UROPATHOGENS AND THEIR SUSCEPTIBILITY PATTERNS AT KING HUSSEIN MEDICAL CENTER-JORDAN

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ÖZET

Ürdün Kral Hüseyin Tıp Merkezi'nde Üropatojenler ve Duyarlılık Sonuçları

Temmuz 2000- Aralık 2001 tarihleri arasında Ürdün, Amman'da Kral Hüseyin Tıp Merkezinde yatan ve ayakta tedavi edilen hastalardan alınan toplam 21600 idrar örneği, kültür ve antimikrobiyal duyarlılığını belirlemek üzere test edildi. Bunlardan 2537 örnekte (%11.74) belirgin bakteriuri gözlendi. Kadın hastaların erkeklere oranı 1523:1014 (1.50:1.00) bulundu. En sık soyutlanmış patojenler, E.coli (%58.90), Klebsiella pneumoniae (%12.90), Pseudomonus aeruginosa (5.20%), Enterococcus fecalis (4.80%) ve Proteus mirabilis (4.20%) olarak belirlendi. Değişik antibiyotik gruplarına olan duyarlılıklar Vitek-1 sistemi (Bio Merieux, Fransa) kullanılarak incelendi. Sonuç olarak, Pseudomonas aeruginosa dışındaki Gram negatif bakteriler karbenisillin (88.00%), ampicillin (87.00%), sefalotin (78.00%), sefazolin (75.00%) ve trimetoprim/sulfamethoksazole (60.00%) nisbeten dirençli bulundu.
Anahtar Kelimeler : *Vitek, Üropatojen, Duyarlılık.*

SUMMARY

From July 2000 to Dec. 2001, a total of 21600 urine specimens were collected from inpatients and outpatients of King Hussein Medical Center, located in Amman/Jordan for culture and antimicrobial susceptibility testing. Among these, 2537 specimens (11.74%) showed significant bacteriuria. The ratio of female-to- male patients was 1523:1014 (1.50:1.00). The most frequently recovered pathogens were E.coli (58.90%), Klebsiella pneumoniae (12.90%), Pseudomonus aeruginosa (5.20%), Enterococcus fecalis (4.80%) and Proteus mirabilis (4.20%) . In this study, all isolates were tested for their antimicrobial susceptibilities against different groups of antibiotics, with Vitek-1 system (Bio Merieux, France) to determine their susceptibility patterns. As a result, (88.00%) of the Gram-negative isolates other than Pseudomonas aeruginosa were found to be respectively resistant to carbenicillin, (87.00%) to ampicillin, (78.00%) to cephalothin, (75.00%) to cefazolin and (60.00%) to trimethoprim/sulphamethoxazole.
Key Words : *Vitek, Uropathojen, Susceptibility.*

INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections observed in clinical practice among community and hospitalized patients(1). It has been estimated that urinary tract infections account for approximately 40.00% of all hospital-acquired infections(2), and that 25.00-35.00% of all females suffer from UTI at some stage in their lives(3).

UTI is a therapeutic problem, a cause of morbidity, renal scarring and end stage renal disease(4), and it has also been documented that catheter associated urinary tract infections are a major antecedent of gram-negative septicemia, a potentially serious condition with a mortality of 20.00-50.00% (5,6).

The choice of antibiotics should depend upon the causative organism and their susceptibility pattern to various antibiotics (7). Proper management and prevention of bacteriuria can reduce the incidence of the life- threatening consequences of urinary tract infections.

The aim of this study was to assess the incidence of causative organisms, and antibiotic susceptibilities of the isolates from July 2000 to Dec. 2001 at King Hussein Medical Center, an 800-bed hospital located in Amman/ Jordan.

MATERIAL AND METHODS

A total of 21600 clean-catch midstream and catheter urine samples from outpatients and inpatients were collected over a period of 18 months from July 2000 to December 2001. Specimens of urine were collected in a sterile universal container and transported to the laboratory within 30 minutes. Culture of urine and determination of significant bacterial count were performed by the semi quantitative method using the calibrated loop, direct-streak

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method (8). The loop used was checked by a procedure outlined by Barry et al (9). A calibrated platinum loop was used to deliver 0.001 ml from urine. Flame sterilized and cooled loop inserted in the well-mixed urine sample vertically and allowed urine to adhere to the loop, and one loopful delivered to a plate of MacConkey agar, and another loopful to a plate of blood agar. After streaking, the plates were incubated aerobically at 35-37 ^{O}C and examined after 18 to 24 hours. A cut-off point of 100000 CFU/ml was used for this study. The colonies on each plate were counted, and if more than 100 colonies were present, the urine sample was considered to have greater than 10^5CFU/ml, indicating significant bacteriuria(10).

