

ASSESSMENT OF RISK FACTORS OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME FOLLOWING PERCUTANEOUS NEPHROLITHOTOMY AND THEIR IMPACT ON PATIENT OUTCOMES

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Abstract

Background: To identify perioperative risk factors for postoperative systemic inflammatory response syndrome (SIRS) following percutaneous nephrolithotomy (PCNL) and suggest potential modifications to reduce morbidity. **Materials and Methods:** A prospective observational study was conducted at the Department of Genitourinary Surgery, Government Medical College, Kottayam, over a period of 12 months (June 2018 to May 2019). The study included 80 patients undergoing PCNL with sterile preoperative urine culture. Exclusion criteria encompassed diabetic patients, those on immunosuppressants, ASA grade 3 and 4 patients, anatomical abnormalities, tumors, heart/kidney failure, and preoperative fever requiring antibiotics. Intraoperative samples of renal pelvic urine and stone fragments were cultured. Postoperative monitoring for SIRS was performed, and correlations between various perioperative factors and SIRS development were analyzed statistically using SPSS version 22. **Result:** The mean age of patients was 49.64 ± 14.76 years, with a male predominance (75%). The incidence of SIRS was significantly correlated with operative duration (>45 minutes, $p=0.03$), positive renal pelvic urine culture ($p<0.005$), and positive stone culture ($p=0.02$). Among 80 patients, 11 had a positive renal pelvic urine culture, with 10 developing SIRS. Additionally, 15 patients had positive stone cultures, of whom 11 developed SIRS. Stone culture exhibited the highest sensitivity (97%) and negative predictive value (96%) in predicting post-PCNL infection. The study also highlighted an increased risk of SIRS with tubeless PCNL with DJ stent placement compared to totally tubeless PCNL. **Conclusion:** The study identifies prolonged operative duration, positive renal pelvic urine culture, and positive stone culture as significant risk factors for post-PCNL SIRS. Preoperative screening for risk factors, intraoperative measures to minimize procedural time, and postoperative monitoring of high-risk patients are recommended to reduce morbidity.

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) has become the standard of care for large (>2 cm) renal stones. Despite significant advancement in technique and instrumentation and availability of broad spectrum antibiotics over the past few decades, fever and sepsis are dreadful complications associated with PCNL that are still commonly encountered in the postoperative period.^[1-3] Postoperative fever (not always related to infections) is one of the most

common complications after PCNL and can affect upto 30% of patients⁴. Rates of systemic inflammatory response syndrome (SIRS) can be as high as 23.4–29% and rates of sepsis range from 0 to 3%.^[5]

SIRS, which is defined as any of the following 2 are positive, which includes

- Body temperature more than 38 degree C or less than 36 degree C,
- Heart rate more than 90 beats/ min,

- Respiratory rate more than 20 breaths/min or arterial carbon dioxide tension (PaCO₂) less than 32 mmHg.
- WBC count more than 12,000 or less than 4000 or more than 10% immature forms

SIRS is poorly understood non-infectious inflammatory response of the body to stress and has the potential to progress to multiple organ failure.^[5-8]

These prolong the hospital stay, add to health care costs, and are one of the common causes of rare perioperative mortality.

Several factors such as age, composition of stone, antibiotic prophylaxis, degree of hydronephrosis, preoperative urine culture, intra-operative renal pelvic or stone culture and operative time have been implicated to increase the risk of postoperative SIRS or sepsis.^[9] This prospective study will be aiming at detecting perioperative risk factors for post PCNL SIRS and sepsis, to identify potentially modifiable factors and to suggest alterations in usual practice to reduce morbidity.^[10,11]

MATERIALS AND METHODS

It was a Prospective Observational Study conducted at Department of Genitourinary surgery, of Government Medical College, Kottayam for a period of 12 months (JUNE 2018 to MAY 2019).

Inclusion Criteria

- All patients undergoing percutaneous nephrolithotomy in our institution.
- Patients with negative urine culture and no evidence of any source of infection.

Exclusion Criteria

- Patients who are diabetic or taking immunosuppressive agents or ASA grade 3 and 4.
- Patients with anatomic abnormalities like horseshoe kidney, polycystic kidney or ureteropelvic junction stricture.
- Patients with tumors or with hematopathy.
- Those having a heart rate greater than 90 beats/min before surgery.
- Those with heart or kidney failure.
- Preoperative fever treated with antibiotics.
- Patients who are having second PCNL, minimally invasive PCNL (18 fr), PCNL with other procedure.
- Patients who have intra operative complications like pleural injury, bowel injury.

Sampling Procedure

Sample size - 75

Sample size = 4 PQ/D2

P (prevalence) Q= (100-P) D(absolute precision)= 10

Above values are taken from following article with power of study – 80% according to study conducted by TuncErdil at al,^[12] the prevalence of renal pelvic urine culture positive which is one of the important risk factors is 22.5%.

