ORIGINAL ARTICLE

Antibiogram and susceptibility pattern of bacterial isolates of urinary tract infection among children and adolescents at a tertiary care hospital

Salman Arshad, Shahid Rasheed, Mudassar Hussain, Saqib Munir, Nadia Qamar, Abdul Sattar

Khawaja Muhammad Safdar Medical College (Allama Iqbal Memorial Teaching Hospital), Sialkot Pakistan

ABSTRACT

Background: UTI is one of the major causes of morbidity among children and adolescents in developing countries like Pakistan, where precise knowledge of causative micro-organisms and their antimicrobial susceptibility patterns remains inadequate. To identify common organisms involved in urinary tract infection and their antimicrobial sensitivity patterns among children & adolescents.

Material and Methods: This retrospective descriptive study was conducted on urine cultures reports of children less than 18 year presented with suspected UTI in Allama Iqbal Memorial Teaching hospital between the periods of January 2020 to December 2022 were taken. Urine sample cultured on CLED agar plates, micro-organism were identified by performing their morphological & biochemical tests.

Results: Urine culture reports of 500 patients of age <18 years with suspected UTI were collected, out of which 102 were positive. The most common age for UTI was 5-11 years. The ratio of boys and girls was 30 and 72 respectively. Both Gram-negative and Gram-positive bacterial species were recovered. The ratio of gram negative to gram positive was 94 and 8 respectively. Among Gram-negative bacterial species, *E. coli* was the most common organism. Antimicrobial susceptibility pattern of *E. coli* showed that susceptibility to commonly prescribed drugs as follows Gentamicin (80%), co- amoxiclav (52%), Trimethoprim- Sulfamethoxazole (19%), Cephalosporin's (8%), and Amoxicillin (5%). Susceptibility to Nitrofurantoin & Fosfomycin was 80% and 63% respectively.

Conclusion: *E.coli* was most common organism Isolated. Co-amoxiclav, Nitrofurantoin and Fosfomycin have good susceptibility profile among the oral drugs and Gentamicin has high susceptibility among injectables.

Keywords: Urinary tract infection, Antibiotic sensitivity, Urine culture

BACKGROUND

Urinary tract infection is the presence of bacteria (> 10^5) in the urine.[1] Urinary Tract Infection is one of the most common infections around the world that can affect both the upper and lower urinary tract. It can be acquired from the hospital or community at any age.[2] The term UTI is applied to variety of clinical conditions ranging from the asymptomatic bacteruria to severe infection of the kidney leading to sepsis. If diagnosis in not made in time it can result in long term complications in the form of hypertension, failure to thrive and end stage renal disease[3]. The overall prevalence of UTI is approximately seven percent in febrile infants and young children but it differs according to age, sex and circumcision status. It is more common in un-circumcised males, especially who are younger than three years old. Girls have two-to-four-time increased risk of UTI than circumcised Boys [4]. females are more prone to UTI due to short urethra, absence of prostatic secretion, pregnancy and fecal contamination of Urinary tract.[1]

Worldwide about 150 million people are diagnosed with UTI annually, costing almost more than 6 billion dollars.[5] In the developing countries various studies have been conducted which showed that about 10% of children who presents with febrile illness are suffering from UTI. This can be increased to 8-35% if the children are suffering from malnutrition.[3] UTI can involve both upper and lower urinary tract system so the clinical presentation depends on the area of involvement. Lower urinary tract symptoms include dysuria, urgency increased urinary frequency and suprapubic tenderness.[6] In childhood the risk of developing UTI is 3-10% in girls and 1-3% in males.[7] The most common organism causing UTI is *E.coli* followed by *Klebsiella Pneumonia, Pseudomonas aeruginosa, Staphylococcus saprophyticus,* and *Enterbobacter species.* with variability in sequence of their prevalence.[8] However, the organisms and

Correspondence: Dr. Salman Arshad, Senior Registrar, Khawaja Muhammad Safdar Medical College (Allama Iqbal Memorial Teaching Hospital), Sialkot Pakistan

Email: salman.arshaf@gmail.com

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antimicrobial susceptibility in pediatric UTI differ from one place to another place and even within the same place between various geographical areas.[7] Thus, precise knowledge about the causing organisms and its susceptibility pattern is necessary.[9]

The increasing antibiotic resistance in the management of UTI is a serious public health concern, particularly in developing countries where other than poverty, ignorance and poor hygienic practices, there is prevalence of substandard drugs in the market. Urinary Pathogens having strong ability for invasion, adhesion and virulence along with emerging increased antibiotic resistance is becoming a great concern throughout the world.[10] Although very few studies have shown the status of UTI in general population, larger studies are limited towards specific target population such as HIV patients, diabetic patients, pregnant woman, children and students.[1] Similar situation applies to Pakistan and limited data on UTIs, risk factors, and drug resistance profiles are available from the general population.[1] Information about causative organisms and its sensitivity to the available drug is paramount for judicious selection of antibiotics and to develop suitable prescribing policies in the institute.[5] Commonly Prescribed empirical antibiotics in the treatment of UTI are cephalosporin, Gentamicin, ciprofloxacin, Co-amoxiclav, Trimethoprim-sulphmethoxazole, nitro-furantoin and cephalexin.[11-12] This study was carried out to see the microbial pattern of UTI as well as build the current antibiogram that will help the local practioners to use effective antibiotics in the treatment of UTI in children.

