Original Article

DOI: 10.7860/IJARS/2023/62084.2945

Post-percutaneous Nephrolithotomy Urosepsis: Does Stone Culture Add Value?

Surgery Section

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ABSTRACT

Introduction: Percutaneous Nephrolithotomy (PCNL) is the most commonly performed intrarenal surgery worldwide for the management of renal stones. Despite the administration of perioperative antibiotic prophylaxis, a significant number of patients develop Systemic Inflammatory Response Syndrome (SIRS), and several research articles have reported post-PCNL sepsis in 0.4-3% of cases. Despite having a sterile preoperative urine culture, the incidence of sepsis mentioned above could possibly be attributed to the presence of organisms in the stone. These organisms may enter the bloodstream during surgery and manifest as urosepsis.

Aim: To determine whether the microbial spectrum of preoperative urine and postoperative stone culture can serve as predictors of urosepsis.

Materials and Methods: A prospective observational study was conducted at the Department of Urology at Bharati Medical College and Hospital, Pune, Maharashtra, India involving all patients (sample size=167) undergoing PCNL between August 2019 and July 2021. The PCNL procedure was performed according to standard guidelines. To obtain a renal stone culture, authors followed the technique described by Nemoy NJ and Stamey TA. Postoperatively, patients were closely monitored for signs of systemic inflammatory response. Demographic and continuous variables were summarised using mean and standard deviation, while categorical variables (such as urine culture and stone culture, organisms isolated) were summarised using frequency and percentage. Statistical analysis was performed using unpaired t-test for quantitative variables and Chi-square test for qualitative variables, with a significance level set at 5%.

Results: The mean age of the study participants was 39 years. Although the spectrum of organisms differed in many cases, *E.coli* (11.4% versus 12.6%) was more prevalent in stone cultures compared to *Enterococcus* (9% versus 7.2%). *Staphylococcus saprophyticus* (66.6%) was isolated from stone cultures, while *E.coli* (66.6%) was predominant in urine cultures. Sepsis/SIRS was effectively managed with antibiotic treatment based on stone culture (p=0.001) rather than urine culture (p=0.047).

Conclusion: Routine stone culture not only helps in better prediction of potential sepsis but also guides the appropriate choice of antibiotics for sepsis management.

Keywords: Intrarenal surgery, Microbial spectrum, Mid-stream sample of urine

INTRODUCTION

Urolithiasis is a significant urological problem in our region. Renal stones significantly contribute to the morbidity of urological diseases. Percutaneous Nephrolithotomy (PCNL) is the most commonly performed intrarenal surgery for the management of renal stones [1]. At the study Institute, all modalities of percutaneous surgeries (such as PCNL, Mini perc, Ultra-mini perc, Retrograde intrarenal surgery) are routinely used for the treatment of renal stones. Following PCNL, 10% to 35% of patients may experience Systemic Inflammatory Response Syndrome (SIRS), with a small percentage developing sepsis [1]. Postoperative fever and urosepsis/SIRS, if not promptly treated with appropriate antibiotics and support, can have catastrophic consequences. According to guidelines, a sterile preoperative urine culture is recommended. Patients undergoing PCNL receive appropriate antibiotic coverage for at least 24 hours or longer if, necessary. However, despite perioperative antibiotic prophylaxis, many patients still develop SIRS and sepsis. Several research articles have reported post-PCNL sepsis in the range of 0.4-3%, even with a sterile preoperative urine culture [2,3]. One possible source of infection could be the presence of organisms in the stone, which enter the bloodstream following breakage and manipulation during surgery, leading to urosepsis.

Mariappan P et al., conducted a study involving 54 patients comparing pelvic urine and stone culture with Midstream Urine Sample (MSUS). They found that stone culture strongly correlated with episodes of sepsis [4]. Similarly, Walton-Diaz A et al., conducted a study involving 122 patients and noted a weak correlation between urine culture and infective complications, as compared to pelvic urine and stone culture [5].

