Community-Acquired Urinary Tract Infections in a Rural Area: Predominant Uropathogens, and their Antimicrobial Resistance

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Abstract

Introduction: Urinary tract infections (UTIs) are among the most common bacterial infections and frequently recurring problems encountered by clinicians in community practice. The approach to these infections remains a difficult and sometimes controversial issue, especially in asymptomatic and symptomatic bacteruria. The objectives of this study were to determine the incidence of community acquired UTI in a rural area, the clinical characteristics, risk factors, the uropathogens and their antimicrobial susceptibilities to commonly used antimicrobials.

Methods: Urine cultures and urine analysis were performed on 250 urine specimens collected from patients diagnosed as having a urinary tract infection upon admission. Quantitative bacteriologic cultures, identification of isolates, and antimicrobial susceptibility tests were performed by standard methods.

Results: Escherichia coli was the predominant uropathogen (46.4%) isolated from acute uncomplicated infections (46.4%), followed by Candida spp. (14.9%) Klebsiella spp, Proteus spp., and Pseudomonas spp. Staphylococcus saprophyticus accounted for (7.8%) of the female cases and was associated with uncomplicated UTIs. The lowest incidence of UTIs (10%) was seen among the 13-20 year old age group. Complains of frequent infections of the lower urinary tract accounted for 40.5% of the cases. Resistance of the isolates to used antimicrobials were consistent with those reported in the literature.

Conclusions: The incidence of UTIs is high and was influenced by the patient’s age, sex, and previous antibiotics use. The high frequency of single and multiple antimicrobial resistance of the pathogens to the prescribed antibiotics in this rural community demonstrated decreased usefulness of common antibiotics and emphasizes the need for frequent re-evaluation of the prevalence of uropathogens in such areas and the adjustment of the empirical first-line treatment accordingly.

Introduction

Urinary tract infections (UTIs) are the most common hospital-acquired infection. However, in the community, they are exceeded by respiratory tract and gastrointestinal infections. Upper and lower UTIs are frequently recurring problems encountered by clinicians in a community practice [1, 2].

In community-acquired UTIs, women are significantly more likely to experience these infections during their lifetime than men [3, 4]. Recurrent infection is a common problem and can affect women of all ages, particularly the elderly and pregnant women [5]. The diagnosis of these infections is made based on the symptoms and bacteriuria of more than 105 colony forming units (CFUs) per milliliter of the same organism [6,11].

Host and bacterial virulence factors are important in the pathogenesis of recurrent infections. The etiology of these infections is affected by underlying host factors that complicate the infection, such as age, diabetes, spinal cord injury, or catheterization [7]. Other host factors predisposing to recurrent infections are genetic factors, ageing, the menopause, urogenital dysfunction, sexual behavior, and previous pelvic surgery [5].

Members of the Enterobacteriaceae are the most common organisms isolated from uncomplicated UTI [8]. While, Candida is an increasing nosocomial problem, however, isolation of yeast from urine does not necessarily always indicate infection [9].

The goals of the management of UTIs are to prevent the progressive renal disease by prompt eradication of the bacterial pathogen, identification of abnormalities of the urinary tract, prevent recurrent infections, and resolution of the acute symptoms of the infection [8]. Delay in initiation of the antibacterial therapy is associated with increased risk of renal scarring, which may lead to hypertension and end stage renal disease. The initial choice of antibacterial therapy is based on the knowledge of the predominant pathogens in the patient's age group, antibacterial susceptibility patterns in the practice area, and the clinical status of the patient. Nevertheless, it is difficult to accurately assess the incidence of UTIs, because they are not

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reportable diseases in several countries [3] including Jordan. This situation is further complicated by the fact that accurate diagnosis depends on both the presence of symptoms and a positive urine culture, although in most outpatient settings this diagnosis is made without the benefit of culture. [3].

A previous article suggested utilizing the "enhanced" urinalysis, not as a replacement to culture but as a potential sensitive predictor to allow therapy to be given while awaiting culture results [10]. Initial antimicrobial therapy for UTIs is generally empiric, therefore, it is important to account for local susceptibility trends when selecting an antimicrobial agent [11].

The objectives of this study were to determine the incidence of UTI, the clinical characteristics, risk factors, and causative organisms in a rural area in the north east of Jordan. The susceptibility of urinary pathogens to common antimicrobials was investigated.

Methods

A midstream urine sample of the early urine was collected in a sterile container from 250 patients diagnosed as having a UTI upon admission. Symptoms reported by patients were dysuria (burning pain on passing urine), urgency, frequency, some patients had fever and low back pain. These patients were seen by physicians in several governmental health centers in the Badia, a rural area in the north east of Jordan during two-year period. Information concerning demographic characteristics of the patients, their underlying diseases and the previous use of antibiotics were recorded.