MATERIAL AND METHODS

This was a retrospective descriptive study conducted at Allama Iqbal Memorial Teaching Hospital (AIMTH). Children less than 18 years old, whose urine cultures were sent between January 2020 to December 2022, were included in the study. Cultures of both out door and hospitalized patients were included. Children who were on steroid therapy, taken previous antibiotics, were excluded from the study. Urine specimen was collected by 3 methods depending on the age i.e.2-24 month of age - urinary catheterization, suprapubic aspiration method, and toilet trained - mid-stream clean catch method. After collecting the urine sample in the urine container, they were labeled with patient registration number and samples were sent to the lab. The total samples collected were 500. Urine sample were cultured on CLED agar plates. The samples showing no growth on CLED agar were also excluded. The significant growth of organism considered only if there were up to two organisms' growth in significant number of colonies. Significant bacteruria was identified as more than 100,000 CFU/ml in mid-stream clean catch specimen, or > 50,000 CFU/ml in sample collected by urethral catheterization, or any number of colonies if sample collected by suprapubic aspiration. Probably significant bacteruria was defined as 1000-100,000CFU/ml in a mid-stream specimen [7].

Colonies which appeared on CLED agar plates were characterized on the basis of color and colony. From the CLED agar plates a total of 102 bacterial strains were identified. A total of 102 bacterial isolates, which were isolated were further screened for confirmation of organism species by performing their morphological and biochemical tests. Purification of bacterial isolates was done on several types of CLED-inhibited colonies. A total of 102 bacterial strains were designated names accordingly. The morphological characterization of 102 strains obtained from samples. Gram-staining was performed. All strains were tested for oxidase activity, catalase activity, triple sugar iron test, gas production, urease activity, and citrate utilization. Indole test was also performed. The disk diffusion method was used to assess the in.vitro susceptibility of the positive samples to the most commonly used antimicrobial drugs for UTI treatment including ceftriaxone (30ug), ceftazidime (30ug), cefixime (5ug), cefoperazone/ sulbactam (105/ 30ug), cefipime (20ug), cefotaxime (30ug), cefoperazone (105ug), amoxicillin (10ug), amoxicillin-clavulanic acid (20/10ug), ciprofloxacin (5ug), fosfomycin (200ug), nitrofurantoin (300ug), trimethoprim-sulamethoxazole (5/250ug), amikacin (30ug), gentamicin (10ug), imepenem (10ug), meropenem (10ug), piperacillin-tazobactam (30ug) and pipemidic acid (20ug).

Culture and sensitivity reports were obtained from laboratory of Allama Iqbal Memorial Teaching Hospital. Data were presented as descriptive statistics (frequency tables, charts and percentages). Data analysis was carried out using Microsoft Excel 2023 version 16.72. Approval for the conduct of this research was obtained from ethical review board of Allama Iqbal Memorial Teaching Hospital, Sialkot.

RESULTS

Urine culture of 500 patients of age <18 years with suspected UTI were collected, out of which

102(20.4%) showed significant bacterial growth. (Figure-I).

The most prevalent age group for UTI was 5-11 years (39.2%) followed by 11-18 (25.4%), 2-5 (19.6%) and < 2year of age (15.6%). The ratio of boys and girls was 30(29%) and 72(71%) respectively (Table-I).

Both Gram-negative and Gram-positive bacterial species were recovered. The ratio of gram negative to gram positive was 94/102 (93%) and 8/102 (7%) respectively. Among Gram-negative bacterial species, *E. coli* (70%) was the most frequently isolated bacteria followed by the *Providencia species* (9%) and *Enterobacter cloacae* (8%). Among the gram-positive species there were only eight isolates six of them were *Enterococcus fecalis* while only two were *Staph aureus.* Antimicrobial susceptibility pattern of *E. coli* showed that it was 100% sensitive to meropenem and imipenem, followed by amikacin (94%), piperacillin-tazobactam (86%). Sensitivity to gentamicin, cefoperazone-sulbactam, and nitrofurantoin was 80%, followed by fosfomycin (63%) and then co-amoxiclav (52%). Cephalosporins (cefepime, cefixime, ceftriaxone, cefoperazone, cefotaxime, and ceftazidime) and trimethoprim- sulphmethoxazole had sensitivity of only 8% and 19% respectively. Amoxicillin showed very high resistance with susceptibility of only 5% (Table-II).