Patients who were undergoing PCNL in our institute were included in this study. The study was approved of institutional review board.

Methodology: After enrolling candidates for study based on inclusion and exclusion criteria, well informed written consent was taken. Patients who were undergoing percutaneous nephrolithotomy, all pre operative information was collected. All patients had preoperative bladder urine culture done and those patients were included who had sterile urine culture. Patients who had positive urine culture were treated with appropriate antibiotics for specific period. Those patients were included in the study that had sterile bladder urine culture. Intra operatively pelvic urine was sent for culture and sensitivity. We followed Nemoy & Stamey Technique of processing stones for culture and sensitivity. The basic principle is to wash off surface contaminants and culture bacteria within the stone and avoid cross contamination. The stone fragments were washed in 5 sequential bottles containing sterile saline and then crushed in the fifth bottle, of which the contents were sent as stone for C&S. All data regarding method of procedure were recorded including intra op tachycardia, number of tracts, any complications, size of the stone, procedure time specifically irrigation time, clearance of stone and others. Stone fragments were sent for culture and sensitivity. Post operatively patients were monitored for tachycardia, tachypnoea, increased or decreased temperature and leucocyte count. If evidence of inflammatory response is present, then blood for culture and sensitivity were sent to identify evidence of sepsis. Pelvic urine culture and stone culture report were followed up.

Statistical Analysis: Data collected from above will be tabulated on Microsoft excel and analyzed by SPSS software version 22. Various qualitative data will be analyzed using chi square TES.

RESULTS

In our study group of 80 patients who underwent PCNL, age distribution ranged from 20 to 78 years with mean age was 49.64 + 14.76 years of standard deviation. The maximum cases were in the age group of 56 to 65 years (22 cases, 27.5%) followed by 46 to 55 years (17 cases, 21.3%).

Table 1: Age wise distribution of study subjects.

S. No	Age in years	Frequency	%	Mean age + SD
1	<25	5	6.3	49.64+/- 14.768
2	26-35	11	13.8	
3	36-45	13	16.3	
4	46-55	17	21.3	
5	56-65	22	27.5	
6	>65	12	15.0	
	Total	80	100.0	

Table 2: Gender wise distribution

Frequency		Percent
Males	60	75.0
Females	20	25.0
Total	80	100.0

In this study, 60 males and 20 females were involved.

Table 3: Correlation of duration of the procedure with SIRS

	SIRS		Total
	0	1	
Within 45 min	49	12	61
45 to 60 min	15	3	18
More than 60 min	0	1	1
Total	64	16	80

Mean duration of procedure is 43.94 min with standard deviation of 9 min. As the duration of the procedure increased the incidence of SIRS increased in our study which is statistically significant. (P value – 0.03).

Table 4: Correlation of renal pelvic urine culture with SIRS

		SIRS		Total
		0	1	
Pelvicurineculture	0	62	7	69
	1	1	10	11
Total		63	17	80

Out of 80 patients, 11 patients had renal pelvic urine culture positive. Among these 11 patients 10 patients had SIRS which is statistically significant. P <0.005. All the patients who had urinary bladder culture positive were treated with appropriate antibiotics. These patients underwent surgery once the bladder urine culture became negative.

Most common organisms grown in bladder urine culture were E. Coli followed by Klebsiella and Pseudomonas aeruginosa. These organisms were usually sensitive to fluoroquinolones and piperacillin and tazobactam combination.

Table 5: Correlation of stone culture and SIRS

		SIRS		Total	
		0	1		
Stoneculture	0	60	5	65	P-0.02
	1	4	11	15	
Total		64	16	80	

In our study, 15 patients had positive stone fragment culture among which 11 patients had SIRS. it had positive predictive value of with 81%.

Table 6: Comparison of bladder urine, pelvic urine and stone culture

	Bladder urine C&S	Pelvic urine C&S	Stone C&S
Sensitivity (%)	25	83	97
Specificity (%)	97	94	78
PPV	0.90	0.94	0.81
NPV	0.47	0.83	0.96
RR (95%CI)	1.9 (1.4-2.7)	5.6 (2.7-11.7)	21(3.1-145.4)
P-value	0.01	<0.01	<0.01

