bacterium.[13] However, amikacin had a lower sensitivity frequency (33.3%), compared to study done by Ma et al (100%).[13] For staphylococci, ampicillin is commonly reported as highly resistant, which is supported by the study's findings. Amikacin and cefotaxime are generally effective against staphylococci, and the study found similar results.[14] However, ceftriaxone had a low sensitivity frequency, which is not commonly reported in literature.

Multiple investigations have noted an elevated occurrence of neonatal sepsis attributed to gram-negative bacteria, including E. coli, klebsiella, and pseudomonas, in contrast to gram-positive bacteria like staphylococcus.[15,16] The current study found no statistically significant difference in the frequency of different types of organisms causing neonatal sepsis between males and females. Specifically, the frequency of E. coli, klebsiella, staphylococcus, and pseudomonas infections had no significant difference between the two genders ($p>0.05$). This observation is consistent with some previous studies. For example, a study conducted in Ethiopia found no significant difference in the incidence of neonatal sepsis among females and males.[17]Similarly, a study conducted in India also found no significant difference in the incidence of neonatal sepsis between two genders.[18]

However, other studies have reported conflicting results. A Nigerian study documented a higher incidence of neonatal sepsis among males compared to female infants.[19] Additionally, a study conducted in Iran reported a higher incidence of gram-negative bacterial infections in male infants compared to female infants.[20]

**Limitations of the study** include its single-center nature, potentially limiting generalizability. Additionally, the study's reliance on catheterized urine samples may not accurately reflect the true prevalence of UTIs, as catheterization itself can introduce contamination.

Overall, while the current study found no significant difference in the frequency of different types of organisms causing neonatal sepsis between males and females, further research is needed to fully understand the impact of gender on neonatal sepsis.

## CONCLUSION

The study concluded that E. coli is the most frequently isolated organism in neonatal UTIs, with varying resistance and sensitivity patterns to different antibiotics. Understanding these patterns is crucial for guiding treatment decisions and developing effective strategies for the prevention and management of UTIs in neonates with LOS.

**Conflict of interest:** None

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