Providencia was the second most common isolated organism which showed that resistant strains to carbapenem are emerging with susceptibility of 80%. The susceptibility to amikacin was (80%), followed by 60% to piperacillin-tazobactam, and cefoperazone-sulbactam while only 40% towards Gentamicin (Table-II). *Enterobacter cloacae* was the most resistant among the isolates with uniformly low susceptibility i.e. 75% to meropenem, imipenem, piperacillin-tazobactam, gentamycin, cefoperazone-sulbactam and nitrofurantoin. The susceptibility to cephalosporins is 25%. All strains were resistant to amoxicillin (Table-II).

Table-I: Demographic feature of children & frequency of bacteria isolated in urine culture.

Patient Characteristics	*E. coli n=72 (70%)*	*Providencia species 10 (9%)*	*Enterobacter Cloacae 8 (8%)*	*Enterococcus faecalis 6 (5%)*	*Klebsiella Pneumonia 2 (2%)*	*Staph Aureus 2 (2%)*	*Enterobactor species 2 (2%)*	Total n 102 (%)
Age								
<2years	12	-	2	-	2	-	-	16(15.6%)
2–5years	16	4	-	-	-	-	-	20(19.6%)
5–11years	22	6	4	4	-	2	2	40(39.2%)
11-18 years	22	-	2	2	-	-	-	26(25.4%)
Gender								
Male	20	4	2	2	2	-	-	30 (29%)
Female	52	6	6	4	-	2	2	72(71%)

Table-II: Antimicrobial susceptibility pattern among gram negative micro-organisms.

Antibiotics	*E.coli* (72)	*Providencia species* (10)	*Enterobacter cloacae* (8)	Overall sensitivity
Meropenem	100%	80%	75%	85%
Imipenem	100%	80%	75%	85%
Amikacin	94%	80%	0%	58%
Piperacillin-tazobactam	86%	60%	75%	73%
Gentamicin	80%	40%	75%	65%
cefoperazone-sulbactam	80%	60%	75%	71%
Nitrofurantoin	80%	0%	75%	77%
Fosfomycin	63%	0%	0%	63%
Co-amoxiclav	52%	0%	0%	52%
Ciprofloxacin (quinolones)	33%	0%	0%	11%
Pipemidic acid	27%	0%	0%	9%
trimethoprim-sulphmethoxazole	19%	0%	0%	6%
Ceftriaxone	8%	0%	25%	11%
Cefipime	8%	0%	25%	11%
Cefotaxime	8%	0%	25%	11%
Cefixime	8%	0%	0%	2.6%
Ceftazidime	8%	0%	25%	11%
Cefoperazone	8%	0%	25%	11%
Amoxicillin	5%	0%	0%	1.6%
Cefradine	0%	0%	0%	0%

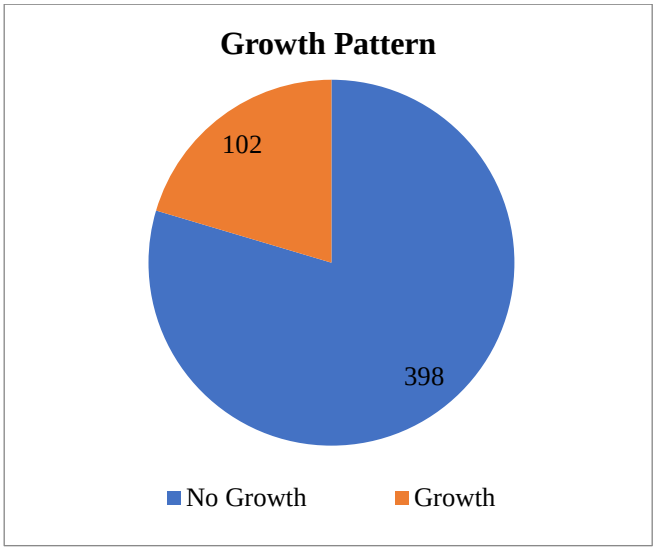

Figure-I: Growth pattern of organisms (n=500).

