Research Article

Bacterial Pathogens and Antimicrobial Resistance Patterns in Pediatric Urinary Tract Infections: A Four-Year Surveillance Study (2009–2012)

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The aims of this study were to assess the common bacterial microorganisms causing UTI and their antimicrobial resistance patterns in Bandar Abbas (Southern Iran) during a four-year period. In this retrospective study, samples with a colony count of $\geq 10^5$ CFU/mL bacteria were considered positive; for these samples, the bacteria were identified, and the profile of antibiotic susceptibility was characterized. From the 19,223 samples analyzed, 1,513 (7.87%) were positive for bacterial infection. UTI was more frequent in male (54.9%). E. coli was reported as the most common etiological agent of UTI (65.2%), followed by Klebsiella spp. (26%), Pseudomonas aeruginosa (3.6%), and Staphylococcus coagulase positive (3.7%). Results of antimicrobial susceptibility analysis for E. coli to commonly used antibiotics are as follows: Amikacin (79.7%), Ofloxacin (78.3%), Gentamicin (71.6%), Ceftriaxone (41.8%), Cefotaxime (41.4%), and Cefixime (27.8%). Empirical antibiotic selection should be based on awareness of the local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal or even national guidelines. In this study, Amikacin and Gentamicin were shown to be the most appropriate antibiotics for empiric therapy of pyelonephritis, but empirical therapy should only be done by specialist physicians in cases where it is necessary while considering sex and age of children.

1. Introduction

Urinary tract infection (UTI) is a common health problem during the childhood period and it is an important cause of morbidity and mortality in the first 2 years of life [1–4]. The reported incidence of UTI is 7% among girls and 2% among boys during the first 6 years of life [5]. The main objects in childhood urinary tract infections are rapid recovery from complaints and prevention of related complications, such as urosepsis, urolithiasis, and renal abscess, as well as the prevention of permanent renal parenchymal damage [6]. To achieve these aims, empirical antibiotic prescription is often endorsed even before the culture results are available [7]. On the other hand, antibiotic resistance of urinary tract pathogens has been known to increase worldwide, especially to commonly used antimicrobials [8, 9]. The increasing antibiotic resistance trends are likely to have important clinical implications for the empirical use of antibiotics [10]. For this reason, knowledge of the etiology pathogens of UTIs and their antimicrobial resistance patterns in specific geographical locations may aid clinicians in choosing the appropriate antimicrobial empirical treatment [11]. Prior to this study, the frequency of bacterial species causing UTI and their susceptibility patterns to most commonly used antibiotics has
growth was higher than $10^5$ CFU/mL. The prevalence of UTI among male and female children suspected to have UTI was 5.1% (845/16282; 95% CI 4.78–5.43%) and 22.4% (659/2941; 95% CI 20.9–23.9%), respectively. Only the first urine sample of one patient and monomorphic bacterial growth samples was considered in this study. 176 of these samples were Staphylococcus coagulase negative (rather a contamination microorganism) and were excluded from the study. So, finally, 1209 samples were included. 664 (54.9%) of these patients were males and 545 (45.1%) were females. Of these patients, 437 (36.1%), 377 (31.2%), and 395 (32.7%) were neonates (<28 days), infants (28 days to 1 year), and children (1 year to 14 year), respectively. The predominant agents of UTI were successively E. coli (65.2%; 95% CI 62.5–67.8%), Klebsiella spp. (26%; 95% CI 23.6–28.4%), Pseudomonas aeruginosa (3.6%; 95% CI 2.6–4.6%), Staphylococcus coagulase positive (3.7%; 95% CI 2.7–4.7%), Citrobacter (0.9%; 95% CI 0.4–1.3%), Enterobacter spp. (0.4%; 95% CI 0.1–0.7%), and Proteus mirabilis (0.2%; 95% CI 0.0–0.4%) (Table 1).

Analysis of the results according to patient gender represented that, although E. coli is the predominant isolated pathogen from both sexes, it occurred more frequently in females (70.8% in females compared to 60.5% in males: significant at $\rho = 0.001$ (chi square = 11.359)), whereas the prevalence of UTI due to Klebsiella spp. was higher in males than in females (28.3% in males compared to 23.1% in females, respectively. Significant at $\rho = 0.001$ (chi square = 11.359)). And the prevalence of UTI caused by Pseudomonas aeruginosa was significantly higher in males at $\rho = 0.035$ (chi square = 4.45).

