### **Original Research Article**

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## Clino-pathological features of urinary tract infection: a study at Nishtar University Hospital Multan, Punjab, Pakistan

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#### ABSTRACT

**Background:** Urinary tract infection (UTI) is a common clinical issue among pediatric population and might progress into renal scaring, hypertension as well as end stage kidney disease. This study was aimed at finding clinopathological features of UTI and antibiotic sensitivity against most common causative agents involved at a tertiary care hospital of South Punjab, Pakistan.

**Methods:** This descriptive case series study was conducted at department of Paediatric Medicine, Nishtar University Hospital Multan from July to December 2019. A total of 100 children fulfilling the inclusion criteria, presenting in outpatient department or emergency section of paediatric medicine department, having positive urine culture and sensitivity were selected. Their detailed history, clinical examination and relevant investigations were done.

**Results:** Out of the 100 children, 73 (73.0%) were female and 27 (27.0%) were male. There were 57 (57.0%) children from 1 year to 4 years age group and 43 (43.0%) were of more than 4 years. Most common clinical presentations were fever 83 (83.0%), urinary symptoms, vomiting 52 (52.0%) and pain abdomen 48 (48.0%). Most common aetiological agents were *Escherichia coli* 74 (74.0%) and *Klebsiella pneumoniae* 9 (9.0%).

**Conclusions:** UTI is more common in female children. Most common presentation observed was fever and/or urinary symptoms while most common aetiological agent was *E. coli*.

Keywords: Escherichia coli, Dysuria, Fever, Failure to thrive, Urinary tract infection

#### **INTRODUCTION**

Urinary tract infection (UTI) is described as presence of single bacterial growth as  $>10^5$  colony forming units/ml in a clean-catch, mid-stream urine sample or  $>10^3$  organisms/ml in a catheter or suprapubic aspirate of urine.<sup>1</sup> UTIs are also noted as common reason of hospitalization among children and might progress into renal scarring as well as hypertension or end stage kidney disease.<sup>2,3</sup> Differences exist in the prevalence of UTIs among pediatric population as predominantly more males are affected in the 1st year of life ranging in between 3-5:1 in comparison to females.<sup>4</sup> Onwards, prevalence of UTIs are more observed among female children and found to be as high as 10 times compared to male

children.<sup>4</sup> Up till 16 years of age, 12% female and 4% male children are found to have at least 1 episode of UTIs whereas recurrence of UTI is also a common phenomenon.<sup>5</sup>

UTI can be symptomatic as well as asymptomatic but studies have shown that infants and children accompanying UTI often present with fever as their only clinical presentation. Commonest symptoms of UTIs among children are fever, urinary symptoms (e.g. dysuria, frequency, urgency, incontinence, hematuria) and abdominal pain.<sup>6</sup> Older children can also present having inability to thrive as well as nephropathy or hypertension.<sup>7</sup> *Escherichia coli* and *Klebsiella pneumoniae* are the commonest uropathogens involved among children while *Enterobacter cloacae* and *Proteus mirabilis* are some of the other most common uropathogens involved.<sup>8,9</sup> Viral infections especially due to adenovirus are also noted to be present mainly among children having cystitis.<sup>10</sup>

Rising antimicrobial resistance is a matter of concern all around the world and it is very important to find out current trends of causative agents as well as their patterns of antibiotic sensitivity. So, this study was conducted to find out clino-pathological features of UTI and antibiotic sensitivity against most common causative agents involved at a tertiary care hospital of South Punjab, Pakistan.

#### **METHODS**

This descriptive case series study was carried out in the Department of Paediatric Medicine, Nishtar University Hospital Multan, Pakistan from July to December 2019. A total of 100 children using non probability convenient sampling technique were enrolled.

#### Inclusion criteria

• Children of both gender, aged 1 to 7 years, presenting with fever and/ or urinary symptoms like dysuria, frequency, urgency, incontinence, hematuria or dribbling, and having positive urine culture and sensitivity.

#### Exclusion criteria

• Children having dysmorphic features or suspected cases of respiratory tract infections, malaria, or meningitis.

