

ORIGINAL ARTICLE

Prevalence, Etiology, Antimicrobial Susceptibility Testing and Predictors of Urinary Tract Infection among Neonates with Clinical SepsisUNAIZA SYED¹, ZAHID RASHID², ZARMAST KHAN³, RABIA RIAZ⁴, AHMAD BILAL⁵, QAMAR UZ ZAMAN⁶¹Senior Registrar Pediatric Medicine, Mohi ud Din Medical College and Teaching Hospital Mirpur AJK²Assistant Professor Pediatrics Medicine, Avicenna Medical College, Lahore³Associate Professor Pediatrics, Niazi Medical and Dental College, Sargodha⁴Registrar Paediatrics, Mohuidin Teaching Hospital, Mirpur AJK⁵Senior Registrar Pediatrics, Shalamar Medical and Dental College, Lahore⁶Assistant Professor Pediatrics, Shalamar Medical and Dental College, LahoreCorresponding author: Zarmast Khan, Email: dzarmastkhan@ymail.com**ABSTRACT**

Background and Aim: The most common pediatric infection is urinary tract infection (UTI). Neonates who suffer from neonatal sepsis remain among the most vulnerable to death and morbidity, especially in developing countries. The present study aimed to determine the prevalence, etiology, and susceptible antimicrobial agents of UTIs among neonates with clinical sepsis.

Patients and Methods: This cross-sectional study was carried out on 128 sepsis diagnosed neonates admitted to the Department of Pediatrics, Microbiology and Infectious Diseases, Niazi Welfare Teaching Hospital, Sargodha from September 2021 to May 2022. All neonates aged ≤ 28 days diagnosed of clinical sepsis and consent provided by their parents/guardian were enrolled. An interviewed based questionnaire was used for data collection from neonate's parents or caregiver. The questionnaire included information on the socio-demographics and clinical presentations of neonates, as well as maternal history and laboratory examinations. The history is taken from prenatal to postnatal, including birth weight analysis and birth conditions. Neonates underwent general and local examinations to determine their state of consciousness, vital signs, and weight. We examined the abdomen (for tenderness and abdominal distention) and the nervous system (to elicit suckling and motor reflexes). A hematological analyzer was used to test the full blood picture (FBP). SPSS version 27 was used for data analysis.

Results: Of the total 128 neonates, there were 76 (59.4%) females and 52 (40.6%) male neonates. The overall mean age was 6.4 ± 0.36 days with majority of neonates 112 (87.5%) were < 7 days. The low birth weight and low Apgar score were found in 13 (10.2%) and 16 (12.5%) neonates respectively. Of all neonates, the failure to breastfeed was found in 26 (20.3%) being the most common clinical symptom followed by an increase in breathing rate 21 (16.4%), diarrhea 19 (14.8%), grunting 16 (12.5%), altered mental status 12 (9.4%), and jaundice 11 (8.6%). The incidence of UTI was 20.3% (n=26). The prevalence of separated bacterial agents such as *Klebsiella pneumoniae* and *Enterobacter* spp. was 61.5% (n=16) and 38.5% (n=10) respectively. Ciprofloxacin and amikacin were both effective against 90% and 60% of the bacterial isolates, respectively. The UTI potential predictors involved prolong labour, positive leucocyte esterase test, Low Apgar score, and positive urine nitrite test.

Conclusion: The present study found that the prevalence of UTI was 20.3%. Failure to breastfeed was the most common clinical symptom followed by an increase in breathing rate, diarrhea, grunting, altered mental status, jaundice, convulsion, and cyanosis. *Klebsiella pneumoniae* and *Enterobacter* spp. were the most prevalent separated bacterial agents. Ciprofloxacin and amikacin were both effective in bacterial isolates.

