Prevalence and anti-microbial resistance of bacteria isolated from patients with urinary tract infection in north-western provenance, Libya

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Abstract

Background: Urinary tract infection (UTI) is one of the most important infections in adults and children. Escherichia coli is a common cause of urinary tract infection (UTI) affecting both male and female worldwide, however data on the incidence and antibiogram of the various strains of bacteria including E. coli isolated from UTI samples in Libyan population is scanty hence this present study. **Objectives:** To determine the prevalence and antibiogram of bacteria causing UTIs from a referral hospital in north-western provenance in Libya (Zawia teaching hospital). **Methods:** A cross-sectional study of mid-stream urine specimens collected from 2286 patients over 2 years, was conducted at Zawia teaching hospital. Each sample was cultivated on blood agar and Mac Conkey agar and incubated at 37°C for 24 hours. Bacterial isolates were identified with Gram stain, biochemical test was done using AP120 and antimicrobial susceptibility tests were done using Kirby-Bauer test (disc diffusion method). **Results:** Urine samples of the 2286 patients were included in this study of which 788 (34.5%) were children and 1498 (65.5%) were adults. Out of 788 children samples tested 123 (15.6%) were positive for bacterial growth. *E. coli* were isolated from 61% of the samples, *K. Pneumonia* in 15.4%, *S. aureus* in 12.2%, and *Enterobacter* in 10% and 1.6% showed growth of other bacteria. In adults out of 1498 samples tested 355 (23.7%) were reported positive and 1143 (76.3%) were negative for bacterial growth. In adult samples about 37.5% were positive for *E. Coli* and 14.1 % for *K. Pneumonia*, 10% *S. aureus*, and *Enterobacter* in 10%, Acientobacter in 2.5%, Pseudomonas in 1.4%, Proteus in 4.5%. Most bacterial isolates showed high sensitivity to Ciprofloxacin, Amoxicillin-clavulanic

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acid, Nalidixic acid, Cefotaxime and Ceftriaxone with resistance to Ampicillin, and Trimethoprim-sulfamethoxazole. **Conclusion:** Data shown in this study concluded that in urinary tract infection *E. coli* is an important causative agent both in children and adults. Effective infection prevention measures and physician awareness and education regarding drug resistance should be implemented to reduce the prevalence of this important disorder in adults and children.

Keywords: UTI, Antibiogram, E. coli

■ **ملخص:**

خلفية: تعد عدوى المسالك البولية (UTI) من أهم أنواع العدوى التي تصيب البالغين والأطفال. و تعتبرالإشريكية القولونية (E. Coli) سبب شائع لعدوى للمسالك البولية (UTI) التي تصيب كل من الذكور والإناث في جميع أنحاء العالم. ومع ذلك فإن البيانات حول حدوثها والمضادات الحيوية للسلالات المختلفة من البكتيريا بما في ذلك E. coli المعزولة من عينات UTI في السكان الليبيين هزيلة وبالتالي كانت هذه الدراسة الحالية. **الأهداف:** لتحديد مدى انتشار البكتريا المسببة لالتهابات المسالك البولية والمضاد الحيوي لها المستخلصة من عينات المرضي في الشمال الغربي لليبيا المحالة إلي المستشفى المركزي (مستشفى الزاوية التعليمي). **طرق البحث:** تم إجراء دراسة مقطعية لعينات من البول في منتصف التيار و التي تم جمعها من 2286 مريضًا على مدى عامين في مستشفى الزاوية التعليمي. تمت زراعة كل عينة على أجار الدم وأجار Mac Conkey وحضنت عند درجة 37 مئوية لمدة 24 ساعة. تم التعرف على العزلات البكتيرية باستخدام صبغة جرام، وتم إجراء اختبار الكيمياء الحيوية باستخدام AP120 وتم إجراء اختبارات الحساسية لمضادات الميكروبات باستخدام اختبار كيربي باوير (Kirby-Bauerبم طريقة انتشار القرص). **النتائج:** تم تضمين عينات بول من 2286 مريضًا في هذه الدراسة ، منهم 788 (a34.5٪) من الأطفال و 1498 (65.5٪) من البالغين. من بين 788 عينة أطفال تم اختبارها، كانت 123 (15.6٪) إيجابية لنمو البكتيريا. تم عزل E. coli من 61٪ من العينات ، و K. Pneumonia في 15.4٪، S. aureus في 12.2٪، و Enterobacter في 10٪ و 1.6٪ أظهرت نمو بكتيريا أخرى. في البالغين من بين 1498 عينة تم اختبارها، تم الإبلاغ عن 355 (23.7٪) إيجابية و 1143 (76.3٪) كانت سلبية لنمو البكتيريا. أظهرت عينات البالغين أن حوالي 37.5٪ كانت موجبة للإشريكية القولونية (E. coli) و 14.1٪ K. Pneumonia ، و 10٪ بكتريا S. aureus ، و 10٪ Enterobacter ، و 2.5٪ Acientobacter ، و Pseudomonas في 1.4٪ ، والبروتيوس (Proteus) في 4.5٪. أظهرت معظم العزلات البكتيرية حساسية

