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RESEARCH ARTICLE

Urinary Tract Infection in Infants <1 Month of Age: Demographic, Clinical, and Microbiological Characteristics

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Abstract: ***Background:*** This cross-sectional study was conducted on 232 infants aged <1 month with proven UTI admitted to three major teaching hospitals for the period 2010-2018 to assess clinical, demographic, and laboratory findings of urinary tract infection in this age group.

Methods: All information was extracted from the medical records. Urinary tract infection was defined as ≥ 50,000 colony-forming units per milliliter of a single uropathogen isolated from a catheterized or suprapubic aspiration or greater than 100,000 colony-forming units per milliliter from a midstream, clean-catch sample.

Results: The most common pathogen isolated was *E. coli* (78.4%), followed by *Enterobacter* and *Klebsiella*, accounting for 12.1 and 4.7% respectively. The main presenting clinical manifestation was jaundice, which was found in 54.7% of cases; it was followed by restlessness (45.6%) and fever (40%).

Conclusion: During infancy, the signs and symptoms of UTI are often nonspecific and although urine culture is a gold standard diagnostic tool specimen collection is challenging and urine contamination is common in children, therefore it makes the diagnosis difficult. UTI in infants may indicate underlying genitourinary abnormalities; therefore, appropriate diagnosis and immediate initiation of antibiotic therapy are crucial to decrease long-term complications like renal scarring. According to our study, the most common clinical features were jaundice, restlessness, and fever, therefore it is suggested that urine culture should be performed for all infants presenting with these signs and symptoms.

Keywords: Urinary tract infection, infant, *Escherichia coli*, fever, jaundice, urine culture.

1. INTRODUCTION

Urinary tract infection (UTI) is one of the most common infectious diseases during infancy that may be ignored because in many cases it is not associated with specific clinical signs and symptoms [1-4]. In the first 6 months of life, the occurrence of UTI in male infants decreases and in females increases simultaneously [5]. The incidence of UTI is approximately 0.7% in females and 2.7% in uncircumcised males within the first year of life [6, 7]. UTI may be associated with genitourinary tract abnormalities, however, it can occur in the setting of normal anatomy [8]. The majority of UTI cases appear to be caused by ascending bacteria from the periurethral area [6, 9-11]. Hematogenous spread can also occur but it is more common in the first few months of life [5]. Gram-negative bacteria are the most common pathogens causing UTIs in children and adults. Similar to other age groups, *Escherichia coli* (*E. coli*) is the most common bacterial etiology for neonatal UTI, which is found in approximately 80% of neonatal cases [3, 12-14]. Other enteric gram-negative bacteria can also cause UTI, including *Klebsiella*, *Pseudomonas*, *Proteus*, *Enterobacter*, and *Citrobacter spp* [3, 4]. UTI is usually diagnosed when infants are screened for fever because it may be the only presenting manifestation of UTI in this age group. Newborns are at higher risk for disseminated bacteremia, septicemia and severe related complications due to cellular and humoral immune system insufficiencies during infancy [15, 16]. It is suggested that urine culture should be considered for all infants with fever (≥ 38°C), weight loss, poor feeding, prolonged jaundice, vomiting, diarrhea, tachypnea and other suspicious signs and symptoms. The clinical manifestations in premature infants are similar [15, 17-20]. UTI occurs frequently during infancy and if there is a delay in diagnosis and proper treatment it can lead to severe irreparable complications like permanent kidney scar that can be prevented with immediate and appropriate antibiotic treatment [13]. Because of the importance of early diagnosis and treatment of UTI in infants, we conducted this cross-sectional cohort study to evaluate the epidemiological, clinical and microbiological characteristics and also laboratory findings of UTI in

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infants <1 month in three major teaching hospitals from 2010 until 2018 in Khoramabad, Iran.