Table 1 illustrates incidence of the main bacterial pathogens implicated in urinary tract infection, according sex and age during the study period. Significant (Kruskal-Wallis test, $\rho < 0.05$) changes in the main bacterial pathogens responsible for UTI were observed during the study period. In general, the incidence of Staphylococcus coagulase positive increased and the incidence of Klebsiella spp. decreased during the period of the study (Figure 1).

*In vitro* sensitivity testing showed that the mean susceptibility E. coli had a sensitivity rate of 79.7% to Amikacin and
Table 1: The main bacterial pathogens implicated in urinary tract infection by sex and age throughout the study period.

| Bacteria       | Totala (N = 437) | Neonates  | Infants  | Children  | Totala (N = 377) | Maleb (n = 217) | Femaleb (n = 160) | Totala (N = 395) | Maleb (n = 187) | Femaleb (n = 208) |
|----------------|------------------|-----------|----------|-----------|------------------|-----------------|------------------|------------------|-----------------|------------------|
| *E. coli*      | 57.7             | 54.2      | 62.7     | 70.8      | 66.8             | 76.3            | 68.1             | 62.0             | 73.6            |                  |
| *Klebsiella*   | 36.2             | 38.1      | 33.3     | 19.4      | 21.2             | 16.8            | 21               | 23.0             | 19.2            |                  |
| *P. aeruginosa*| 2.3              | 3.1       | 1.1      | 5.0       | 6.0              | 3.8             | 3.8              | 5.3              | 2.4             |                  |
| S. coagulase positive | 1.6  | 2.3       | 0.6      | 3.2       | 4.1              | 1.8             | 6.6              | 9.2              | 4.3             |                  |
| *Citrobacter*  | 1.6              | 1.5       | 1.7      | 0.8       | 0.5              | 1.3             | 0.3              | 0.0              | 0.5             |                  |
| *Enterobacter* | 0.6              | 0.8       | 0.6      | 0.5       | 0.9              | 0.0             | 0.0              | 0.0              | 0.0             |                  |
| *Proteus*      | 0.0              | 0.0       | 0.0      | 0.3       | 0.5              | 0.0             | 0.3              | 0.5              | 0.0             |                  |

*aPercentage determined in relation to N; †percentage determined in relation to n.*

Figure 1: Incidence of the main bacteria implicated in UTI by age during the study period.

77.1% to Ciprofloxacin. In this study, the highest resistance rate of this germ was to Ampicillin (83.5%) followed by Trimethoprim-sulfamethoxazole (75.4%). The *E. coli* resistance to Trimethoprim-sulfamethoxazole (one of the most important UTI empirical therapy options) changed significantly over the study period (chi square test, \( \rho < 0.001 \)). In general, the resistance rate has been increased in females but has been reduced in males (Table 2). *Klebsiella* spp., the second common germ producing UTI, showed the highest sensitivity to Ciprofloxacin (81.3%) and Amikacin (86.4%), and Gentamycin (84%). The antibiotic resistance patterns of *E. coli* (the most common germ) and *Pseudomonas aeruginosa* (the most antibiotic resistant germ) agents of UTI are presented in Figures 2 and 3.

4. Discussion

Urinary tract infection (UTI) is of major clinical importance owing to considerably high morbidity and mortality rates among children [3]. In this study, of 19223 patients who were
suspected to UTI and from whom urine samples were taken, only 7.87% had a urinary tract infection. Its relative ratio varies in different areas of Iran. In studies carried out in Tabriz and Qazvin, 13.2% and 7.2% of pediatric suspected of urinary tract infection had a positive urine culture [10, 13] that was similar to our results. This is possibly because UTI symptoms are not a dependable indicator of infection and in children younger than 2 years of age are nonspecific [10] therefore, urine culture of suspected children is necessary for a definitive diagnosis of UTI.

In this study, E. coli, as the most common pathogen, incidence among females was significantly higher than in males and incidence of Klebsiella, as the second most common pathogen, was significantly higher in males. On the other hand, in this study, 70.5% of UTI caused by Pseudomonas aeruginosa were in males and only 29.5% were in females. Pseudomonas aeruginosa is an opportunistic uropathogen for community-acquired UTI [12] and also totally resistant to first line empirical antibiotics (special importance of this pathogen) [14]. Be male, received recent antibiotic therapy, have a neurogenic bladder and have a history of urinary tract procedures such as catheterization are known as risk factors for UTI caused by Pseudomonas aeruginosa [15]. So similar to other literature, sex might influence the etiology of UTI and must be considered in empirical therapy [12].

