Relationship between demographic characteristics and community-acquired urinary tract infection

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العلاقة بين الخصائص الديموغرافية وبين التهابات المسالك البولية المكتسبة من المجتمع

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الخلاصة: لدراسة تأثير كل من العمر والجنس والحالة الزواجية على العوامل الممرضة المسببة لالتهابات المسالك البولية المكتسبة من المجتمع، ومقاومة تلك العوامل الممرضة لمضادات المكروبات، فقد تم جمع عينات من 270 مريضا من مراجعي العيادات الخارجية وتحليلها وزرع 121 منها، وتعيين الجراثيم الممرضة وتحسسها لـ 14 من مضادات المكروبات. ثم دراسة علاقة النتائج مع العمر والجنس والحالة الزواجية للمرضى. وتخلص الدراسة إلى فهم تأثير العوامل المختلفة على التهابات المسالك البولية المكتسبة من المجتمع ومقاومتها لمضادات المكروبات مما يساعد على التدبير العلاجي الملائم لها.

ABSTRACT To investigate the effect of age, sex and marital status on the etiology of community-acquired urinary tract infection and the antimicrobial resistance of uropathogens, urine specimens collected from 270 outpatients were analysed and 121 significant monomicrobial cultures obtained. The microorganisms were identified and their susceptibility to 14 selected antimicrobial agents was determined. These results were then related to the age, sex and marital status of the patients. This study concludes that understanding the effect of the different factors on community-acquired urinary tract infections and their antimicrobial resistance will aid the proper management of this disease.

Relation entre les caractéristiques démographiques et les infections urinaires communautaires

RESUME Afin d'examiner l'effet de l'âge, du sexe et du statut marital sur l'étiologie des infections urinaires communautaires et la résistance des pathogènes urinaires aux antimicrobiens, des échantillons d'urine recueillis chez 270 patients des consultations externes ont été analysés et 121 cultures monomicrobiennes significatives ont été obtenues. Les micro-organismes ont été identifiés et leur sensibilité à 14 agents antimicrobiens sélectionnés a été déterminée. Ces résultats ont ensuite été associés à l'âge, au sexe et au statut marital des patients. La présente étude conclut que la compréhension de l'effet des différents facteurs sur les infections urinaires communautaires et leur résistance aux antimicrobiens permettra une prise en charge correcte de cette maladie.

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Introduction

Urinary tract infections (UTI) are any type of urothelial inflammatory response resulting from bacterial invasion of the urinary tract [1]. UTIs are considered community acquired if the specimens are collected from outpatients or within 48 hours of hospital admission [2].

Worldwide, an estimated 150 million people are diagnosed with UTI each year, with a cost to the global economy of more than 6 billion US dollars [1]. Complicating these staggering figures is the emerging pattern of antimicrobial drug-resistant UTI [3,4]. Antimicrobial resistant UTIs have continued to increase at an alarming rate over the past 15 years [1].

The majority of community-acquired UTIs can be attributed to microbial species that are members of the intestinal microflora, the most common of which are *Escherichia coli*, *Klebsiella* species, *Enterococcus* species and *Proteus mirabilis* [5]. Several host factors, such as sex, age, sexual activity, urine biochemistry and pregnancy are implicated in the etiology of community acquired UTIs [6].

This study was carried out to elucidate the effect of the age, sex and marital status of adult patients on the etiology of community-acquired UTI and the antimicrobial resistance of the isolated uropathogens.

Methods

This study was carried out at Khan Younis Hospital Laboratory, Gaza Strip, Palestine during the period January to July 2000. A single, clean, voided midstream urine sample was collected from each of 270 adult outpatients with suspected UTI (178 female and 92 male) with a mean age of 33.5 years (range 18–65 years). Samples were stored at 2–4 °C until being processed on the same day. UTI was defined as the culture of a single microorganism at a concentration of ≥ 10^5 CFU/mL [7].

