Severe Urinary Tract Infection in Men Caused by *Enterobacter cloacae*

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Abstract

A urinary tract infection (UTI) is a bacterial infection that affects part of the urinary tract. When it affects the lower urinary tract it is known as a simple cystitis (a bladder infection) and when it affects the upper urinary tract it is known as pyelonephritis (a kidney infection). Urinary catheterization increases the risk for urinary tract infections. The risk of an associated infection can be decreased by catheterizing only when necessary, using aseptic technique for insertion, and maintaining unobstructed closed drainage of the catheter. 60 urine samples from male patients suffering from UTI were examined. 25 of them were a catheter samples of urine and 35 of them were asymptomatic, showed *Enterobacter cloacae* were isolated.

Keywords: *Enterobacter cloacae*- UTI

خمج المجاري البولية الحاد عند الرجال نتيجة الاصابة بجرثومة الانتيروبكتر كلوكي

الخلاصة

عند إصابة القسم السفلي من القناة البولية بالاخماج المختلفة تؤدي إلى حدوث خمج المثانة، أما في حالة إصابة القسم العلوي من الجهاز البولي فيؤدي إلى حدوث خمج الكليتين. لوحظ أن المرضى الذين يستخدمون أنابيب تفريغ الادرار يكونون أكثر عرضة للاصابة بالاخماج خصوصا عند سوء الاستخدام وكذلك في اجواء غير معقمة.

أظهرت هذه الدراسة تسجيل حالات إصابة خمج المجاري البولية بهذه الجرثومه ومسببة شدة مرضية عالية من خلال فحص ٦٠ أنموذجا من إدرار المرضى لمجموعتين الاولى تحتوي على ٢٥ أنموذج لمرضى يستخدمون قناني تفريغ مختلفة والباقي ٣٥ أنموذج لمرضى لا تظهر علامات الالتهاب لكن تبين وجود تلك البكتريا فى إدرارهم.

Introduction

Urinary tract infections (UTIs) are caused by germs, usually bacteria that enter the urethra and then the bladder. This can lead to infection, most commonly in the bladder itself, which can spread to the kidneys [1]. Most of the time, your body can get rid of these bacteria. However, certain conditions increase the risk of having UTIs. A UTI is a bacterial infection that affects part of the urinary tract. When it affects the lower urinary tract it is known as a simple cystitis (a bladder infection) and when it affect the upper urinary tract it is known as pyelonephritis (a kidney infection) [2]. Symptoms from a lower urinary tract include painful urination and either frequent urination or urge to urinate (or both), while those of pyelonephritis include fever and flank pain in addition to the symptoms of a lower UTI, in the elderly and the very young, symptoms may be vague. The main causal agent of both types is *Escherichia coli,* however other bacteria, viruses or fungus may rarely be the cause [3]. Urinary tract infections occur more commonly in women than men, with half of women having at least one infection at some point in their lives, recurrences are common [2]. Risk factors include female anatomy, sexual intercourse and family history [3]. Pyelonephritis, if it occurs, usually follows a bladder infection but may also result from a blood borne infection. Diagnosis in young healthy women can be based on symptoms alone, in those with vague symptoms, diagnosis can be difficult because bacteria may be present without there being an infection [3]. In complicated cases or if treatment has failed, a urine culture may be useful. In those with frequent infections, low dose antibiotics may be taken as a preventative measure. In uncomplicated cases, urinary tract infections are easily treated with a short course of antibiotics, although resistance to many of the antibiotics used to treat this condition is increasing [3,12]. In complicated cases, longer course or intravenous antibiotics may be needed, and if symptoms have not improved in two or three days, further diagnostic testing is needed. In women, urinary tract infections are the most common form of bacterial infection with 10% developing urinary tract infections yearly [3]. The bacteria that cause urinary tract infections typically enter the bladder via the urethra, however, infection may also occur via the blood or lymp. It is believed that the bacteria are usually transmitted to the urethra from the bowel, with females at greater risk due to their anatomy [3]. After gaining entry to the bladder, E. Coli are able to attach to the bladder wall and form a biofilm that resists the body's immune response up the bladder and kidneys and cause an infection [4,11]. Women tend to get more bladder infections than men, this is probably because women have shorter urethras, so it is easier for the germs to move up to their bladders, having sex can make it easier for germs to get into your urethra [4]. The bacteria that cause kidney infections (pyelonephritis) are generally the same bacteria that cause cystitis, there is some evidence, however, *E. coli* strains in pyelonephritis are more virulent (able to spread and cause illness). For reasons that are not well understood, some women get bladder infections again and again [13].

