Original Article

UTI in Patients with Urinary Stone

Prevalence of Urinary Tract Infection in Patients with Urinary Stone Disease and Their Antibiotic Sensitivities

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ABSTRACT

Objective: To find out the frequency of common bacteria causing urinary tract infection in patients with urinary stone disease and to determine the antibiogram of common bacteria causing urinary tract infection in patients with urinary stone disease.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at Urology Out-patient Department, Shaikh Zayed Hospital Lahore from 1st February 2020 to 30th July, 2020.

Materials and Methods: Sixty five patients with urinary stone diseases were enrolled. All urinary stone patients of both genders and 13-65 years were included. their clean-catch mid-stream urine samples were sent to microbiology laboratory for culture and sensitivity testing.

Results: The mean age was 45.09±15.49 years with 35 (53.8%) male and 30 (46.2%) female patients. The most common pathogens isolated were E. coli (61.5%), K. Pneumonia (9.2%), Enterococcus species (9.2%), methicillin-resistant Staphylococcus aureus (6.2%) and P. mirabilis (4.6%). Most of the isolates were found to be highly resistant to commonly prescribed antibiotics including cephalosporins, quinolones and penicillin-derivatives.

Conclusion: An overall high prevalence of E. coli causing UTI in patients with USD. For gram-positive isolates, low levels of resistance were detected against teicoplanin, linezolid and vancomycin while gram-negative isolates were most sensitive to colistin, meropenem and imipenem. Multi-drug resistant urinary tract bacteria are becoming widespread in patients with USD, probably due to frequent and unwarranted use of antibiotics. The surveillance of UTI and antimicrobial resistance patterns are essential to reduce the emergence of more resistant strains of these bacteria.

Key Words: Urinary Tract infection, Urinary stone disease, Urolithiasis, Bacteriuria

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INTRODUCTION

Urinary tract infection is very common in patients with urolithiasis. Persistent infections caused by urease-producing bacteria will form infection stones consisting of monoammoniumurate, struvite (magnesium ammonium phosphate), and/or carbonate apatite.[1]

Secondarily infected stones, the non-struvite and non–calcium carbonate apatite stones are also associated with UTIs.[2]

Complications of urolithiasis, i.e. asymptomatic bacteriuria, UTI, and sepsis have been recognized after treatment with extracorporeal shock-wave lithotripsy. Patients with severe or multiple stones might develop postoperative systemic inflammatory response syndrome after a percutaneous nephrolithotomy (PCNL), with a small percent progressing to urosepsis, which could lead to a catastrophic even, such as septic shock. All infections of the urogenital tract, pyelonephritis is very severe and leads to dangerous complications.[3] The frequency of urinary tract infection in stone disease, which has a high incidence in Pakistan need to be studied to find out the risk and help in the treatment of disease.[4]

In majority of studies, *E. coli* was found to be the most frequently encountered pathogen causing UTI and accounts for more than 50% of the isolates in several studies.[5-7] Similarly, in one of the studies, the majority of isolates were *E. coli* (52.7%) followed by Staphylococcus (21.4%), Moraxella (8%), Klebsiella (7.4%) and Enterococcus (5.9%). Other isolated organisms were Citrobacter (4%), Streptococcus (3.5%), Pseudomonas (2.4%), Sphingomonas (1.2%), Kocuria (0.8%), Acinetobacter (0.8%), Providencia (0.8%), Francisella (0.4%) and Morganella (0.4%).[8]

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Ampicillin had the highest overall resistance rate (78.3%) whereas tazobactam/piperacillin combination had the highest overall sensitivity rate (17.7%). *E. coli*; the most commonly found uropathogen was most sensitive to nitrofurantoin (20%) while most resistant to ampicillin (77.8%).[8] While in another study the same organism was found to be most sensitive to imipenem (93%) followed by amikacin (78%), tazobactam (69%), fosfomycin (60%) and nitrofurantoin (59%). In this study similar patterns were shown by Klebsiella and Staphylococcus Aureus, the other two most common uropathogens of the study.[9]

The primary aim of this study is to identify the common pathogens associated with UTI in patients with urinary tract stone disease and to determine their sensitivity patterns. One of the main criteria for selecting antimicrobial drugs for treating UTI is data on the antibiotic resistance of uropathogens.[6] The results of this study will help the urologists and other doctors dealing with such infections especially locally to choose appropriate antibiotic regime at initial stage in the absence of culture and sensitivity reports and will also help in devising guidelines for appropriate empirical antibiotic therapy. Furthermore, as the pathogens causing urinary tract infections are developing resistance against commonly used antibiotics, this study will also shed light on the changing sensitivity patterns of these pathogens when compared to the previous studies.