Keywords: UTI, Clinical sepsis, Neonates, Antibiotic sensitivity

INTRODUCTION

Bacteria, parasites, viruses, and fungi are different infectious agents that causes urinary tract infections (UTIs) that exist and proliferate in urinary system sections such as urethra urethritis, bladder cystitis, urine bacteriuria, and kidney pyelonephritis [1]. UTIs might be symptomatic or asymptomatic infections that can transpire in complicated or uncomplicated individuals [2]. UTIs is one of the most prevalent causes of febrile illness in children, with a global frequency of 2-20% [3, 4]. They can cause significant morbidity and long-term consequences include renal scarring, hypertension, and chronic renal failure [5, 6]. Many pediatric UTI infections go undiagnosed due to a lack of specific symptoms and indications, particularly in newborns and young children [7]. It is believed that around 50% of UTIs in children are overlooked [8]. Early detection and treatment reduce the incidence of renal scarring and associated consequences [9]. Empirical antibiotics are frequently used for this purpose even before culture results are available. Antibiotic resistance in urinary tract infections, on the other hand, has been growing internationally [10].

Neonatal sepsis is defined as a clinical illness marked by systemic signs and symptoms of bacterial infection in the first 28 days of life [11]. It is a medical emergency that requires immediate diagnosis and treatment to avoid death [12]. Globally, it is estimated that 3 million babies die from sepsis each year, with neonatal sepsis accounting for 30% of all fatalities in children under the age of five [13]. Due of their immature immune system, newborns are especially vulnerable to infectious pathogens. The systemic inflammatory response to infection is decreased in newborns due to low immunoglobulin levels, poor complement

activation, low neutrophil storage, and impaired neutrophil migration from the circulation to infection sites [14].

The diagnosis of newborn UTI is commonly neglected since the symptoms are typically vague and obtaining clean samples is difficult. Systemic signs of UTI in the infant include prolonged jaundice, poor weight growth, temperature irregularity, lethargies, inability to breastfeed, and abdominal distension [15]. *Escherichia coli* is the most frequent bacterium that causes UTI in newborns and babies, accounting for 90% of cases [16]. *Klebsiella pneumoniae* and enterococci are two more bacteria. These species are located mostly in the proximal gastrointestinal tract and inhabit the perineum [17]. The absence of UTI was not ruled out by negative microscopic results for dipstick tests for nitrite and leukocyte esterase [18]. Gestational age, male gender, birth weight, chronological age, feeding exposure, UTI, and poor Apgar score >7 at 5 minutes are all predictors of UTI in a neonatal population [19].

METHODOLOGY

This cross-sectional study was carried out on 128 sepsis diagnosed neonates admitted to the Department of Pediatrics, Microbiology and Infectious Diseases, Niazi Welfare Teaching Hospital, Sargodha from September 2021 to May 2022. All neonates aged ≤ 28 days diagnosed of clinical sepsis and consent provided by their parents/guardian were enrolled. An interviewed based questionnaire was used for data collection from neonate's parents or caregiver. The questionnaire included information on the socio-demographics and clinical presentations of neonates, as well as maternal history and laboratory examinations. The history

is taken from prenatal to postnatal, including birth weight analysis and birth conditions. Neonates underwent general and local examinations to determine their state of consciousness, vital signs, and weight. We examined the abdomen (for tenderness and abdominal distention) and the nervous system (to elicit suckling and motor reflexes). A hematological analyzer was used to test the full blood picture (FBP). Blood of two milliliters were taken aseptically and placed in clot activator tube and allowed for at least 15 minutes to guarantee that it clotted. The serum was drained, placed in the disc, and then placed in the machine.

A container comprised of urine specimen were stored and transported to laboratory in order to prevent organism growth in those samples. This technique was completed within 1 hour of the sample being collected. In cases where test was not performed immediately, it was chilled at temperatures ranging from 4 to 8 °C, and the procedure was completed within 4 hours. For data analysis, SPSS version 27 was used. For continuous data, the mean was computed. Chi-square test was used for comparative association between categorical variables. Multivariate regression analysis was done to define the UTIs associated independent factors among neonates with clinical sepsis.

