



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

<http://doi.org/10.5281/zenodo.3956136>Available online at: <http://www.iajps.com>

Research Article

**ANTIMICROBIAL SUSCEPTIBILITY, PATHOGENS AND
ASSOCIATED RISK FACTORS OF CHILDREN WITH ACUTE
URINARY TRACT INFECTIONS**Dr. Muhammad Hassnain Saleem¹, Dr. Sadaf Ejaz², Dr. Najia Nazeer¹¹ United Medical & Dental College, Karachi² Dow University of Health Sciences, Karachi**Article Received:** May 2020**Accepted:** June 2020**Published:** July 2020**Abstract:**

Introduction: Adequate treatment of acute urinary tract infections (UTIs) in children depends on knowledge of the local pattern of causative pathogens and associated risk factors. We explored these patterns and risk factors in a group of children who attended the Pediatric department of Mayo Hospital Lahore with symptoms of acute UTI.

Methods: This is a prospective hospital study conducted in the Pediatric department of Mayo Hospital Lahore for one-year duration from March 2019 to March 2020. Urine culture and sensitivity testing was performed for symptomatic children who had positive urine dipstick tests for nitrates and leukocyte esterase.

Results: Acute UTI was confirmed in 100 children, 74% of them were below 5-years of age and 35% were infants. The male-female ratio of affected children was 2.1:1 among infants, and 1:1.2 among older children. Uncircumcision and infancy were significantly more prevalent among children confirmed to have UTI compared to children with non-significant bacteriuria. *E. coli* was the most commonly isolated pathogen (60%). Mean susceptibility of all isolates was high to gentamicin (96%), ciprofloxacin (94%), ceftriaxone (90%), and cefixime (85%). Mean susceptibility was moderate to cefuroxime (75%), nalidixic acid (74%), and nitrofurantoin (70%), and low to cephalixin (51%), cotrimoxazole (26%), amoxicillin-clavulanate (19%) and ampicillin (14%). Ultrasound scan was feasible in 89 children with confirmed UTI, revealing renal stones in six children (6.7%). Micturating cysto-urethrogram (MCUG) was indicated for 28 children but was feasible for only 15 children, revealing low-grade vesico-ureteric reflux (VUR) in five of them.

Conclusion: *E. coli* was the commonest causative organism of acute UTI in our setting. Isolated pathogens were highly resistant to conventional empiric therapy. Male uncircumcision was significantly associated with UTI among the study patients.

Keywords: Acute Urinary Tract Infections, Children, Pathogens, Antimicrobial susceptibility.

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Please cite this article in press Muhammad Hassnain Saleem et al, *Antimicrobial Susceptibility, Pathogens And Associated Risk Factors Of Children With Acute Urinary Tract Infections.*, Indo Am. J. P. Sci, 2020; 07(07).

INTRODUCTION:

Urinary tract infection (UTI) is a common disease in pediatric practice. Early diagnosis and emergency treatment can reduce long-term sequelae such as scarring and renal hypertension, and end-stage renal disease¹⁻³. Appropriate treatment for acute urinary tract infection depends on the local pattern of pathogens, antimicrobial resistance and related risk factors. The changing pattern of microbial susceptibility to bacterial pathogens causing acute urinary tract infection is an increasing problem. Sudan is a third world country where drug prescriptions are not under strict control. As a result, many organisms, including those that cause acute urinary tract infections, can develop high resistance to many antibiotics in current use⁴⁻⁶. Also, organisms that are not known to cause acute urinary tract infections may also appear as major causative pathogens⁷⁻⁸. Therefore, information on the local pattern of urinary pathogens and their susceptibility to various antimicrobials is required to choose appropriate empirical treatment in children with acute urinary tract infection⁹⁻¹⁰. This study was conducted to investigate possible risk factors and local patterns of causal organisms and antimicrobial sensitivity to assess new empirical treatment options in children with acute urinary tract infection.

METHODS:

This is a prospective hospital study conducted in the Pediatric department of Mayo Hospital Lahore for one-year duration from March 2019 to March 2020. This study accepts children from one day to sixteen years old. Included children are then transferred for further treatment. The researcher recruited children with symptoms indicating acute urinary tract infection. Children recently taking antibiotics and children with urinary tract disorders and / or stones were excluded from the study. All cases were initially examined using urine indicator (nitrate and leukocyte esterase) rod tests and urine microscopy.