MATERIALS AND METHODS

This cross-sectional study undertaken in the Department of Urology, Shaikh Zayed Hospital, Lahore from 01-02-2020 to 31-07-2020. Sixty five patients were included from 13 to 65 years of age and both genders with evidence of stone disease on CT-KUB plain. Those excluded from the study who refusing to give consent, patients with indwelling catheter or history of catheterization in past 6 weeks, with any history of instrumentation or surgery in past 6 weeks and with any history of antibiotic usage in last 3 days. The samples of mid-stream urine were sent to microbiology laboratory for culture and sensitivity testing. There urine samples were inoculated onto Cysteine Lactose Electrolyte Deficient medium using a calibrated loop with a capacity of 1µl in safety cabinet. All inoculated plates were incubated at 37 C for 24-48hours and the number of colonies were counted. Colony counts yielding bacterial growth of$>10^5$ per ml of urine (≥100,000 colonies) were regarded as significant for bacteriuria. Urine samples yielding more than 3 bacterial species were not considered for further investigation. Then gram staining of smear of the urine was prepared for identification of gram positive or negative bacteria. Specimen ID was confirmed by biochemical panel using api (analytical profile index) 20E and Whitek 2 system. The sensitivity of the isolated bacteria to specific antibiotics (as specified by CLSI (clinical and laboratory standards institute) 2019 guidelines for each bacterium) were then tested using NCCLS (National laboratory for Clinical Standards) Modified Kirby-Bauer disc diffusion technique and the bacteria were labelled sensitive(S) or resistant(R) after measuring zones of inhibition.

RESULTS

The age ranged from 15-65 years of patients with a mean of 45.09±15.49 years. Majority of the patients were in age group of 41-65 years (60.0%) followed by the age group of 15-40 years (40.0%).

Table 1: Frequency of different bacteria isolated (n=65)

Bacteria	Frequency	Percent
Escherichia coli	40	61.5
Klebsiella pneumonia	6	9.2
Enterococcus species	6	9.2
Methicillin-resistant Staphylococcus aureus	4	6.2
Proteus mirabilis	3	4.6
Pseudomonas aeruginosa	2	3.1
Coliform species	2	3.1
Serratia species	1	1.5
Acinetobacter species	1	1.5
Total	65	100.0

Table No.2: Antibiotics sensitivity and resistance patterns of gram-positive bacteria

Antibiotics	Gram Positive			
	Enterococcus species (%)		Staphylococcus aureus (%)	
	S	R	S	R
TPN	100	0	100	0
LNZ	100	0	100	0
VAN	100	0	100	0
NIT	83.3	16.7	100	0
FOS	60.0	40.0	100	0
AMX	50.0	50.0	0	100
AMP	50.0	50.0	0	100
AUG	50.0	50.0	0	100
PEN	40.0	60.0	0	100
GEN	-	-	33.3	66.7
AMK	-	-	0	100
IMI	-	-	0	100
CXA	-	-	0	100
CFX	0	100	0	100
CTR	0	100	0	100
CTX	0	100	0	100
CIP	0	100	0	100
CEF	0	100	0	100

There were 35 (53.8%) male and 30 (46.2%) female patients with a male to female ratio of 1.16:1.The most common pathogens isolated were *E. coli* (61.5%), K. Pneumonia (9.2%), Enterococcus species (9.2%),

methicillin-resistant Staphylococcus aureus (6.2%) and P. mirabilis (4.6%). Other isolated pathogens were P. aeruginosa (3.1%), Coliform species (3.1%), Serratia species (1.5%) and Acinetobacter species (1.5%) (Table-1).

There were only 2 Gram-positive bacteria among the isolates: Enterococcus species and methicillin-resistant Staphylococcus aureus (MRSA). Both of these bacteria were found to be fully sensitive (100%) to Teicoplanin (TPN), Linezolid (LNZ) and Vancomycin (VAN) whereas both were highly resistant (100%) to ciprofloxacin (CIP) and most cephalosporins (Cefuroxime CFX, Ceftriaxone CTR, Cefotaxime CTX and Cephradine CEF). Moreover, Enterococcus was found to be resistant to half of the drugs tested while MRSA was found to be resistant to 2/3rd of the tested drugs (Table 2).