Sensitivity: Bladder urine culture & sensitivity (C&S) has the lowest sensitivity (25%), indicating a high rate of false negatives. Pelvic urine C&S shows significantly higher sensitivity (83%). Stone C&S has the highest sensitivity (97%), making it the most reliable in detecting infection. **Specificity:** Bladder urine C&S has the highest specificity (97%), meaning it correctly identifies negative cases most of the time. Pelvic urine C&S follows with 94% specificity. Stone C&S has the lowest specificity (78%), indicating a higher false-positive rate. **Predictive Values: Positive Predictive Value (PPV):** Bladder urine C&S: 0.90 (high confidence in positive results). Pelvic urine C&S: 0.94 (even higher

accuracy in predicting infection). Stone C&S: 0.81 (slightly lower than the others but still significant). **Negative Predictive Value (NPV):** Bladder urine C&S: 0.47 (poor at ruling out infection). Pelvic urine C&S: 0.83 (good at ruling out infection). Stone C&S: 0.96 (best at ruling out infection). **Relative Risk (RR) and Confidence Interval (CI):** Bladder urine C&S: RR = 1.9 (1.4-2.7), indicating a lower relative risk. Pelvic urine C&S: RR = 5.6 (2.7-11.7), showing a stronger association. Stone C&S: RR = 21 (3.1-145.4), the highest risk association. All p-values are significant: Bladder urine C&S: 0.01 (significant). Pelvic urine C&S: <0.01 (highly significant). Stone C&S: <0.01 (highly significant).

Table 7: Correlation of SIRS with type of PCNL

		SIRS		Total
		0	1	
Type of PCNL	1	54	12	66
	2	10	3	13
	3	0	1	1
Total		64	16	80

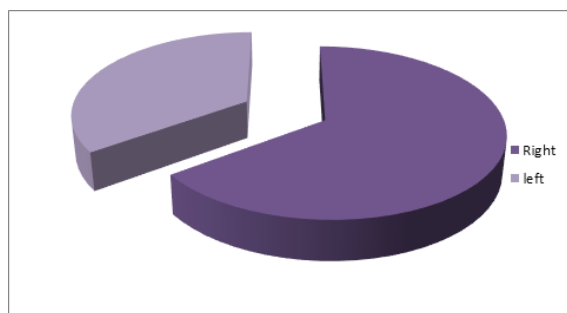
In our study, majority of the patients underwent totally tubeless PCNL (66 out of 80), 13 patients underwent tubeless PCNL with DJ stent and 1 patient had classical PCNL with both DJ stent and nephrostomy tube.

18% of the totally tubeless PCNL group had SIRS. Whereas 30 % of the tubeless PCNL with DJ stent had SIRS and the 1 patient who had both the tubes, had SIRS.

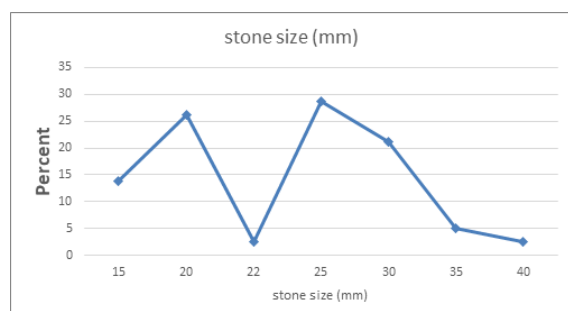
Table 8: Correlation of SIRS with number of tracts

		SIRS		Total
		0	1	
Tracts	1	61	13	74
	2	3	3	6
Total		64	16	80

In the study group, 74 patients had single tract among which 13 developed SIRS. 6 patients had 2 tracts entry among which, 3 patients had SIRS.

**Figure 1: Sidewise distribution of the patients**

In the study, 52 patients underwent PCNL on right side and 28 patients underwent on left side and none were on both sides.

**Figure 2: Stone size distribution**

The mean stone size among these patients is 24.18mm with standard deviation of 6.01mm ranging from 15mm to 40mm.

DISCUSSION

Endourological procedures are most commonly performed surgical procedures for stone disease. Because of their minimally invasive nature (need to fragment the stone) and need to raise intra pelvic pressure (for visualization), these procedures are at

higher risk of infectious complications. This holds true for PCNL also. The introduction of percutaneous nephrolithotomy (PCNL) in the 1970s marked a turning point in the interventional treatment of nephrolithiasis with an overall stone-free rate of 85% to 95 %, depending on stone size and complexity of their minimally invasive nature (need to fragment the stone) and need to raise intra pelvic pressure (for visualization), these procedures are at higher risk of infectious complications. Despite that urine culture is routinely performed before urological surgery to ensure sterility, and appropriate antibiotics were used for patients with infection, urosepsis is still considered as a serious complication in patients undergoing PCNL. Post PCNL SIRS is commonly reported in about 20–30% of patients according to various studies and has the potential to progress to severe sepsis (0–3%), which has mortality rates of 50–60%.^[2,3,6,] Thus, minimizing infection-related complications is priority to maintain low morbidity rates.^[8,9]

In the study conducted by Prabjoth Singh et al, the incidence of SIRS was about 17.6% another study conducted by Turdil et al, had incidence of SIRS about 16.7%. Majority of studies had incidence of SIRS in the range of 12 to 30 %. In our study we had incidence of SIRS of 20% which is similar to most of the studies.^[10,12]

