

Clinical and Etiological Profile of Complicated Urinary Tract Infection in Children: A Health Facility-Based Cross-Sectional Study

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ABSTRACT

Background: Urinary tract infection (UTI) is known to be the most frequent bacterial infection in the paediatric population.

Objective: To determine the clinical profile and etiology of complicated urinary tract infection (UTI) in children.

Methods: This cross-sectional study was done at the Department of Nephrology and Neonatology, National Institute of Child Health, Karachi from 1st January 2022 to 30th June 2022. In 241 children of either gender, (male and female) aged up to 15 years having structural or functional anomalies of the kidney and urinary tract or recurrent infection due to underlying kidney or urinary tract abnormalities were enrolled. Demographic and clinical characteristics along with laboratory parameters and etiological agents of complicated UTI were noted. Ultrasonography examination and dimercaptosuccinic acid (DMSA) renal scan (where indicated) were performed.

Results: Of 241 children, 179 (74.3%) were male. The mean age was 3.08±3.63 years. Capillary refill time was prolonged in 78 (32.4%) children. Fever/chills, nausea/vomiting, urinary urgency, and dehydration were the most frequently noted clinical presentations reported in 232 (96.2%), 109 (45.2%), 91 (37.8%), and 89 (36.9%) children respectively. Ultrasonography findings were evident of bilateral moderate hydronephrosis in 60 (24.9%) children. *E. coli* followed by *Pseudomonas* and *Klebsiella* species were the most commonly found etiological agents noted in 98 (40.7%), 50 (20.7%), and 40 (16.6%) children respectively.

Conclusion: The majority of the children with complicated UTIs were male. Fever/chills, nausea/vomiting, urinary urgency, and dehydration were the most frequently noted clinical presentations. The most commonly observed ultrasonography findings were bilateral moderate hydronephrosis.

Keywords: Dehydration, *E. coli*, fever, hydronephrosis, urinary tract infection.

INTRODUCTION

Urinary tract infection (UTI) is known to be the most frequent bacterial infection in the paediatric population, either in outpatient or hospitalized children, and is considered the 3rd commonest cause behind febrile ailment among paediatric age groups [1, 2]. UTI is described as the growth of a significant number of microorganisms of a single species in the urine [3].

Symptoms of UTI vary according to age groups like, young children have non-specific symptoms like fever while younger infants may exhibit irritability, failure to thrive, jaundice, vomiting, and diarrhoea or oliguria/polyuria. Relatively older children present with symptoms of upper or lower urinary tract symptoms such as pyelonephritis presenting with high-grade fever, flank pain, and/or vomiting whereas in cystitis, these children might be presenting with dysuria, frequency, new onset incontinence, and mal-odorous urine [4, 5]. UTIs have been classified based on location and severity, if it occurs in the upper urinary tract known as pyelonephritis, and if it occurs in the lower urinary tract it is known as cystitis,

based on the severity it is classified into uncomplicated and complicated [6, 7].

When UTI occurs in children without any structural or functional anomalies it is known as uncomplicated UTI or complicated UTI when it occurs in the presence of any underlying structural or functional anomalies of the urinary tract, urinary tract devices (catheter), if it is recurrent or associated with immunodeficiency [7, 8]. Complicated UTI could be due to renal, pelvoureteric, vesicoureteric junction, bladder, urethra related abnormalities [8, 9]. UTI is generally diagnosed by positive urine culture and evidence of pyuria or bacteriuria [10]. Ultrasound kidney ureters and bladder (KUB) findings are categorized as hydronephrosis, renal or ureteral dilation, renal parenchymal changes, or bladder findings [11].

Many studies on various aspects of renal problems in children have been done but the importance of complicated UTIs is not highlighted in Pakistan while complicated UTIs commonly present late with sepsis or obstructive uropathy, or renal failure. There is international literature available on the subject, which evaluated the causes of complicated UTIs [1-3, 12]. With this study, we may be able to diagnose the cases of complicated UTIs in their early stages and prevent them from complications. This study was performed to

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determine the clinical profile and etiology of complicated UTIs in children.