Urine samples were collected using the mean flow method in children trained to go to the toilet and using pure trapping methods or a sterile bladder catheter in young children and infants. Positive urine samples were then sent to an *in vitro* culture and sensitivity test strip. The culture was carried out with semi-quantitative tests in medium with cystine and lysine electrolyte deficiency (CLED). A culture was considered positive if a single organism was isolated in the presence of bacterial growth exceeding 100,000 CFU / ml. Sensitivity was tested by Muller and Hinton agar gel diffusion technique. Ultrasound was requested for all patients with a positive culture. According to the guidelines of the American Academy of Pediatrics, a urinary cysto-urethrogram (MCUG) was planned for children, whether they were between 2 months and 2 years old, or with a family history of vesico-ureteral reflux disease (VUR) or urinary dilatation or ultrasonic hydronephrosis (USS). Ethical approval was obtained from the Ethics Committee. The researchers received the oral consent of each child's parents before being included in the study. Data were analyzed using the Social Science Statistics Pack (SPSS) version 18.0. The ratios were compared using the Chi square test; P values <0.05 were considered statistically significant.

RESULTS:

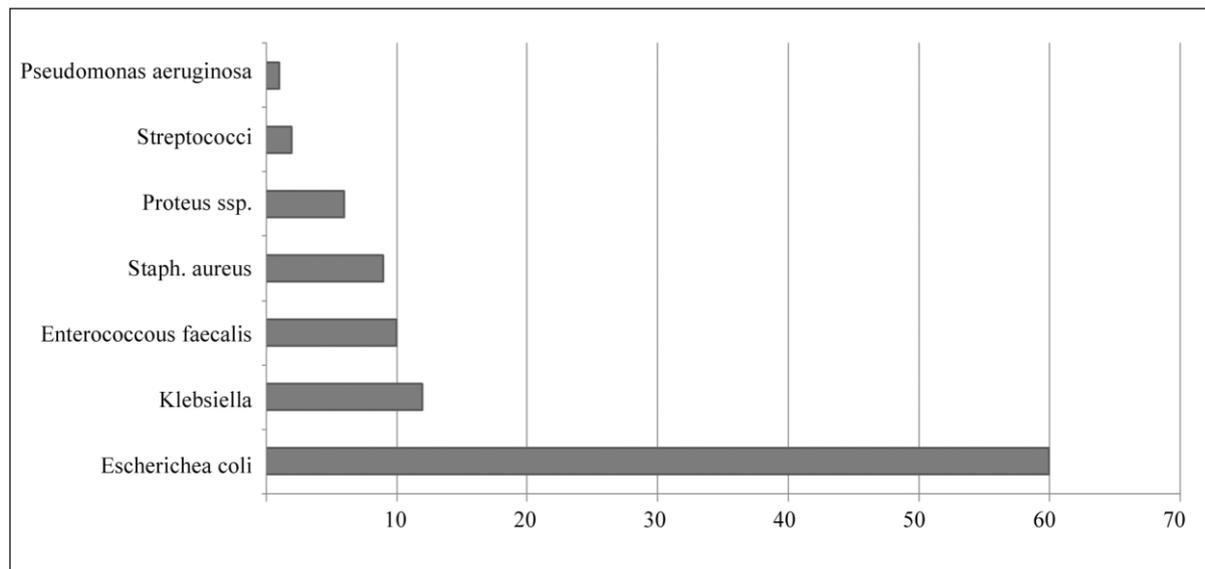
In 221 (55.2%) of 400 children suspected of acute urinary tract infection, nitrate and leukocyte esterase, i.e., positive bacteriuria urine stick tests and urine samples were sent for breeding. Of these, 100 patients (45.2%) had a significant increase in urine culture and met the criteria for the diagnosis of acute urinary tract infection. The average age of children with UTI was 3.4 years (SD 3.6, range of 15 days - 14 years) and 35% of infants. Most children with UTI are men (53%), the majority were under 5 years (74%).

Table 1: Clinical characteristics of children with positive leukocyte esterase test, whose urine samples were submitted to cultureAli *et al***Table 1: Clinical characteristics of children with positive leukocyte esterase test, whose urine samples were submitted to culture**

Characteristic		UTI group	No UTI group	P value
Age	< 1 year	35 (35%)	22 (18.2%)	0.008
	1-4 years	39 (39%)	50 (40.5%)	
	5-16 years	26 (26%)	49 (41.3%)	
Gender	Male	53 (53%)	67 (54.5%)	0.8
	Female	47 (47%)	54 (45.5%)	
Male circumcision	No	42 (77.8%)	40 (60.6%)	0.04
	Yes	12 (22.2%)	26 (39.4%)	
History of UTI	Yes	14 (14%)	12 (10%)	0.35
	No	86 (86%)	109 (90%)	
Constipation	Yes	12 (12%)	6 (5%)	0.057
	No	88 (88%)	116 (95%)	
Pinworm infestation	Yes	5 (5%)	6 (5%)	0.98
	No	95 (95%)	115 (95%)	