2. MATERIALS AND METHODS

This cross-sectional cohort study was conducted on 232 infants <1 month of age with proven UTI diagnosis admitted to three major teaching hospitals (Shahid Rahimi, Shahid Madani and Asalian Hospitals) that serve a population of about 400,000 people, from 1st January 2010 to 31st December 2018 in Khoramabad, Iran. During this period, 6800 infants aged <1 month were seen in the mentioned hospitals. Our study included 232 (3%) infant patients who were diagnosed with UTI: 197 cases at Shahid Madani Hospital, 20 cases at the Asalian Hospital and 15 cases at the Shahid Rahimi Hospital. All cases were identified retrospectively through medical records. All information including initial clinical manifestations, gestational age, gender, age on admission, past medical history, method of urine collection, laboratory results and discharge diagnosis were extracted from the medical records. Patients with nosocomial urinary tract infection, congenital metabolic disorders, infants with severe systemic diseases including congenital metabolic disorders, neuromuscular diseases, malignancy, acquired or congenital immunodeficiency and also infants with genitourinary devices were excluded from our study (Fig. **1**). All urine samples were collected by urinary bladder catheterization or suprapubic approach. All cases had evidence of positive urine culture in their medical records according to the definition of UTI in clinical guidelines issued in 2011 for the diagnosis and management of UTI. Based on these guidelines a positive urine culture for UTI is defined by the isolation of a single uropathogen at a density of greater than 50,000 colony-forming units (CFUs)/mL from a catheterized or suprapubic aspiration, or greater than 100,000 CFU/mL from a midstream, clean-catch sample [21].

Approval to conduct this research was obtained from the Ethics Committee of Lorestan University of Medical Sciences (IR.LUMS.REC.1397.198). This manuscript conforms to the Helsinki Declaration as well.

Data were analyzed using the IBM SPSS for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA) and the categorical data are expressed as percentage and shown by tables. Continuous data are shown as mean ± SD.

3. RESULTS

The study population consisted of 232 infants aged below 1 month with confirmed UTI, including 125 females (54%) and 107 males (46%). All male infants were uncircumcised. Gestational age was not available for 20 (9%)

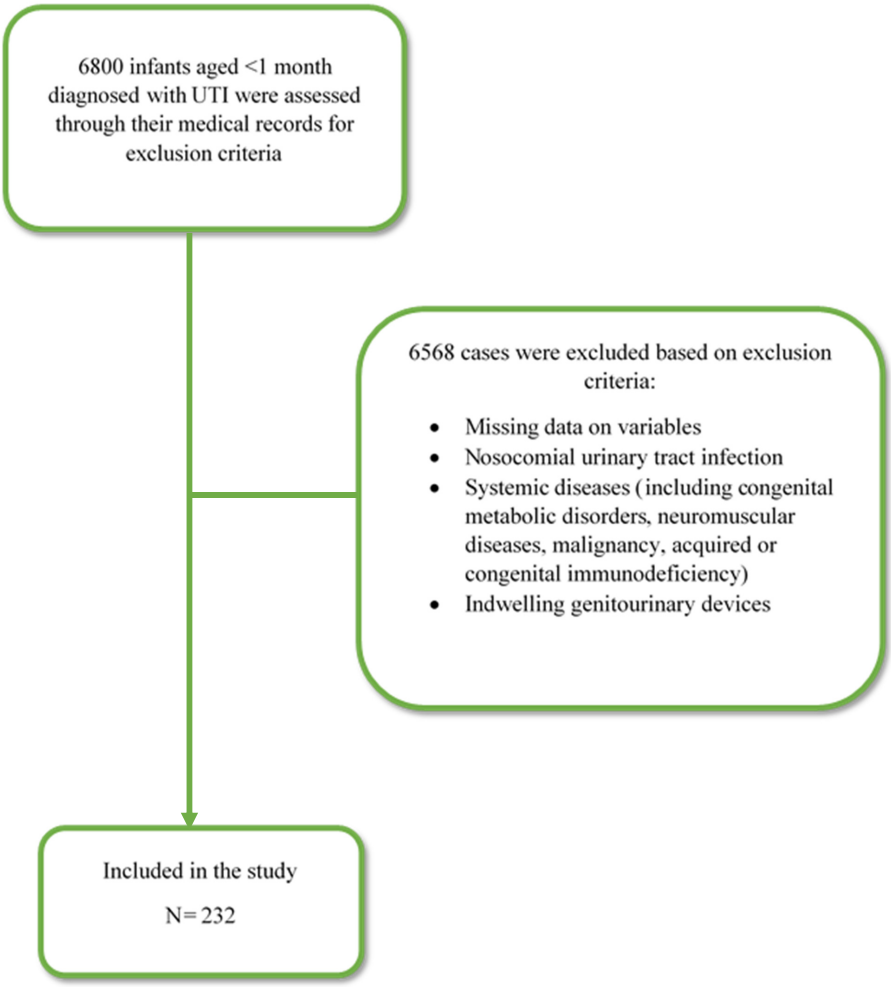

Fig. (1). Flowchart of the study.