عالية للسيبروفلوكساسين ، وحمض الأموكسيسيلين- الكلافولانيك ، وحمض الناليديكسيك ، والسيفوتاكسيم ، والسيفترياكسون مع مقاومة الأمبيسلين ، وتريميثوبريم-سلفاميثوكسازول. **خاتمة:** خلصت البيانات الموضحة في هذه الدراسة إلى أن الإشريكية القولونية عامل مسبب مهم في عدوى المسالك البولية لدى الأطفال والبالغين. يجب تنفيذ تدابير فعالة للوقاية من العدوى وتوعية الطبيب وتثقيفه فيما يتعلق بمقاومة الأدوية للحد من انتشار هذا الاضطراب المهم عند الأطفال و الكبار. يجب تنفيذ تدابير فعالة للوقاية من العدوى وتوعية الطبيب وتثقيفه فيما يتعلق بمقاومة الأدوية للحد من انتشار هذا الاضطراب المهم لدى البالغين والأطفال

Introduction

UTI is considered one of most common health problems in clinical practice affecting both male and female patients worldwide, and are one of the most common nosocomial infections requiring empiric antibiotic selection, pending the results of urine culture and sensitivity testing (Montini et al., 2011). Although the prevalence of infection differs with age, sex, predisposing factors such as systemic illness, and structural and functional abnormality of urinary tract (Griebling, 2001), previous studies have shown that females are more prone to infection than males both in children and adults due to their short urethra and its anatomical proximity to the anal orifice (Hummers-Pradier and Kochen, 2002; McLaughlin and Carson, 2004). Young children develop urinary tract infections (UTIs) fairly often, before age 6, approximately 7% of girls and 2% of boys experience this painful condition.

In treating patients with UTI, physicians often select antibiotics empirically and may do so with little consideration of local and national antibiotic resistance patterns. Poor choice of empirical antibiotic therapy can lead to unnecessary patient suffering, increased costs, additional office or emergency department visits, and even hospital admission.

Many organisms are involved including bacteria, fungi, protozoans or viruses. Bacterial agents are the most common and invasive cause, in addition, antimicrobial resistance of bacterial pathogen are complicating treatment and recovery of infected individuals (Hummers-Pradier and Kochen, 2002; McLaughlin and Carson, 2004).

The symptoms and signs of urinary tract infection include urinary frequency, dysuria, haematuria and flank pain. However, urine analysis and culture for isolation of causative organism and antimicrobial sensitivity test are needed for confirmation of diagnosis and proper treatment of UTI because the symptoms or signs are non-specific for certain bacterial infection such as Escherichia coli which is the most common bacterial cause of UTI (Miller and Tang, 2004).

Since the natural course of UTI shows a low rate of spontaneous cure and it is considered as a frequent cause for prescribing antibiotics, the decision about which antibiotic should be prescribed has to be considered very carefully. Normally, when antibiotics for treating an acute UTI are prescribed in primary health care the nature of the causative organism and its antibiotic sensitivity can only be presumed because information regarding antibiotic resistance from the primary health care sector are very limited (Allerberger et al, 2008; Hoffmann et al., 2011). In order to reduce the risk of antibiotic resistances regularly updated data on the local microbial prevalence and antibiogram (antimicrobial resistance patterns), have to be sought and respected (Butler et al., 2006; Apfalter et al., 2010; Mittermayer et al., 2009; Schito et al., 2009; Kahlmeter et al., 2003).

In addition, it is necessary to obtain antibiogram data from the primary health care sector for community acquired infection and not only from hospitals or specialized centres because these resistances differ from that seen in the ambulatory sector (Magee et al., 1999).

Urinary tract infections in paediatric patients often remain under-diagnosed due to nonspecific signs and symptoms (Chander and Singla, 2008). The diagnosis and treatment of urinary tract infection especially in children is essential, as it could be the first presentation of underlying urological anomalies, and could lead to significant morbidity such as renal scarring, hypertension, and eventually renal failure (Cunningham et al., 2005).