DISCUSSION

Urine culture yield is variable and depends upon laboratory methods, geographical location and countries. In our study urine culture yield was 20.4% which is much higher than the study conducted at Mexico (16.9%)[13], Ethiopia 16.7%[3], and Kuwait 13.7%.[9] However, it was much lower than the previous studies conducted in Pakistan 32.8%[2], 65.1%[1] and 66.5%.[18] Similarly, a study in south India showed slightly higher yield 21.2%.[7] There was one study in northern India[8] which showed highest yield of around 77%, but they included patients of all age groups. Furthermore, one study in Iran showed bacterial growth of only 6.7% probably because they had taken large sample size of 21604.[15]

Our study shows UTI was more prevalent among 5-11 year of age which was similar to study conducted in Kuwait and Ethiopia.[9,3] However, studies in Mexico and Tanzania shows that UTI was more prevalent among age less than 5 year.[13,14] One study conducted in south India that included children less than 15 years of age found that UTI was more prevalent in children less than 1 year age group.[7] Few studies conducted in Pakistan in which they include all age group patients they found UTI was more common among patient of age 26 to 35year.[1,2]

Our study shows that UTI was more common in females than males and this gender predilection is similar in studies conducted at Pakistan India, Mexico, Ethiopia, Iran, Kuwait and Nigeria. [2-1-10-18,6,13,3,15,9, 5] However, one study conducted in south India shows no gender difference[7], whereas a study conducted in Northern India where they included all age patients found that after the age of 80-year UTI was more prevalent in males than females.

Our study shows that gram negative organisms are more common than gram positive in causing UTI. Among gram negative organisms *E. coil* was most the most common isolate. These results were similar to all the studies conducted previously in Pakistan, Nigeria, Kuwait, Ethiopia, India, Uganda and Tanzania. [18,1,5,2,9,3,6,16,14]

In our study *E. coli* was 100% sensitive to imipenem and meropenem. Previous studies conducted in Pakistan shows 98%[2], 85.3%[18], 76%[1], and 72%[10] sensitivities to meropenem and imipenem. Previous studies in other countries also showed the similar results 100%[7,9,13], 97%[3], 98%[9], 94%[16] and 83%.[18] In our study *E. coli* was 94% sensitive to amikacin whereas in other studies sensitivity to amikacin were 89.5%[19], 87%[7], 81%,[2] 95.5%[9], 40.4%,[1] 51%[18], and 63%.[10] In our study sensitivity to cefoperazone-sulbactam, piperacillin-tazobactam and Nitrofurantoin was >80%. Other studies in the past also shows the similar results for nitrofurantoin 98%, 85.3%, 82%, 97%, 88%, 83%, and 82%.[9,19,2,13,16,9,3] However, one study showed only 43% sensitivity to nitrofurantoin.[5] Surprisingly one study in Pakistan shows 0% sensitivity toward nitrofurantoin [1]. Sensitivity to piperacillin-tazobactam in previous studies was 98%, 85%, 87%, 75%, 75% and 50%.[9,13,16,7,2,1]

Sensitivity to Fosfomycin in our study was 63%, whereas in previous studies it was 90%[16] and 85.3%.[18,1] Sensitivity to co-amoxiclav in our study was 53% whereas in previous studies it was 71%[9], 52%[7], 35%[16], 26.5%[18], 18%[2], 18.5%[1] and 18%[3]. Sensitivity to trimethoprim- sulphmethoxazole in our study was 19% only, while in previous studies it was 97 %[16], 70%[19], 63%[9], 50%[2], 42%[3], 39%[13], 26%[7], and only 6%.[10] Sensitivity to cephalosporin in our study was only 8% which is qui*et al*arming situation for our geographic area because in previous studies sensitivity to cephalosporins was quite good, i.e., it was 85% to cefoxitin, 82% to cefotaxime, and 75% to ceftazidime in one study[3] while in other studies it was 93 % to ceftriaxone [16], 74% to cefotaxime[9] and 19.8% to cefixime.[1] Similarly studies conducted in Pakistan previously which shows sensitivity of 32.3%, 39%, 21.3% and only 10% to ceftriaxone[18,1,19,10] whereas sensitivity to cefotaxime 23.8% and 22.5%.[18,19] The

greatest resistance was noted to Amoxicillin which has only 5% sensitivity which differs from one study conducted in Pakistan[1] which shows 25% sensitivity towards amoxicillin. However, our results were similar to Previous Study[17] in which only 15.2% and in other studies[18] conducted in Pakistan shows 5%, sensitivity to Amoxicillin found. Whereas, surprisingly in study[10] all strains were resistant to amoxicillin.

CONCLUSION

Our study concludes that *E. coli* was the most common isolate, has higher susceptibility to carbapenems, which needs to be preserved. The sensitivity to trimethoprim- sulphmethoxazole, third generation cephalosporin and amoxicillin was very low. These drugs should not be used as first line keeping in view the higher resistance. The sensitivity to the commonly used antibiotics like Gentamicin, co-amoxiclav, nitrofurantoin and Fosfomycin is good, so they are better choice to be used as first line.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Salman Arshad: Study design, methodology, manuscript writing

Shahid Rasheed: Data collection, statistical analysis, results interpretation

Mudassar Hussain: Literature review

Saqib Munir: Data collection, statistical analysis, results interpretation

Nadia Qamar and Abdul Sattar: Data collection

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