Bacteria that enter the urethra and travel up the urinary tract are the usual cause of urinary tract infections (UTIs), bacteria that normally live in the large intestine and are present in feces are the most common source of infection [5,8,9] . Complicated UTIs that are related to physical or structural conditions are apt to be caused by a wider range of organism. *E. coli* is still the most common organism, but others include *Klebsiella*, *P. mirabilis*, and *Citrobacter* [6,7,10].

Material and Methods

Amid-stream urine samples from 350 patients males ages between 45 -80 years old and suffering from UTI were attended a urology clinic in Medical city in Baghdad from July to November 2012 performed into sterile container immediately urinalysis examines the physical, chemical, and microscopic properties of urine. In a standard urinalysis, the odor, color, and clarity of urine are first evaluated for the possible presence of urine with a strong odor, hematuria (red urine), pyuria (cloudy urine), or phosphate crystal deposits (cloudy urine) were inoculated with standard platinum loop (Jorgensen tungsten alloy, 4-mm calibrated wire loop, 0.01 ml of urine was inoculated on MacConkey agar and Trypticase soy agar with 5% sheep blood and Levine eosin methylene blue agar(Scott Labs) and then incubated aerobically and anaerobically at 37°C for 48 h. Organisms were quantitated and then identified by API 20E (Biomerioux, France) and biochemical test reaction character done see table (4) .We identified 60 patients males whose urine contained a pure culture of a member of the *Enterobacter cloacae* in account of 100,000 organisms per ml or greater. 25 of these patients did practice intermittent catheterization and they had a Foley catheter, suprapubic catheter or ileal –loop bladder, the remainder males who did not practice inter mitten catheterization ; these asymptomatic men had previously been subjected to urological procedures particularly transurethral reseoction to relieve obstructive uropathy and were followed in the outpatient clinic regularly over a period of one year as part of an established post operative assessment program. These subjects were given no medication and were asked to return to the laboratory within one week to have a second urine culture. When the patients returned another specimen was obtained that was processed in a manner identical to the first.

The diagnosis of urinary tract infection was based on microscopic finding of more than 5 white blood cells per high power field on urine microscopy and a colony count of 10^5/ ml of single pathogen. In moribund patients the urine was also collected through the supra pubic puncture or urinary catheterization, after washing the genital region with soap and water. Mid stream, clean, early morning specimens were collected in a sterilized container. All the antibiotics were discontinued 72 hours before collecting the urine for culture and sensitivity. Urine sample was delivered to the laboratory within 1 hour of collection. In case of delay the urine samples was kept at 4^oC and analyzed within 6 hours of the collection. The urine samples were cultured in 5% sheep blood agar and MacConkey agar medium. Inoculation was done with the help of a 0.001ml caliber loop. All the sample plates were incubated for 48 hrs at 37^oC in 5-10% carbon dioxide for anaerobic growth. Bacterial identification was done by hand lens and standard biochemical tests. Multiple growths were obtained in the case of scanty growth; the culture was repeated again before accepting the results. The details of each patient were recorded in a proforma.

Catheterization refers to the presence of a Foley, condom, or suprapubic catheter for 48 hours or more. Catheter duration was calculated by measuring the number of days between the first day of catheterization and the day of the urine culture collection, including any catheter-free period of 48 hours or less see table (1). Chronic catheterization was defined as catheter duration of more than 30 days. A serum white blood cell count greater than 10 000/µL (to convert to $\times 10^9$/L, multiply by 0.001) was considered leucocytosis. More than 10 red blood cells and 10 white blood cells per high-power field via automated microscopy of the urine defined microscopic hematuria and pyuria respectively (Table 2).

