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Antibiotic resistance for UTI in pediatric age groups and association bacteria

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قال تعالى

{وَإِذ تَأَذَّنَ رَبّكم لَئِن شَكَرتم لَأَزِيدَنَّكم وَلَئِن كَفَرتم إِنَّ عَذَابِي لَشَدِيدٌ}

وقال تعالى أيضًا: {فَاذكرونِي أَذكركم وَاشكروا لِي وَلَا تَكفرونِ}

صدق الله العلي العظيم

Acknowledge

I dedicate this graduation of mine to the one who taught me giving and to the one whose name I carry with pride, and I hope that God will extend your life so that you see fruits whose time has come to be harvested after a long wait “my dear father” and to my angel in life and to the meaning of love, tenderness and devotion and to the smile of life and the secret of existence and to the one whose supplication was the secret of my success is my dearest beloved “my beloved mother” and to the one who has great merit in encouraging and motivating me and from whom I learned perseverance and diligence and to whom I am older and upon whom I rely and to whom with their presence I gained limitless strength and love and to those with whom I knew the meaning of life “my brothers and sisters” and to those who were fraternal and they were distinguished by loyalty and giving. To those who accompanied them in the happy and sad paths of life, I walked and to those who were with me on the path of success and goodness, “my dear friends.”

Abstract

Background: Urinary tract infections (UTI) are a commonly encountered infection in the pediatric age group.Therefore, it is necessary to have a current understanding of the antibiotic susceptibility (AS) pattern of uropathogens to manage UTI effectively.The aim of this study is to describe the prevalence and the antimicrobial resistance patterns of the pathogens causing UTI in the pediatric age group in Al-Batoul Teaching Hospital which is care hospital in Baquba of Iraq.

Patients and Methods: This is a retrospective cross-sectional study, conducted in Al-Batoul Teaching Hospital which is care hospital in Baquba of Iraq. The inclusion criteria consisted of patients between 0 - 10 years or more of age admitted to the Pediatrics department at with bacteriologically proven UTI between the months of August 2022 and February 2023. Patients who were identified to have chronic urinary tract conditions or neurodevelopmental problems involving the urinary tract were excluded from the study.

Results: A total of 144 cases with positive culture were included. The most common bacteria causing UTI in this sample were successively *Escherichia coli* (77.76%), *Klebsiella pneumoniae* (14.4%), *Staph*ylococcus spp (23.04%) and *staph.hemolytics* (14.4%) and *Streptococcus* spp (7.2%) and *Staph.aureus* (2.88%). *E. coli* was most resistant to azthromycim (14.04%), followed by ceftazidime (13.5%), whilst it was most sensitive to meropenem (23.22%%) followed by nitrofurantoin (14.58%). *K. pneumoniae* showed the highest rate of resistance to ceftazidime (0.6%) followed by azthromycin (0.4%), while having the highest sensitivity rate to Imipenem (0.9%), followed by meropenem (0.8%). *Staph*.spp had the highest resistance to ceftazidime (2.24%) followed by azthromycin (0.96%), while having the highest sensitivity to meropenem (1.76%). In the other hand, the samples showed no growth was (67.68%).

Conclusion: *E. coli* is the most common cause of UTI in the pediatric population and it was found to be most resistance to azthromycin and ceftazidime whilst being relatively sensitive to meropenem and nitrofurantoin.

Keywords: Uropathogenic *Escherichia coli*, antibiotics resistance, paediatric, urinary tract infection.

Introduction

Urinary tract infections (UTI) are a commonly encountered infection in the pediatric age group. Knowledge of the causative pathogens and their antimicrobial resistance patterns in specific geographical locations is important to provide optimum care. The aim of this study is to describe the prevalence and the antimicrobial resistance patterns of the pathogens causing UTI in the pediatric age group in Iraq. Urinary tract infections (UTIs) are inflammatory disorders caused by microorganisms that have proliferated abnormally in the uinary system (1). UTIs are known to induce short-term orbidities such as fever, dysuria, lower abdominal pain, and may result in permanent kidney scarring (Leung *et al*.,2019).Urinary tract infection is more common in women than in men because of the anatomical proximity of the urethra to gut opening (2). Therefore, UTIs are currently treated empirically, particularly in rural and small-town settings where the facility of urine culture is unavailable, resulting in antibiotic misuse (3). Therefore, screening for susceptibility in each location is critical for producing up-to-date epidemiological data (4). Unfortunately, the resistance profile of community-acquired uropathogens in diverse geographical regions of India has not been adequately explored (5). Worldwide, Centers for Disease Control and Prevention (CDC) 2017 in National Health prevalence survey reported UTI prevalence rate of 0.48%, and among them, 80% were symptomatic UTI cases. Complications of UTIs mainly include kidney failure due to extensive renal damage and sepsis, which occurs when the infection spreads from the lower urinary tract to other parts of the body. UTIS, particularly uncomplicated UTIs like acute uncomplicated cystitis and acute uncomplicated pyelonephritis, are the most frequent reasons for consulting a general practitioner in most of the developed countries, which are being treated by antibiotics.Sensitivity analysis determines the effectiveness of antibiotics against microorganisms such as bacteria that have been isolated from cultures. Antibiotic sensitivity pattern is an important tool to choose the right antibiotics by the clinicians for the patient with