SIRS, according to 1991 consensus is defined as any of the following 2 are positive, which includes

- Body temperature more than 38* C or less than 36*C ,
- Heart rate more than 90 beats/ min,
- Respiratory rate more than 20 breaths/min or arterial carbon dioxide tension (PaCO₂) less than 32 mmHg.
- WBC count more than 12,000 or less than 4000 or more than 10% immature forms

The incidence of sepsis following PCNL in the world literature ranges from 0 to 3%. Prabjoth Singh et al¹⁰, reported 3.4% of sepsis and 0.4 % patients had septic shock. O'Keeffe et al, reported that 9 out of 700 (1.3 %) patients developed severe sepsis, and six of the nine (66 %) died. In our study, 3 patients out of 80 had sepsis and none had septic shock who were managed with culture antibiotics. The comorbidities like diabetes mellitus, chronic kidney disease, or any other immuno suppressive state, presence of active urinary tract infection which are known risk factors for SIRS and hence sepsis. These patients were excluded from our study.

There was no correlation found between developing SIRS and demographic parameters such as age of the patient, gender of the patient, side of the surgery, which was similar finding in most of the similar studies. Prabjoth Singh et al, reported higher incidence of SIRS in younger age group, but in our study we could not find such association.^[10,11]

Factors which were found to be associated with SIRS significantly in our study are duration of the procedure, need of blood transfusion, positive pelvic urine culture and stone culture. As the duration of the procedure increased, the risk of SIRS increased which was found to be statistically significant. In our study patients were divided into 3 groups according to duration of the procedure, group 1: less than 45 minutes, group 2: 45 to 60 minutes, group 3: more than 60 minutes. Majority of the patients who had SIRS, were in group 2 and 3. Similar result was found many studies. Prabjoth Singh et al,^[10] mentioned Long operative times are associated with higher postoperative sepsis rates because of a longer duration of high intra pelvic pressures and associated higher chance of pyelovenous backflow and irrigant absorption.

Though bladder urine culture was negative in all the patients, renal pelvic urine and stone fragments were sent for culture and sensitivity in all patients as mentioned in the methodology part. 11 patients out of 80 patients (13.75%) had positive renal pelvic urine culture. Among these patients, 10 patients had SIRS and 2 patients had sepsis. Most common organism isolated was E.Coli followed by pseudomonas and klebsiella. The data regarding this in the literature had slightly higher incidence of positive pelvic urine culture. Prabjoth Singh et al,^[10] showed 18.5% of positive renal pelvic urine culture. Similarly stone fragments removed were washed in 5 sequential bottles containing sterile saline and then crushed in the fifth bottle, of which the contents were sent as stone for C&S. 15 out of 80 patients had positive stone culture and among these, 11 patients had SIRS. The organism isolated were similar to renal pelvic urine culture organisms. The most common was E.Coli followed by pseudomonas and klebsiella. The bacteriological profile is similar to other studies where most of studies had E. Coli as most common organism.^[10-12]

In patients who had SIRS, blood culture was sent and 2 patients had evidence of sepsis with positive blood

culture and organisms isolated were similar to that of stone culture grown organisms. These patients were managed with appropriate antibiotics. In contrast to preoperative cultures, those obtained intraoperatively are more predictive of SIRS. Even though all the patients had negative bladder urine culture before the procedure, still 11 patients had positive renal pelvic urine culture positive. This usually results from obstructed system, repeated infection by the organisms which are colonizing over the stone. Similarly, most of the stones are harbor bacteria as laminated layers. Once the stone was broken these bacteria are released systemic endotoxins are released resulting in SIRS and sepsis. Other factors such as number of tracts, type of calyceal entry, presence or absence of DJ stent or nephrostomy tube were not contributing to development of SIRS in our study.

CONCLUSION

SIRS is one of the immediate complications of the PCNL surgery and can lead to sepsis, septic shock and thus leading to increased hospital stay, morbidity and even increased mortality following the surgery. As the majority of the patients will be in the young or middle age group, these patients will have major loss in terms of economic losses because of the prolonged hospital stay and increased morbidity. Hence the important risk factors found out in the study, which are statistically significant and modifiable are pre-op sterile bladder urine culture, duration of the procedure, need of blood transfusion.

All the guidelines recommend pre-operative bladder urine culture should be sterile and it is universally followed. But regarding renal pelvic urine culture and stone fragments for culture, which are better markers of urinary tract infection than bladder urine, these not followed universally. Hence we recommend strongly that all the patients undergoing PCNL renal pelvic urine and stone fragments should be sent for culture and sensitivity. And also monitoring the post PCNL patients for SIRS and managing them with broad spectrum antibiotics and later tapering to stone and renal pelvic urine culture specific antibiotics is the key to reduce morbidity and mortality.

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