Results

Our data confirm the statement that adult non catheterized males without an ileal-loop bladder, showed that a single clean mid stream urine samples that contain more than 100,000 CFU *Enterobacter cloacae* per ml in pure culture can be considered diagnostic of an asymptomatic urinary tract infection (Tables 1, 2, and 3). The isolate was identified as *Enterobacter cloacae* by using biochemical reactions (Table 4) and was confirmed by using API 20E systems. Minimal inhibitory concentration was performed using different antimicrobial agents (Table 5). The reproducibility of a single urine culture containing significant bacteriuria occurred independently of the tissue source of the infection. A single urine culture containg more than 100,000 organisms per ml in adequate to establish the diagnosis of asymptomatic urinary tract infection and in patients with urinary catheterization. However, in the asymptomatic patient, cloudy or foul smelling urine is not an indication for urinalysis, culture, or antimicrobial treatment. A study of residents in long-term care facilities with chronic indwelling catheters and bacteriuria who were treated with antibiotics or no therapy showed no differences in the incidence of fever or reinjection; however, patients who received antibiotic therapy had twice the incidence of subsequent microbial resistance. We showed that Patients distribution duration of introduced catheter (Foley and suprabubic) increase the mean CFU/ml more than 30 days duration more colonies of *Enterobacter cloacae* harvested see table (6). Regarding the antimicrobial sensitivity profile of the uropathogenes, we observed that the isolated *Enterobacter cloacae* strains were sensitive at similar rate to ampicillin, Gentamicin, Carbenicillin, kanamycin, Tobramycin, Amikacin and cephotaxime , and resistant to Cephalothin , Tetracycline, Chloramphenicol, Methprime and Nitrofurantoin, determining sensitive and resistant bacteria to antibiotics by measuring the diameter of inhibition zone by mm and then compared with the standard diameters that installed in the standard scale (Tables 3,7). Culture positivity rates were found almost same in diabetes mellitus and In-patient in both UTI and ABU groups ($p < 0.001$). These data obtained according (SAS) statistical Analysis System 2004 (Statistical Anaylsis System Users Guide. Statistical Version 7th ed. SAS .Inst. Inc. Cary N.C. USA) (Tables 2,8,9, and 10).

Discussion

This study describe the first time isolate and identified *Enterobacter cloacae* in Iraq causes UTI in both in both asymptomatic and non catheterization males patients see table (1). Despite the limited utility of pyuria in making the diagnosis of enterococcal UTI, we found that it was associated with a more than 3-fold increase in the inappropriate use of antibiotics see table (3) . Recent guidelines specifically state that “pyuria accompanying asymptomatic bacteriuria is not an indication for antimicrobial treatment.. We found that infectious complications with *Enterococcus* were rare, lending support to the recommendation not to treat ABU, even in our patient population with *Enterococcus* have multiple medical co-morbidities see table (2).

The characteristics associated with UTI as opposed to ABU shown in (Table 2). Whereas immunocompromise of any cause was not significantly associated with UTI compared with ABU see table (3),

Catheterization was associated with a nearly 2-fold increase in UTI compared with ABU. Having at least 10^5 CFU/mL of Enterococcus was associated with a 3 times greater likelihood of having UTI compared with ABU, with a sensitivity of 41% and a specificity of 83%.

The longer any urinary catheter is in place, the higher the risk for growth of bacteria and an infection. In most cases of catheter-induced UTIs, there are no symptoms. Because of the risk for wider infection, however, anyone requiring a catheter should be screened for infection. Catheters should be used only when necessary and should be removed as soon as possible.

However, in the asymptomatic patient, cloudy or foul smelling urine is not an indication for urinalysis, culture, or antimicrobial treatment. A study of residents in long-term care facilities with chronic indwelling catheters and bacteriuria who were treated with antibiotics or no therapy showed no differences in the incidence of fever or reinfection; however, patients who received antibiotic therapy had twice the incidence of subsequent microbial resistance to antibiotics see table (3) .

The characteristics associated with UTI as opposed to ABU shown in (Table 2,. 3), the neutropenic (absolute neutrophil count <1000/µL) subset was more than 3 times more likely to have UTI than nonneutropenic patients. Catheterization was associated with a nearly 2-fold increase in UTI compared with ABU. Having at least 10^5 CFU/ml of *Enreococcus* was associated with a 3 times greater likelihood of having UTI compared with ABU, with a sensitivity of 41% and a specificity of 83%. Whereas peripheral leukocytosis was not associated with UTI, pyuria was 3.2 times and microscopic hematuria was 2.6 times more likely to be associated with UTI as opposed to ABU. However, the sensitivity and specificity were low for the relationship of pyuria to UTI and the relationship of microscopic hematuria to UTI (Table -2).

The older residents in long-term care facilities have shown no benefits from screening for or antimicrobial treatment of asymptomatic bacteriuria. Although antimicrobial treatment does not decrease symptomatic infection or improve survival, there is an increased incidence of adverse antimicrobial effects and re-infection with antibiotic-resistant organisms.