UTIs. It is also found that the prevalence of resistance to commonly prescribed antibiotics in primary care among children with UTIs due to *Escherichia coli* is high, particularly in countries outside the Organization for Economic Co-operation and Development, where the antibiotics are available over the counter. Based on the above points, it was considered suitable by the investigator to study the drug utilization and antibiotic sensitivity pattern of bacterial pathogens in patients suffering from UTI. Moreover, this UTI-related study will help in establishing a proper antibiotic utilization guideline as well as in promoting the rational prescribing of antibiotics. Therefore, keeping these facts in the mind, this study was conducted to assess the drug of choice for the empirical antibiotic therapy and to find the changing susceptibility pattern of urinary pathogens to commonly used antimicrobials among urinary tract-related infectious diseases.

Some risk factors for UTI have already been identified, including sex, ethnicity, vesicoureteral reflux, neurogenic bladder, phimosis, anatomical abnormalities of the lower urinary tract, constipation and the presence of LUTS. Some LUTS such as urinary retention, elevated residual urine volume, infrequent voiding and voiding postponement have been reported to be associated with UTI . Overactive bladder is the most common lower urinary tract disorder; however, its association with UTI remains to be clarified. The objectives of the present study were to evaluate the incidence of UTIs in children with isolated overactive bladder and identify the possible predictors of UTI (Sood and Gupta, 2012).

In neonates, symptoms and signs of urinary tract infection are nonspecific and include poor feeding, diarrhea, failure to thrive, vomiting, mild jaundice (which is usually direct bilirubin elevation), lethargy, fever, and hypothermia. Neonatal sepsis may develop.Infants and children < 2 years with UTI may also present with poorly localizing signs, such as fever, gastrointestinal symptoms (eg, vomiting, diarrhea, abdominal pain), or foul-smelling urine. About 4 to 10% of febrile infants without localizing signs have UTI.In children > 2 years, the more classic picture of cystitis or pyelonephritis can occur. Symptoms of cystitis

include dysuria, frequency, hematuria, urinary retention, suprapubic pain, urgency, pruritus, incontinence, foul-smelling urine, and enuresis. Symptoms of pyelonephritis include high fever, chills, and costovertebral pain and tenderness.Physical findings suggesting associated urinary tract abnormalities include abdominal masses, enlarged kidneys, abnormality of the urethral orifice, and signs of lower spinal malformations. Diminished force of the urinary stream may be the only clue to obstruction or neurogenic bladder.

Children usually need to pass urine more often than adults because their bladders are smaller and they tend to drink more fluids relative to their size. In addition, young children may feel the need to pass urine more urgently because it takes a long time—several years—to develop mature control of the muscles that open and close the bladder. If a child has pain on urination, a UTI is the most likely reason, but several other conditions can also cause pain.

Patients and methods

The aim of this retrospective cross-sectional study is to assess the prevalence of the pathogens isolated from the collected urine cultures in children admitted with microbiologically confirmed UTI during the duration starting from August 2022 and ending in January 2023, in addition to assessing the prevalence of antimicrobial resistance for these organisms. This study was conducted in the Pediatric department in Al-Batoul Teaching Hospital which is care hospital in Baquba of Iraq.The ICD-10 code for unspecified UTI was used in order to identify patients who have been diagnosed with a UTI in the electronic medical records. The electronic records of patients under this code were reviewed and patients with bacteriologically proven UTI were selected for inclusion in this study. Data on age, gender, urine culture results and sensitivity patterns for identified pathogens were obtained from the electronic medical records. All the recorded data were encrypted and no personal information about the patients was included. In Al-Batoul Teaching Hospital , the final diagnosis of UTI is confirmed

based on clinical presentation and is further supported with the microbiology results. The collected urine sample is then sent to the microbiology department for analysis in addition to culture and sensitivity testing. A manual colony count is done using a standardized loop (loop size of 1 microliter) as a tool for obtaining the standard urine quantity. Antibiotic sensitivity test was done to determine the antibiotic sensitive and resistance for the bacteria that cause UTI in children. Common antibiotics used to treat UTI in the pediatric age group were included in this study. These antibiotics are azthromycin, nitrofurantoin, meropenem, ciprofloxacin, and ceftazidime, levofloxacin, amoxicillin.