MATERIALS AND METHODS

This cross-sectional study was conducted in the inpatient and outpatient department of Nephrology and Neonatology, “National Institute of Child Health (NICH)”, Karachi from 1st January 2022 to 30th June 2022. Approval from Institutional Ethics Review Board was acquired. Informed and written consent was sought from parents/caregivers of all study participants. Considering the 6% prevalence of UTI among unwell children with a 95% confidence level and a 3% margin of error, the sample size was estimated as 241 [13].

Inclusion criteria were children of either gender (male and female) aged up to 15 years having structural or functional anomalies of the kidney and urinary tract, diagnose by history, clinical examination, and lab investigation, or recurrent infection due to underlying kidney/urinary tract abnormality. Exclusion criteria were children whose parents/caregivers were not willing to be part of this study. Children with chronic constipation with no association with bladder abnormality were also not included. Among enrolled children, medical history was taken, clinical examination was performed and lab investigations were ordered. Complicated UTI was defined as UTI that occurred in the presence of any underlying structural or functional anomalies or indwelling catheter with or without renal impairment, characterized by any of the following features: the presence of fever greater than 39°C, systemic toxicity (anorexia, nausea, vomiting, sepsis, symptoms of the lower urinary tract (frequency, urgency, dysuria) or tenderness in flanks. Renal angle tenderness was labeled as the reaction of pain, discomfort, or tenderness upon palpation and pressure application on the renal angle area. Palpable bladder or kidney was termed as the feeling or detection of the kidney during the physical examination. UTI was labeled as positive urine culture s growth of microorganism >5x10⁴CFU/ml by catheterization or midstream clean catch, any count via suprapubic aspiration. Drug sensitivity was measured as diameter (mm) by the zone of inhibition by applying drugs on Mueller Hinton agar plates incubated for 72 hours by the modified Kirby Bauer disc diffusion method. Recurrent UTI was labeled as a child who had two or more discrete episodes of UTI within the last 6 months.

Data were analysed using “Statistical Package for Social Sciences (SPSS)” version 26.0. Mean and standard deviation were estimated for quantitative variables while frequency and percentages were calculated for categorical variables. The chi-square test was applied for the comparison of qualitative data considering p<0.05 as significant.

Table 1: Demographic and clinical characteristics of children with complicated UTI (n=241).

| Characteristics | | Number (%) / Mean±SD |
|-----------------------------------|--------|----------------------|
| Gender | Male | 179 (74.3%) |
| | Female | 62 (25.7%) |
| Age (years) | | 3.08±3.63 |
| Height (cm) | | 82.30±25.06 |
| Weight (kg) | | 12.17±10.95 |
| Heart Rate (beats/minute) | | 102.77±11.25 |
| Respiratory Rate (breaths/minute) | | 36.64±7.98 |
| Temperature (Celsius) | | 38.89±0.41 |
| Prolonged Capillary Refill Time | | 78 (32.4%) |
| Renal Angle Tenderness | | 8 (3.3%) |
| Palpable Bladder | | 23 (9.5%) |
| Palpable Kidneys | | 34 (14.1%) |
| Glomerular filtration rate (GRF) | ≥90 | 41 (17.0%) |
| | 60-89 | 31 (12.9%) |
| | 30-59 | 42 (17.4%) |
| | 15-29 | 59 (24.4%) |
| | <15 | 68 (28.2%) |

RESULTS

Of 241 children, 179 (74.3%) were male. The mean age was 3.08±3.63 years ranging between 2 months to 13 years. Mean height and weight were 82.30±25.06 cm and 12.17±10.95 kg respectively. Capillary refill time was prolonged in 78 (32.4%) children. The mean GFR was calculated to be 51.83±67.79. Table 1 is showing characteristics of children with complicated UTIs.

Fever/chills, nausea/vomiting, urinary urgency, and dehydration were the most frequently noted clinical presentations reported in 232 (96.2%), 109 (45.2%), 91 (37.8%), and 89 (36.9%) children respectively.