RESULTS

Of the total 128 neonates, there were 76 (59.4%) females and 52 (40.6%) male neonates. The overall mean age was 6.4 ± 0.36 days with majority of neonates 112 (87.5%) were < 7 days. The low birth weight and low Apgar score were found in 13 (10.2%) and 16 (12.5%) neonates respectively. Of all neonates, the failure to breastfeed was found in 26 (20.3%) being the most common clinical symptom followed by an increase in breathing rate 21 (16.4%), diarrhea 19 (14.8%), gritting 16 (12.5%), altered mental status 12 (9.4%), and jaundice 11 (8.6%). The incidence of UTI was 20.3% (n=26). The prevalence of separated bacterial agents such as *Klebsiella pneumoniae* and *Enterobacter spp.* was 61.5% (n=16) and 38.5% (n=10) respectively. Ciprofloxacin and amikacin were both effective against 90% and 60% of the bacterial isolates, respectively. The UTI potential predictors involved prolong labour (AOR= 5.41, 95% CI, 1.30-20.46, p=0.001), positive leucocyte esterase test (AOR= 6.59, 95% CI, 1.51-30.26, p=0.015), Low Apgar score (AOR = 11.82, 95% CI = 4.21–38.92, p<0.001), and positive urine nitrite test (AOR = 25.74, 95% CI = 7.82–90.69, p<0.001). The demographic and clinical details of neonates and maternal is shown in Table-I and Table-II. Participants' clinical features are shown in Table-III. Urine culture test was performed on positive and negative neonates on urine dipstick test and it was observed that 20.3% (26/128) of the neonates had positive urine culture and 79.7% (102/128) of the neonates had negative urine culture findings. *Klebsiella pneumoniae* accounted for 61.5% (n=16) of the pathogenic organisms identified in neonates urine culture among, followed by *Enterobacter spp.*, which accounted for 38.5% (n=10) as depicted in Figure-1. Ciprofloxacin, meropenemamikacin, and nitrofurantoin were shown to be susceptible to *Klebsiella pneumoniae* and *Enterobacter spp.*, whereas ampicillin, ceftriaxone, and gentamycin were completely resistant to the isolated organisms as shown in Figure-2. Predictors of neonatal urinary tract infection (UTI) are represented in Table-IV.

Table-1: Neonatal baseline and medical features (n=128)

Features	Frequency N	Percentage %
Neonates age (days)		
<7	112	87.5
≥7	26	12.5
Gender		
Male	52	40.6
Females	76	59.4
Birth weight (g)		
Normal (≥2500)	114	89.1
Low (<2500)	14	10.9

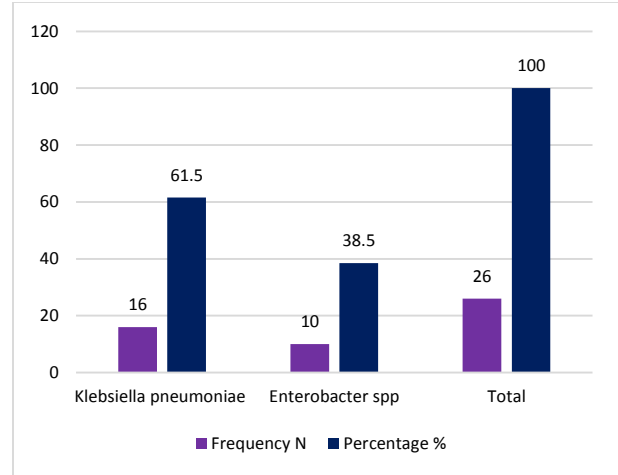


Figure-1: Prevalence of UTIs (n=26)

Table-2: maternal baseline and medical features (n=128)

Features	Frequency N	Percentage %
Maternal age group (years)		
<20	15	11.7
21-35	92	71.9
>35	21	16.4
Maternal Occupation		
Employed	46	35.9
Unemployed	82	64.1
Gestational Age		
First trimester	12	9.4
Second trimester	92	71.9
Third trimester	24	18.8
UTI antibiotics		
Yes	5	31.3
No	11	68.7
Labour duration (hrs)		
>18	11	8.6
≤18	117	91.4
Mode of delivery		
Cesarean section	9	7.0
Spontaneous vaginal delivery	119	93

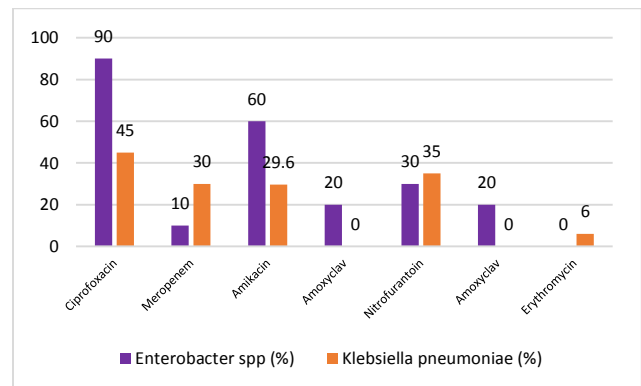


Figure-2: Patterns of antibiotic sensitivity in infants with urinary tract infection

