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HIGH PERVASIVENESS OF MULTIPLE DRUG RESISTANCE AMONGST ESCHERICHIA COLI INFECTIONS IN PEDIATRIC PATIENTS

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Abstract:
Antimicrobial resistance is a major health risk. The number of infections caused by numerous drug-resistant microorganisms is increasing, making community-acquired infections a physician's nightmare.
Objective: *A survey was conducted to assess the prevalence of multiple drug-resistant urinary tract pathogens affecting children.*
Place and Duration: *In the Pediatric Unit of Shalamar Medical and Dental College Lahore for one-year duration from March 2019 to March 2020*
Methods: *Urine samples were collected from children under five years of age. Urine samples were considered positive cultures when a single bacterial species with a colony count> 105 CFU / ml was grown. A total of 240 urine samples were collected, of which only 67 were positive. It was found that 67% and 18% of the infections were caused by E. coli and Staphylococcal species, respectively. Other bacteria that cause urinary tract infections include Klebsiella, Citrobacter, and Pseudomonas. The antimicrobial susceptibility pattern of E. coli isolates was tested on 10 commonly prescribed antimicrobial drugs for urinary tract infections because E. coli was the predominant uropathogenic factor.*
Results: *About 66 percent of the isolates were resistant to 3 or more drugs. 46 percent of E. coli isolates were resistant to the 5 antibiotics tested. Augmentin (64%) showed the highest resistance. E. coli resistance to Norfloxacin and Cefuroxime was 60%. Approximately 94% of the isolates were sensitive to netilmicin. None of the investigated drugs were effective against all E. coli isolates.*
Conclusion: *This type of questionnaire can serve as a guideline for initiating the empirical treatment of community-acquired urinary tract infections pending the generation of culture reports.*
Key words: *multi-drug resistance, E. coli, urinary tract infection, children, children.*

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INTRODUCTION:

The second most common infectious disease in community medical practice is urinary tract infection (UTI) [1-2]. UTIs account for the majority of causes of unexplained fever in children under 3 years of age. The risk of UTIs is greatest in the first year of life. About 1% of boys and 3% of girls experience a UTI usually before the age of eleven, and recurrences of UTIs are common in childhood. According to available social studies, boys under the age of 1 and girls under the age of 5 are most at risk of developing UTI [3-4]. The incidence of UTIs in children with fever is 20%. The vast majority of feverish young children with UTIs have pyelonephritis, which can lead to scarring of the kidneys and long-term kidney failure. Unfortunately, in a toddler or toddler, the classic symptoms of UTI and pyelonephritis are not present or are easily perceived, as in older children and adults. The most common symptom of a UTI in an infant is fever [5-6]. Echerichia coli is the major etiological factor associated with UTI in children. The sensitivity to antimicrobial agents of urinary pathogens has changed over the years; both in the social and hospital environment. Factors such as the unregulated use of antibiotics in developing countries, the widespread use and inappropriate use of antimicrobials may contribute to altering the microbiological profile of uropathogens. In hospital conditions, most cases of UTI are initially treated empirically[7-8]. Empirical treatment is based on local rates of antimicrobial resistance and disease severity. In an infant or child with acute symptoms who have pyelonephritis, treatment should be started prior to urine culture and hypersensitivity, as delay in treatment may cause permanent kidney damage. The antibiotic susceptibility pattern of uropathogens in the population is critical to determining empirical treatment as the use of inappropriate empirical therapy has been found to predict mortality in patients with urinary sepsis. In Pakistan, the pattern of resistance to community-acquired uropathogens has not been extensively studied. The study was conducted to identify patterns of antibiotic resistance among uropathogens affecting children to help formulate local guidelines for empirical treatment of community-based UTIs with antibiotics.