Informed consent was sought from parents/guardians of all study participants. Approval from the institutional ethical committee was seeked. Detailed history, clinical examination and relevant investigations like urinalysis, urine culture examination, complete blood count, renal parameters and abdominal ultrasonography (USG) were done in all cases. Positive urine culture was labeled as growth of single bacteria as more than  $10^5$  colony forming units/ml in a clean-catch mid-stream urine sample or  $10^3$  organisms/ml in a catheter or suprapubic aspiration.

All urine samples were submitted to the institutional laboratory immediately after collection for urine culture and sensitivity testing. All procedures involved in the study were carried out under full aseptic measures.

#### Statistical analysis

SPSS version 24.0 was utilized for data analysis. Descriptive statistics were used to calculate mean±SD for age, weight, height of the patients. Frequencies and

percentages of variables of clinical presentation [i.e. fever, urinary symptoms (including dysuria, urgency, frequency, incontinence, hematuria or dribbling), abdominal pain, failure to thrive or swelling of body] and aetiological agents were calculated.

#### **RESULTS**

Out of 100 children enrolled, 73(73.0%) were female and 27(27.0%) male. Most, 57(57.0%) children were from 1 year to 4 years of age whereas remaining 43(43.0%) were of more than 4 years. Table 1 shows distribution of age groups with respect to gender. Overall, mean age was found to be  $3.75\pm1.05$  years, mean weight  $15.41\pm2.3$  kg and mean height  $96.1\pm7.97$  cm.

# Table 1: Distribution of age groups with respectto gender.

Age Groups (Years)	Male (n=27)	Female (n=73)
1-4	18 (66.7%)	39 (53.4%)
>4	9 (33.3%)	34 (46.6%)

The most common symptoms noted in this study are highlighted in Table 2. Fever 83 (83.0%), urinary frequency 57 (57.0%), vomiting 52 (52.0%), pain abdomen 48 (48.0%), and dysuria 36 (36.0%). Clinical findings noted in the study were generalized abdominal tenderness in 34 (34.0%), suprapubic tenderness 23 (23.0%), lumber tenderness 21 (21.0%), pallor 17 (17.0%), palpable urinary bladder 11 (11.0%), failure to thrive 9 (9.0%), high blood pressure 9 (9.0%), periorbital oedema 4 (4.0%) and palpable kidneys in 3 (3.0%) cases.

Table 3 shows findings of abdominal tenderness with respect to age groups among study cases.

Mid-stream urine catch was the most popular method of collecting the urine, done in 54 (54.0%) cases, followed by catheterization 43 (43.0%) and suprapublic aspiration 3 (3.0%). Table number 4 shows urinalysis of study cases.

Regarding the aetiological agents, *Escherichia coli* was responsible for UTI in 74 (74.0%) cases, *Klebsiella pneumoniae* in 9 (9.0%), *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa* and *Streptococcus fecalis* in 4 (4.0%) each. Proteus was found in 3 (3.0%) and *Candida albicans* in 2 (2.0%) cases. Twenty four cases were associated with malnutrition. Four cases of UTI (3 females, 1 male) were associated with nephrotic syndrome. Of these two patients were 1-4 years of age group and the remaining two were more than 4 years.

Following complications were noted in the present study: Renal scarring 19 (19.0%), vesicoureteral reflux 11 (11.0%), hypertension 9 (9.0%), hydronephrosis 7 (7.0%) and renal stone in 2 (2.0%) cases. Following congenital anomalies were noted: Posterior urethral valve in 5 (5.0%) and pelvic ureteric junction obstruction in 2 (2.0%) cases. Meropenem and Cefoperazone Sulbactam (93.2%), Imipenem (91.9%), Fosfomycin (89.2%), amikacin (77.0%), Amoxicillin clavulanate (75.7%) and nitrofurantoin (74.3%) were noted to have good

sensitivities against *E. coli* while other commonly used antibiotics like amoxicillin (31.1%), ceftazidime (45.9%) and ciprofloxacin (48.6%) were having antimicrobial sensitivities less than 50% (Table 5).