Table-3: Participants' clinical features

Clinical features	Frequency N	Percentage %
Failure to breastfeed	26	20.3
Breathing rate	21	16.4
Diarrhea	19	14.8
Gritting	16	12.5
Altered mental status	12	9.4
Jaundice	11	8.6
Convulsion	14	10.9
Cyanosis	9	7.0
Total	128	100

Table-4: urinary tract infection (UTIs) predictors of neonates

UTIs predictors	AOR, 95% CI	P-value
Prolong labour	5.41 (1.30-20.46)	0.001
Positive leucocyte esterase test	6.59 (1.51-30.26)	0.015
Low Apgar score	11.82 (4.21–38.92)	<0.001
Positive urine nitrite test	25.74 (7.82–90.69)	<0.001

DISCUSSION

The present study mainly focused on the incidence, etiology, and susceptible antimicrobial agents of UTIs among neonates with clinical sepsis and found that UTI was found in 20.3% of neonates. The most prevalent clinical sign was failure to breastfeed, followed by an increase in respiratory rate, diarrhea, grunting, changed mental state, jaundice, convulsion, and cyanosis. Enterobacter spp. and Klebsiella pneumoniae are the most prevalent separated bacterial agents. Both ciprofloxacin and amikacin were effective against bacterial isolates. UTI is the most prevalent bacterial infection, affecting primarily children, and can have serious consequences in cases if not cured promptly. Disease established scope, predictors of risk factors, and causative agents for infection are all critical steps in the therapeutic therapy of newborns.

The frequency of UTI among newborns was found to be 20.3%, and the only bacterial isolates involved in causing UTI were Klebsiella pneumoniae and Enterobacter spp. Ampicillin, gentamycin, and ceftriaxone were all completely ineffective against the isolated bacteria in the research; however, ciprofloxacin showed response to both isolates. Moreover, the UTIs independent predictors were leucocytes, lower Apgar score, and nitrite positive test. The incidence of UTI among newborns in our study was 20.3%, which was comparable to the incidence of 18% reported by Fatima et al. in India among neonates (< 4 weeks) [20].

The incidence of UTI discovered in this investigation was greater than the prevalence of 6%, 6.4%, 7.2%, 12.5%, and 14.5% recorded in various studies [21–25]. The difference in prevalence between studies might be attributed to differences in technique. The UTIs most prominent cause in the present study was Klebsiella pneumoniae, which is consistent with the findings in our study [26, 27]. In terms of antibiotic sensitivity, nitrofurantoin, ciprofloxacin, and amikacin showed significant resistance to Enterobacter spp. In contrast, Klebsiella pneumoniae was sensitive to Cipro, nitrofurantoin, and amikacin. A Nigerian based study reported that Klebsiella pneumoniae was the most prevalent bacterial isolated among neonates followed by Enterobacter spp. The former was sensitive to gentamicin (33.3%), nitrofurantoin (83.3%), and ciprofloxacin (33.3%) [28].

Low Apgar score neonates were 12 to 13 times more prone to UTI as compared to normal Apgar score and their association was found statistically significant [29]. The majority of neonates delivered with low Apgar scores are owing to difficulties in the delivery process, particularly delays during the 2nd stage of labour. Furthermore, UTIs among neonates have been associated with maternal diseases such as anemia and malaria [30].

Anorectal abnormalities and gastrointestinal issues have also been observed to enhance the odds of newborns developing UTI. Vesicoureteral reflux, for example, has been shown to occur in 20–47% of children with anorectal abnormalities [31]. Furthermore, the risk of UTIs rises with increased vesicoureteral reflux, which can contribute to renal impairment due to renal scarring. [32].