infants, out of 212 cases, 22 infants (10%) were preterm (20-37 weeks) and 190 infants (90%) were full-term. For 212 cases with recorded gestational age, the mean gestational age was 37.61 ± 1.288 weeks, data from 20 cases were not available. 127 infants (55%) were delivered by vaginal delivery and 105 infants (45%) by caesarian section. All infants were between 1 and 29 days old and the median age on admission was 16.62 ± 7.09 days. According to the medical records, 121 infants (52%) were exclusively breastfed, 49 infants (21%) were fed on formula and 62 infants (27%) were fed from both. Overall, the common manifestations at presentation were jaundice (54.7%), restlessness (45.6%), fever (40%), irritability (13.7%), weight loss (10.3%), poor feeding (9.9%) and poor weight gain (6%) (Table **1**). We evaluated all available laboratory findings including the presence of white blood cells (WBCs), red blood cells (RBCs) and the nitrite test result in the first sterile urine sample. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were also assessed as inflammatory markers in the blood sample. All of our cases (100%) had more than 5 WBCs/HPF in urinalysis. The result of the urine nitrite test was positive for 138 cases (59.5%). A total of 40 infants (17.2%) had more than 5 RBCs/HPF in the urine sample (Table **2**). In terms of inflammatory markers in the blood sample, for 219 infants (94.4%) CRP levels were greater than 5mg/L and ESR levels were above 10 mm/h in all patients (100%). A total of 60 patients had leukocytosis ≥ 15000/mm^3. The mean value of WBCs/mm^3 was 12294 ± 4466 (Table **3**). We also evaluated the results of the urine culture of all patients and it was shown that the most common pathogen isolated was *E. coli* (78.4%), followed by Enterobacter and Klebsiella, accounting for 12.1 and 4.7% respectively. Other microorganisms such as Proteus spp. and coagulase-negative staphylococcus were relatively rare (Table **4**). 229 patients had renal ultrasonography results in their medical records, of which 79 cases (34.5%) had abnormalities on renal ultrasound.

Table 1. Common clinical manifestations.

Signs and Symptoms	n
Fever	7
Fever + Restlessness	32
Fever + Poor feeding	16
Fever + Jaundice	6
Fever + Jaundice + Restlessness	10
Fever + Poor feeding +Restlessness	6
Fever + Restlessness + Irritability	8
Fever + Restlessness + Poor weight gain	1
Fever + Irritability	5
Fever + Poor weight gain + Jaundice	2
Jaundice	62
Jaundice + Poor weight gain + Restlessness	4
Jaundice + Restlessness	19
Jaundice + Restlessness + Irritability	1
Jaundice + Poor weight gain	1
Jaundice + Weight loss	21
Jaundice + Poor weight gain + Irritability	1
Restlessness	5
Restlessness + Irritability	17
Restlessness + Weight loss	3
Poor weight gain	4
Poor weight gain + Poor feeding	1

Table 2. Urinalysis findings.

Variable	-	N (%)
Nitrite test	Positive	138 (59.5)
	Negative	94 (40.5)
WBCs > 5/HPF	-	232 (100)
RBCs > 5/HPF	-	40 (17.2)

Abbreviations: WBC, White blood cell; RBC, Red blood cell; HPF, High-power field.

Table 3. Laboratory findings.

Variable	N (%)
CRP > 5mg/L	219 (94.4)
ESR > 10 mm/h	232 (100)
Blood counts with WBCs ≥ 15000/mm^3	60 (25.8)
Mean WBCs/mm^3 ± SD	12294 ± 4466

Abbreviations: CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; WBC, White blood cell.

Table 4. Distribution of etiological agents.

Etiological Agents	N (%)
E. coli	182 (78.4)
Enterobacter spp.	28 (12.1)
Klebsiella spp.	11 (4.7)
Coagulase negative Staphylococcus	7 (3.0)
Proteus spp.	4 (1.7)
Total	232 (100)

Abbreviation: *E. coli, Escherichia coli*.