#### Table 2: Frequency of signs and symptoms of urinary tract infection.

Symptoms		Patients age groups (Years)		
		1-4 (n =57)	>4 to 7 (n=43)	Total (n=100)
Fever		49(85.9%)	34(79.0%)	83(83.0%)
Urinary Symptoms	Frequency	24(42.1%)	33(76.7%)	57(57.0%)
	Dysuria	9(15.7%)	27(62.7%)	36(36.0%)
	Urgency	1(1.7%)	7(16.2%)	8(8.0%)
	Incontinence	1(1.7%)	3(6.9%)	4(4.0%)
	Dribbling	3(5.2%)	1(2.3%)	4(4.0%)
Vomiting		28(49.1%)	24(55.8%)	52(52.0%)
Diarrhoea		22.8(21%)	4(9.3%)	17(17.0%)
Pain abdomen		17(29.8%)	31(72.0%)	48(48.0%)
Periorbital swelling	5	2(3.5%)	2(4.6%)	4(4.0%)
Loss of appetite		11(19.2%)	9(20.9%)	20(20.0%)
Constipation		2(3.5%)	5(11.6%)	7(7.0%)
Failure to thrive		9(15.7%)	0(0%)	9(9.0%)
Irritability		8(14%)	3(6.9%)	11(11.0%)
Pyuria		2(3.5%)	3(6.9%)	5(5.0%)
Gross Haematuria		1(1.7%)	2(4.6%)	3(3.0%)
Polyuria		2(3.5%)	5(11.6%)	7(7.0%)

Table 3: Abdominal tenderness in patients with urinary tract infection.

Age	Absent (n=22)	Generalized (n=34)	Lumber (n=21)	Suprapubic (n=23)
1-4 years	13(13.0%)	23 (23.0%)	9(9.0%)	12(12.0%)
>4 years	9(9.0%)	11(11.0%0	12(12.0%)	11(11.0%)

#### Table 4: Urinalysis of study cases (n=100).

Findings		Number (%)
Pus cells	>5/HPF	93 (93.0%)
RBCs	+	17 (17.0%)
RBC cast	+	11 (11.0%)
WBC cast	+	8 (8.0%)
Proteinuria	≥1+	7 (7.0%)

#### DISCUSSION

In terms of gender, female predominance in the current study is aligned to many other national and international findings.<sup>11-14</sup>

Authors saw fever as the most common presenting symptom, noted among 83.0% cases. Urinary frequency 57.0% and vomiting 52.0% were the other commonest observations. Qureshi AM reported fever to be present among 92% cases with UTIs while dysuria (68%) and

failure to thrive (31%) were some of the other most common symptoms in that study.<sup>15</sup> Hafeez F et al, also noted 73.3% cases with UTIs to have fever while they noted vomiting and pallor each to be present in 40% of the cases.<sup>16</sup> Ahmad A et al, noted fever, pain abdomen and dysuria to be the most frequent symptoms in their study.<sup>17</sup> From the current findings, it is evident that UTI in children has no specific symptoms. The children having fever, urinary frequency, vomiting, pain abdomen, dysuria and diarrhea etc. when no other cause can be found, must be investigated for the presence of UTI.

Clinical findings noted in the study were generalized abdominal tenderness in 34 (34.0%), suprapubic tenderness 23 (23.0%), lumber tenderness 21 (21.0%), pallor 17 (17.0%), palpable urinary bladder 11 (11.0%), failure to thrive 9 (9.0%), high blood pressure 9 (9.0%), periorbital oedema 4 (4.0%) and palpable kidneys in 3 (3.0%) cases. In the study conducted by Qureshi AM, 48% of the patients did not have any pain.<sup>15</sup> Others presented with generalized abdominal pain 21%, lumber

tenderness 18% and hypogastric pain 13% in descending order of frequency. Similar findings were observed by Qureshi AM, reported palpable urinary bladder in 11% patients.<sup>15</sup>

