Association of Preoperative mid-stream urine culture, Renal pelvic urine culture and Renal stone culture in the detection of Systemic inflammatory response syndrome/urosepsis post Percutaneous Nephrolithotomy

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ABSTRACT

Introduction: Urosepsis post Percutaneous Nephrolithotomy (PCNL) is a dreaded complication with high mortality rate. Objective: To find the association of preoperative midstream urine culture (PMUC), renal pelvic urine culture (RPUC) and renal stone culture (RSC) in the post-operative development of Systemic Inflammatory Response Syndrome (SIRS) and urosepsis. **Methods:** It was a prospective cross-sectional observational study. The study included all symptomatic patients meeting the inclusion criteria who underwent Percutaneous Nephrolithotomy from 18th August, 2019 to 28th March, 2020. PMUC, RPUC and RSC were done and analyzed accordingly. **Results:** A total of 140 (73 males, 67 females) patients underwent PCNL. PMUC was positive in 15% (21/140) as compared to RPUC and RSC which were 7.9 % (11/140) and 4.3% (6/140) of total cases. None of the patients had simultaneous culture positivity in all the three types of specimens. Only two (1.42%) patients had simultaneous positivity in pelvic urine culture and stone culture. The organisms obtained in pelvic urine culture and stone culture were same i.e. Klebsiella and Escherichia coli respectively. Only two (1.42%) patients developed SIRS post PCNL, where in both the cases stone culture were positive but PMUC and RPUC were negative. Urosepsis was found in none of the patients. In the Fischer Exact test PMUC and RPUC were not statistically significant in the detection of SIRS post PCNL. Whereas only RSC showed statistical significance in the detection of SIRS. **Conclusion:** Stone culture has high prediction for SIRS and it might be considered for patients undergoing PCNL in order to prevent stone related infective complications.

Keywords: Percutaneous nephrolithotomy, Sepsis, Urine culture

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INTRODUCTION

Percutaneous Nephrolithotomy (PCNL) is considered as the procedure of choice for a complex and large volume nephrolithiasis in all age groups.[1-3] But the procedure is not devoid of complications as fever occurs in 21% to 39.8% of patients undergoing PCNL.[4] The incidence of urosepsis is 0.3% to 9.3% and the septic shock is 1% in which the mortality reaches up to 66 to 80% post PCNL.[5-8] Hence, the factors leading to urosepsis in PCNL should be considered seriously in order to prevent the dreaded complications.

Factors responsible for post-operative urosepsis are the number of stones, duration of operation, bleeding and presence of residual stones.[9] Despite these factors, preoperative Urinary Tract Infection (UTI) also leads to post-operative urosepsis if urine is not made sterile before PCNL. Antibiotic prophylaxis is advised by the American

Urological Association (AUA) for the prevention of post-operative urosepsis but despite prophylaxis the incidence of urosepsis is 8-10%.[10] Thus control of urinary tract infection (UTI) is needed which is best correlated by Renal Pelvic Urine Culture (RPUC) and Renal Stone Culture (RSC) as compared to Pre-operative Midstream Urine Culture (PMUC).[11]

It is imperative to control UTI to prevent post-operative urosepsis and reduce the morbidity and mortality. Hence, this study aimed to find the association of PMUC, RPUC and RSC in the post-operative development of Systemic Inflammatory Response Syndrome (SIRS) and urosepsis.

MATERIALS AND METHODS

This was a prospective cross-sectional observational study conducted at the Department of Surgery, Lumbini Medical College and Teaching Hospital effectively from 18th August, 2019 to 28th March, 2020. Ethical approval was taken from the Institutional Review Committee of Lumbini Medical College and Teaching Hospital (IRC-LMC 06-G/019).

The sample size was calculated using the formula: Sample Size (S)= Z^2Pq/d^2, where: Z= Confidence Level of 95% (Standard Value – 1.96), P= Estimated Prevalence of Renal Stones (That corresponds to around 10%)[12], q= 1-P, d= Margin of error (0.05), Calculating sample size from above formula, the minimal sample required was 140. So, we decided to take the number of samples of 145.

All patients with renal stone size more than 10 mm in the largest dimension were included in the study, whose stone burden was calculated by multiplying the largest two dimensions of the stone. Patients not giving consent for the study, those having persistent preoperative midstream urine culture positivity and untreated coagulopathy were excluded from the study. Five cases were excluded from the study as three cases did not give the consent and the rest of the two had persistent coagulopathies. Routine preoperative and diagnostic investigations including ultrasonography of abdomen and pelvis, intravenous urogram and the preoperative midstream urine culture (PMUC) were done in all patients along with Computed Tomography –Intravenous urogram (CT-IVU) in selected cases. All patients were treated with empirical antibiotics for three days before the PMUC report arrived and the PMUC negative cases were taken for surgery, whereas for PMUC positive cases, culture specific antibiotics were administered for two weeks prior to the surgery and the PMUC was repeated. In every patient surgery was performed only when the PMUC report came out to be negative. All patients received intravenous antibiotics i.e. third generation cephalosporin (Cefoperazone Sulbactum combination) of dose 1.5gms for adults and 750mg for children along with aminoglycosides (Amikacin) of dose 15mg/kg/day a day prior to the surgery according to the local hospital protocol which was carried out till the third postoperative (POD) day which was then subsequently converted into oral antibiotics continued up to seven days post-operatively.