The study was fully explained to all the participants, and their informed consent was obtained. Each specimen was inoculated onto both blood agar (with 5% defibrinated sheep blood) and MacConkey agar plates using a 0.001 mL standard loop (for semi-quantitative counts) and incubated aerobically at 37 °C for 24–48 hours. The number of colonies was then counted. A direct smear for Gram staining was prepared from the centrifuged sediment of each specimen. Significant growth was identified biochemically and serologically in a systematic way according to standard methods [7,8]. Antimicrobial agent susceptibility was assessed according to the Kirby–Bauer method [9] using the following antimicrobial drugs: amoxycillin, trimethoprim–sulfamethoxazole, nalidixic acid, norfloxacin, ofloxacin, ciprofloxacin, doxycycline, cephalexin, cefuroxime, ceftazidime, nitrofurantoin, amikacin, gentamicin and amoxycillin–clavulanate (Augmentin). The isolated microorganisms and their antimicrobial resistance patterns were analysed with respect to age, sex and marital status of the patients. Only a single positive culture per patient was included in the study.

Statistical analysis was performed using the chi-squared test and Fisher exact test, with a significance cut-off value of $P < 0.05$.

Results

A total of 270 urine specimens were subjected to bacteriological analysis; of these 121 showed positive monomicrobial cultures. The overall sex distribution of the participants was 34.1% (92) males and

Table 1 **Distribution of the 121 positive cultures by marital status and sex of the patients**

Marital status	Males No.	Males %	Females No.	Females %
Single	9	7.4	24	19.8
Married	21	17.4	66	54.5
Others	0	0.0	1	0.8
Total	30	24.8	91	75.2

χ^2 = 0.46, P = 0.79.

65.9% (178) females and the sex distribution for the 121 positive cultures was 24.8% (30) males and 75.2% (91) females. The difference in distribution by sex and culture results was not statistically significant. The majority of participants were in the age-group 18–41 years (73%) and positive cultures were found mainly in this age group. The proportion of females with positive cultures was higher in all age groups except for 50–57 years. Table 1 illustrates the distribution of positive cultures according to the marital status and sex of the patients.

Gram-negative aerobic and facultative anaerobic rods accounted for 90.9% of the positive cultures, while Gram-positive cocci represented the remaining 9.1%. The nature of the isolated microorganisms and their frequencies among the total sample were as follows: *E. coli* (70, 25.9%), *Proteus* species (12, 4.4%), *Enterobacter* species (9, 3.3%), *Klebsiella* species (8, 3.0%), *Pseudomonas* species (7, 2.6%), *Staphylococcus saprophyticus* (6, 2.2%), *Enterococcus* species (4, 1.5%), *Acinetobacter* species (3, 1.1%), *Citrobacter* species (1, 0.4%) and *Staph. aureus* (1, 0.4%).

Isolated uropathogens were analysed with reference to the age and sex of the

Table 2 **Distribution of the isolates among the positive samples by age**

Isolate	Age group (years)												Total[a] (*n* = 121)	
	18–25 (*n* = 47)		26–33 (*n* = 31)		34–41 (*n* = 12)		42–49 (*n* = 8)		50–57 (*n* = 6)		58–65 (*n* = 17)			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Escherichia coli	26	55.3	22	71.0	7	58.3	6	75.0	4	66.7	5	29.4	70	57.9
Klebsiella sp.	3	6.4	0	0.0	1	8.3	1	12.5	0	0.0	3	17.6	8	6.6
Proteus sp.	6	12.8	3	9.7	0	0.0	0	0.0	0	0.0	3	17.6	12	9.9
Enterobacter sp.	6	12.8	0	0.0	0	0.0	0	0.0	0	0.0	3	17.6	9	7.4
Pseudomonas sp.	2	4.2	1	3.2	3	25.0	0	0.0	0	0.0	1	5.9	7	5.8
Acinetobacter sp.	1	2.1	1	3.2	0	0.0	0	0.0	1	16.7	0	0.0	3	2.5
Citrobacter sp.	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
Staphylococcus saprophyticus	2	4.2	2	6.4	1	8.3	0	0.0	1	16.7	0	0.0	6	5.0
Enterococcus sp.	1	2.1	0	0.0	0	0.0	1	12.5	0	0.0	2	11.8	4	3.3
Staph. aureus	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8