In this study, among children who have a positive urine culture, 55.9% were males and 44.1% were females. Also, most of the participants were infants and neonates (65.2%) and 34.8% were children. Male children are infected more than girls during the first 3 months of their life but, incidence of
UTI among girls who have more than one year old is much more [16] possibly because the structural anomalies incidence in first 3 months among boys is more. Boys were more at risk of wrong diagnosis of UTI than female children too. In this study, the frequencies of positive cultures were 5.1% for males and 22.4% for females (ratio~1:4). Farajnia et al. reported this ratio 1:2 [10] and Farrell et al. reported this ratio 1:4.1 [17]. The cause of this needs more study.

Chi square test showed that pathogens differed significantly ($p < 0.001$) across the three age groups of study. E. coli prevalence was higher in infants (63.1%), incidence of Klebsiella was higher in neonate (32.9%), and Pseudomonas aeruginosa incidence was higher in infants, but the Staphylococcus coagulase positive prevalence was higher in children (5.4%). So age might influence the etiology of urinary tract infection as has been shown in the study of Afsharpaiman et al. [16]. Overall, these results indicate that urine culture is necessary for a definitive diagnosis of UTI and that empirical therapy should only be done by specialist physicians in case where it is necessary while considering sex and age of children.

E. coli is the leading uropathogen and was isolated from 56.6–84.6% of Iranian children with febrile UTI [16, 18]. The results of this study in this context are in agreement with previous literature findings. E. coli was the most causative organism responsible for 65.2% of urinary tract infections. But the resistance pattern of this germ to antibiotics was very different in comparison with other studies. For example Sharifian et al. reported the highest susceptibility percentage of E. coli to Ceftriaxone (97.8%) and Cefotaxime (95.2%) in 2006 in Tehran [19]. But, in this study, E. coli specimens were 52.2% and 56.2% resistant to Ceftriaxone and Cefotaxime, respectively, probably because the pattern of the sensitivity of microorganisms to antibiotics varies over time and between different geographical locations. There was no study before this study for physicians of this region to estimate the most common pathogen and its resistant pattern in pediatrics, but they empirically consider E. coli as the most causative agent and Ceftriaxone and Cefixime as the most appropriate choice for UTI treatment but the results of this study have shown that Ceftriaxone probably cannot be the best choice hereafter. On the other hand, according to the results of this study, E. coli specimens were 64.8% resistant to Cefixime and 75.4% resistant to Trimethoprim-sulfamethoxazole. Although Cefixime probably cannot be the best choice, it is better than Trimethoprim-sulfamethoxazole for outpatient treatment option.

In a study conducted in Khartoum, Ali and Osman reported that the mean susceptibility of all isolates was too high to Gentamicin (96%), Ciprofloxacin (94%), and Ceftriaxone (90%) whereas the lowest percentages of susceptibility were reported for Amoxicillin clavulanate (19%) and Ampicillin (14%) [20]. In a study conducted in the US hospitals, resistance among E. coli was highest for Trimethoprim-sulfamethoxazole (24%) but lower for Nitrofurantoin (<1%) and Cephalothin (15%) [5]. This study revealed a high E. coli resistance rate to antibiotics. Except for Nitrofurantoin and Ciprofloxacin that are not appropriate options for UTI treatment in children [19], the highest percentages of susceptibility were seen for Amikacin (79.7%), Ofloxacin (78.3%), and Gentamicin (71.6%), whereas the highest percentages of resistance for this pathogen were found for Ampicillin (83.5%), Cotrimoxazol (75.4%), and Cefalexin (69.8%). Other studies in Iran have also indicated a high resistance rate to antibiotics. For example, Farajnia et al. reported resistance rate of 90.7% to Ampicillin, 51.8% to Cotrimoxazol, and 26.5% to Cefalexin, whereas the highest percentages of susceptibility were seen for Amikacin (96.6%) and Gentamicin (92.9%) in 2008 in Tabriz [10]. These significantly higher bacterial resistance rates to antibiotics in our country in comparison with other countries seem to be the result of two factors: first, a higher rate of antibiotic usage by families even in the absence of a prescription and, second, a population with a high percentage of young individuals since UTI is more common in the early years of life (UTI is most common in girls aged 3 to 5 years) [19]. The other factor that probably caused this study to show higher bacterial resistant rates of antibiotic is the empirical therapy itself because the results of this study showed that only 7.87%, of who were suspected to UTI, had a urinary tract infection in reality. Probably a high rate of antibiotics using resulted in various antibiotic resistance patterns in different parts of Iran.

In conclusion, we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal or even national guidelines. In this study, Amikacin and Gentamicin were shown to be the most appropriate antibiotics for empiric therapy of pyelonephritis, but, empirical therapy should only be done by specialist physicians in cases where it is necessary while considering sex and age of children.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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