According to the instructions were provided by the manufacturer, Vitek 1 system (Bio Merieux, France) was used for identification of the isolates, using V 1306 Vitek GNI card for Gram negative bacilli, and V 1305 Vitek GPI card for Gram positive microorganisms, and for antibiotic susceptibility testing of the isolates using V 4525 Vitek GNS-203 card for Gram negative bacilli, V 4523 Vitek GNS-113 card for Pseudomonas spp., and V 4511 Vitek GPS-101 card for Gram positive bacteria.

E.coli ATCC 25922, Staphylococcus aureus ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality control organisms.

RESULTS

A total of 21600 urine specimens were collected during the 18 months period of study; 12312 (57.00%) out of them were from outpatient clinics and 9288 (43.00%) were inpatients from different services. Significant bacteriuria was detected in 2537 specimens (11.74%). Among them, 1599 (63.00%) were specimens from outpatients and 938 (37.00%) were from inpatients. Table-I shows the number of patients with significant bacteriuria categorized by sex and clinics (inpatients and outpatients).

TABLE - I
Number of Patients With Significant Bacteriuria Categorized By Sex and Clinics (Inpatients and Outpatients)

Category	Number	%	Significant bacteriuria	%	Prevalence rate %
Female	12672	58.66	1523	60.03	-
Male	8928	41.33	1014	39.96	-
Total	21600	100.00	2537	11.74	-
Inpatients	9288	43.00	938	36.97	10.09
Outpatients	12312	57.00	1599	63.03	12.98
Total	21600	100.00	2537	11.74	-

Note that significant bacteriuria was more common in outpatients than in inpatients, and urinary tract infections were more common in females than in males.

The microorganisms isolated from urine specimens were shown in Table-II.

TABLE - II
Microorganisms Isolated From Urine

ORGANISMS	Number	%
Acinetobacter sp.	42	1.65
Candida albicans	6	0.24
Candida sp.	8	0.32
Citrobacter sp.	32	1.26
Enterobacter sp.	82	3.23
Enterococcus fecalis	121	4.76
Enterococcus sp.	2	0.08
Escherichia coli	1495	58.92
Klebsiella pneumoniae	328	12.92
Morganella morganii	28	1.10
Proteus mirabilis	106	4.17
Proteus vulgaris	6	0.24
Providencia sp.	5	0.20
Pseudomonas aeruginosa	132	5.20
Salmonella sp.	2	0.08
Serratia sp.	19	0.75
Staphylococcus aureus	19	0.75
Staphylococcus saprophyticus	5	0.20
Staphylococcus coagulase-negative	33	1.31
Streptococcus agalctiae group B	28	1.10
Streptococcus sp	13	0.52
Shigella sp.	2	0.08
Other organisms	23	0.92

The most frequently recovered pathogens were *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus fecalis* and Proteus mirabilis.

The antimicrobial susceptibilities of Gram-negative organisms except *P.aeruginosa* were shown in Table-III, for Gram-positive isolates in Table-IV, and for *Pseudomonas aeruginosa* in Table-V.

E.coli was found more resistant to ampicillin, carbenicillin, and cephalothin, but respectively sensitive to nitrofurantoin, ceftriaxone, and cefuroxime-sodium. *Klebsiella pneumoniae* showed a high resistance pattern to ampicillin, carbenicillin, and nitrofurantoin; 76.00% of *P. aeruginosa* strains showed resistance to gentamicin. *Proteus mirabilis* showed a high resistance pattern to nitrofurantoin, ampicillin and cephalothin.

As a result, 86.60% of Gram-negative isolates except *P.aeruginosa* strains were sensitive to ceftriaxone 79.46% to tobramycin, 76.00% to gentamicin, 75.00% to nitrofurantoin, 74.06% to cefuroxime-sodium, 74.00% to ciprofloxacin, 73.41% to ofloxacin and 73.19% to norfloxacin.