Among the 7 Gram-negative bacteria identified, percent of isolates sensitive to polymyxin B (PB), Colistin (CST), meropenem (MEM) and imipenem (IMI) were 96.1%, 90.6%, 88.2% and 87.0% respectively, whereas all gram-negative isolates were fully resistant (100%) to amoxicillin (AMX), ampicillin (AMP) and Cephradine (CEF) (Table 3).

Table No.3: Antibiotics sensitivity and resistance patterns of gram-negative bacteria

Antibiotics	Gram Negative						
	Escherichia coli	Klebsiella species	Proteus species	Pseudomonas aeruginosa	Coliform species	Serratia species	Acinetobacter species
	S	S	S	S	S	S	S
CST	100	100	0	100	50	0	100
PB	100	100	100	100	50	0	100
MEM	97.3	60	100	50	50	100	0
IMI	95	66.7	100	50	50	-	0
AMK	91.7	33.3	100	50	50	-	0
ETP	89.2	60	-	0	100	100	0
NIT	80.6	0	0	0	0	0	0
FOS	79.4	0	-	-	-	-	-
SCF	75.7	33.3	100	50	50	100	0
TZP	73.7	40	100	50	50	100	-
GEN	54.1	33.3	100	50	50	-	0
AUG	28.9	0	0	-	0	0	0
CAZ	23.3	16.7	66.7	0	50	100	0
CTX	18.9	20	66.7	-	100	100	0
CTR	18.2	0	100	-	0	-	-
CIP	10.5	0	-	50	0	100	0
CFX	5.6	0	66.7	0	50	0	0
AMX	0	0	0	-	0	-	0
AMP	0	0	0	-	0	0	0
CEF	0	0	-	-	-	-	-

DISCUSSION

Urinary tract infection in patients with urinary stone disease is an increasing clinical problem. Urease producing bacteria have long been recognized to contribute to struvite stones and are almost always present in infection stones; however, the association of bacteria with other types of calcium and non-calcium stones has not been extensively investigated. Several findings do indicate a possible correlation between urinary stones and bacteria and higher rate of UTI in urinary stone patients.[10]

The incidence of urinary stone disease in males is 2 to 3 times higher than females as documented by many studies.[11-13] The lower male to female ratio in our study and other similar studies can be explained on the basis that although stone disease is more common in males, but urinary tract infection is very higher in females like to males.[14]

E. coli was the much frequent isolated pathogen causing UTI in patients with accounting for 61.4% of isolated pathogens. Although E.coli is the most frequent uropathogen in almost all studies, the prevalence of *E. coli* in our study was slightly less than its prevalence (64.41%) from a study in Jamshoro.[15] Whereas it is relatively higher when compared with the studies from Lahore and Karachi which identified *E. coli* isolates in 34.01% and 40% of the patients respectively.[16] This higher prevalence of *E. coli* in our study indicate that E.coli may be associated with urinary stone formation through unknown mechanism as also suggested by studies from Thailand and India.[17]E.coli is also the most prominent bacteria in urology.[18]

Other bacteria isolated in this study were K. Pneumonia (9.2%), Enterococcus species (9.2%), methicillin-resistant Staphylococcus aureus (6.2%), P. mirabilis (4.6%), P. aeruginosa (3.1%), Coliform species (3.1%), Serratia species (1.5%) and Acinetobacter species (1.5%). These findings are in line with the studies done in Jamshoro (K. Pneumonia: 11.31%, Enterobacter: 11.31%, P. mirabilis: 7.86%, P. aeruginosa: 3.27%, Citrobacter: 1.74%) and Thailand.[15,18] Another study done in Lahore showed similar trend with some variations (K. Pneumonia: 18.78%, S. aureus:6.6%, S. epidermidis: 4.57%, P. aeruginosa: 4.57%, P. mirabilis: 1.52%, Citrobacter: 1.52%) whereas the study from India identified isolates with significantly different prevalence of (K. Pneumonia: 30%, P. aeruginosa: 19%, S. aureus: 5%, E. faecalis: 4%, P. mirabilis: 2%).[16] These differences could be due to the poor hygiene and sanitation in India.

