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Diagnosis and Antibiotic Resistance Distribution in Children with Urinary Tract Infection: A Single Center Experience

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Abstract

Background

Urinary tract infection is a common disease in childhood, yet the appropriate approach for a child is still a matter of controversy. The aim of this study was to determine the diagnostic performance of urinary analysis, assess the role of urine culture in determining its necessity and evaluate etiologic agents and antimicrobial resistance patterns in children with urinary tract infection.

Materials and Methods

Our study was made by evaluating the patients who applied to the Antalya Research and Training Hospital- Turkey, between 2015 and 2017. A total 237 urine analysis and urine culture were retrospectively analyzed. Culture results were taken a reference for microscopic and chemical examination of urine and diagnostic accuracy of the test parameters, and the performance of urine analysis were calculated. The culture and antibiogram results were examined and antibiotic resistance with infectious agents frequency was evaluated.

Results

The 42.4% of culture negative samples showed leukocyte esterase, nitrite, bacterial and leukocyte counts, which are indicative of infection in urine analysis, were found in normal range. The highest sensitivity (90%) was in the presence of leucocyte esterase and bacteria, while the highest specificity (99.4%) was in the presence of nitrite alone or with other components (leucocyte or leucocyte esterase). The highest antibiotic resistance was found in beta lactam antibiotics. The lowest antibiotic resistance was detected in the Carbapenem followed by fluoroquinolone group antibiotics.

Conclusion

Microscopic and chemical examination of urine analysis can give us information about urine culture requirement. The observation of increasing overall resistance to antibiotics authorize further studies that lead to new recommendations to antibiotic use in children and adolescents.

Key Words: Antibiotic resistance, Children, Sensitivity, Specificity, Urinary tract infection.

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1- INTRODUCTION

Urinary tract infection (UTI) is a common disease in children; 3-5% in girls and 1% in boys (1). Pediatric patients with UTI, may present with non-specific signs and symptoms, therefore it can be difficult to diagnose. Despite all improvements in diagnosis and treatment in UTI, diagnosis can be missed and after it can lead to hypertension, renal scarring and chronic kidney disease in children (2, 3). UTI can be diagnosed by history and clinical approach, but for definite diagnosis urinary culture should be done after appropriate chemical and microscopic evaluation of urine (4). Some studies reported that, urine chemical analysis, especially leukocyte esterase and nitrite test positivity, microscopic analysis leucosyte and bacterial detection confirming UTI, tests negativity can exclusion of the disease diagnosis (5). Urine culture is a gold standart to diagnose UTI (6).

Escherichia coli (E.coli) is the most common bacterial uropathogen accountable for UTI and assumes for 85-90% of cases (7). Beta lactam antibiotics and trimethoprim-sulfamethoxazole (TMP-SMX), commonly used as first-choice treatments in pediatric UTIs, have increased antibiotic resistance. Therefore selection of antibiotics to be used in prophylaxis and empirical treatment is gaining importance (8). The aim of this study was to determine the diagnostic performance of urinary analysis, assess the role of urine culture in determining its necessity and evaluate etiologic agents, determination of antimicrobial resistance distributions in children with urinary tract infection.

2- MATERIALS AND METHODS

A total 237 patients, resorting to our policlinic between January 2015 to October 2017, urine analysis and urine culture were examined. Children of both gender, age between 2 to 18 years, and diagnosed with UTİ were selected. Mean age was 9.4 ±3.25 years. Patients whose urine culture result did not meet the definition for UTI according to the clinical practice guidelines for the diagnosis and management of UTI were excluded from the study. Our hospital fully automatic urine analyzer (IQ 200 IRIS Diagnostics, USA) using the urine as both microscopic chemical analysis are performed.

Autio as the urine strip Stiks 10EA (Arkray Factory, Inc., Shiga, Japan) is used. Strip for leukocyte analysis < 25 cells/ml; while accepting negative result on this value was considered positive. Microscopy leukocyte cell analysis > 5/hpf was considered positive. Sterile container collected urine samples for urinary culture, 5% sheep in the microbiology laboratory agar and Eosin-methylene blue (EMB) (Merck KGaA Darmstadt, Germany) after aerobic seeded agar is incubated at 35 ± 2 ° C for 18 to 24 hours at ambient. This included significant bacteriuria with recovery of at least 100.000 CFU/ml (colony forming unit per milliliter) of a single uropathogen from a clean catch or sterile urine bag specimen.

Reproducible bacteria are produced by conventional methods identified; antibiotic susceptibilities "Clinical and Laboratory Standards Institute "(CLSI) methods in accordance with the disc diffusion method. Expanded spectrum on the detection of beta lactamase (ESBL) production, CLSI screening and verification tests were carried out in line with standards (9). Our study was performed according to the guidelines of the Declaration of Helsinki and accepted by the Ethics Committee. Written informed consent was confirmed by the patients or their parents.