There are also reports suggesting that other factors such as prolonged intraoperative time, residual stone, and patient co-morbidities may also contribute to the development of postoperative urosepsis. While the American Urological Association (AUA) does not recommend routine stone culture, the European Urological Association (EAU) suggests that intraoperative renal stone culture may help in selecting postoperative antibiotics [4,5].

Therefore, authors decided to investigate stone culture as a possible and logical source of infection leading to urosepsis in the post-PCNL setting. Authors excluded pelvic urine culture from the study, as it may be well represented in the bladder sample, as the same urine flows from the pelvis to the bladder. The present study aimed to assess the microbial spectrum of preoperative urine and postoperative stone culture and to determine the association between episodes of sepsis and urine and stone culture.

MATERIALS AND METHODS

A prospective, observational study was conducted at the Department of Urology from August 2019 to July 2021 on a sample size of 167 patients undergoing PCNL at Bharati Medical College and Hospital, Pune, Maharashtra, India. All necessary approvals from the Ethical Committee were obtained (BVDUMC/IEC/14), and written informed consent was obtained from all participants.

Inclusion criteria: The study included all patients of both sexes, aged 9-75 years, undergoing PCNL.

Exclusion criteria: Patients with a stent or PCN In-situ, those on dialysis, and patients with features of acute pyelonephritis were excluded from the study.

Study Procedure

All patients underwent a detailed history taking and physical examination. Laboratory investigations, including haemogram, renal function tests, blood sugar level, coagulation profiles, urinalysis with urine culture and sensitivity, and intraoperative stone culture, were performed as required. Appropriate antibiotics were administered preoperatively based on the sensitivity pattern if urine culture showed evidence of infection. Patients with no positive urine culture were started on prophylactic antibiotic Cefuroxime 1.5 gm twice daily for 24 hours postoperatively. Surgery was scheduled after achieving sterile preoperative urine whenever possible. PCNL was performed following standard guidelines and procedures [6-8]. The Nemoy NJ and Stamey TA technique was used to obtain a renal stone culture [3]. This involved taking a sample of the extracted stone fragments, rinsing them in 0.9% normal saline (five times), crushing them with a sterile instrument, and sending them in a sterile tube with a small amount of 0.9% normal saline for microbiological evaluation as a stone culture.

Postoperatively, patients were monitored for systemic inflammatory response, characterised by two or more of the following conditions:

- Body temperature below 36ºC or above 38ºC.
- Heart rate greater than 100 beats per minute.
- Respiratory rate greater than 20 breaths per minute.
- Leukocyte count greater than 12,000 white blood cells per cubic mL or fewer than 4,000 white blood cells per cubic mL. Blood cultures were drawn in all patients who met the SIRS criteria [9].

Intravenous antibiotics were discontinued after 24 hours in patients without SIRS. Vitals were monitored every four hours, and postoperative X-rays were performed to check for residual stones.

STATISTICAL ANALYSIS

Demographic and continuous variables were summarised using the mean and standard deviation, while categorical variables were summarised using frequency and percentage based on the outcome or exposure variables. The association between outcome and exposure variables was analysed using the chi-square test to determine the significance. A p-value <0.005 was considered statistically significant.

RESULTS

Among the total study 176 participants , there were 85 (50.9%) females and 82 (49.1%) males. The age range of the study participants was 9-75 years, with mean age of 39 years. *Escherichia coli* was prevalent in urine culture in 19 cases (11.4%), while *Enterococcus* was prevalent in 15 cases (9.0%). *E. coli* was prevalent in stone culture in 21 (12.6%) cases while *Enterococcus* was prevalent in 12 (7.2%) cases. Sepsis occured in 3 (1.8%) cases while, fever and tachycardia was seen in 34 (20.4%) cases. Respiratory rate was higher in 3 (1.8%) cases [Table/Fig-1]. The association between stone culture and episodes of sepsis was highly significant (p=0.001) [Table/Fig-2].