Urine cultures and urine analysis were performed on the urine specimens within 1-4 hours of collection; they were kept in the refrigerator at 4oC until processed. Colony forming units (CFU) per milliliter were counted. UTI was defined as >105 CFU per milliliter except for Candida species where CFU number of yeasts were considered if >10 4 per milliliter and bacteria are present in low numbers or are absent. Specimens were examined macroscopically for cloudy appearance or blood strained. A drop of urine was examined microscopically for the presence and number of white blood cells, and counts of 10 cells/ milliliter urine was considered significant. Presence of red blood cells, epithelial cells, bacteria and crystals were also recorded.

Urine specimens were cultured on MacConkey agar, blood agar, and Sabouraud dextrose agar, and plates were incubated for 24 hours at 37oC. Counts of >105 CFU/ milliliter of urine were considered significant. [12] Antimicrobial susceptibilities of the isolates were assayed with the disk diffusion method [12]. The pathogens were tested for their susceptibility to antimicrobials used in the treatment of UTIs. The antimicrobials tested included ampicillin, carbenicillin, cefuroxime, chloramphenicol, ciprofloxacin, cotrimoxazole, nalidixic acid, nitrofurantoin, and tetracycline.

Statistical analysis: A multivariate analyses were performed to test for the risk factors for developing a community-acquired UTI.

Results

Of the 250 urine specimens tested, 168 (67.24%) were culture positive for counts of >105 organisms per milliliter. All infections were due to a single species. Mean age of the patients was 43 (2 - 84 years). Females were 102 (63%), of whom 58 (56.9%) were ≥ 35 years old. The lowest incidence of infection (10%) was seen among the age group 13-20 year old, and 12 years old patients (20%).

The cases were categorized mild, or severe depending on the symptoms. Mild symptoms were reported by the elderly male patients. Uncomfortable pressure above the pubic bone, were experienced by women. Irritative voiding symptoms, and slight fever were reported in cases with urinary structural abnormalities.

The most common pathogen isolated mainly from uncomplicated cases was Escherichia coli 78 (46.4%), with 70% in the female patients. The other pathogens are listed in Table 1.

The two gram-positive isolated species were Staphylococcus saprophyticus 8 (4.8%), and Enterococcus faecalis 4 (2.4%). Staphylococcus saprophyticus isolates were from young, healthy women, but, it was not associated with complicated infections. While, Enterococcus and Pseudomonas spp. were isolated from complicated UTIs.

Three (1.8%) cases of non-typhoidal Salmonella (NTS) bacteriuria were identified and was the sole pathogen isolated in these patients. Patients had symptoms of an acute UTI, which did not differ clinically from infections caused by other members of the Enterobacteriaceae. Salmonella was isolated from stools of two of these patients who presented with concomitant gastroenteritis and experienced episodes of diarrhea during the weeks before the UTIs.

Stenotrophomonas (Xanthomonas) maltophilia was isolated from 2 (1.2%) of the patients and the clinical course of infection was severe. Both patients had fever; one had bacteremia and urinary structural

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abnormalities.

In cases of Candida spp., the number of CFU was higher than 104/milliliter and bacteria were present in very low numbers or were absent. It was identified by conventional methods (germ tube test). The presence of pyuria was observed in some cases, but no antifungal therapy was administered. C. albicans was isolated in 15/25 (60%) of Candida cases mainly in children with urogenital abnormalities or elderly patients with diabetes. The major predisposing factor associated with candiduria was previous antibiotic therapy 16 (64%).

Patients with frequent infections (more than three episodes per year) of the lower urinary tract accounted for 68 (40.5%) of the cases. Thirty-two (47%) of these may be considered relapses, since they were caused by the same species of organism. E. coli caused 22 (68.8%) of the relapses, other causative agents included Candida spp., Klebsiella spp., Pseudomonas spp., and Proteus spp. In thirty-six of the 68 (53%) patients, infections occurred at least one month after the index episode and were regarded as recurrent infections since they were caused by different organism. Men and women with frequent UTIs were 70%, and 30% respectively.

Antibiotic resistance: The highest and lowest mean resistance among gram-negative bacteria to common antibiotics were 72.6% to ampicillin and 25% to chloramphenicol. The most resistant pathogens were found to be E. coli and Proteus species (Table 2) shows the proportion of the isolates and E. coli resistance to antibiotics used.

Cotrimoxazole and nalidixic acid showed increased resistance in patients with complicated cases.