Statistical analysis:

Statistical package for social sciences (SPSS) version 19 was used to analysis the data that was collected. It was expressed the quantitative data by frequencies and percentages.

Results

Urine samples from 144 pediatric cases between 0 - 10 years or more in age were submitted for analysis and culture from August 2022 to February 2023 to confirm an initial clinical diagnosis of urinary tract infection.Thirty cases were excluded from the study due to the presence of chronic urinary tract conditions and neurodevelopmental problems involving the urinary tract. The percentages of confirmed UTI among male and female cases suspected to have UTI were 40.76% (53/130). Thirty-seven cases (53.28%) were included from 2022 and 77 cases (65.44%) from 2023.

The samples included 40 male cases (57.6%) and 104 female cases (78.10%) ($p<0.01$ between males and females) as shown in Table 1. The included cases were categorized into three age groups: 14 cases (1.70%) were neonates (<28 days), 28 cases (21.10%) were infants (28 days - one year) and 102 cases

(77.20%) were children (one year - 14 years) ($p<0.01$ between the age groups) as shown in Table 2.

Table 1: Classification of patients according to gender.

Total Number	144
Male	40
Female	104

Table 2: Classification of patients according to their ages.

Age	**Number of cases**
1day – 3 months	14
3 months – 6 months	15
6 months - 1yrs	13
1yrs - 3yrs	19
3yrs - 6yrs	26
6yrs - 10yrs	18
More than 10 yrs	39

The five most predominant agents were successively different bacteria were identified as the causative organism in our samples; *E. coli* 54 cases , *Klebsiella pneumoniae* 10 cases, *Staph.*spp 16 , *Staph.hemolytics* 10, and *Staph.aureus* 2 and no growth 47 cases as shown in Table 3.

Table 3: The types of bacteria that cause UTI in children.

Types of Bacteria	**Number of cases**
E.coli	54
Staph.spp	16
Klebsiella.p	10
Staph.hemolytics	10
Strept.spp	5
Staph.aureus	2
No Growth	47

The antibiotic sensitivity test was done and the results for *Staphylococcus aureus* shown in Table 4 and for *E.coli* in Table 5.

Table 4: The results of antibiotic susceptibility test for *Staphylococcus aureus.*

Antibiotics	**Sensitive**	**Resistance**
NIT	1(0.02%)	1(0.02%)
CL	1(0.02%)	1(0.02%)
PM	1(0.02%)	0
LE	1(0.02%)	0
CAZ	0	1(0.02%)
Do	0	1(0.02%)

Table 5: The results of antibiotic susceptibility test for *E.coli.*

Antibiotics	Sensitive	Resistance
AZM	10(5.4%)	26(14.04%)
LE	22(11.88%)	7(3.78%)
MRP	43(23.22%)	1(0.54%)
NX	21(11.34%)	14(7.56%)
NIT	27(14.58%)	2(1.08%)
CAZ	11(5.94%)	25(13.5%)

The antibiotics sensitivity test for *Staph. Hemolytics* was showed in Table 6 and for *Klebsiella pneumoniae* in Table 7. The antibiotic sensitivity test for *Staphylococcus* spp was showed in Table 8 and for *Steptococcus* spp in Table 9.

Table 6: The results of antibiotic susceptibility test for *Staph.hemolytics*.

Antibiotics	Sensitive	Resistance
CL	6(0.6%)	1(0.1%)
IPM	9(0.9%)	0
CAZ	0	9(0.9%)
TCC	3(0.3%)	3(0.3%)
NIT	7(0.7%)	0
MRP	9(0.9%)	0

Table 7: The results of *Klebsiella.pneumoniae* susceptibility test.

Antibiotics	Sensitive	Resistance
MRP	8(0.8%)	1(0.1%)
IPM	9(0.9%)	1(0.1%)
CAZ	2(0.2%)	6(0.6%)
AZM	2(0.2%)	4(0.4%)
NA	3(0.3%)	2(0.2%)
NIT	8(0.8%)	1(0.1%)

Table 8: The results of *Strept*.spp susceptibility test

Antibiotic	Sensitive	Resistance
AZM	2(0.1%)	1(0.05%)
IPM	5(0.25%)	0
MRP	3(0.15%)	1(0.05%)
AMP	1(0.05%)	1(0.05%)
E	1(0.05%)	4(0.2%)
CTR	1(0.05%)	1(0.05%)

Table 9: The results of *Staph*.spp susceptibity test.