Variables		Count	n (%)
Sex Age range (9-75 years) Mean age: 39 years	Female	85	50.9%
	Male	82	49.1%
Preoperative organism isolated urine culture	*Candida*	8	4.8%
	Escherichia Coli	19	11.4%
	Enterococcus	15	9.0%
	No growth	91	54.5%
	Others	12	7.2%
	Proteus	10	6.0%
	Staphylococcus saprophyticus	12	7.2%
Stone culture	*Candida*	8	4.8%
	Escherichia Coli	21	12.6%
	Enterococcus	12	7.2%
	No growth	102	61.1%
	Others	7	4.2%
	Proteus	7	4.2%
	Staphylococcus saprophyticus	10	6.0%
Sepsis (Yes/No)	N	164	98.2%
	Y	3	1.8%
Fever (°C)	N	133	79.6%
	Y	34	20.4%
Tachycardia	N	133	79.6%
	Y	34	20.4%
Respiratory rate (breaths/min)	High (More than 20 breaths/min)	3	1.8%
	Normal (12-20 breaths/min)	164	98.2%

[Table/Fig-1]: Bacterial spectrums of urine culture and stone culture.

Variables		Sepsis (Y/N)				p-value*
		N		Y		
		Count	n (%)	Count	n (%)	
Gender	Female	83	97.6%	2	2.4%	0.581
	Male	81	98.8%	1	1.2%	
Preoperative organism isolated in urine culture	*Candida*	8	100.0%	0	0.0%	0.049
	Escherichia Coli	17	89.5%	2	10.5%	
	Enterococcus	14	93.3%	1	6.7%	
	No growth	91	100.0%	0	0.0%	
	Others**	12	100.0%	0	0.0%	
	Proteus	10	100.0%	0	0.0%	
	Staphylococcus saprophyticus	12	100.0%	0	0.0%	
Stone culture	*Candida*	8	100.0%	0	0.0%	0.001
	Escherichia Coli	20	95.2%	1	4.8%	
	Enterococcus	12	100.0%	0	0.0%	
	No growth	102	100.0%	0	0.0%	
	Others**	7	100.0%	0	0.0%	
	Proteus	7	100.0%	0	0.0%	
	Staphylococcus saprophyticus	8	80.0%	2	20.0%	

[Table/Fig-2]: Culture and sepsis association.
Chi-square test was used; **Others include mixed bacterial flora: Urine (4), Stone (0), *Klebsiella oxytoca*: Urine (3), Stone (1), *Stapylococcus hominis*: Urine (2), Stone (3), *Citrobacter freundii*: Urine (3), Stone (3)

DISCUSSION

Post-PCNL sepsis is a serious complication that not only poses a threat to life but also significantly increases hospitalisation costs. The reported incidence of sepsis after PCNL in the literature ranges from 0.9% to 4.7% [2,10]. There are several reasons why sepsis may occur after PCNL, including stone manipulation and fragmentation, prolonged surgery duration, female gender, use of nephrostomy tube, amount of irrigation fluid used, and renal insufficiency [11-13]. Bacteria present within the stones and pelvic urine can be released and introduced into the patient's circulatory system through reflux in the pyelotubular, pyelolymphatic, and pyelovenous pathways. Elevated intrarenal pressures during surgery can exacerbate this reflux [12]. The bacteria and associated endotoxins that enter the bloodstream subsequently trigger