Six out of eight (75%) Staphylococcus isolates were as well resistant to ampicillin.

Resistance to more than one and up to four antibiotics was observed in 76 (45.2%) of the uropathogens isolated. Two of the NTS isolates were resistant to three antibiotics

Significant risk factors for developing a community-acquired UTI as determined by multivariate analyses were antibiotic exposure (OR = 2.68, P = 0.005); female gender (OR = 3.87, P = 0.03); age (OR= 3.90 P = 0.03) and pregnancy (OR = 1.91, P = 0.046).

Discussion

Members of the Enterobacteriaceae are the most common organisms isolated from uncomplicated UTIs. Results of this study showed that E. coli (46.4%) is the most common pathogen isolated and was resistant to more than one antibiotic. Considerable evidence supports the concept that the initial event leading to community acquired UTI is intestinal colonization with a uropathogenic strain of E. coli. Once colonization has occurred, the strain may remain part of the colonic flora for months, whether or not it causes a UTI. Its persistence in the colonic flora is facilitated by the same bacterial adhesins that promote attachment to the uroepithelium [13]. The association of highly urovirulent strains of E. coli with antimicrobial resistance may thus arise because prolonged enteric colonization facilitates the acquisition of antimicrobial-resistance genes, which in turn further prolong colonization. Exactly how enteric colonization occurs initially and how uropathogenic E. coli strains are transmitted among members of the community are not clear [4].

The majority (68.8%) of the relapses in the current study were caused by E. coli. These results are in agreement with a previous study, which reported that 73% of the relapses were due to E. coli in women with community acquired UTI [14].

The isolation of Candida spp. from 25 (14.9%) cases was surprising since these species are known to be mainly associated with nosocomial infections after instrumentation of the urinary tract, critically ill patients, diabetic patients or in children with urogenital abnormalities [8,15-19]. The etiological role of Candida species in the pathogenesis of UTIs can be hypothesized if the CFU number of yeasts is higher than 10 4/milliliter and bacteria are present in low numbers or are absent [17]. The patients who had candiduria in the current study were children with urogenital abnormalities or elderly patients with diabetes. The major predisposing factor associated with candiduria in these patients (64%) was previous antibiotic therapy.

Staphylococcus saprophyticus accounted for 4.8% of the total infections and 7.8% of the female cases, but was not associated with complicated infections. These results are consistent with previous studies that reported 10% to 15% infection rates in acute uncomplicated community acquired infections [7, 11].

NTS was the sole pathogen isolated from three patients who had symptoms of acute UTI. Recurrence of bacteriuria occurred in one patient, two patients presented with concomitant gastroenteritis and Salmonella was isolated from their stools. These two isolates were resistant to three common antibiotics. While some urinary isolates of NTS may be fecal contaminants, the three isolates recovered from urine during this study were considered to be the cause of symptomatic UTI. Similar results were reported in a study, which reviewed cultures performed at the Mayo

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Clinic (Minn.) [20]. None of the three patients had urologic abnormalities or was undergoing immunosuppressive therapy, which was suggested as a cause of cases of urinary salmonellosis [21, 22].

Serratia marcescens, long considered a non pathogen, is now found to be responsible for outbreaks of nosocomial infections and more frequently isolated from children with urogenital abnormalities and/or undergoing invasive instrumental investigations. It was isolated from three patients who previously had antibiotic therapy. The three most important reported conditions that preceded isolation of Serratia were the use of indwelling urethral catheters, antibiotic therapy and operation. An epidemiological survey showed that the organism is present in the environment, even in the absence of active infection [23].

Stenotrophomonas (Xanthomonas) maltophilia has emerged as a causative agent of serious nosocomial infections. However, well-documented cases of UTI with this organism have rarely been reported. Stenotrophomonas maltophilia UTI is usually associated with a severe clinical course. It was isolated from two patients in the current study that experienced severe symptoms; one was a child who was diagnosed to have urogenital abnormalities. Risk factors for urinary colonization by this organism include hospitalization, urinary catheterization, and administration of inactive antibiotics [24].

The primary risk factor associated with isolation of S. maltophilia in a case control study was antibiotic use (e. g. ampicillin, cefotaxime) and suggested that judicious use of antibiotics may prevent some cases of S. maltophilia infection [25].

The role of Plesiomonas shigelloides, which was isolated as the sole bacteria in two patients could not be substantiated. The isolation of Stenotrophomonas maltophilia and Plesiomonas shigelloides may result through the uncontrolled use of antibiotics in rural areas, improper usage of doses and duration, as well as usage of inactive antibiotics [24].