Antibiotics	Sesitive	Resistance

CAZ	0	14(2.24%)
AZM	0	6(0.96%)
CTR	3(0.48%)	1(0.16%)
NIT	9(1.44%)	3(0.48%)
MRP	11(1.76 %)	2(0.32%)
CTX	2(0.32%)	0

Discussion

The goal of this study was to evaluate the antibiotic sensitivity pattern of microbiological isolates and antibiotic recommendation in pediatric cases suffering from UTIs admitted in the Pediatric department in Al-Batoul Teaching Hospital which is care hospital in Baquba of Iraq(1). Antimicrobial susceptibility testing of individual isolates is important to confirm sensitivity to chosen empirical antimicrobial agents(2). Prevalence was highly influenced by the gender and age of the patients(3). The present study demonstrated a higher incidence of infections in males in comparison to female patients in contrast to previous studies(4). Digging deeper, we observed that male to female proportion of UTIs cases was much greater in between the age of 0–2 months (2:1), and this proportion almost reverses in higher age group children (1:3)(5). The most chances of higher prevalence in male neonates and infants are due to poor hygiene particularly due to lack of circumcision as reported in earlier studies(6). However, the UTIs were reported to be more prevalent in the female young and middle-aged population and thought to be due to lesser distance between the anus (the usual source of uropathogens) and the urethral meatus, the greater length of the male urethra, and the antibacterial activity of prostatic fluid in male. Furthermore,

this may be due to the vaginal colonization with uropathogens or entry of colonizing uropathogens into the bladder via urethra. This is well-evidenced that many drugs, as well as foods like milk, egg nuts, and seafood, can trigger anaphylactic reactions in children. Concurrent to this, it was observed an allergy to fish and milk in our study. But no drug allergy was noticed in any patients indicating the safety of drugs prescribed among the patients. Pyelonephritis has been reported to be a major cause of pain and fever in UTIs . Consistent with previous study, it was observed severe fever, diarrhea, and vomiting as the commonest symptoms for hospital admission. Moving forward, we also observed seizure as the most common concomitant condition in children having UTIs. In line of the above discussion, fever was a major symptom in UTIs and this febrile seizure in pediatric population may be due to raised body temperature. E. coli was the most causative organism of UTIs and has been reported to be present in 75–90% of UTI isolates . Concurrently, the present study confirmed a higher prevalence of isolates of *E. coli* (77.76%) followed by staph.spp (23.04%) *K. pneumoniae* (14.4%). Moreover, many more microorganisms like *Klebsiella pneumoniae* (14.4%), and *staph.hemolytics* (14.4%),strept.spp (7.2%) and staph.aureus(2.88%) have been reported to be prevalent in our study. These findings indicated a prevalence of the highly diverse type of microbes in UTIs as reported earlier. The present study showed that *E.coli* have sensitivity in 92.86% of cases, to amikacin, ceftriaxone, levofloxacin, ertapenem, gentamycin, meropenem, piperacillin-tazobactam, tigecycline, and ceftazidime. Among antibiotics, ampicillin showed high resistance in the case of *E. coli* isolates (100%) like previous studies. Therefore, rational use of antibiotics must be implemented after keeping these facts in mind. Concurrently, meropenem was also observed to be effective in 100% of cases of *K. pneumoniae* followed by tigecycline and amikacin as reported earlier. As mentioned above, various other isolates were also reported in our study. In case of *Staph.hemolytics*, 100% of cases were susceptible to cefepime, ciprofloxacin, levofloxacin, gentamycin,

ceftazidime, and piperacillin-tazobactam. However, amikacin, imipenem, meropenem, and aztreonam were effective in 66.67% of cases . Studies reported that among enterococci, *E. faecalis* play a major role in various infections. However, it was observed *E. faeciumas* UTI isolates and reported to be susceptible with tigecycline, linezolid, and vancomycin in 100% of cases followed by quinupristin/dalfopristin and teicoplanin. Other cases related to , *S. aureus*, *staph*.spp and *Strept*.spp and its sensitivity to antimicrobial agents were in line with previous studies. Looking forward, ceftriaxone (29.55%), vancomycin (25%), meropenem (20.45%), and cefuroxime (15.91%) have been reported to be the four most commonly prescribed antibiotics in UTIs in children. The reason behind this may be ease of route of drug administration and bacterial sensitivity to antibiotics in pediatric population. Almost all drugs were administered intravenously possibly due to the nature of antibiotics and treatment recommendations about the route of drug administration in children. Various authors reported similar evidence in different studies. Our study highlights the continuous implementation of rational use of antibiotics in case of UTIs. It was strongly recommend an antibiotic sensitivity test before deciding treatment plan for UTIs considering proper disease management and its prevention toward multidrug resistance . This is the only way to keep the treatment plan on track and should be carried out frequently to keep eye on resistance to antibiotics in the different clinical setups.

Conclusions

E. coli is the most common cause of UTI in the pediatric population and it was found to be most resistance to azthromycin and ceftazidime whilst being relatively sensitive to meropenem and nitrofurantoin. Similarities between our study and previous studies around the world were found when comparing the antibiotics resistance patterns. Nevertheless, it is our recommendation that

empirical antibiotic selection should be tailored to the local data collected from the region.

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