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A comparison of pre-operative urine culture with intra-operative stone culture: a prospective observational study

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Abstract

Background: It is well known that urinary calculi are associated with urinary tract infections. Post-operative sepsis is one of the major complications after various endourological procedures for stone surgeries. These episodes of sepsis occur even in negative urine cultures. Stones have been found to harbour bacteria which on fragmentation causes bacteremia and sepsis. Thus, usual practice of pre-operative urine culture cannot truly predict the occurrence of post-operative sepsis. It also seems logical that intra-operative stone cultures could guide us for early management of such episodes of sepsis. The purpose of this study was to determine if there exists any association between urine and stone cultures in patients undergoing endourological stone surgeries.

Methods: This is a prospective comparative observational study, in patients undergoing endoscopic procedures for calculus in urinary tract. Mid-stream urine cultures were obtained 3 to 5 days prior to surgery and crushed stone culture during the surgery. Comparison was then made between the two with respect to positivity, location of calculus and bacterial flora.

Results: A total of 122 cases of urolithiasis were included, in which 30 (24.59%) cases had a positive urine culture, whereas 62 (50.82%) patients were positive for stone culture. This significant difference was maintained only in renal stones on subset analysis (p value < 0.0001). Both cultures were positive in only 15% of cases, and bacteriological analysis showed same organism in just 6.5% of cases. In our study, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of urine culture against the stone culture were 29.03%, 80%, 60%, 52.17% and 54.09%.

Conclusion: The results of our study suggests that pre-operative urine cultures have a poor predictive value and accuracy for infective organism in the renal stone. Therefore, stone culture should be included in routine protocols during renal endourologic surgery for stones.

Keywords: Mid-stream urine culture, Stone culture, Urosepsis, Endoscopic procedures, Cost-effective

1 Background

Urinary tract infections (UTIs) and urosepsis remain among the most common reasons for urological consultation both pre- and post-operatively, increasing the cost of medical treatment, morbidity and mortality. Urinary calculi have been well known to be associated with infection for many years [1]. This association between urinary calculi and infection can trigger a systemic inflammatory response syndrome (SIRS) before, during or after medical and/or surgical treatment [2]. It is also not uncommon for patients with a sterile pre-operative urine culture to develop post-operative sepsis after stone manipulation or fragmentation possibly because of release of bacteria

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in blood stream [3, 4]. This condition may even progress to multi-organ failure and even death if not managed promptly and aggressively. Thus, urosepsis in post-operative period may prove to be catastrophic despite adequate pre-operative antibiotic coverage, and negative urine culture. Bacterial flora of the stone could thus be used as an early guide for treatment or prevention of post-operative urosepsis. Stone culture is not a usual practice in endourologic surgeries, and pre-operative urine cultures have been heavily relied on for treatment of post-operative infections and sepsis. The aim to of this study was to find association between pre-operative urine culture and intra-operative stone culture obtained during endourologic procedure so as to predict whether urine culture can be used as a surrogate marker for stone bacterial flora.

2 Methods

This non-randomized observational study was conducted from May 2019 to October 2019 after appropriate approval from local ethics committee of our institution (Approval No. 287 MC/EC/2019). In this study, we analysed culture specimens, namely midstream urine (MSU) and crushed stones culture of 122 patients after endoscopic procedures. Urine cultures were obtained 3–5 days prior to scheduled surgery. All patients with negative pre-operative urine culture were given a single shot of ceftazidime 1g IV 2 h before the urological procedure and patients who had a positive urine culture were treated with antibiotics for 3 to 5 days before surgery based on sensitivity. Stone fragments were aseptically collected during the procedure and were sent for culture and antibiotic sensitivity.

2.1 Inclusion criteria

Both male and female between age of 18 and 70 years with urolithiasis (renal, ureter or bladder calculi) without prior treatment or instrumentation.

2.2 Exclusion criteria

(1) Patients with urogenital malignancy.
(2) Patients with others causes of sepsis.
(3) Severely immune compromised patients (diabetes, HIV, etc.)
(4) Patients already on broad spectrum antibiotic before obtaining urine culture.
(5) Patients on steroids.
(6) Patients with congenital urologic anatomical anomalies.
(7) Patients on prolonged catheterization or stents.

2.3 Urine culture studies

MSU samples were obtained with all necessary precautions. After inoculation on MacConkey agar, samples were incubated at 37 °C for 24 h. If no growth was observed after 24 h, incubation samples were considered sterile. The colony characteristics of the growth from culture plate were examined after 48 h and studied for morphology, motility, biochemical test and antibiotic sensitivity. Antibiotic sensitivity was done by using disc diffusion method. The sensitivity of organisms to antibiotics was studied using standard techniques.