2-2. Statistical analysis

Data were recorded in a Microsoft Excel spreadsheet and were analyzed using SPSS for Windows v.17.0 (SPSS, Inc., Chicago IL). The culture results were accepted as

reference for strip and microscopy analysis. The sensitivity, specificity and positive predictive values were calculated for each combination based on the original clinical information using SPSS program. P-value less than 0.05 were statistically significant.

3- RESULTS

A total 237 patient (58 (24.5 %) male, 179 (75.5%) female), follow-up with UTI diagnosis, with a mean age 9.4 ±3.25 years, were included in the study. Urinary analysis and urine cultures of these patients were examined. There were 160 (67.5%) urine culture negative and 77 (32.5%) urine culture were positive. The results of the strip and urine microscopy of culture negative and positive urine specimens are given in **Table.1**. The 42.4% of culture negative samples showed leukocyte esterase, nitrite, bacterial and leukocyte counts, which are indicative of infection in urine analysis, were found in normal range. **Table.2** shown the sensitivity and specificity of the components of the dipstick urinalysis. The highest sensitivity (90%) was found in the presence of leucocyte esterase and bacteria; while the highest specificity (99.4%) was found in the presence of nitrite alone or with other components (leucocyte or leucocyte esterase).

Escherichia coli (E. coli) was found the most common gram-negative uropathogen in 60 (77.9%) patients in both gender. Gram positive uropathogens are rare and enterococci 6 (7.8%) was the most frequently found. **Table.3** and **Figure.1** shown the distribution and frequency of uropathogens by gender. Also, when antibiotic resistance was evaluated, the highest antibiotic resistance was found in beta lactam antibiotics, mainly ampicillin. The lowest antibiotic resistance was detected in the carbapenems followed by fluoroquinolone group antibiotics (**Figure.2**).

Table-1: Urinary chemical and microscopy test results from positive and negative culture examples

Urine dipstick parameters	Negative Cultures		Positive Cultures	
	Negative	Positive	Negative	Positive
	Number (%)	Number (%)	Number (%)	Number (%)
Leucocyte esterase	119(74.4)	41(25.6)	21(27.3)	56(72.7)
Nitrite	158(98.7)	2(1.3)	37(48)	40(52)
Leucocyte-M	125(78.1)	35(21.9)	21(27.3)	56(72.7)
Bacteria-M	127(79.4)	33(20.6)	25(32.5)	52(67.5)

L-ES: Leucocyte esterase; M: Microscopy.

Table-2: The sensitivity and specificity of the components of the dipstick urinalysis

Urine dipstick parameters	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
L-ES	72.4	74.7	57.9	84.9
Nitrite	52.6	99.4	97.6	81.3
Leucocyte-M	75.3	79.9	64.4	87.0
Bacteria-M	70.1	81.0	64.3	84.8
L-ES+ Leucocyte-M	77.3	80.3	64.6	88.4
L-ES+ Nitrite	71.1	100.0	100.0	90.0
L-ES+ Bacteria-M	90.0	86.7	69.2	96.3
Leucocyte-M+Bacteria-M	88.9	89.3	75.5	95.6
L-ES+ Leucocyte-M+Nitrite	78.0	100.0	100.0	92.7
L-ES+ Leucocyte-M+ Bacteria-M	89.2	88.5	71.7	96.2
L-ES+ Leucocyte-M+Nitrite + Bacteria-M	89.7	100.0	100.0	97.1

L-ES: Leucocyte esterase; M: Microscopy.

Table-3: Distribution and frequency of uropathogenes by gender

Pathogens	Male	Female	Total
Escherichia coli	4(5.2)	56(72.7)	60(77.9)
Proteus species	2(2.6)	2(2.6)	4(5.2)
Klebsiella Klebsiella	2(2.6)	1(1.3)	3(3.9)
Enterococcus species	2(2.6)	4(5.2)	6(7.8)
Grup B streptococcus	2(2.6)	2(2.6)	4(5.2)
Total	12(15.6)	65(84.4)	77(100)