Incidence, prevalence, and antibiogram of UTI differ from country to country and within the same country between different geographical areas and also in different age groups (Bachur and Harper, 2001; Twaij et al., 2000). The microbiological profile of infections has not been fully reported from this part and other parts of Libya. In addition, data on the incidence and antibiogram of the various strains of bacteria isolated from urine samples from patients suspected of having UTI in Libya is scanty. Hence, this study was undertaken to determine the microbial profile and antibiogram of UTI.

Furthermore, empirical treatment is largely employed and acquiring of antibiotics over the counter is very easy as there are no laws or policies organizing use of antibiotics in the country and due to variations and frequent changes in antibiotic sensitivity patterns frequent reports and documentation of antibiotic sensitivity is needed in order to use empirical therapy properly before the results of sensitivity test is made available to the treating medical professionals.

Lack of national or regional treatment guidelines in Libya regarding the use of antibiotics for treatment of different infectious diseases including empirical treatment; necessitate extensive and urgent studies to explore this

important area of medicine. Therefore, the goal of this study was to determine the prevalence of bacteria causing UTIs and to investigate the antibiotic susceptibility to commonly used agents for urinary tract infections in urine samples obtained from a referral hospital in Libya.

Subjects and Methods

This retrospective analysis of bacterial pathogens and their antimicrobial sensitivity was undertaken on urine samples collected from patient referred to Zawia teaching hospital over a period of 2 years. Analysis of urine culture results was performed at the department of microbiology, and 2286 urine samples collected from children and adults were involved in the study.

The sex and age of patients, the organism isolated and the antimicrobial susceptibility profiles were collected from the registration records using a standard data collection form. The data were entered into Excel for analysis.

Midstream urine samples were collected unless otherwise mentioned and supra-pubic aspiration or from catheterized patients. Samples were processed immediately in the following manner: wet mount microscopy was performed to detect pyuria, bacteriuria, hematuria, or candiduria then urine samples were inoculated on blood agar and MacConkey agar and incubated overnight at 37°C. Significant growth was determined as $\geq 10^5$ colony forming units (CFU)/ml of midstream urine, $\geq 10^2$ CFU/ml of a catheter specimen and any number of colonies from a supra-pubic sample (Forbes et al., 2002). Bacterial isolates were identified with Gram stain and standard biochemical tests (using AP120), as described by Mackie and McCartney (Colles et al., 1996). Antibiotic susceptibility testing was done by disc diffusion method using commercially available antibiotic discs.

All isolates were tested against nalidixic acid, trimethoprim-sulfamethoxazole, ciprofloxacin, Amoxicillin-clavulanic acid, cefotaxime, Ceftriaxone and Ampicillin, that was the most commonly used antibiotics in the region.

Results

A total of 2286 urine samples were included in this study, samples were collected from patient referred to Zawia Teaching Hospital, suspected of having urinary tract infection (UTI) and seen at in-patients or out-patients clinics over 6 months period. Children from 1 to 18 years old accounted for 788 (34.5%) samples and 1498 (65.5%) samples were adults aging between 19 and 90 years (Table 1).

Some patients were admitted to hospital either due to severity of symptoms or for further investigation. Out of paediatric samples studied 274 (34.8%) were from inpatients and 514 (65.2%) were from outpatients (Table 1). Three

hundred forty four (44%) urine samples were from male and 444 (56%) were from female patients with male to females ratio of 1: 1.3; data shown indicated that urinary symptoms were more frequent in female children than male children as a cause of seeking medical advice (Tables 1).

Regarding adult patients, 265 (17.7%) were taken from inpatients and 1233 (82.3%) were from outpatients and symptoms of UTI were more frequent in adult female patients than adult male patients as a cause of seeking medical advice; 420 (28%) urine samples were from male and 1078 (72%) were from female patients with male to females ratio of 1: 2.5 (Table 1).

Table 1: Number of patients seen with suspicion of having urinary tract infection

	Children			**Adults**		
Clinic	Males	Females	total	Males	Females	total
Inpatients	144	130	274	98	167	265
Outpatients	200	314	514	322	911	1233
Total	344	444	788	420	1078	1498

UTI symptoms requiring medical advice in children were more frequently seen in the age group 11-18 years old and the number of males and females are about equal, however, the differences were more obvious at younger age groups with female children more frequently affected (Figure 1).