2.4 Stone culture studies

Calculi were collected during the procedure in a sterile container and washed multiple times in sterile normal saline. These were then crushed before being subjected to culture, and the crushed calculi core was cultured in blood agar and Mac Conkeys agar and incubated at 37 °C for 48 h. The growth from culture plates was examined for a number of colonies. The colony was studied for morphology, motility and biochemical reactions. The identification of bacterial isolate was done by conventional methods. Also, the antibiotic sensitivity of bacterial isolates was done by using disc diffusion method.

3 Statistical analysis

Descriptive and inferential statistical analysis was carried out in the using computer software (SPSS Trial version 23). The qualitative data were expressed in proportion and percentages, and the quantitative data expressed as mean and standard deviations. The difference in proportion was analysed by using Chi-square test. Significance level for tests was determined as 95% ($p < 0.05$).

4 Results

Of the 122 cases of urolithiasis enrolled in this study, 74 (60.65%) were male and 48 (39.34%) were female (M/F ratio was 1.5:1) with mean age of 39.14 ± 15.68 years. All patients were divided into 3 groups according to the location of calculus. Among the study population, 24.59% had a positive pre-operative urine culture, whereas 50.82% patients were positive for stone culture (Table 1).

Most common bacteria isolated in urine culture were *E. Coli* (33.3%), followed by Pseudomonas (26.67%), Enterococcus (13.33%), Enterobacter (13.33%), coagulase-negative Staphylococcus aureus and Klebsiella (6.67% each). The most common bacteria isolated in stone culture was Pseudomonas followed by Enterobacter, *E. coli* and others (Table 2).

On comparing the result of bacteriological analysis of stone and urine culture, it was seen that only 18 (14.75%) patients were positive for both stone and

Table 1 Distribution of patients with urolithiasis

		No. of patients (*N* = 122)
Sex	Male	74 (60.65%)
	Female	48 (39.34%)
Location of stone	Renal stone	96 (78.68%)
	Ureteric stone	16 (13.11%)
	Vesical stone	10 (8.19%)
Pre-operative urine culture	Positive	30 (24.59%)
	Negative	92 (75.41%)
Post-operative stone culture	Positive	62 (50.82%)
	Negative	60 (49.18%)

urine culture of which same organism was isolated in only 8 patients (6.56%). It was also found that 12 patients (9.83%) had positive urine culture and negative stone culture, whereas 44 patients (36.06%) had positive stone culture and negative urine culture (Table 3).

On subgroup analysis based on location of the stone, significant variance in MSU and stone culture was only apparent in renal stones (p value < 0.0001) (Table 4).

When overall urine cultures were cross-tabulated with stone cultures, no significant association was found between the two based on Chi-square analysis ($p = 0.241$) (Table 5).

Using these data, we calculated sensitivity, specificity, PPV, NPV and diagnostic accuracy of urine culture against the stone culture to be 29.03%, 80%, 60%, 52.17% and 54.09%. It is however important to note

Table 3 Bacteriological analysis of stones and urine culture

		No. of patients (*N* = 122)
Both positive	Same organisms in both cultures	8 (6.56%)
	Different organism in both cultures	10 (8.19%)
Urine culture positive and stone culture negative		12 (9.83%)
Urine culture negative and stone culture positive		44 (36.06%)
Both negative		48 (39.34%)

that bacteriological concordance between the cultures is just 6.56%.

On further analysis, we found that the same result (both negative and both positive culture with same organism growth) was seen in 45.9% of cases (56/122), while different result (either growth only in one culture or both positive with different organism growth) was seen in 54.1% of cases (66/122). Thus, we found that urine culture cannot determine the bacteriology of stone with precision.

5 Discussion

Obtaining MSU culture has been a standard practice prior to any stone surgery. This is usually done at least a week prior to surgery and treated with appropriate antibiotics for 3–5 days. It is then repeated to confirm sterility of the urine. Antibiotic prophylaxis before endourological procedure is given in accordance with standard guidelines [5]. Even with proper pre-operative preparation and sterile urine cultures, patients still develop systemic and sometimes catastrophic infections [6, 7]. As per the literature, post-PCNL sepsis can occur

Table 2 Culture results

	Organism	No. of patients
Mid-stream urine culture	*E. coli*	10 (33.33%)
	Pseudomonas	8 (26.67%)
	Enterococcus	4 (13.33%)
	Enterobacter	4 (13.33%)
	Coagulase-negative staph	2 (6.67%)
	Klebsiella species	2 (6.67%)
Intra-operative stone culture	Pseudomonas	20 (32.25%)
	Enterobacter	12 (19.35%)
	E. coli	10 (16.13%)
	Coagulase-positive staph aureus	8 (12.9%)
	Enterococcus	4 (6.4%)
	Proteus	4 (6.4%)
	Citrobacter	2 (3.22%)
	Klebsiella species	2 (3.22%)

Table 4 Comparison of urine and stone culture based on stone location

	Urine culture positive	Stone culture positive	*p* Value
Bladder ($n=10$)	2	6	0.0752
Renal ($n=96$)	28	56	< 0.0001
Ureter ($n=16$)	0	0	–
p Value	0.54	0.92	

