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A Study on Positive Stone Culture and its Association with Rate of Sepsis after Urological Procedures

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A B S T R A C T

This prospective study was done to determine correlation between urine and/or stone cultures with postoperative sepsis in patients treated for renal and ureteral calculi. This prospective study was carried out in Department of Microbiology, Government medical college Kota between July 2015 and June 2016. The incidence of renal stone was more in male (N 70) (70%) as compared with female (N 30) (30%) i.e., in the ratio of 2:1. Urine culture was positive more in females (63.67% in female vs. 37.32% in male approx. ratio 2:1), however infected stone rates are almost similar in male and female (64.67% in male vs. 62.60% in female). Out of 100 patients 43 cases showed infection in preoperative urine culture, while rests 57 were sterile. Similarly 64 patients were positive for stone culture and rest 36 were sterile. 28 patients had both stone and urine culture positive. Most common bacteria isolated in urine culture were *E. coli, Klebsiella* positive urine culture) cases. Post operatively 35% (N 35) patient show signs of SIRS. Out of 35 patients who had sepsis 30 patients were positive for stone culture while 20 patients were positive for urine culture. The result was significant on chi square test (Observed P value is 0.036). The results of this study suggest that in patients undergoing surgery for urolithiasis, stone cultures are better predictors of urosepsis than bladder urine C and S. Positive stone culture may guide clinicians regarding selection of antibiotics, especially in cases of severe

Introduction

USD is an expanding problem. Approximately 10% of people will have a urinary stone during their lifetime (1). The key component in urinary stone formation is supersaturation, a process by which the concentration of substances in urine, such as calcium and oxalate, exceed the limits of their solubility (2). The bacterial contribution to USD formation has long been recognized. Incidence of urinary tract infection in stone patients varies from 7% to 60% reported in previous studies. The predominant bacteria found in the nuclei of urinary calculi are *Staphylococcus* and *Escherichia coli*. Urea splitting organisms like Proteus, *Pseudomonas* and *Klebsiella* are under the urine alkaline and hence are known to promote stone formation in both clinical and experimental studies. These are the required conditions for the formation of magnesium

ammonium phosphate calculi which are generally staghorn. Other bacteria like *E. coli* commonly observed in urinary infection are not urea splitting. (3) For study of aetiology and treatment of patients with urinary calculi it is necessary to perform urine and stone culture. Urinary tract infection and urinary stone can trigger a Systemic Inflammatory Response Syndrome (SIRS) before, during or after medical treatment (i.e. antibiotics) and/or surgical manipulation of infected urinary stones. It is believed that SIRS is due to the release of bacteria and their endotoxins from infected urinary stones, developing endotoxemia, bacteremia and urosepsis. Stone may be infected with a different organism than that infecting the bladder and urine. Low Penetration of antibiotics in the stone prevents complete eradication of urinary tract infection by conventional antibiotic therapy and thus leads to development of resistant organisms with intermittent shedding in urine. In this prospective study we shall determine the correlation between different sites of urine sampling, including stones.

Materials and Methods

This prospective study was carried out in Department of Microbiology, Government medical college Kota between July 2015 and June 2016.

Patients with urogenital malignancy, others cause of sepsis and those who were severely immunocompromised were excluded from the study. Before giving antibiotic treatment pre-operative mid-stream sample of urine was collected in sterile container after cleaning the external genital organs. Samples were inoculated using calibrated (4mmdia.) loop on blood agar and MacConkeys agar. Cultures were incubated at 37°C for 24 hours. Also microscopy and Gram stain of urine samples were performed. 3-7If no growth observed after 24 hours of incubation samples were considered sterile. The identification of bacterial isolate was done by using standard biochemical test. Antibiotic sensitivity was done by using disc diffusion (Kirby and Baur) method. The sensitivity of organisms to antibiotics will be studied (Ampicillin, chloramphenicol, tetracyclin, floroquinolones, cephalosporin group of antibiotics, imepenem, meropenem aminoglycosides, macrolide group of antibiotics, linezolid etc. Urinary calculus was collected after the operation in a sterile container. Culture of calculus by giving 4-5 washes and finally by crushing the calculus in sterile mortar and pestle with 5ml in sterile saline, The crushed calculi core was cultured in 5 ml thioglycolate broth which was incubated at 37°C for 18-24 hours, and then subcultures were made on blood agar and Mac Conkey's agar plate for isolation of etiological agents (9,10,11). Cultures were incubated at 37°C for 24 hours. The growth from culture plates were examined for number of colonies. The identification of bacterial isolates was done by conventional methods. Also the antibiotic sensitivity of bacterial isolates was done by using disc diffusion (Kirby Baur) method (8)

Results and Discussion

Total 100 cases of urolithiasis were enrolled in this study out of which70 were male and 30 were female.

Out of 100 patients observed 43 cases showed infection in preoperative urine culture, while rest 57 were urine culture sterile. Similarly 64 patients were positive for stone culture and rest 36 were sterile. 28patients had both stone and urine culture positive.

Urine culture was positive more in females (63.67% in female vs. 37.32% in male approx. ratio 2:1), however infected stone rates are almost similar in male and female (64.67% in male vs. 62.60% in female).

Most common bacteria isolated in urine culture were *E. coli* (24.44%), *Klebsiella* (17.77%), *Pseudomonas* (13.33%) coagulase negative Staphylococcus (17.77 and *Enterococcus* 8.88%), etc.

Preoperative urine culture results

Most of the bacteria isolated from urine culture were resistant to all antibiotics (32.33%), 33.11% of these showed sensitive to carbapenem group of antibiotics, 25.67% to third generation cephalosporin, 21% to floroquinolons and 17.71% to aminoglycosides.