TABLE - III
Susceptibilities of Gram-Negative Organisms Except *P.aeruginosa*
Strains Isolated from Urine (%)

Antibiotics	Acinetobacter sp.	Citrobacter sp.	Enterobacter sp.	E.coli	Klebsiella pneumoniae	Morganella morganii	Proteus mirabilis	Proteus vulgaris	Providencia sp.	Salmonella sp.	Serratia sp.	Shigella sp.	Number of susceptibil M.O **M:organisms	%
Amoxicillin/CA	25.70	4.00	18.50	47.90	57.30	0.00	84.10	0.00	0.00	0.00	0.00	50.00	1025	44.97
Ampicillin	0.00	8.00	0.00	17.40	0.34	0.00	21.60	0.00	0.00	0.00	0.00	50.00	289	12.63
Carbenicillin	42.80	48.00	11.10	18.90	0.34	50.00	26.10	100.00	33.30	0.00	21.40	50.00	274	12.00
Cefazolin	2.86	12.00	40.70	21.00	60.30	0.00	25.00	0.00	0.00	0.00	7.10	50.00	579	25.40
Ceftriaxone	5.71	56.00	81.50	93.80	73.30	88.40	94.30	75.00	66.60	100.00	78.60	100.00	1973	86.60
Cefuroxime/sod.	2.86	28.00	55.50	87.20	69.10	0.00	90.90	0.00	0.00	100.00	7.10	100.00	1688	74.06
Cefuroxime/axetil	0.00	24.00	51.80	83.40	64.70	0.00	88.60	0.00	0.00	100.00	7.10	100.00	1609	70.60
Cephalothin	2.86	16.00	22.20	18.40	53.90	0.00	25.00	0.00	0.00	0.00	0.00	50.00	504	22.11
Ciprofloxacin	48.60	52.00	74.00	76.50	84.70	76.90	82.90	50.00	66.70	100.00	64.30	100.00	1686	73.97
Gentamicin	37.10	72.00	74.00	83.30	69.50	65.30	76.10	100.00	0.00	50.00	92.90	100.00	1733	76.03
Minocycline	100.00	32.00	29.60	49.00	72.20	15.30	0.00	0.00	0.00	100.00	85.70	100.00	1079	47.34
Nalidixic acid	48.60	48.00	66.60	65.30	73.20	30.80	61.40	50.00	0.00	50.00	64.30	50.00	1398	61.33
Nitrofurantoin	0.00	100.00	55.50	97.70	43.00	61.50	9.10	0.00	0.00	50.00	0.00	100.00	1709	75.00
Norfloxacin	-	52.00	70.40	76.20	83.70	76.90	93.20	50.00	66.70	100.00	64.30	100.00	1668	33.19
Ofloxacin	48.60	44.00	70.40	76.50	83.70	65.40	85.20	50.00	0.00	100.00	64.30	100.00	1673	73.41
Ticarcillin/CA	82.86	48.00	59.30	57.10	55.20	30.80	95.40	75.00	33.30	0.00	21.40	50.00	1308	57.40
Tobramycin	45.70	68.00	74.00	85.60	69.50	84.60	94.30	100.00	0.00	100.00	85.70	100.00	1811	79.46
Trimethop./sul.	34.30	56.00	48.10	40.40	56.30	34.60	27.30	0.00	33.30	0.00	64.30	100.00	915	40.10

Total number of Gram negative isolates are 2279.

TABLE - IV
Susceptibilities of Gram-Positive Organisms Isolated from Urine (%)