E. coli was the most prevalent bacterium linked with pediatric UTI. Our findings are comparable with those of other research [33, 34]. E. coli is the most frequent etiological agent for UTI, regardless of age, community, and gender accounting for 50–90% of infections. Uropathogenic E. coli (UPEC) enter the bladder through the urethral orifice after emerging from the intestinal flora [35].

CONCLUSION

The present study concluded that the prevalence of UTI was 20.3%. Failure to breastfeed was the most common clinical symptom followed by an increase in breathing rate, diarrhea, grunting, altered mental status, jaundice, convulsion, and cyanosis. Klebsiella pneumoniae and Enterobacter spp. were the most prevalent separated bacterial agents. Ciprofloxacin and amikacin were both effective in bacterial isolates.

REFERENCES

- Lugira, Y.S., Kimaro, F.D., Mkhoyi, M.L. et al. Prevalence, aetiology, antimicrobial susceptibility testing, and predictors of urinary tract infection among neonates with clinical sepsis: a cross-sectional study. *Egypt Pediatric Association Gaz* 70, 2 (2022). <https://doi.org/10.1186/s43054-021-00088-6>.
- Lo DS, Rodrigues L, Koch VHK, Gilio AE (2018) Clinical and laboratory features of urinary tract infections in young infants. *J Bras Nefrol* 40:66–72.
- Bahat Ozdogan E et al (2018) Urinary tract infections in neonates with unexplained pathological indirect hyperbilirubinemia: Prevalence and significance. *Pediatr Neonatol* 59:305–309.
- Kumar S, Shankar B, Arya S, Deb M, Chellani H (2018) Healthcare associated infections in neonatal intensive care unit and its correlation with environmental surveillance. *J Infect Public Health* 11:275–279.
- Gidabayda JG et al (2017) Patterns of urinary tract infection amongst children admitted at Kilimanjaro Christian Medical Centre. *East African Heal Res J* 1:53–61.
- Masika WG, O'Meara WP, Holland TL, Armstrong J (2017) Contribution of urinary tract infection to the burden of febrile illnesses in young children in rural Kenya. *PLoS ONE* 12:1–13.
- Amelia N, Amir I, Trihono PP (2016) Urinary tract infection among neonatal sepsis of late-onset in Cipto Mangunkusumo Hospital. *Paediatr Indones* 45:217
- Gunduz S, Uludağ Altun H (2018) Antibiotic resistance patterns of urinary tract pathogens in Turkish children. *Glob Heal Res Policy* 3:1–5
- Ding Y, Wang H, Pu S, Huang S, Niu S (2021) Resistance trends of klebsiella pneumoniae causing urinary tract infections in Chongqing, 2011–2019. *Infect Drug Resist* 14:475–481
- Ballén V et al (2021) Antibiotic resistance and virulence profiles of Klebsiella pneumoniae strains isolated from different clinical sources. *Front Cell Infect Microbiol* 11:1–11
- Gidabayda J et al (2017) Prevalence, aetiology, and antimicrobial susceptibility patterns of urinary tract infection amongst children admitted at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. *East African Heal Res J* 1:53–61.
- Fenta A, Dagne M, Eshetie S, Belachew T (2020) Bacterial profile, antibiotic susceptibility pattern and associated risk factors of urinary tract infection among clinically suspected children attending at Felege-Hiwot comprehensive and specialized hospital, Northwest Ethiopia A prospective study. *BMC Infect Dis* 20:1–10
- Samancı S, Çelik M, Köşker M (2020) Antibiotic resistance in childhood urinary tract infections: a single-center experience. *Turk Pediatr Ars* 55:386–392
- Chokshi A, Sifri Z, Cennimo D, Horng H (2019) Global contributors to antibiotic resistance. *J Global Infect Dis* 11:36–42.
- Beahm NP, Nicolle LE, Bursley A, Smyth DJ, Tsuyuki RT (2017) The assessment and management of urinary tract infections in adults: Guidelines for pharmacists. *Can Pharm J* 150:298–305.
- Fair RJ, Tor Y (2014) Antibiotics and bacterial resistance in the 21st century. *Perspect Medicin Chem*:25–64. <https://doi.org/10.4137/PMC.S14459>
- Mikkelsen LF, Rubak S (2020) Reversible lung fibrosis in a 6-year-old girl after long term nitrofurantoin treatment. *BMC Pulm Med* 20:1–4
- Gebremedhin D, Berhe H, Gebrekirstos K (2016) Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia, 2015: Unmatched case control study. *PLoS ONE* 11:1–10.
- Glen P, Hawary A, Prashar A (2016) Sterile pyuria: a practical management guide. *Br J Gen Pract* 66:e225–e227.
- Fatima S, Muhammad IN, Usman S, Jamil S, Khan MN, Khan SI. Incidence of multidrug resistance and extended-spectrum beta-lactamase expression in community-acquired urinary tract infection among different age groups of patients. *Indian J Pharmacol*. 2018;50(2):69–74.
- Bellazreg F et al (2019) Diagnostic value of dipstick test in adult symptomatic urinary tract infections: results of a cross-sectional Tunisian study. *Pan Afr Med J* 33:1–6