All patients received the above mentioned intravenous antibiotics one hour before the procedure. Five French (Fr) ureteric catheter was introduced into ipsilateral ureter via 20 Fr cystoscope (Karl Storz, Germany) in lithotomy position and foley's catheterization was done. Later, the position was changed into prone and under fluoroscopic guidance using C-arm (Allengers, India) after the instillation of urografin 76% via ureteric catheter, targeted calyceal puncture was done using 18 Gauge (G) needle. Pelvic urine was aspirated from the puncture site and was sent for the culture in 3ml sterile urine within one hour of collection. Subsequent dilatation of the track with the help of fascial dilators (Cook, Germany) was done using Seldinger's technique with the introduction of 0.035 inches guide wire. After the dilatation of track Amplatz sheath of size 20 Fr were used. Nephroscope (Wolf, Germany) of size 18 Fr was introduced and the stones were visualized and broken down into fragments using lithotripter (Nidhi lith, India). The stones were taken out using forceps. The fragmented stones were washed with normal saline and sent in fresh normal saline for the culture. Double J stent (DJ stent) was routinely kept in all patents. Nephrostomy drain of size 18 Fr was also placed routinely at the end of the procedure. Nephrostomy drains were removed on the third postoperative day while DJ stents were removed three weeks after the procedure. Patients were closely monitored for any signs of SIRS (Systemic Inflammatory Response Syndrome) and urosepsis postoperatively. UTI was defined as urine test having pus cells equivalent to or more than five in number per high power field in microscopic examination.[13] SIRS was defined as patients having two or more of the following criteria i.e. hypothermia (body temperature less than 36 degree Celsius) or hyperthermia (body temperature more than 38 degree Celsius), leukocytosis (total leucocyte count more than 12,000/$mm^{3)}$ or leucopenia (total leucocyte count less than 4,000/mm^3), tachycardia (heart rate more than 90 beats/min) or tachypnea (respiratory rate more than 20 beats/min). Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[14] Sepsis secondary to urinary tract infection was considered as urosepsis.

All the pre, intra and post-operative data were collected in a preformed proforma and entered into Microsoft Excel spreadsheet 2013. The data were checked for consistency and validity. They were then imported to Statistical Package for Social Sciences (SPSS™) software version 16 for statistical analysis. Categorical variables were analysed as the Fisher exact test and chi-square tests to determine associations among the various groups and subgroups. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and association risks were calculated. P value less than 0.05 was considered statistically significant.

RESULTS

There were 140 patients which included 73 males and 67 females. The mean age of the patient was 39.9 ± 14.8 years. The mean operation time was 40.61 ± 13.4 minutes. Table 1 shows mean age, mean operation time and stone burden of the patients under study.

Table 1: Patient and stone demographics

Mean Age ± SD(in years)	39.97±14.87
Mean Stone Burden± SD(in mm^2)	190.97±177.5
Mean Operative Time± SD ((in minute)	40.61 ±13.4

PMUC was the most prevalent culture positive specimen with 21 cases (15%) with Escherichia coli (7.1%) being the commonest organism Isolated. RPUC was positive in 11 cases (7.9%) with Proteus mirabilis (3.6%) infection being the commonest organism cultured. Stone culture was positive in six cases (4.3%) where Proteus mirabilis (1.4%) was the commonest organism cultured. Table 2 depicts the same.

Table 2: Types of organism obtained in PMUC, RPUC and RSC

PMUC positive Organisms cultured (N=21)	Frequency	Percent
Staphylococcus aureus	1	0.7
Mixed growth	1	0.7
Klebsiella	4	2.9
Proteus mirabilis	5	3.6
E.coli	10	7.1
RPUC positive Organisms cultured (N=11)	Frequency	Percent
E.coli	3	2.1
Klebsiella	3	2.1
Proteus mirabilis	5	3.6
RSC positive Organisms cultured (N=6)	Frequency	Percent
E.coli	1	0.7
Klebsiella	1	0.7
Staphylococcus aureus	1	0.7
Pseudomonas	1	0.7
Proteus mirabilis	2	1.4

None of the patients had simultaneous culture positivity in all the three types of specimens. Only two (1.42%) patients had simultaneous positivity in pelvic urine culture and stone culture. The organisms obtained in pelvic urine culture and stone cultures were same i.e. Klebsiella and E.coli respectively. Only two (1.42%) patients developed SIRS post PCNL, where in both the cases stone culture were positive but PMUC and RPUC were negative. Urosepsis was found in none of the patients.