Ultrasonography findings were evident of bilateral moderate hydronephrosis in 48 (55.2%) children. “Dimercapto succinic acid (DMSA)” scan identified bilateral vesicoureteral reflux (VUR) in 60 (24.9%) children. Laboratory parameters of children with complicated UTI showed that hemoglobin, TLC, Platelet count, Creatinine, GFR, and Leucocyte Esterase were 9.4±1.6 (g/dl), 17.7±13.0 (x10⁹/L), 420±201 (x10⁹/L),

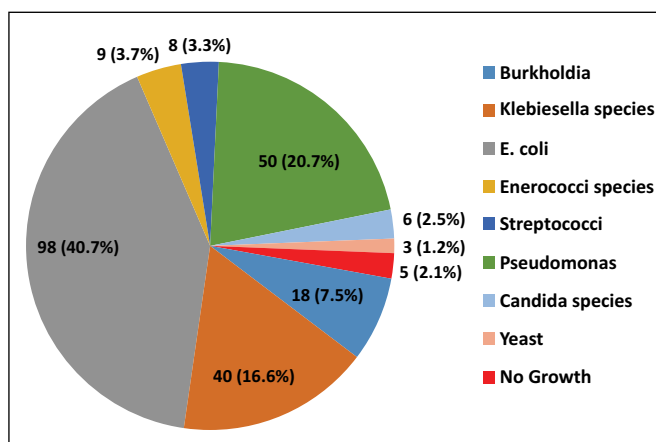


Fig. (1): Frequency distribution of microorganisms among children with complicated UTI (n=241).

1.77±1.57 (mg/dl), 51.83±67.79 (ml/min/1.73m) and 352.38±187.69 (ul) respectively.

E. coli followed by *Pseudomonas* and *Klebsiella* species were the most commonly found etiological agents noted in 98 (40.7%), 50 (20.7%), and 40 (16.6%) children respectively. **Fig. (1)** is showing the complete frequency distribution of microorganisms among children with complicated UTIs. *E. coli* were most sensitive to ciprofloxacin imipenem (94.3%), meropenem (91.4%), cefoperazone sulbactam (85.7%), tazobactam (82.9%) and gentamicin (71.4%) while highest resistance patterns were shown for ampicillin (85.7%), ofloxacin (77.1%), ceftriaxone (71.4%) and ciprofloxacin (65.7%). *Pseudomonas* species showed highest rates of sensitivities against imipenem (94.7%), piperacillin/tazobactam (84.2%) and amikacin (73.7%) whereas highest resistance rates were shown for cefuroxime (94.7%), cotrimoxazole (94.7%), co-amoxiclav (84.2%) and cefipime (78.2%). *Klebsiella* species were most sensitive to meropenem (93.3%), imipenem (93.3%), fosfomycin (80.0%) and cefoperazone-sulbactam (80.0%) while most resistance rates were shown for sulfamethoxazole (80.0%), ciprofloxacin (73.3%) and ceftriaxone (66.7%). **Table 2** is showing the distribution of frequency of clinical presentations concerning gender and age groups.

DISCUSSION

Complicated UTI has been related to factors linked with abnormal urinary tract functioning, host defense, and foreign bodies while management of complicated UTI is found to be challenging [14, 15].

In this study, 74.3% of children with complicated UTIs were male. *Wu et al.* also reported 51.5% of children with complicated UTIs are male [3]. Studies evaluating adult patients with complicated UTIs have shown a female predominance (61.4%) [16].

Fever/chills, nausea/vomiting, urinary urgency, and dehydration were the most frequently noted clinical presentations reported in 96.2%, 45.2%, 37.8%, and 36.9% of children respectively. Literature reports fever, systemic toxicity, persistent vomiting, and dehydration

as the most commonly found presenting features/complaints in complicated UTI so our findings were quite consistent with what has been reported in the literature in the past [17].