[a] *Among positive samples.*

Table 3 **Distribution of isolates among the total sample according to sex**

Isolate	Male (*n* = 92) No.[a]	%	Female (*n* = 178) No.[a]	%	Total (*n* = 270) No.[a]	%
Escherichia coli	14	15.2	56	31.5	70	25.9
Klebsiella sp.	2	2.2	6	3.4	8	3.0
Proteus sp.	2	2.2	10	5.6	12	4.4
Enterobacter sp.	4	4.3	5	2.8	9	3.3
Pseudomonas sp.	5	5.4	2	1.1	7	2.6
Acinetobacter sp.	1	1.1	2	1.1	3	1.1
Citrobacter sp.	1	1.1	0	0.0	1	0.4
Staphylococcus saprophyticus	0	0.0	6	3.4	6	2.2
Enterococcus sp.	1	1.1	3	1.7	4	1.5
Staph. aureus	0	0.0	1	0.8	1	0.4
Total	30	32.6	91	51.1	121	44.8

[a]*No. = number of isolates.*

patients and the results are shown in Tables 2 and 3. The isolated bacterial strains showed wide differences in their susceptibility to the tested antimicrobial drugs. The relation between antimicrobial resistance of the isolates and the age of the population studied is presented in Table 4.

Discussion

We describe the relationships between age, sex and marital status, and the etiology and antimicrobial resistance of UTIs. The study was confined to community-acquired UTIs in adults.

The sex distribution of patients in our study is consistent with those of other reported studies, showing a statistically significant predominance of females with UTI (75.2% of the positive cultures). This result is similar to those reported from many other centres [*10–12*]. The elevated incidence of infection among females is related to differences between the male and female genitourinary systems in anatomy and microflora [*13*].

Although increasing age is associated with increased risk of UTI, our results showed that most of the positive as well as the negative cultures were from patients aged 18 to 41. The positive cases in those age groups may be due to the higher sexual activity and incidence of pregnancy in this age group.

The distribution by sex and marital status is shown in Table 1, where married females represented 54.6% of the positive cultures. This may be due to the effect of sexual intercourse on promoting the migration of bacteria inhabiting the periurethral introitus to the bladder [*13*].

The uropathogens identified in our study are similar to those of many other studies conducted in different countries

Table 4 Resistance (%) against each antimicrobial agent, by age group

Age group (years)[a]	AMX	AMC	AN	GM	TMP–SMZ	DOX	CF	CTX	CTZ	CIP	NOR	OFX	NA	NTFN
18–25 (47)	35.2	34.9	16.7	28.6	39.2	37.8	39.0	34.5	28.6	20.0	18.2	20.0	34.5	40.6
26–33 (31)	27.3	27.9	33.3	21.4	24.1	23.1	25.4	27.6	14.3	0.0	9.1	0.0	20.7	18.8
34–41 (12)	11.4	11.6	16.7	21.4	11.4	11.1	10.2	13.8	28.6	20.0	18.2	20.0	10.3	12.5
42–49 (8)	6.8	9.3	0.0	3.6	7.6	6.1	8.5	10.3	14.3	20.0	0.0	0.0	3.5	0.0
50–57 (6)	4.5	2.3	0.0	7.1	3.8	6.1	5.1	0.0	0.0	0.0	9.1	0.0	6.9	9.3
58–65 (17)	14.8	14.0	33.3	17.9	13.9	15.8	11.8	13.8	14.3	40.0	45.4	60.0	24.1	18.8
Total (121)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
P	0.857	0.827	0.613	0.209	0.881	0.814	0.950	0.633	0.528	0.266	0.023*	0.001*	0.535	0.269