Table 5 Comparing of urine culture with stone culture results

Urine culture	Stone culture		Total
	Positive (*N*)	Negative (*N*)	
Positive	18 (60%)	12 (40%)	30
Negative	44 (47.82%)	48 (52.17%)	92
Total	62	60	122

**Chi-square = 1.342 with 1 degree of freedom; $p=0.241$

in 10–15% of cases [8]. Various risk factors have been associated with sepsis with common ones including long duration of the procedure, urinary bacterial load, severity of obstruction by stone and infection in the stone [3]. Other risk factors described in the literature include use of nephrostomy tube, renal insufficiency, amount of irrigation fluid used and high fluid pressure during operative procedure [4, 9, 10]. It is a usual practice to obtain a pre-operative mid-stream urine culture and procedure is undertaken with antibiotics based on its culture results. However, several authors have reported a poor concordance between organism in the stone and bladder urine specimens [8, 11]. In the series by Fowler et al, stone culture was positive in 77% of the patients, whereas a simultaneous bladder urine sample was positive in only 12.5% of the patients [12]. Another study by Mariappan et al. also reported discordance between urine and stone culture with MSU culture being positive in only 11.1%, whereas stone culture positivity was in 35.2% cases [3]. Devraj et al in 2016 also reported stone culture positivity in 30.1% compared to MSU positivity in just 10.8% of the patients [13].

In our study, we found that the stone culture was positive in 50.82% of patients, whereas mid-stream urine culture was positive in 24.59% of patients. We also observed that urine culture has a poor sensitivity, specificity, PPV, NPV and diagnostic accuracy to predict stone culture positivity. Another interesting observation in our study was that urine cultures and stone cultures vary significantly in cases of renal stones where stone cultures were found to be positive in significantly larger patients (58.3%) as compared to pre-operative MSU cultures (29.16%) (p value < 0.0001). This, however, was not true for bladder stones. Since in patients of ureteric stones, none of cultures turned out to be positive, association cannot be made, thereby limiting our interpretation for the same. Thus, the above observation of difference between MSU and stone cultures appears to be most important in cases of renal stones.

Microbiology of stone and urine predominantly includes gram-negative bacterial infection with fewer infections by gram-positive organisms [14]. In our study, most common organism isolated in stone culture was *Pseudomonas aeruginosa* and Enterobacter and those in urine culture were *E. coli* and Pseudomonas. These results corroborate with the present literature [14]. However, we noted that most often identified organism in both samples differ which was also found in the study by MC Songra et al in 2015 [2]. In their study, they also found bacteriology of stone as a better predictor of post-operative sepsis than urine culture. Annerleim Walton-Diaz et al in their study also demonstrated that urine culture and stone cultures were discordant and that post-operative sepsis correlated significantly with intra-operative stone cultures rather than pre-operative urine culture [8].

Thus, stones in kidney have higher chances of harbouring microorganisms when compared with urine and a negative urine culture does not rule out infection within the stone. Microbiological environment of the stone is also quite different from that found in urine. Thus, stones remain one of the most important sources of sepsis post-operatively. Various studies have demonstrated positive association of stone culture and post-operative sepsis specially when pre-operative urine cultures were negative [2, 3, 8, 13]. Stone cultures can be easily obtained at the time of surgery at minimal additional cost. This not only reduces the hospital stay but overall cost of treating an episode of post operative sepsis. This not only reduces the hospital stay but overall cost of treating an episode of post operative sepsis. This study thereby brings to light the importance ofintra-operative stone culture in addition to routine use ofurine culture.

6 Conclusions

Urine culture has poor predictive value and accuracy to predict bacteriology of stone and therefore, cannot be used as a surrogate marker for it. This has maximal clinical significance in cases of renal stones. Hence, obtaining stone cultures during PCNL is a valuable practice that should be included as a routine protocol.

7 Limitations

One of the limitations of this study was that it included microbiological aspects of endourologic procedures for stones and differences were not compared with post-operative sepsis. Study also did not include differences in susceptibility to antibiotics even when the same organisms were found in urine and stone cultures. Thirdly, stones parameters like size and composition were not evaluated against bacteriology, and only associations with urine cultures were considered.

Abbreviations

UTI: Urinary tract infections; SIRS: Systemic inflammatory response syndrome; MSU: Mid-stream urine.

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None.

Authors' contributions

AG helped in study concept, design, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, editing and review. NV contributed to study concept, design, manuscript editing and critical review. GS contributed to manuscript editing and review. SP helped in manuscript editing and review. DM contributed to manuscript review. PS helped in data analysis, statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The present study protocol was reviewed and approved by the Ethics committee of SMS Medical College and attached Hospitals, Jaipur (Approval Number 287 MC/EC/2019). Written informed consent was obtained by all subjects when they were enrolled.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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