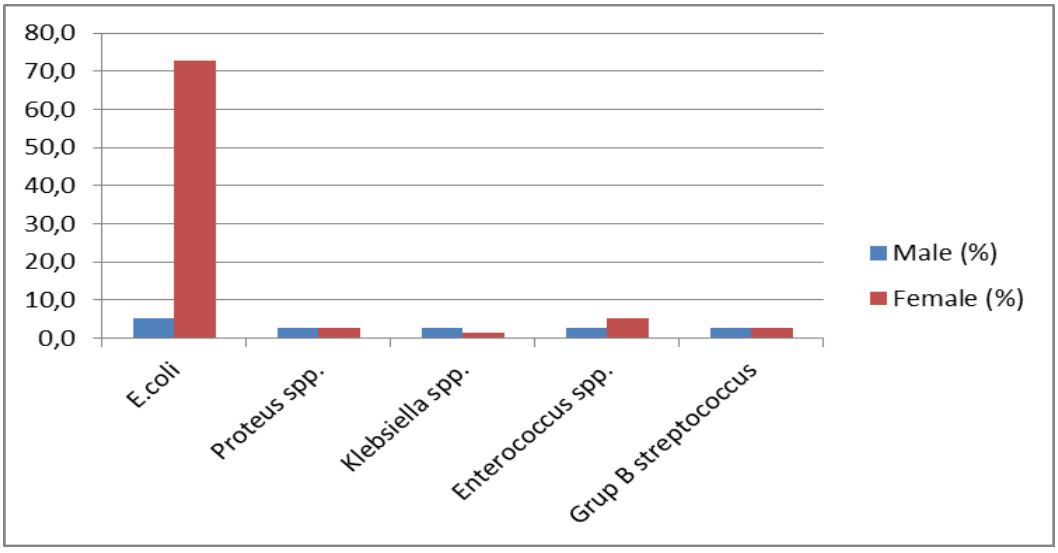

Fig.1: Percentage of uropathogenes by gender.

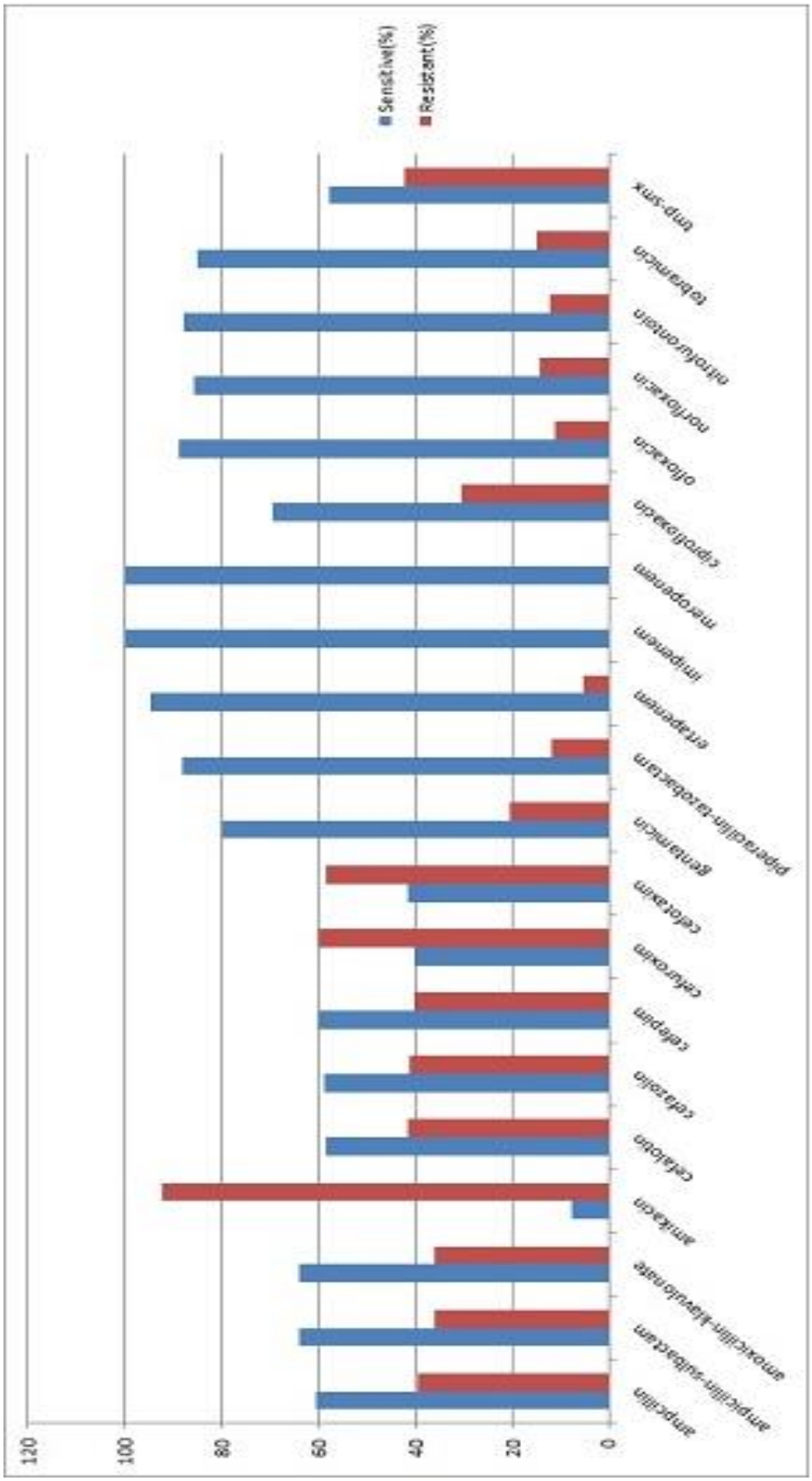

Fig.2: Sensivity and resistance rate distribution of antibiotics (percentage).