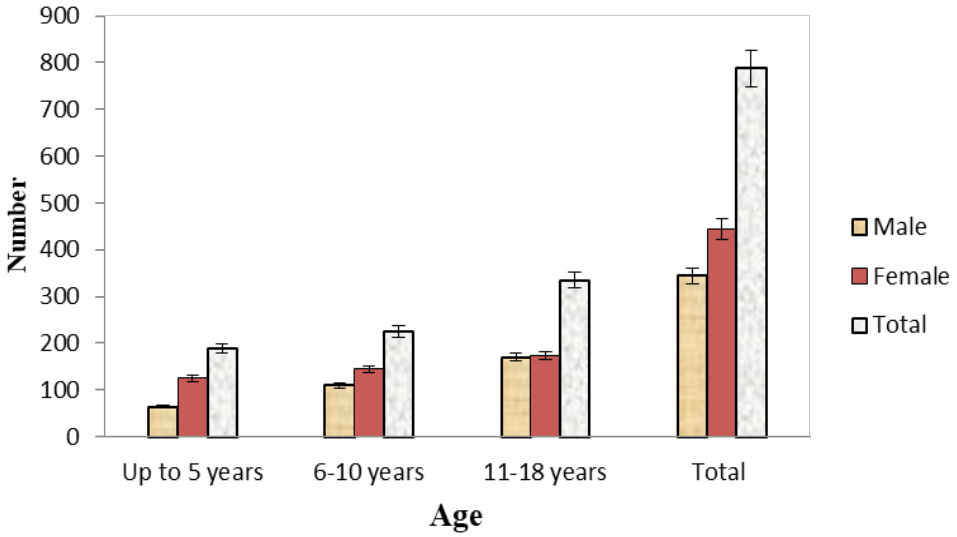

Figure 1: Age and sex Distribution of paediatric patients

Similarly to data obtained from children cases, this work showed that in older age groups UTI symptoms requiring referral to hospital for specialist opinion and management were more frequent in females than males. In adults female patients 478 were from age group 19 to 35 years old, 353 from 36 to 50 years age group and 247 from 51 to 90 years age group. Whoever, in male patients 183 was from age group 19 to 35 years, 133 from 36 to 50 years age group and 104 from 51 to 90 years age group (Figure 2).

Figure 2: Age and sex Distribution of adult patients

Data collected from results of urine cultures showed that, out of 788 paediatric samples tested, 123 (15.6%) were positive for bacterial growth and 665 (84.4%) showed negative results (Figure 3). In adults 355 samples (23.7%) were positive for bacterial growth and 1143 (76.3%) of the samples tested were negative (Figure 3).

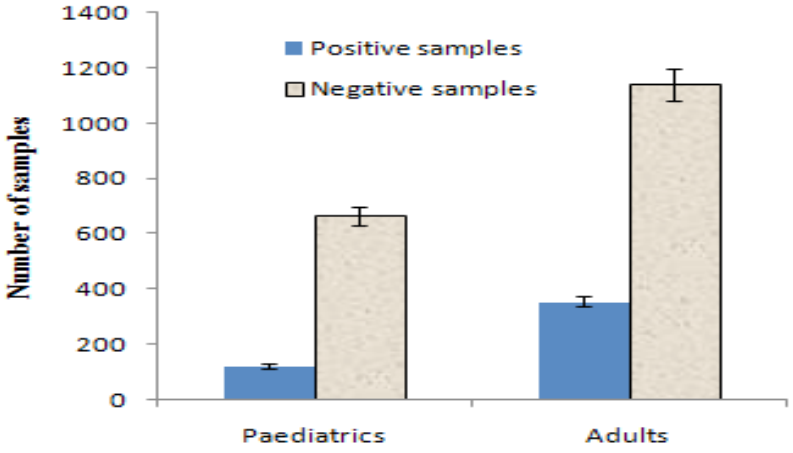

Figure 3: Number of positive and negative urine cultures

In children more positive results were seen in samples from female patients accounting for 59.3%, with 40.7% of positive samples were collected from male children. Number of positive samples was increased by increasing the age of the child, as seen in table 2, both in male and female patients with highest numbers recorded at the age group of 11 to 18 years.

Table 2: Number of positive and negative samples according to age and sex of paediatric patients

Age (in years)	Male		Female	
	Positive	Negative	Positive	Negative
Up to 5 years	4	60	13	112
6-10 years	16	94	20	125
11-18 years	30	140	40	134
Total	50 (6%)	294 (37%)	73 (9%)	47%))371

Similar to the results shown in table 2, there was more positive results seen in samples from adult female patients accounting for 71.8% of the total adult positive samples. Adult male patients account for 28.2% of the total adult positive samples. Positive samples were highest at age group 19-35 years both in male and female patients (Table 3).