The incidence rate among boys and girls was 2.1: 1 among infants and 1: 1.2 among older children. Circumcision was more common in children confirmed with UTI (77.8% vs. 60.6%, $p = 0.04$) than in insignificant bacteriuria. Early age (<1 year) was more common in children with confirmed UTI than in insignificant bacteriuria patients (35% vs. 18.2%, $p = 0.008$). Gender, history of UTI, constipation and roundworm infection did not differ significantly between the two groups (Table 1). Among the positive culture samples, the most commonly isolated pathogen (60%) were other Gram-negative organisms, such as *E. coli*, followed by *Klebsiella* (12%) and *Enterococcus faecalis* (10%) (Fig. 1). In vitro sensitivity tests, average sensitivity of isolated pathogens was high in gentamicin (96%), ciprofloxacin (94%), ceftriaxone (90%) and cefixime (85%), medium to cefuroxime (75%), nalidixic acid (74%) and nitrofurantoin (70%) and low cefalexin (51%), cotrimoxazole (26%), amoxicillin-clavulanate (19%) and ampicillin (14%). *E. coli* had similar sensitivity to antibiotics (Table 2-3).

Figure 1: Frequency of different pathogens isolated from urine of children with acute UTI (N = 100)



Ultrasound can be used in 89 (89%) of 100 children with confirmed urinary tract infections. Twenty-nine children had abnormal USS results (32.6%); six children had kidney stones and 23 children had variable urinary tract dilatation. Due to some difficulties, it was not possible to perform micturition cystourethrography (MCUG) for all patients who showed these tests. MCUG is indicated for 28 children, but it can only be used for 15 children. MCUG was carried out 4-6 weeks after the diagnosis of UTI. The results showed vesicoureteral reflux disease (VUR) (I-II) in five children; three women and two men. DMSA scans were not made for any children.

DISCUSSION:

In this study, the incidence of women among children affected by acute urinary tract infections is consistent with previous reports, excluding childhood. The role of circumcision in men in the prevention of urinary tract infections in men is controversial. Some studies have shown that circumcision protects or prevents the recurrence of symptomatic urinary tract infection in male children¹⁰⁻¹¹. However, the task force of the American Academy of Pediatric Circumcision found this data insufficient to recommend routine neonatal circumcision. In this series it was much more common among children confirmed by uncircumcised UTI than in patients with bacteriuria¹². This finding suggests that circumcision may predispose men to acute urinary tract infections and is supported by earlier studies in men from Sudan. Shaikh *et al.* performed a meta-analysis to determine the total incidence of urinary tract infection (UTI) in men by age, sex, race, and circumcision status. Urinary tract infection was found in 2.4% of circumcised men and 20.1% of uncircumcised men in febrile boys under the age of 3 months. In another meta-analysis of 12 male circumcision studies, including a randomized controlled trial, circumcision was shown to be associated with a significantly reduced risk of urinary tract infection with a probability of 0.13. However, given the low risk of urinary tract infection in healthy children, the authors concluded

that the clinical benefit only applies to children at high risk for urinary tract infection. In this Sudanese series for children *E. coli* is the most common pathogen causing acute urinary tract infection and accounts for 60% of cases. This is in line with previous reports of Sudanese children, as well as from other parts of the world. Isolates that cause UTI in children were resistant to co-trimoxazole, ampicillin and amoxicillin clavulanate in our series, according to reports from Sudan and reports from other countries¹³. The high resistance to amoxicillin clavulanate demonstrated in these and other studies reflects the increased resistance of urinary pathogens to conventional antibiotics, but resistance to even newly added antibiotics is alarming. Sensitivity, Tunisia, Turkey, Iran and third generation gentamicin based on data obtained from Taiwan was higher compared to ciprofloxacin and cephalosporins. For this reason, we recommend using gentamicin and ceftriaxone as the primary parenteral empirical treatment for children with acute urinary tract infection. Cefixime can be used in people who tolerate oral medications¹⁴. Although reported from Turkey, high sensitivity, moderate sensitivity to nalidixic acid and nitrofurantoin are in line with reports of Yemen. Among the 15 children who received MCUG, the results showed low quality VUR in five children (5%)¹⁵. This may not reflect the true incidence of VUR in our environment, because MCUG is only performed for half of the children with whom it is identified.

However, the incidence is much lower than the numbers given in the literature, so 30-35% of children with the first acute urinary tract infection had VUR.

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