[a]*The number in brackets is the number of positive cases in that age group.*
**Significant at* $P < 0.05$.
AMX = amoxycillin; AN = amikacin; AMC = amoxycillin-clavulanate; TMP-SMZ = trimethoprim–sulfamethoxazole; DOX = doxycycline; CF = cephalexin; CTX = cefuroxime; CTZ = ceftazidime; CIP = ciprofloxacin; NOR = norfloxacin; OFX = ofloxacin; NA = nalidixic acid; NTFN = nitrofurantoin.

either in the region or internationally [*14–17*]. In the United States, however, different results have been reported [*3*]. The similarities and differences in the type and distribution of uropathogens may result from different environmental conditions and host factors, and practices such as healthcare and education programmes, socioeconomic standards and hygiene practices in each country. Apart from the Gram-positive uropathogens, all other isolates are inhabitants of the large bowel, the most common source of community acquired UTIs [*18*].

The Gram-positive uropathogens, and especially the enterococci, are rarer in uncomplicated UTI. Infection with these organisms may be due to sources other than the large bowel, such as previous catheterization [*19*]. The occurrence of most of the isolated enterococci in elderly patients (Table 2) further supports this hypothesis.

An association seems to exist between sex and the nature of the uropathogens. As can be seen in Table 3, almost all types of bacterial strains were more prevalent in females except for *Pseudomonas* species, which was commoner in male patients. The biased distribution of the isolates by sex, although not statistically significant for all uropathogens, can be attributed to host factors, i.e. that females favour colonization by most the isolates. The predominance of *Pseudomonas* species in male patients may be due to the source of infection, which is commonly associated with indwelling catheterization, bacteraemia and prostate enlargement [*20*].

Regarding the resistance pattern of the isolates, the highest level of resistance was found to amoxycillin (73.6%), followed by doxycycline (68.6%) and trimethoprim–sulfamethoxazole (66.1%). Similar results have been reported by other authors [*10,15,21*]. This high resistance is mainly due to the widespread and indiscriminate use of these antibiotics. Therefore, these three drugs should no longer be prescribed for UTI unless susceptibility testing indicates otherwise.

The most effective antimicrobial agents were ciprofloxacin (95.9% of the isolates were susceptible), amikacin (95%) and ceftazidime (94.2%). The low level of resistance to these antibiotics might be due to the fact that these drugs are not widely used. Exposure to these antimicrobials is limited because of their high price and limited tolerability. In order to decrease the chance of organisms becoming resistant, these drugs should be used with restraint.

In our study the Gram-negative aerobic and facultative anaerobic isolates showed high susceptibility to nalidixic acid (82.7%). Comparable results have also been reported by Oren et al. [*21*]. We suggest that nalidixic acid be used for the empirical treatment of uncomplicated acute UTI, especially for Gram-negative uropathogens. Moreover, it is an economical treatment option in comparison with third-generation cephalosporins and fluoroquinolones.

A high percentage of multiple-drug resistance was also observed for most of the isolated strains, especially for *Pseudomonas* species. This resistance has probably emerged in the community as a result of overcrowding, an increase in the number of elderly people, increased travel, the widespread use of broad spectrum antibiotics, the sale of over-the-counter medicines and self-medication with antibiotics, the inappropriate use of antibiotics, and decreased funding for public health surveillance [*14*]. Therefore, the establishment of regulations for dealing with antimicrobial resistance could contribute to better prevention and management of resistance to these agents. It is also likely that limiting the use of broad-spectrum antibiotics will change resistance patterns.

The continued evolution of antimicrobial resistance among community-acquired isolates is worrying, and mandates national and international coordination on surveillance, data exchange and new approaches to slow its emergence.

As can be seen in Table 4, there is variation in isolate resistance between the different age groups. The effect of age can clearly be seen when we consider the fluoroquinolones, where there is a significantly higher proportion of resistance in the age group 58–65 years. Thus, age-related changes in host physiology may influence the effect of antimicrobial agents on the uropathogens. This result shows that patient age is an important factor when considering an antimicrobial agent for treatment of UTI: fluoroquinolones should not be used to treat elderly UTI patients without first conducting a sensitivity test.