In this study, we found multidrug resistance strains which are resistant to most of the antimicrobials agent tested. This reflected the fact that ampicillin, tetracycline, and streptomycin were the most commonly prescribed antibiotics in the hospital even before the results of urine analyses and also the most easily available in the market without prescription and because they were also very cheap in terms of cost. A summary of the different antibiotics used during the study period was shown in Table 1 evaluated the prevalence of *Enterobacter cloacae* implicated in UTI to ascertain their antimicrobial drugs. Gentamicin and Cefotaxime that still show high efficacy against *Enterobacter cloacae* because of its multiple mechanisms of action seem to have enabled it to retain potent activity against pathogens. The overall rate of resistance to SXT found in this study was significant and higher than those reported by many workers in past others (Zhanel et al., 2000). For the past decades, SXT or trimethoprim alone has been used widely as an empirical therapy for urinary tract infections caused by *E. coli*. In this study, we found multidrug resistance strains of *Enterobacter cloacae* which are resistant to ampicillin, tetracycline, were the most commonly prescribed antibiotics in the hospital even before the results of urine analyses and also the most easily available in the market without prescription and because they were also very cheap in terms of cost .In this study showed resistance to at least 4 different antibiotics, indicating the presence of strong selective pressures from the antibiotics in the community. Although little information are available on prevalence of uropathogenic *Enterobacter cloacae* in Iraq [15, 16], this study may be an important addition of UTIs studies caused by serious this pathogen in Iraq.

Conclusion

Enterobacter cloacae were isolated from both UTI and asymptomatic bacteriurea. Indwelling catheters for urgency incontinence may not result in continence or the relief of recurrent infections. Asymptomatic bacteriuria is highly prevalent in elderly persons, compared with other age groups studied.

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Table 1: Mean CFU/ML according to patients characteristic

Case	Number of patients	Mean CFU/Ml
Out-Clinic urological patient		
Older community-dwelling	**5**	110
Older long-term care residents	**5**	115
Patients with spinal cord injuries(Intermittent catheter)	**2**	115
Sphincterotomy and codom catheter	**1**	110
Patients with an indwelling catheter(short-term)	**3**	100
Patients with an indwelling catheter (long-term)	**6**	120
Out patients		
Asymptomatic	**23**	120
Foley catheter	**5**	110
Suprabubic catheter	**5**	110
Ileal-loop bladder catheter	**2**	100

Table 2: Associations between Patients and UTI

Characteristics	Combined	UTI	ABU	P value
Age > 45 years	60	25	35	0.004
Male (sex)	60	25	35	0.004
Immunocompromised	21	8	13	0.002
Diabetes mellitus	60	2	-	< 0.001
In-Patients	5	3	-	< 0.001
Out-Patients Clinic	60	25	35	0.004
Catheter Present (>48h)	32	8	3	0.006
Catheter Chronic (>10days)	32	20	12	0.006
Pyurea (< 10 WBCs/HPF)	60	20	22	0.005
Microscopic haematurea (<10 RBCs/HPF)	60	8	2	0.008

ABU: Asymmptomytic bacteriurea

Table 3: Summary of distant Infections Complications by *Enterococcus cloacae*

Patients No.	Co-morbidity	Symptoms	Diagnosis	Treatment	Infected site
5	None	Delirium	UTI	Ampicillin	Bacteriuria
2	Diabetes mellitus	Fever	UTI	None	Bacteriuia
10	None	Fever	UTI	Gentamicin	Bacteriuria
13	Immunocompromised	None	ABU	None	Bacteriuria
3	Immunocompromised	Urgency, fever	UTI	Cefotaxime	Bacteriuria
5	Immunocompromised	Fever	UTI	Amoxicillin	Bacteriuria
22	None	None	ABU	Trimethoprime-sulfamethaxazol	Bacteriuria

Table 4: Biochemical reactions of *Enterobacter cloacae*

Biochemical Test	Reaction/48 h
Indole	-
Voges-proskauer	+
Simmon"s Citrate	+
H_2S production	-
Phenylalanine deaminase	-
Ornithine decarboxylase	+
Gas from glucose	+
Acid from D-glucose	+
Lactose	+
Arabinose	+
Deoxyribonuclease	-
Oxidase	-
Catalase	+
Yellow pigment in Tryptic soy agar at 25^oC	+
Urea	-