4. DISCUSSION

This cohort study aims to address clinical and laboratory findings about UTI in infants aged below 1 month. The incidence of UTI is approximately 0.7% in females and 2.7%

in uncircumcised males within the first year of life [6, 7]. In our study, all infected male infants were uncircumcised which is in accordance with previous studies [3, 8, 22, 23]. During infancy, the incidence of UTI in boys is higher than in girls [22]. After one year of age, females are much more likely than males to develop UTI [5]. However, we did not find a significant difference between genders having UTIs. In our study, a total of 125 cases (53.9%) were female and 107 cases (46.1%) were male. Most UTIs in infants are caused by gram-negative bacilli; *Escherichia coli* accounts for 85 to 90% of cases [3]. In our study, *E. coli* was isolated in 78.4% of patients, followed by *Enterobacter* and *Klebsiella*, accounting for 12.1 and 4.7% respectively. In the neonatal period, the clinical manifestations of UTI are often nonspecific, making the diagnosis difficult. A neonate may present with anorexia, poor feeding, diarrhea, vomiting, lethargy, irritability, temperature instability, or prolonged jaundice. Foul-smelling urine is a rare manifestation, but a more specific symptom of UTI for infants [5, 19]. In our cohort, the main presenting clinical manifestation was jaundice, which was found in 54.7% of cases; it was followed by restlessness (45.6%) and fever (40%). The gold standard method of assessing pyuria has been centrifugation of the urine sample and microscopic analysis, the presence of ≥ 5 white blood cells per high-power field (HPF) is defined as pyuria [21]. However, pyuria is not diagnostic of UTI [24, 25]. It has a specificity of approximately 81% and a sensitivity of 73% [21]. In our study, all cases (100%) had more than 5 WBCs/HPF in urinalysis. A nitrite test is not sensitive enough to rule out UTI, particularly for infants, because they empty their bladders frequently and there is no adequate time for the conversion of nitrate into nitrite. Additionally, infection with non-nitrate-reducing bacteria (*e.g.*, *Pseudomonas spp*., *Enterococcus spp*., *Staphylococcus saprophyticus*) may lead to a false-negative test result. The positive nitrite test can be helpful because it is highly specific [5, 21]. Based on the results of our search, out of 232 cases, 138 infants (59.5%) had positive nitrite tests and 94 infants (40.5%) had negative nitrite test results. Occurrence of UTIs in the first 3 days of life is very rare (0%–1%) in the United States [8] and higher in developing countries up to 1.8% [26, 27]. Our results also did not report the occurrence of UTI on the first day of birth.

5. STUDY LIMITATIONS

The main limitation of our study comes from its retrospective nature, and some data could have been missing or incomplete. Our study was only limited to hospitalized infants <1 month with confirmed UTI, therefore our findings may not apply to the general pediatric population. We also excluded a significant number of cases due to our restricted inclusion criteria or negative urine culture, because they may have used antibiotics before being visiting the hospital.

CONCLUSION

The purpose of this study was to assess the common presenting clinical and laboratory findings of infants aged below 1 month with UTI. During infancy the clinical manifestations of UTI are often nonspecific, making the diagnosis difficult. UTI in infants may indicate an underlying renal disorder; therefore, appropriate diagnosis and prompt initiation of therapy are crucial to decrease long-term complications like renal scarring. In our study the most common clinical manifestations were jaundice, restlessness and fever, therefore our findings suggest that urine culture should be performed for all infants presenting with these clinical manifestations. Additional prospective studies should be performed to overcome limitations and follow up on the patients and the long-term complications of UTI.

LIST OF ABBREVIATIONS

CRP	=	C-Reactive Protein
ESR	=	Erythrocyte Sedimentation Rate
RBCs	=	Red Blood Cells
UTI	=	Urinary Tract Infection
WBCs	=	White Blood Cells

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval to conduct this research was obtained from the Ethics Committee of Lorestan University of Medical Sciences, Iran, with the approval number (IR.LUMS.REC.1397.198).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants.

STANDARDS OF REPORTING

STROBE guideline has been followed.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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