MATERIALS AND METHODS:

This study was held In the Pediatric Unit of Shalamar Medical and Dental College Lahore for one-year duration from March 2019 to March 2020. Urine samples were collected from patients visiting clinical laboratory. Only samples from children under 5 years of age (both men and women) were included in the study. All patients had clinical signs of urinary tract infection as determined by the attending physician. Only one positive culture per patient was included in the analysis. The study excluded patients without clinical signs of infection and multiple pathogens in the urine culture. A semi-quantitative urine culture was performed using a calibrated loop. The samples were inoculated onto blood agar plates, Mac Conkey agar, and nutrient agar. Plates were read after overnight incubation at 37 ° C. Significant monomicrobial bacteriuria was defined as a culture of one bacterial species from a urine sample at a concentration> 105 cfu / ml. Significant pathogens were identified using standard biochemical procedures. Antimicrobial susceptibility testing was carried out using the disk diffusion method as described by the Clinical Laboratory Standard Institute (CLSI) [6]. Antimicrobials tested and reported (disks) were obtained from Pathogen Biological Laboratories, Gujarat. Susceptibility tests were performed for Ampicillin + Sulbactam (AM; 10 + 10 = 20mcg), Augmentin (AG; 20 + 10 = 30mcg), Ceftriaxone (RP; 30mcg), Cefoperazone (CP; 75mcg), Cefuroxime (CB; 30mcg), Ciprofloxacin (RC; 5mcg), Doxycycline (DX; 30mcg), Gentamicin (GM; 10mcg), Netilmicin (NT; 30mcg), and Norfloxacin (NX; 10mcg).

RESULTS:

Of the 240 processed urine samples, 173 (72%) were sterile and 67 (28%) showed significant monomicrobial growth.

Table: 1. Frequency and Distribution of Uropathogens

Serial No.	Microorganism Identified	No. Of Isolates
1	*Escherichia coli*	45
2	*Staphylococci* (coagulase positive)	06
3	*Staphylococci* (coagulase negative)	06
4	*Klebsiella sp.*	04
5	*Citrobacter*	02
6	Non-hemolytic *Streptococci*	01
7	*Proteus*	01
8	*Pseudomonas*	01
9	*Enterobacter*	01

Data on the frequency of uropathogens (Table 1) showed that E. coli (45) is one of the most common pathogens of the urinary system among children. Gram-negative rods accounted for 87.6%, and Gram-positive rods accounted for the remaining 19.4% of all uropathogens (Fig. 1).

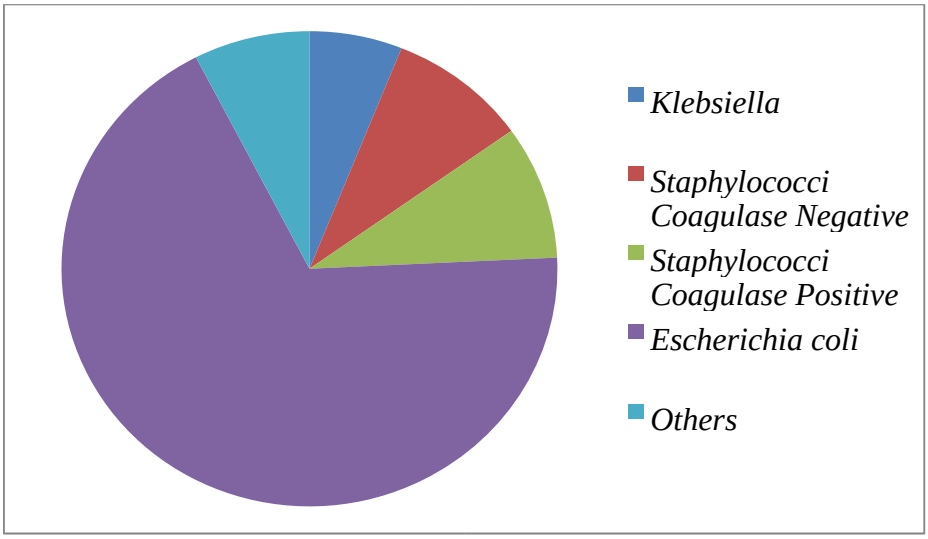

Fig. 1: Relative distribution of uropathogens isolated from children

The antimicrobial agents with the highest level of activity against E. coli isolates were netilmicin and gentamicin. Augmentin showed the highest resistance (64%; table: 2).