Table 5: Antimicrobial susceptibility test results for *Enterobacter cloacae*

Antimicrobial agent	MIC ug/ml	Interpretation
Ampicillin	2.00	Susceptible
Cephalothin	20.00	Unsusceptible
Gentamicin	0.50	Susceptible
Tetracycline	1.50	Unsusceptible
Carbenicillin	16.00	Susceptible

Chloramphenicol	3.00	Unsusceptible
Kanamycin	2.00	Susceptible
Tobramycin	0.50	Susceptible
Amikacin	2.00	Susceptible
Cefotaxime	2.00	Susceptible
Nitrofurantoin	32.00	Unsusceptible
Metheprim	28.00	Unsusceptible

Table 6: Patients distribution according to duration of introduced catheter (Foley and suprabubic) and mean CFU/Ml

Duration (days)	**Symptomatic/25 patients**	**Mean CFU/ML**	**Asymmptomatic/35 patients**	**Mean CFU/ML**
<30	8	100	16	110
>30	17	120	19	125

Table 7: Antimicrobial Sensitivity according to Patients Characteristics

Patients Characteristics	**Most Sensitive to Antibiotic**	**Resistant to Antibiotic**
Out Patients		
Diabetes mellitus	Cefotaxime	Tetracycline
Neurogenic bladder	Gentamicin	Methprim, Nitrofurantoin
Immunocompromised	Cefotaxime	Tetracycline, Methoprim
None	Ampicillin,Cefotaxime	Methoprim
Foley catheter	Cefotaxime	Chloramphenicol
Suprabubic catheter	Carbenicillin, Cefotaxime	Tetracycline, Methoprim
Ileal-loop bladder catheter	Gentamicin	Tetracycline, Methoprim
Patients with an indwelling catheter(short-term)	Cefotaxime	Ampicillin, Tetracycline
Patients with an indwelling catheter (long-term)	Cefotaxime	Ampicillin, Cephalothin
In-patients		
Diabetes mellitus	Gentamicin, Cefotaxime	Ampicillin,
Neurogenic bladder	Gentamicin,	Ampicillin, Methoprim,
Immunocompromised	Cefotaxime	Tetracycline, Methoprim
None	Ampicillin,Cefotaxime	Methoprim,
Foley catheter	Cefotaxime , Tobramycin	Chloramphenicol, Tetracycline

Suprabubic catheter	Cefotaxime	Tetracycline, Methoprim
Ileal-loop bladder catheter	Cefotaxime	Tetracycline, Methoprim
Patients with an indwelling catheter(short-term)	Cefotaxime, Tobramycin	Ampicillin, Tetracycline, Methoprim
Patients with an indwelling catheter (long-term)	Cefotaxime , Tobramycin	Ampicillin, Tetracycline, Methoprim

Table 8: Patients distribution according to co-morbidities

Patients characteristics	**Symmptomatic/25 patients**	**Asymmptomatic/35 patients**	**p-value**
Out-patients			
Diabetes mellitus	**2**	**2**	0.002
Neurogenic bladder	**5**	**5**	0.002
Immunocompromised	**12**	**8**	0.004
None	**6**	**20**	0.002
In-patients			
Diabetes mellitus	**3**	**5**	0.002
Neurogenic bladder	**4**	**5**	0.002
Immunocompromised	**8**	**13**	0.004
None	**10**	**12**	0.002

<0.001 = Non Significant

Table 9: Patients distribution according to ages

Age/years	**Symmptomatic /25 patients**	**Asymmptomatic/35 patients**	**p-value**
41-50	3	5	**0.002**
51-60	9	10	**<0.001**
61-70	8	10	**<0.001**
71-80	5	5	**<0.001**

<0.001 = Non Significant

Table 10: Patients distribution according to site of Foleys

Out-Patients	**Symmptomatic/25 patients**	**Asymmptomatic/35 patients**	**p-value**
Foley catheter	**21**	**32**	**0.002**
Suprabubic catheter	**2**	**2**	**<0.001**
Iieal-loop catheter	**2**	**1**	**<0.001**
In-patient			
Intermittent catheter for	**3**	**2**	**0.004**

patients with spinal cord injuries			
Sphincterotomy and condom catheter	**2**	**2**	**<0.001**
Short-term indwelling catheter	**10**	**13**	**0.002**
Long-term indwelling catheter	**10**	**18**	**0.004**

<0.001= Non-significant

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