Antibiotics	Enterococcus fecalis	Enterococcus Sp.	Staphylococcus aureus	Staphylococcus saprophyticus	Coagulase-negative Staphylococcus	Streptococcus agalactica	Streptococcus.sp.
Ampicillin	100.00	100.00	10.53	40.00	0.00	95.45	100.00
Ampicillin/sulbactam	-	-	42,11	100.00	50.00	-	-
Cefazolin	-	-	42.11	100.00	50.00	100.00	100.00
Ciprofloxacin	71.74	100.00	78.95	100.00	75.00	-	-
Clindamycin	-	-	84.21	100.00	62.00	95.45	100.00
Erythromycin	-	-	57.89	60.00	37.00	90.91	100.00
Gentamicin	-	-	73.68	100.00	75.00	-	-
Gentamicin 500	68.48	100.00	-	-	-	-	-
Nitrofurantoin	98.91	100.00	100.00	100.00	100.00	100.00	100.00
Ofloxacin	-	-	78.95	100.00	75.00	100.00	100.00
Oxacillin MIC	-	-	42.11	100.00	50.00	-	-
Penicilin-G	92.39	100.00	10.53	40.00	0.00	95.45	100.00
Rifampin	-	-	100.00	100.00	75.00	-	-
Streptomycin 2000	47.83	100.00	-	-	-	-	-
Tetracycline	22.83	-	78.95	100.00	87.50	0.00	0.00
Trimethoprim/Sulfa	-	-	57.89	100.00	75.00	-	-
Vancomycin	96.74	100.00	100.00	100.00	75.00	100.00	100.00

TABLE - V
Susceptibility of *Pseudomonas* Spp. Isolated from Urine

Antibiotics	%
Amikacin	69.70
Ampicillin	0.00
Ampicillin/sublactam	0.00
Cefazolin	0.00
Cefapime	63.64
Cefotaxime	6.06
Cefotetan	6.06
Ceftazidime	66.67
Ciprofloxacin	60.61
Gentamycin	54.55
Imipenem	90.91
Levofloxacin	60.61
Piperacillin	78.79
Piperacillin/tazobac	84.85
Tobramycin	66.67
Trimethoprim/sulfa	0.00

DISCUSSION

This study revealed that there was a female preponderance of urinary tract infection occurrence (the ratio of female to male patients was (1.50:1.00), (1523:1014) at King Hussein Medical Center and our findings agree with those reported elsewhere (11, 12).

The prevalence rate of urinary tract infections in outpatient group was 12.98% (1599/12312) and in the inpatient group was 10.09% (938/9288).

The spectrum of uropathogens isolated from urine in this study is not too different from that reported in literature. Throughout Jordan various studies had been conducted for causative agents of UTI, which reports that *E.coli* and *Klebsiella spp* is the leading pathogens(11,13,14). Our study showed similar finding.

E.coli, K. pneumoniae, P. aeruginosa, Enterococcus fecalis, and Proteus mirabilis were the organisms commonly encountered.

E.coli was the most common organism isolated in this study, the overall incidence of *E.coli* in cases of significant bacteriuria in our series was 58.90% (1495/2537).

E.coli and *K. pneumoniae* showed similar resistant pattern to ampicillin (82.60% and 99.60% respectively) and to carbenicillin (81.20% and 99.60% respectively). The high frequency of resistance was expected, as ampicillin and its derivatives continue to be the most widely used antibacterial drugs used in Jordan as throughout the world, and in our setting where there is no guideline for antibiotic use, unchecked use will increase the resistant strains of previously sensitive bacteria, as reported by some authors (15,16).

Among the Gram-negative non-fermentative bacteria, *P. aeruginosa* is an important nosocomial pathogen, leading to infections especially in compromised host. Since it is resistant to most of the antimicrobial agents, the treatment of pseudomonal infections is usually difficult (17). In this study, *Pseudomonas spp.* showed a sensitivity of 91.00% to imipenem, 85.00% to pipreracillin/tazobactam, 67.00% to the ceftazidime, and 0.00% to the ampicillin.

Enterococcus fecalis is the fourth most common pathogen in our study; similar reporting is done by Nizami et al.(18), showing that now Gram positive bacteria are becoming one of the main uropathogens of UTI. In this study among the Gram-positive isolates, the most effective antibiotic was nitrofurantoin, with a susceptibility rate of 99.80%.

Because of the high level of resistance to ampicillin among the Gram-negative, *Pseudomonas spp*, and *Staohylococcus spp.,* this drug should not be the drug of choice for the treatment of UTI.

As a conclusion, blind treatment of urinary tract infection should be discouraged and culture and susceptibility testing should be performed in each case in order to prevent further increase of resistance rates. It is also recommended to apply strict antibiotic guidelines for rational usage and to screen frequency and antibiotic susceptibility pattern of microorganisms for effective empiric therapy.

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