The current study showed an alarmingly high percentage of resistance to commonly prescribed antibiotics. The all gram-negative isolates were fully resistant to at least 2 antibiotics (MDR). More isolates of Gram-negative bacteria revealed 100% resistance to ampicillin, amoxicillin and cephradine which is much

higher than the resistance pattern of these antibiotics in previousstudies in Lahore, Jamshoro and Karachi.[15-16] Similar higher level of resistance among the gram-negative bacteria was also observed in this study against commonly used antibiotics such as ciprofloxacin (mean resistance of 87.8%), cephalosporins (cefuroxime (89.6%), ceftriaxone (81.3%), cefotaxime (75%), ceftazidime (72.7%)) and co-amoxiclav (77.6%). For comparison the mean resistance for some of these antibiotics in Jamshoro study was ciprofloxacin (27.4%), ceftriaxone (27%) and ceftazidime (24.5%) (16). Recently popular nitrofurantoin and fosfomycin were found to be effective against 2/3rd and 3/4th of the tested isolates. Most of the gram-negative isolates in our study were found to be sensitive to very few antibiotics namely polymyxin b, colistin, meropenem, imipenem, ertapenem and amikacin with mean resistance of only 3.9%, 9.4%,11.8%, 13%, 17.4% and 20% respectively.[19]

Only two species of gram-positive bacteria were identified in our study indicating high prevalence of mainly Gram-negative bacteria in causing urinary tract infection in patients with stone disease. Among Gram-positive bacteria evaluated for antimicrobial drug resistance enterococcus and only methicillin resistant strain of *S. aureus isolated.* Both of these bacteria were highly resistant to most first-line and commonly used antibiotics having zero susceptibility to ciprofloxacin and all tested cephalosporins (cephradine, cefotaxime, ceftriaxone and cefuroxime) while MRSA was also fully (100%) resistant to amikacin, imipenem and cloxacillin for which enterococcus were not tested. Both the strains were 100% susceptible to teicoplanin, linezolid and vancomycin. Although half of the isolates of enterococcus were also susceptible to ampicillin, amoxicillin, penicillin and co-amoxiclav but no isolate of MRSA was susceptible to any of these drugs. Again these findings indicate much higher levels of resistance among the Gram-positive isolates in patients with stone disease as compared to isolates identified in previous studies done in Lahore, Karachi and a similar study in Thailand.[16,17]

The role of typically cultured pathogens in pathologic calcification is largely unknown and unstudied, particularly in the case of kidney stone disease. Our data suggests that UTIs even in patients with stone disease are mainly caused by *E. coli* and not urease-splitting bacteria. Our findings also emphasize that UTIs in stone diseases is not limited to proteus or urease-splitting bacteria rather UTIs caused by other bacteria are more prevalent in the presence of stone disease. These observations could be due to either secondary infection of stones as suggested by a study in USA, alternatively these non-urease producing bacteria may be somehow involved in stone formation or propagation as suggested by a study in Thailand.[2,17]

UTIs associated with urolithiasis is a significant problem for the modern endo-urologist due to the high levels of resistance among the isolates as observed in this study. These bacteria continue to survive in the urine most likely due to multidrug resistance, thus becomes difficult to be eradicated. Another possible explanation of the persistence of these bacteria is that they may get entrapped in the stone periphery. Several factors may be responsible for this alarmingly increased prevalence of highly resistant organisms identified in this study. Most importantly, mis-use of antibiotics because of its easy availability over-the-counter without the requirement of any prescription have resulted in self-medication of these drugs for viral infections and for other irrelevant illnesses. Moreover, widespread quackery as well as failure to adhere to standard treatment guidelines and inadequate or absence of local antimicrobial drug resistance surveillance programs have allowed the pathogens to grow resistant to most antibiotics largely unnoticed.

CONCLUSION

An overall high prevalence of *E. coli* causing UTI in patients with USD. For gram-positive isolates, low levels of resistance were detected against teicoplanin, linezolid and vancomycin while gram-negative isolates were most sensitive to colistin, meropenem and imipenem. Hence, these could be used as empirical therapy for urinary stone patients having UTI in the study area. Multi-drug resistant urinary tract bacteria are becoming widespread in patients with USD, probably due to frequent and unwarranted use of antibiotics.

Author's Contribution:

Concept & Design of Study:	Hafiz Muhammad Aeymon
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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