Table 3: Number of positive and negative samples according to age and sex of adult patients

Age (in years)	Male		Female	
	Positive	Negative	Positive	Negative
19-35	43	140	130	363
36-50	30	103	103	268
51-90	27	77	77	192
Total	100 (28.2%)	320	255 (71.8%)	823

In children, result of the returned positive cultures showed growth of both Gram positive and Gram negative bacterial. The most prominent bacteria isolated from the samples studied were *E. coli,* accounting for 61% of the total isolates, followed by *K. pneumonia* (15.4%), *S.aureus* (12.2%), and *Enterobacter* (10%) and 1.6% of the samples showed growth of other bacteria (Table 4). Detecting more than two types of bacteria in the sample were considered as non-specific growth.

Table 4: Bacterial strains isolated from urine samples in children

Bacteria	Number	Percentage
E. coli	75	61%
K. pneumonia	19	15.4%
S.aureus	15	12.2%
Enterobacter	12	10%
Other bacteria	2	1.6%

In adults, result of the returned positive cultures showed growth of both Gram positive and Gram negative bacterial (Table 5). The most prominent bacteria isolated from the samples studied were *E. coli,* accounting for 37.5% of the total isolates, followed by *K. pneumonia* (14.1%), *S.aureus* (10%), and *Enterobacter* (10%). Detecting more than two types of bacteria in the sample were considered as non-specific growth.

Table 5: Bacterial strains isolated from urine samples from male and female adult patients

Bacteria	Male	Female	Total	Percentage
E. coli	25	108	133	37.5%
K. pneumonia	17	33	50	14.1%
S.aureus	10	25	35	10%
Enterobacter	12	23	35	10%
Pseudomonas	2	3	5	1.4%
Aciento bacter	6	3	9	2.5%
Serratia	1	1	2	0.6%
Proteus	7	9	16	4.5%
Streptococcus	2	3	5	1.4%

The overall susceptibility profiles of bacterial isolates are shown in Table 6. Antibiogram using disc diffusion test for antimicrobial susceptibility applied in the current work showed high sensitivity to Ciprofloxacin, Amoxicillin-clavulanic acid, Nalidixic acid, Cefotaxime and Ceftriaxone with resistance to ampicillin, and Trimethoprim-sulfamethoxazole in most bacterial isolates.

However, *E coli* that accounts for the majority of UTI cases showed

sensitivity to Ciprofloxacin, Nalidixic acid, Cefotaxime and Ceftriaxone and it was found to be resistant to Amoxicillin-clavulanic acid, Ampicillin and Trimethoprim-sulfamethoxazole.

This study reports higher rates of antibiotic resistance among S. Aureus isolates as well. S. Aureus bacteria tested were resistant to Nalidixic acid, Ceftriaxone, Ampicillin and Trimethoprim-sulfamethoxazole and sensitive to Ciprofloxacin, Amoxicillin-clavulanic acid, and Cefotaxime only (Tables 6). Multiple drug resistant was found, all bacterial isolates manifested resistance to two or more antibiotics.

Table 6: Antibiotic sensitivity pattern of most commonly isolated bacterial strains from urine samples

Bacteria	*E. coli*	*K. pneumonia*	*S.aureus*	*Enterobacter*
Ciprofloxacin	S	S	S	S
Amoxicillin-clavulanic acid	R	S	S	S
Nalidixic acid	S	S	R	S
Cefotaxime	S	S	S	S
Ceftriaxone	S	S	R	R
Ampicillin	R	R	R	R
Trimethoprim-sulfamethoxazole	R	R	R	R

Discussion

Urinary tract infections (UTI) are common medical problem encountered in medical practice worldwide.

Many studies should that there are variation in sex distribution of cases in different geographical regions and the occurrence of UTI is more common in girls as compared to boys, but the frequency is more in boys before the age of one (Elder, 2004; Hernández-Porras, 2004; Taneja et al., 2010; Rekha et al., 2010). Females are more prone to infection than males due to their short urethra and its anatomical proximity to the anal orifice which provides

easy access of bacteria to the bladder (Hansson, 1999, Hummers-Pradier and Kochen, 2002; McLaughlin and Carson, 2004).