# Table 5: Antimicrobial sensitivity of *E. coli* to various drugs (in culture and sensitivity reports) (n=74).

Drugs	Sensitivity (%)
Amoxicillin	31.1
Amoxicillin Clavulanate	75.7
Gentamycin	60.8
Amikacin	77.0
Ciprofloxacin	48.6
Piperacillin Tazobactam	67.6
Meropenem	93.2
Ceftriaxone	58.1
Imipenem	91.9
Nitrofurantoin	74.3
Cefoperazone Sulbactam	93.2
Fosfomycin	89.2
Cefoperazone	67.6
Cefixime	67.6
Ceftazidime	45.9
Levofloxacin	49
Moxifloxacin	62
Ofloxacin	57

In the study it was found that *Escherichia coli* (74.0%) were the major cause for UTI. Researchers from around the world have found *Escherichia coli* to be the most commonly found isolate causing UTIs.<sup>18,19</sup> In the present work, *Escherichia coli* was found among 79.5% isolates. A local study from Islamabad among children aged 3 months to 12 years noted *E. coli* to be the most frequent isolate found (57.3%).<sup>20</sup> Another local study from Swabi<sup>11</sup> found that 67.0% culture positive samples had stains of *Escherichia coli* whereas another one found the presence of *Escherichia coli* to be 76.3% in cases of UTIs. Gram negative bacteria, mainly *Escherichia coli* and *Klebsiella pneumoniae* are the predominant causative agents among cases of UTIs.<sup>11,17</sup>

In the present study sensitivity of the *E. coli*, the main organism causing UTI was mainly to Meropenem and Cefoperazone Sulbactam (93.2%), Imipenem (91.9%), Fosfomycin (89.2%), amikacin (77.0%), Amoxicillin clavulanate (75.7%) and Nitrofurantoin (74.3%) were noted to have good sensitivities against *E. coli* while other commonly used antibiotics like amoxicillin (31.1%), ceftazidime (45.9%) and ciprofloxacin (48.6%) were having antimicrobial sensitivities less than 50%. Antimicrobial sensitivity finding regarding various antibiotics used in this region noted that isolated microorganisms showed low-to-poor sensitivity to the commonly used antibiotic options like ciprofloxacin, ceftazidime and ceftriaxone. Ciprofloxacin is commonly adopted as choice of treatment of UTIs but current

findings showed that its effectiveness is not up to the accepted standards. It is also important to keep in mind that fluoroquinolones are thought to have advantages commonly considered antibiotic like over other amoxicillin clavulanate with regards to its pharmacokinetic characteristics. This findings were quite different to another local study where flouroquinolones were noted to have 100% sensitivity against common causative agents of UTIs among children.<sup>20</sup> The difference could be because of changes in trends of antibiotic resistance in this region. Flouroquinolones have always been considered a very good option for treating UTIs but this study shows that their sensitivity is not as good as it is thought to be in this region. On the other hand, amoxicillin clavulanate in the present study showed a sensitivity of 75.7% mainly among Escherichia coli isolates (found among 74.0% of the isolates in the present study) which shows the effectiveness of this affordable and commonly available drug. Other local researchers have also found that fluoroquinolones-resistant to most common uropathogens is increasing noting that to be 59% while extended spectrum β-lactamase producing fluoroquinolone-resistant uropathogenic strains have significantly been increased in the Asian-Pacific region and India.<sup>21,22</sup>

Authors noted good sensitivity of imipenem (91.9%), meropenem (93.2%), cefoperazone sulbactam (93.2%), fosfomycin (89.2%), amikacin (77.0%) and nitrofurantoin (74.3%). These findings are very similar to other local and regional data and demonstrate the effectiveness of these antibiotics as these are less commonly used in this community.<sup>20</sup> The results of this study should help clinicians getting an idea of the commonly involved microbes when treating children of this area having UTIs and also while prescribing, choose the good orally available antibiotics when considering empirical therapy in selective cases. One of the limitations of this study was that authors could not gather treatment outcome data of studied children which would have further provided us some insight about the treatment outcomes as well.

#### CONCLUSION

UTI is more common in female children. Most common presentation observed was fever and urinary symptoms while most common aetiological agent was *E. coli*. Treatment should be based on urine culture and sensitivity due to different causative organisms. A clinician's main goals are early diagnosis, appropriate antimicrobial therapy, identification of anatomic anomalies and preservation of renal function.

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