The significant lower infection rate observed in males in the study area might be partially attributed to circumcision, a cultural and religious practice in all male infants in Jordan. The question of circumcision is an area of long-term interest in the study of UTIs. Data published suggests that uncircumcised males have a higher incidence of urinary tract infection; however, this continues to be a point of controversy [10]. Although, data surrounding medical benefits and risks of this surgery are inconsistent, substantial data exist to support the conclusions that uncircumcised males have greater incidences of UTIs, especially in the first six months of life when complications are greatest [26].

Overall susceptibility testing showed decreased usefulness of common antimicrobials and demonstrated a need for reevaluating their use in the therapy for these infections [27]. The highest resistance rate (73%) among the gram-negative bacteria to common antimicrobials was to ampicillin and the lowest (25%) was to chloramphenicol. The most resistant uropathogens were E. coli and Proteus species, which were also reported by another study [27]. Increasing antimicrobial resistance of uropathogens has led to reconsideration of traditional treatment recommendations in many areas [28]. Amoxicillin, trimethoprim-sulfamethoxazole and cephalosporin were reported to be the first line antimicrobials to treat children with uncomplicated UTI [29].

The low resistance (10.8%) of the E. coli to ciprofloxacin isolated in our study was comparable to that reported by another study (11.9%) [30]. A multicenter study on community-acquired UTIs in India reported a (34.3%) resistance to nitrofurantoin [31], which is lower than our findings (51%) but, higher resistance to ciprofloxacin (64.2%) than our study (51%).

These differences could be related to antibiotic usage, and a statistically significant association between nitrofurantoin use and microbial resistance was reported [33].

The relationship between antibiotic use and resistance is complex. The use of broad-spectrum antibiotic agents as a substitute for precise diagnostics or to enhance the likelihood of therapeutic success increases the rate of selection of resistant bacteria [33]. Factors influencing antibiotic consumption include cultural conceptions, patient demands, diagnostic uncertainty, and the level of training among health staff and pharmacists.

High levels of antimicrobial resistance in urinary and faecal pathogens were also reported with similar rates of resistance occurring to antibiotics commonly used in both out-patients and in-patients (a reflection of high community use of antibiotics) [34].

Routine monitoring of antibiotic resistance provides data for antibiotic therapy and resistance control [35], and information will directly affect selection of empiric therapy for UTI [7]. However, the initial choice of empiric antimicrobial therapy should be based on Gram stain and urine culture and should integrate local sensitivity patterns of the infecting organism [19].

Conclusion(s)

The high frequency of single and multiple antimicrobial resistance of the uropathogens to the prescribed

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antibiotics in this rural community emphasizes the need for frequent re-evaluation of the prevalence of uropathogens involved in such areas and the adjustment of the empirical first-line treatment accordingly. The absence of antibiotic prescribing policies and inadequate information on patterns of bacterial resistance, may all contribute to the emergence of resistant strains. Therefore, medical practices aimed at avoiding over prescription of antimicrobial agents should be implemented. In addition, strict adherence to hygiene practices is necessary to prevent the spread of resistant organisms.

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Authors Contribution(s)

Prof. Laila Nimri: experimental design, excustion of experiments, data analysis, writing the manuscript.
Dr. Raymond Batchoun: excustion of experiments, writing the manuscript

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Illustrations

Illustration 1

Table 1. Distribution of pathogens isolated from 168 Badia patients with symptoms of urinary tract infections.

Organism isolated	Number (%)
Escherichia coli	78 (46.4)
Candida spp.	25 (14.9)
Klebsiella spp.	15 (8.9)
Proteus spp.	12 (7.0)
Pseudomonas spp.	10 (6.0)
Staphylococcus saprophyticus	8 (4.8)
Enterococcus faecalis	4 (2.4)
Enterobacter spp.	4 (2.4)
Serratia marcescens	3 (1.8).
non-typhoidal *Salmonella*	3 (1.8)
Stenotrophomonas maltophilia	2 (1.2)
Citrobacter spp.	2 (1.2)

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Illustration 2

Table 2. The proportion of the isolates and E. coli resistance to the antibiotics used.

Antibiotic	Overall Resistance (n = 168) % resistant	*E. coli* isolates (n = 78) % resistant
Ampicillin	73	73
Carbinicillin	51	36
Cefuroxime	28	20
Chloramphenicol	25	25
Ciprofloxacin	51	10.8
Cotrimoxazole	54	46.8
Nalidixic acid	51	38.5
Nitrofurantoin	50	10
Tetracycline	51	30.7
Multidrug resistant	45	42

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