The present study showed that sex, marital status and age are among the factors that influence the etiology and antimicrobial resistance of uropathogens. We recommend that these factors should be taken into consideration to improve the management of these infections. Better control and prevention of UTIs requires further studies to understand the mechanisms responsible for colonization of the urethra and bladder with different uropathogens, and to define ways of identifying patients at special risk.

References

1. Gonzalez CM, Schaeffer AJ. Treatment of urinary tract infections: what's old, what's new and what works. *World journal of urology*, 1999, 17:372–82.

2. Maartens G, Oliver SP. Antibiotic resistance in community-acquired urinary tract infections. *South African medical journal*, 1994, 84:600–2.

3. Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. *Journal of the American Medical Association*, 1999, 281(8):736–8.

4. Thomson KS, Sanders WE, Sanders CC. USA resistance patterns among UTI pathogens. *Journal of antimicrobial chemotherapy*, 1994, 33(suppl. A):9–15.

5. Tannock GW. The bowel microflora: an important source of urinary tract pathogens. *World journal of urology*, 1999, 17:339–44.

6. Plorde JJ. Urinary tract infections. In: Sherris JC, ed. Medical microbiology. *An introduction to infectious diseases*, 2nd ed. New York, Elsevier, 1990.

7. Burnett RW et al. *Clinical laboratory medicine*. Philadelphia, Williams and Wilkins, 1994.

8. Vandepitte J et al. *Guidelines for antimicrobial resistance surveillance*. Alexandria, WHO Regional Office for the Eastern Mediterranean, 1996:13–22 (WHO Regional Publications, Eastern Mediterranean Series, No. 15).

9. Bauer AM et al. Antibiotic susceptibility testing by a standard simple disk method. *American journal of clinical pathology*, 1966, 45:493–6.

10. Abu Shaqra Q. Occurrence and antibiotic sensitivity of *Enterobacteriaceae* isolated from a group of Jordanian patients with community acquired urinary tract infections. *Cytobios*, 2000, 101:15–21.

11. Neu HC. Urinary tract infections. American journal of medicine, 1992, 92:63S–70S.

12. Sobel JD, Kaye D. Host factors in the pathogenesis of urinary tract infections. *American journal of medicine*, 1984, 76:122–30.

13. Strom BL et al. Sexual activity, contraceptive use, and other risk factors for symptomatic and asymptomatic bacteriuria. A case–control study. *Annals of internal medicine*, 1987, 107:816–23.

14. Escolano Vizcaino M et al. Infecciones de vias urinarias en atencion primaria: gérmenes predominantes y su sensibilidad antibi tica. [Urinary tract infections in primary care: predominant microbes and their antibiotic sensitivity.] *Aten primaria*, 1989, 6:165–8.

15. Barrett SP et al. Antibiotic sensitivity of bacteria associated with community-acquired urinary tract infection in Britain. *Journal of antimicrobial chemotherapy*, 1999, 44:359–65.

16. Urassa WK et al. Susceptibility pattern of uropathogenic Gram negative bacilli to antimicrobial chemotherapeutic agents in a National Hospital in Dar es Salaam. *East African medical journal*, 1997, 74:162–5.

17. Khalifa K et al. Retrospective two-year study of urinary tract infection in the Ismailia area of Egypt. *Chemioterapia*, 1987, 6:500–2.

18. Finegold SM, Sutter VL, Mathisen GE. Normal indigenous intestinal flora. In: Hentges DJ, ed. *Human intestinal microflora in health and disease*. New York, Academic Press, 1983.

19. Weber G et al. Changing trends in frequency and antimicrobial resistance of urinary pathogens in outpatient clinics and a hospital in Southern Israel, 1991–1995. *European journal of clinical microbiology and infectious diseases*, 1997, 16:834–8.

20. Lipsky BA. Urinary tract infections in men. Epidemiology, pathophysiology, diagnosis and treatment. *Annals of internal medicine*, 1989, 110:138–50.

21. Oren B et al. [Antimicrobial susceptibility of organisms infecting the urinary tract in Northern Israel.] *Harefuah*, 1991, 120: 60–2 [In Hebrew].

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