The comparison of micro-organisms isolated from pre-operative urine, showed that *E. coli* was predominant whereas from predominant organism isolated from crushed stone core culture was *Klebsiella*.

Most of these organisms (40%) were resistant to all antibiotic, 36% show sensitivity to carbapenem group of antibiotic, 16% to 3rd generation cephalosoprins, 12 % to floroquinolons and 10% to aminoglycosides

Stone culture was done in all 100 cases, out of which 64% of stone were culture positive. In 20 patients previous urine culture was positive and in remaining 24 patients previous urine culture was negative (only stone culture positive).

Post operatively 35% (N 35) patient show signs of SIRS. Out of which 30 were stone core culture positive. 20 Patients had urine culture positivity. p value was significant in for both urine and stone culture.

Bacteria and USD are clinically associated because they often occur in the same patients and USD patients often have positive urine and/or stone cultures. Antibiotics prophylaxis has been done in accordance with European Association of Urology (modified from Infectious Diseases Society of America, and European Society of Clinical Microbiology and Infectious Diseases) guidelines.12 Urosepsis and shock have been found to occur in direct proportion to the duration of the procedure, urine bacterial load, severity of obstruction by stone and infection in the stone. 13 O'Keefe *et al.,* retrospectively reviewed a series of 700 patients undergoing upper tract manipulation. 14 Rao *et al.,* observed minor forms of septicemia in 37% of 27 patients undergoing PCNL. 15

Our study was conducted on 100 patients of urolithiasis which include identification of causative micro-organisms from preoperative urine and crushed stone core culture.

In our study we found that infected urine is more common in females as compared to male (approx. ratio 2:1). However infected stone rates are almost similar. The higher incidence of renal stones in males in comparison to females may be due to higher serum testosterone level favours increased endogenous oxalate production by liver which in turn predisposes to oxalate stone formation. Moreover, increased urinary citrate concentration in females may help in protection against calcium urolithiasis.16

Increased incidence of recurrent urinary tract infection in females is due to close proximity of urethra to anus, short urethra and sexual activity additionally serves to increase chance of bacterial contamination of female urethra. The pregnancy causes anatomical and hormonal changes that favour development of urinary tract infection. A change in genitourinary tract mucosa due to menopause may play a role in colonization of the introit us by coliforms, a major background factor for recurrent bladder infection in females.17

In our study urinary stones were mainly observed in kidney (64%) and urinary bladder (21%) as compared to stones in ureter (15%).

Baron, Peterson *et al.,* 17 found that 82.97% kidney stones were found to be sterile on culture whereas in urinary bladder, infection stones were more frequent (48.57%). High rates of kidney stones are present as it acts as the first barrier filter for crystals and the damaging tubular epithelium which acts as nidus for stone formation.

In our study Urine cultures were positive in 43% of patients. Whereas in a study by Bratell *et al.,* who reported 60% of patients with positive urine cultures.18. In present study *E. coli* (27%) is predominant isolated organism from urine culture. It correlates well with Jennis *et al.,* they found *E. coli* (25.7%). In present study *Klebsiella* (49.23%) was most frequently isolated from stone culture. Whereas in a study by Gault *et al.*, *Pseudomonas* was the predominant isolate.19 In a study by Songra *et al.,* (20) *Pseudomonas* was the predominant isolate.

Table.1 Distribution of patients with urolithiasis

Type of urolithiasis	No. of patients
Renal stone	30
Pelvic stone (Staghorn)	34
Ureteic stone	13
Vesical stone	23
Total	100

Table.2 Results of urine and stone culture

Specimen	Positive	Negative	P value
Preoperative urine culture	43	57	<0.05 significant
Post-operative stone core culture	64	36	

Table.3 showing various organism isolated from preoperative urine culture

Organism	No. of patients (N=43) (%)
E. coli	12(27%)
***Klebsiella* spp**	8(18.6%)
Pseudomonas	8(18.6%)
CONS	7(16.2%)
Proteus	4(9%)
Enterococcus	2(4%)
Citrobacter frendii	2(4%)

Table.4 Post-operative stone culture

Organism	No. of patients (N=64)
Klebsiella	29(45.3%)
Pseudomonas	27(42.18%)
E. coli	21(32.8%)
Proteus	14(21.8%)
CONS	02(3%)
Citrobacter	01(1.5%)

Table.5 Comparison between urine and stone culture and occurrence of sepsis

Name of specimen	Total No. of patients	Sepsis present	Sepsis absent	P value
Stone culture positive	64	30	34	P value <0.05, significant
Stone culture negative	36	05	31	
Urine culture positive	43	20	23	P value <0.05, significant
Urine culture negative	57	15	42	

Table.6 Culture in patients of sepsis

CULTURE	Sepsis present	Sepsis absent	P value
STONE	30	05	P value <0.05, significant
URINE	20	15	

In a similar study of 328 patients Jairam R. Eswara and Ahmad Sharif *et al.*, found that 3% (11/328) developed postoperative sepsis. 73% (8/11) had positive stone cultures.

While none had a positive preoperative urine culture. 8% (8/96) with positive stone cultures and 1% (3/232) with negative stone cultures developed sepsis (P = 0.003).

These results suggest that stone culture is more informative than preoperative urine culture for determining treatment of postoperative sepsis.21

In conclusion, the results of this study suggest that in patients undergoing surgery for urolithiasis, stone cultures are better predictors of urosepsis than bladder urine C&S. Many times urine C&S may be negative or stones may be infected with different organism, in such cases positive stone culture may guide clinicians regarding selection of antibiotics, especially in cases of severe life threatening urosepsis.

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