4- DISCUSSION

In childhood, UTI is an important cause of morbidity, renal scar was shown in 12% of children who had UTI and in about 1/4 of recurrent UTI (10). Urine culture is the gold standard method of diagnosing UTI (7). Unfortunately, it takes at least 18 hour to detect pathogen growth and 48-72 hours to identify which antibiotics would be appropriate. Thus, when deciding whether to start empirical antibiotic treatment, clinicians rely on their clinical index of suspicion and the events of urinary analysis (7). The urine dipstick results are biochemical tests to detect the presence of leucocyte esterase or nitrites. The urine nitrite test is not a sensitive marker for UTI in children (11), as it is highly specific (12). Contrary to urinary nitrites, the sensitivity of the leucocyte esterase test was reported 94% in a clinically suspected UTI (11). The similar of these studies, we found high specificity (99.4%) and low sensitivity (52.6%) in urinary nitrates and high sensitivity (75.3%) in lecocyte esterase. Microscopic analysis of a centrifuged urine specimen can also help diagnosis of UTI.

Ten leucocytes, per high-power field, has been contemplated more reliable to anticipate UTI in children < 2 years of age by the different guidelines (13, 14); but most centres in Canada report the number of leucocytes per high-power field with > 5 being abnormal (15). The visualisation of bacteria in a fresh uncentrifuged urine specimen is a rapid test to identify or exclude UTI (16). We found a high sensitivity (75.3%, 70.1%), and specificity (79.9%,81%) for pyuria and bacteiuria, respectively. Wald and Hoberman showed that the positive predictive value of bacteriuria and pyuria is as high as 84.6% (17). İn our study, the positive predictive value of pyuria and bacteriuria was found to be high in accordance with other studies (18,19). According to literature, a child with a negative urine dipstick for leucocyte esterase and nitrites and no bacteriuria or pyuria on microscopic analysis has a <1% chance of having a UTI (18). İn the present study, patient who have positive urine dipstick and bacteriuria or pyuria on microscopic analysis has an 89.7% sensitivity and 100% specificity of having a UTI. E. coli is most commonly found as uropathogen in our study similar to ours. McGregor et al. (20) and Calzi et al. (21) were detected E.coli at 84.7% and 64.4%, respectively. İn our study, uropathogens were identified E.coli 77.9%, Proteus species 5.2% and Klebsiella species 3.9%. The Extended-Spectrum Beta-Lactamases (ESBL) positivity rate in our study was found to be 19.1%. In studies from our country, the ESBL positive rate among the UTI pathogens varies between 1.6% to 40% (22, 23).

High rates of resistance to ampicillin and TMP-SMX, which are frequently used in empirical therapy are reported in our country. Shao et al. (24) showed that TMP-SMX resistance was 67% and ampicillin resistance was 78.9% in E.coli strains. Yavascan et al. (25), reported an ampicillin and TMP-SMX resistance for E.coli 81.5% and 67%, respectively. İn another study from our country (26) recorded ampicillin resistance 68.9% and TMP-SMX resistance 46.7% for E.coli. İn the present study, we found ampicillin resistance 60.6% and TMP-SMX resistance 42.2% for E.coli.

Aminoglycosides are among the most preferred agents among parenteral antibiotics in UTI. Antibiotic resistance has been reported for amikacin at rates ranging from 4.9% to 52.5% in E.coli strains (24, 25). We found antibiotic resistance for E.coli, amikacin 7.7% and gentamicin 20.3%. According to these studies, due to low resistance of aminoglycosides, they can be preferred in the treatment of UTI. Similar to other reports (26-28), our Fluoroquinolone resistance was 14.4% and antibiotic

resistance against carbapenem group antibiotics was not found.

5- CONCLUSION

Urinary tract infections should be monitored with urine cultures, and microscopic and chemical examination of urine analysis can give us information about urine culture requirement. Selection of appropriate antibiotic treatment, prevention of misuse and overuse will reduce antibiotic resistance rates. The observation of increasing overall resistance to antibiotics authorize further studies that lead to new recommendations to antibiotic use in children and adolescents.

6- CONFLICT OF INTEREST

None of the authors has any conflict of interest, financial or otherwise. This manuscript, or any part of it, has not been previously published; nor is it under consideration for publication elsewhere.

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