Pathogens responsible for UTI largely originate from colonic flora such as E. Coli (Yamamoto et al., 1997; De Backer, 2008), and management of community-acquired urinary tract infections usually starts with empirical antibiotic treatment (Hummers-Pradier and Kochen, 2002; Miller and Tang, 2004; De Backer, 2008). It is acceptable that empirical treatment is a convenient strategy for effective management of UTI if antibiotic susceptibility patterns are regularly updated, and this is especially important in developing countries due to resource constraints which mean that it is often impractical to routinely perform antibiotic sensitivity tests (WHO, 2009). However, reports of uro-pathogens resistant to previously effective antibiotics have emerged globally in recent years (Okeke et al., 2005) and empirical treatment limits opportunities for surveillance of antibiotic resistance among pathogens that cause community-acquired UTI.

Variations in antibiotic resistance patterns commonly occur across different geographical regions, even within the same country (Gupta, 2003; Schito et al., 2009) and such variations must be evaluated regularly in order to inform healthcare providers responsible for treating patients with UTI and who may prescribe empirical treatment to maintain rational antibiotic use and reduce chance of development of antibiotic resistance. Therefore, the best tool for rational prescribing is a local antibiogram, which identifies local outpatient uropathogen prevalence and antibiotic resistance patterns, and can help improve choice of empiric therapy.

This study showed that 15.6% of children and 23.7% of adults with suspected UTI had significant bacteriuria. Both Gram negative and Gram positive bacteria were isolated from positive urine samples included in the study. In children the most prevalent gram negative organism was *Escherichia coli* accounting for 61% of all grown bacteria; a percentage very similar to the results found in other studies (Kahlmeter, 2003; Schito et al., 2009) and *Staphylococcus aureus* was the most prevalent gram positive organism (15.4%).

In addition, data from this study reported high rates of antibiotic resistance in urinary isolates and gave evidence for continuing evolution of resistance to antimicrobial agents. All bacterial isolates examined in the current work were resistant to Ampicillin and Trimethoprim-sulphamethoxazole, in addition, both *S.aureus* and *Enterobacter* were also resistant to Ceftriaxone but none of the isolates were resistant to Ciprofloxacin and Cefotaxime. Multiple drug resistance, where bacteria was found to be resistant to two or more of the antibiotics tested, was seen in all bacterial isolates of the current study. It is worth noting that guidelines suggest that when resistance rates exceed 20%, clinicians should not use the antibiotic.

Concerning the resistance patterns of *E. Coli,* current study data showed resistance to ampicillin, trimethoprim/sulphametoxazole and amoxicillin/ clavulanic acid. The resistant of *E. coli*, which is the most encountered bacterial isolate in urine samples of this study, to amoxillin/clavulanic acid undermines its effectiveness as an empiric agent and is alarming and necessitates revising primary health care providers about prescribing behaviour and the need for national recommendation and guidelines for antibiotic prescribing.

Until now most of Libyan hospitals do not publish complete antibiogram using hospital-based laboratory data. In addition, there are no antibiotic resistance patterns for ambulatory patients or community-based patients. When these are available, it is very important that prescribers and pharmacists make use of them; otherwise, antibiotic susceptibility results from bacteria isolated in prior urine cultures should always supersede an antibiogram when selecting empiric UTI therapy.

Conclusion

The resistance data for *E. coli* in uncomplicated UTIs in both children and adults gained by this study to amoxicillin/clavulanic acid, ciprofloxacin and nalidixic acid should be respected when choosing an appropriate antibiotic for uncomplicated UTIs.

The use of ampicillin and trimethoprim/sulphametoxazole in uncomplicated UTIs should be questioned and the findings of this study should result in a regular surveillance system of resistances emerging in the ambulatory sector.

In addition, to obtain comprehensive resistance data for uncomplicated UTIs that have to be used as basis for national or local guidelines, antibiogram studies have to be performed on a regular base.

In conclusion, data collected in this study concluded that *E. coli* is an important causative agent of urinary tract infection in both children and adults. Furthermore, the best tool in order to avoid or minimise the rate of antimicrobial resistance is developing and periodically updating a local antibiogram, which identifies local outpatient uropathogen prevalence and antibiotic resistance patterns, and can help improve choice of empiric therapy.

The antibiogram pooled from this study is useful for hospitals without sufficient laboratory resources to generate institutional urinary antibiograms. In addition, effective infection prevention measures and physician awareness and education regarding drug resistant should be implemented to reduce the prevalence of this important disorder especially in children.

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