Table: 3. Class of Antibiotics used in this study

Serial No.	Antibiotic	Classification
1	Augmentin (Amoxycillin + Potassium clavulanate)	Penicillin (Pen)
2	Ampicillin + Sulbactam	First Generation Cephalosporin (Cep^1)
3	Cefuroxime	Second Generation Cephalosporin (Cep^2)
4	Cefoperazone	Third Generation Cephalosporin (Cep^3)
5	Ceftriaxone	Third Generation Cephalosporin (Cep^3)
6	Doxycycline	Tetracycline (Tet)
7	Norfloxacin	Fluoroquinolone (Fqn)
8	Ciprofloxacin	Fluoroquinolone (Fqn)
9	Gentamicin	Aminoglycoside (Amn)
10	Netilmicin	Aminoglycoside (Amn)

Only 40% of E. coli isolates were sensitive to Norfloxacin and Cefuroxime. Approximately 94% of the isolates were sensitive to netilmicin. None of the investigated drugs were effective against all E. coli isolates. Approximately 66.6% of E. coli isolates were resistant to 3 or more drugs. 46.6% and 26.6% of E. coli isolates were resistant to the 5 and 6 tested antibiotics, respectively. The lowest degree of resistance was to aminoglycosides. Surprisingly, more than 50 percent of E. coli isolated from pediatric patients were resistant to both of the fluoroquinolone antibiotics used in this study. 22 isolates were resistant to combinations of penicillin and cephalosporins as well as combinations of cephalosporins and fluoroquinolones. About 38% of the isolates were resistant to the three main classes of antibiotics, namely penicillin, cephalosporins and fluoroquinolones. The five isolates showed combined resistance to at least one of the antibiotics of all five classes of antibiotics tested, which is a serious risk in itself.

DISCUSSION:

In our study, E. coli was the most frequently isolated uropathogenic pathogen in community-acquired urinary tract infection among pediatric patients[9-10]. This corresponds to the data obtained by other researchers. The pattern of antimicrobial susceptibility of uropathogens varies greatly from region to region. We show a high level of resistance to Augmentin, Norfloxacin, Cefuroxime and Ciprofloxacin[11]. This is similar to previous research in Pakistan on community acquired urinary tract infections. The most commonly used antibiotics to treat urinary tract infections are fluoroquinolones. The high prevalence of resistance to both tested fluoroquinolones can be attributed to their frequent use as an antimicrobial in the treatment of urinary tract infections in the community[12]. The high degree of resistance to beta-lactam antibiotics observed in our study corresponds to previous reports. A similar study of antimicrobial resistance trends in E. coli isolated from pediatric patients in Kerala also showed high combined resistance to the most commonly used antimicrobials, including β-lactams, quinolones, tetracyclines and aminoglycosides[13-14]. With the widespread use of over-the-counter antibiotics in Pakistan leading to tremendous selection pressure, multi-drug resistance problems may worsen significantly in the near future. This scenario is of serious concern as there are few new antibiotics in the pharmaceutical plans[15]. The lack of a national network system to monitor antimicrobial resistance in Pakistan has heightened the threat of multi-drug-resistant microorganisms.

CONCLUSION:

The increased resistance of E. coli uropathogens to ceftriaxone among pediatric patients is of great concern as it is one of the life-saving drugs in pediatric sepsis. The high rates of oral antibiotic resistance in our study may be due to the uncontrolled consumption of these antibiotics in the Pakistan population in recent decades. On the other hand, resistance to netilmicin, gentamicin and cefoperazone is low, possibly reflecting lower use of these drugs. The greater number of strains resistant to Norfloxacin and Ciprofloxacin was predictable due to their readily available over-the-counter drugs that are commonly used in all intestinal infections. Systematic and prudent action is needed to halt the evolution of antibiotic resistance in Pakistan. Improving the surveillance of the emergence of resistance, better regulation of antibiotic use, and better education of the public, doctors and veterinarians on the correct use of antimicrobials are essential to maintain the usefulness of antimicrobial drugs in Pakistan.

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