In the present research, *E. coli* (40.7%) followed by *Pseudomonas* (20.7%) and *Klebsiella* species (16.6%) were found to be the most common etiological agents among children with complicated UTI. *Wu et al.* revealed *E. coli* to be the causative agent in 53.3% of cases of complicated UTI while *Klebsiella* species and *Pseudomonas* species were the other commonest etiological agents found in 17.8% and 11.1% of children respectively [3]. Literature reports *E. coli* to be the commonest etiological agent behind UTI [18]. *E. coli* isolates have been found among 62-73% of children with community-acquired UTI [19]. A recent study evaluating children with complicated children found *E. coli* to be present in 80.5% positive cultures [20]. In the majority of the cases of UTI, gram-negative bacteria are usually the etiological agent while other less prevalent agents are gram-positive bacteria. The literature exhibits that *Escherichia coli* (*E. coli*) is the most frequent etiological agent behind UTI whereas researchers have shown that *E. coli* is isolated in 80% of UTI community cases and 60% of intra-hospital cases [21, 22]. Moreover, a review stated that the recurrence of UTI could be due to relapse in the preceding *E. coli* infection which might be due to the evidence that *E. coli* can result in invasion and replication within murine bladders, forming stable biofilm-like intracellular reservoirs for recurrent UTI [23]. Among complicated UTI cases, the etiology as well as the susceptibility of the causative agents is not always predictable so in cases of complicated UTI, children need to undergo a urinalysis, moreover, culture and sensitivity analysis also needs to be performed. As global antimicrobial resistance, patterns are showing increasing trends, there is always a challenge when researchers are planning clinical trials aiming for outcomes of UTIs among children.

Not much work is seen evaluating children with complicated UTI so the present study adds to what little is already known about the clinical and etiological profile of children with complicated UTI. Being a single-

Table 2: Distribution of gender and age concerning frequency of clinical presentation.

| Clinical Presentation | Gender | | p-value | Age | | p-value |
|------------------------|------------|-------------|---------|---------------|---------------|---------|
| | Male n(%) | Female n(%) | | <5 years n(%) | ≥5 years n(%) | |
| Fever/Chills | 170 (95.0) | 62 (100) | 0.072 | 180 (96.8) | 52 (94.5) | 0.444 |
| Urinary Urgency | 65 (36.3) | 26 (42.0) | 0.431 | 66 (35.5) | 25 (45.4) | 0.180 |
| Abdominal Pain | 47 (22.9) | 32 (51.6) | 0.001 | 57 (30.6) | 22 (40.0) | 0.165 |
| Nausea/Vomiting | 78 (43.6) | 31 (50.0) | 0.381 | 87 (46.8) | 22 (40.0) | 0.433 |
| Dehydration | 68 (38.0) | 21 (33.9) | 0.378 | 78 (41.9) | 11 (20.0) | 0.003 |
| Dysuria | 21 (11.7) | 18 (29.0) | 0.001 | 30 (16.1) | 9 (16.4) | 0.967 |
| Decreased Urine Output | 41 (22.9) | 13 (21.0) | 0.753 | 45 (24.2) | 9 (16.4) | 0.221 |
| Renal Angle Tenderness | 6 (3.4) | 2 (3.2) | 0.962 | 6 (3.2) | 2 (3.6) | 0.881 |
| Palpable Bladder | 23 (12.8) | 0(0) | 0.003 | 21 (11.3) | 2 (3.6) | 0.090 |
| Palpable Kidneys | 34 (19.0) | 0(0) | 0.001 | 30 (16.1) | 4 (7.3) | 0.097 |

center study with a relatively small sample size, our findings cannot be generalized. We were unable to note treatment trends and outcomes in the current set of children. Further prospective trials involving multiple centers need to be conducted.

CONCLUSION

The majority of the children with complicated UTIs were male. Fever/chills, nausea/vomiting, urinary urgency, and dehydration were the most frequently noted clinical presentations. The most commonly observed ultrasonography findings were bilateral moderate hydronephrosis. Patients presenting with a suspected UTI should be screened for the presence of complicating factors, such as anatomic and functional abnormalities of the genitourinary tract.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Ethical Review Board (IERB) of the National Institute of Child Health (NICH), Karachi, Pakistan as IERB No: 27/2020, dated: 16-07-2021. All procedures performed in studies involving human participants were following the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT OF PUBLICATION

Written informed consent was taken from the parents/guardians of all the participants.

AVAILABILITY OF DATA

The authors confirm that data supporting the results of this study are available upon request to the corresponding author.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

All authors contributed significantly to the study.

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