multiple inflammatory processes that lead to Systemic Inflammatory Response Syndrome (SIRS). Authors institute is a tertiary referral centre that deals with complex stones, including staghorn calculi. Despite the complexity of cases, the incidence of sepsis in present study was low (1.79%). This can be attributed to the strict protocols authors followed to prevent infection. It is important to be able to predict the occurrence of infection/sepsis in the preoperative and postoperative periods in order to provide appropriate counselling to patients and administer appropriate treatment. Preoperative urine culture is a well-known parameter for predicting and preventing postoperative infection/sepsis. However, sometimes infectious organisms may be hidden within stones or may not be shed in the urine. This is particularly important when postoperative fever/sepsis occurs despite a negative preoperative urine culture. Stone culture plays an important role in such cases. It not only helps identify patients who are at risk of developing sepsis, but also guides the selection of appropriate antibiotics for treatment. The microbiology of stone disease has undergone significant changes in recent times, with a shift from predominantly Gram-negative to gram-positive organisms [10,14-17]. In the present study, there was a statistically significant difference in the occurrence of sepsis based on the sex of the patient. However, another study had noted that septic complications are more commonly observed in females [13]. The use of minimally invasive procedures, especially for the clearance of large complex stones, may require repeated endoscopic interventions. This may contribute to changes in the microbial flora of the urinary tract [10].

Mariappan P et al., stated that out of a total of 54 patients suitable for analysis, midstream urine culture and sensitivity were positive in 11.1% of cases, stone Culture and Sensitivity (C&S) were positive in 35.2%, and pelvic C&S were positive in 20.4% (p=0.009) [4]. Pelvic urine C&S was found to be a better predictor of infected stones compared to bladder urine C&S. Among the patients, 37% had Systemic Inflammatory Response Syndrome (SIRS), and three experienced septic shock. Patients with infected stones or positive pelvic urine were found to have a relative risk for urosepsis that was at least four times greater (p=0.0009). Bladder urine did not predict SIRS. Stone C&S had the highest positive predictive value of 0.7. Preoperative hydronephrosis was correlated with infected pelvic urine. None of the patients with urosepsis had positive blood C&S.

However, there are some studies that do not support the use of pelvic urine and stone culture. Singh I et al., in their paper, noted that none of the samples (preoperative urine culture, stone culture, and pelvic urine culture) were sensitive in predicting the occurrence of SIRS/urosepsis in patients undergoing PCNL, with a weak association and poor predictive value [11]. Nevertheless, they recommended the stone culture test, as it may detect stone-colonising bacteria in select at-risk patients to predict potential postoperative sepsis/SIRS. In their study, *E.coli* was the most frequently isolated microbe, followed by *Klebsiella* and *Proteus* [11].

Walton-Diaz A et al., published a similar study involving 122 patients [5]. They noted that positive urine culture demonstrated multidrug-susceptible *Escherichia coli* and *Staphylococcus aureus*, while pelvic urine and stone culture showed multidrug-resistant pathogens and/or fungi. Around 5.7% of patients developed infective complications. There was a weak correlation between urine culture and infective complications compared to pelvic urine and stone culture. The most commonly isolated pathogens in their study were multidrug-resistant bacteria or fungi.

The mineral content of the stone was thought to be an important predictor of bacteria inside the stone. However, Englert KM et al., showed that among positive stone cultures, there was no observed difference among stones of different compositions [18]. Mineral content is an imperfect indicator of the presence of infectious organisms in kidney stones. It may be that some struvite stones developed in the presence of bacteriuria but no longer contain viable organisms. The presence of viable organisms inside stones at the time of surgery is more important for the development of sepsis after PCNL.

Limitation(s)

Due to the small sample size and the fact that it was a single-centre study, the findings cannot be generalised to the entire population.

CONCLUSION(S)

Urine culture and stone culture may have different bacterial spectrums in the same patient. In the event of post-PCNL sepsis, antibiotic treatment based on urine culture alone may misguide the treatment, and a crucial early treatment window may be lost. Stone culture is a better predictor of septic complications and their management. Routinely sending a stone culture at the time of PCNL is recommended for better management of septic complications.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 04, 2023
- Manual Googling: Jun 07, 2023
- iThenticate Software: Jul 03, 2023 (13%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval Obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 03, 2023**
Date of Peer Review: **Apr 05, 2023**
Date of Acceptance: **Jul 04, 2023**
Date of Publishing: **Nov 01, 2023**