Detection of infection of preoperative midstream urine culture and renal pelvic urine culture were correlated with renal stone culture for the detection of infection in renal stones. True and false positivity along with true and false negativity were calculated for the same, which is depicted in the table no.3

Table 3: Table showing parameters of PMUC and RPUC for the detection of infection in renal stones.

Parameters	Preoperative midstream urine c/s	Renal pelvic urine c/s
True Positive	1	2
True Negative	114	125
False Positive	20	9
False Negative	5	4

PMUC and RPUC didn't show significant association with RSC on Fisher exact test where p value was 1 and 0.071. PMUC in our study showed 16.67% sensitivity, 85.07% specificity, positive predictive value of 4.76%, and negative predictive value of 95.8% in 95% confidence interval (CI), in the detection of infection in renal stones. Likewise, renal pelvic urine showed 33.33% sensitivity, 93.28% specificity, 18.18% of positive predictive value, 96.9% of negative predictive value in 95%CI in the detection of infection in renal stones which is shown in table 4.

Table 4: Predicting infected stones with preoperative midstream urine and renal pelvic urine

Diagnostic accuracy	Preoperative midstream urine c/s (%)	Renal pelvic urine c/s (%)
Sensitivity	16.67	33.33
Specificity	85.07	93.28
Positive predictive value (PPV)	4.76	18.18
Negative predictive value (NPV)	95.80	96.90

PMUC had 0% sensitivity, 84.7% specificity, 0% positive predictive value and 98.3% of negative predictive value in 95% CI for the detection of SIRS in post PCNL patient, where as it was 0% sensitivity, 92.03% specificity, 0% of positive predictive value and 98.45% of negative predictive value in 95% CI in RPUC for the detection of SIRS post PCNL. RSC on the other hand had sensitivity of 100%, specificity of 97.10%, and positive predictive value of

33.33% and negative predictive value of 100% with 95% of CI in the detection of SIRS in post PCNL patients. In the Fischer Exact test PMUC and RPUC were not statistically significant in the detection of SIRS post PCNL the p value was 1 in both the cases respectively. Whereas RSC showed statistical significance in the detection of SIRS in the Fischer Exact test p value is 0.002. Table 5 depicts the same.

Table 5: Predicting SIRS using various specimens

Diagnostic accuracy	PMUC (%)	RPUC (%)	RSC (%)
Sensitivity	0.00	0.00	100
Specificity	84.78	92.03	97.10
PPV	0	0	33.33
NPV	98.32	98.45	100
P value(95% CI)	1	1	0.002

DISCUSSION

Postoperative fever in PCNL is bothersome which ranges from 10-15%.[15,16] Fever post PCNL can be due to underlying infection, hence we routinely gave antibiotic prophylaxis three days prior to surgery according to our local hospital protocol. And in cases where pre-operative midstream urine culture was positive, antibiotics were given unless the urine culture report came out to be negative.

Positive preoperative midstream urine culture in our study was 15% and E.coli was the commonest organism detected which is comparable to the study conducted by Gutierrez et al.[1] But in a study conducted by Patel et al[17], PMUC was 51% which is much higher than our study and the reason for it might be due to the absence of patients in our study who were under long-term catheters, nephrostomy tubes.[1] We also aimed to make preoperative urine sterile even in stag horn stones.

Preoperative midstream urine culture is not a good test for the presumption of SIRS or urosepsis post PCNL which is shown by Mariappan et al[18] and Paonessa et al.[19] Sensitivity of preoperative midstream urine culture and the pelvic urine culture for the detection of infected stones were 16.67% and 33.33% respectively in our study which is comparable to the study conducted by Mariappan et al.[18] Likewise, stone culture has the highest value in detecting SIRS/urosepsis as according to the above mentioned studies, which is comparable to the findings of our study.

SIRS in our patient was only 1.42% and no urosepsis was noted, which is much less compared to the study done by Waltondiaz et al.[11] The reason might be due to stringent use of antibiotics preoperatively and continuation of the same postoperatively for seven days in our study.

The present study has few limitations as the surgeries were performed by different consultants. Robust methods for the calculation of stone burden was not carried out. It was a single center study.

CONCLUSION

Stone culture has high prediction for SIRS and it should be considered for patients undergoing PCNL in order to prevent stone related infective complications.

Conflict of interest

Authors declare no conflict of interest

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