22. Wu, C. et al. Risk factors of vesicoureteral reflux and urinary tract infections in children with imperforate anus. (2021).
23. Lendner I et al (2019) Urine dipstick low sensitivity for UTI diagnosis in febrile infants**. *Infect Dis (Auckl)* 51(764–771).
24. Desai DJ, Gilbert B, McBride CA. Paediatric urinary tract infections: diagnosis and treatment. *Aust Fam Physician*. 2016;45(8):558–63.
25. Madhi F, Jung C, Timsit S, Levy C, Biscardi S, Lorrrot M, et al. Febrile urinary tract infection due to extended-spectrum beta-lactamase-producing Enterobacteriaceae in children: a French prospective multicenter study. *PLoS One*. 2018;13(1):e0190910.
26. Parajuli NP, Maharjan P, Parajuli H, Joshi G, Paudel D, Sayami S, et al. High rates of multidrug resistance among uropathogenic *Escherichia coli* in children and analyses of ESBL producers from Nepal. *Antimicrob Resist Infect Control*. 2017;6:9.
27. Badhan R, Singh DV, Badhan LR, Kaur A. Evaluation of bacteriological profile and antibiotic sensitivity patterns in children with urinary tract infection: a prospective study from a tertiary care center. *Indian J Urol*. 2016;32(1):50–6.
28. Iwuafor AA, Ogunsola FT, Oladele RO, Oduyebo OO, Desalu I, Egwuatu CC, et al. Incidence, clinical outcome and risk factors of intensive care unit infections in the Lagos University teaching hospital (LUTH), Lagos, Nigeria. *PloS one*. 2016;11(10):e0165242.
29. Jayaweera J, Reyes M. Antimicrobial misuse in pediatric urinary tract infections: recurrences and renal scarring. *Ann Clin Microbiol Antimicrob*. 2018;17(1):27.
30. Korbel L, Howell M, Spencer JD. The clinical diagnosis and management of urinary tract infections in children and adolescents. *Paediatr Int Child Health*. 2017;37(4):273–9.
31. Garrido D, Garrido S, Gutierrez M, Calvopina L, Harrison AS, Fuseau M, et al. Clinical characterization and antimicrobial resistance of *Escherichia coli* in pediatric patients with urinary tract infection at a third level hospital of Quito, Ecuador. *Bol Med Hosp Infant Mex*. 2017;74(4):265–71.
32. Sorlozano-Puerto A, Gomez-Luque JM, Luna-Del-Castillo JD, Navarro-Mari JM, Gutierrez-Fernandez J. Etiological and Resistance Profile of Bacteria Involved in Urinary Tract Infections in Young Children. *Biomed Res Int*. 2017; 2017:4909452.
33. Masud MR, Afroz H, Fakruddin M. Prevalence of extended-spectrum betalactamase positive bacteria in radiologically positive urinary tract infection. *Springerplus*. 2014;3:216.
34. Wu CT, Lee HY, Chen CL, Tuan PL, Chiu CH. High prevalence and antimicrobial resistance of urinary tract infection isolates in febrile young children without localizing signs in Taiwan. *J Microbiol Immunol Infect*. 2016;49(2):243–8.
35. Bryce A, Hay AD, Lane IF, Thornton HV, Wootton M, Costelloe C. Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. *BMJ*. 2016; 352:i939.