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Original Article

Urology Section

Risk Factors for Post-PCNL Systemic Inflammatory Response Syndrome in Patients with Negative Preoperative Urine Culture: A Prospective Observational Study

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ABSTRACT

Introduction: Percutaneous Nephrolithotomy (PCNL) is the standard treatment for large renal stones. Despite sterile preoperative urine cultures, Systemic Inflammatory Response Syndrome (SIRS) continues to be a common and potentially serious postoperative complication, occurring in up to 30% of cases. This suggests that conventional urine culture alone may not identify all patients at risk. Clinical co-morbidities such as diabetes mellitus, stone burden, operative duration, and inflammatory biomarkers, including C-reactive Protein (CRP), Neutrophil-to-lymphocyte Ratio (NLR), and Platelet-to-lymphocyte Ratio (PLR), have been proposed as potential predictors. Identification of these factors may aid in early recognition and prevention of SIRS.

Aim: To evaluate the proportion of SIRS following PCNL in patients with sterile preoperative urine cultures and to identify associated clinical, biochemical, and intraoperative risk factors.

Materials and Methods: This prospective observational study was conducted at the Department of Urology, IPGMER and SSKM Hospital, Kolkata, West Bengal, India, a tertiary care urology centre, between April 2023 and May 2025. A total of 197 patients undergoing PCNL with sterile preoperative urine cultures were included. Patients were categorised into two groups based on the presence or absence of postoperative SIRS. Preoperative, intraoperative, and postoperative variables were analysed using univariate and multivariate logistic regression analyses.

Results: SIRS developed in 28.9% (57/197) of patients following PCNL. The mean age of patients in the SIRS group was 51.89±9.54 years, compared with 48.75±11.27 years in the non SIRS group (p-value=0.049). The proportion of male patients was comparable between the two groups 54.4% vs. 49.3%, (p-value=0.516). On univariate logistic regression analysis, diabetes mellitus showed a strong association with postoperative SIRS (odds ratio 13.29, p-value <0.001). Other significant predictors included stone size (odds ratio 5.14 per cm^2, p-value <0.001), operative duration (odds ratio 1.09 per minute, p-value <0.001), CRP (odds ratio 1.56 per mg/L, p-value <0.001), and PLR (odds ratio 1.05 per unit, p-value <0.001). On multivariate logistic regression analysis, diabetes mellitus, elevated CRP levels, increased PLR, and multiple access tracts remained independent predictors of postoperative SIRS.

Conclusion: SIRS is a common complication following PCNL, even in patients with sterile preoperative urine cultures. Diabetes mellitus, inflammatory biomarkers, and procedural complexity significantly influence postoperative inflammatory risk. Incorporating these parameters into preoperative risk stratification may facilitate early identification of high-risk patients and improve perioperative outcomes.

Keywords: C-reactive protein, Diabetes mellitus, Inflammatory biomarkers, Neutrophil-to-lymphocyte ratio, Percutaneous Nephrolithotomy , Platelet-to-lymphocyte ratio

INTRODUCTION

The PCNL has become the gold standard treatment for large and complex renal stones. Advances in surgical technique, instrument miniaturisation, and irrigation systems have contributed to a reduction in overall morbidity [1,2]. Nevertheless, SIRS remains a frequent and concerning early postoperative complication, with reported incidence rates ranging from 9% to 29%, depending on patient- and procedure-related factors [2,3]. If not promptly identified and managed, SIRS may progress to sepsis, multiorgan dysfunction, and even mortality.

Preoperative urine culture is routinely used to assess infection risk and guide antibiotic prophylaxis. However, increasing evidence suggests that a substantial proportion of patients with sterile urine cultures still develop postoperative SIRS. This indicates that conventional microbiological screening may not adequately reflect true infectious risk, particularly in the presence of subclinical infection within the renal pelvis or calculi themselves [4,5].

Recent studies have focused on readily available clinical and laboratory parameters- including diabetes mellitus, stone size, operative duration, and inflammatory biomarkers such as CRP, NLR, and PLR- as potential predictors of infectious complications following PCNL [6-9]. The present study was therefore undertaken to identify clinical, intraoperative, and biochemical risk factors associated with the development of SIRS following PCNL in patients with sterile preoperative urine cultures.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Urology, IPGMER and SSKM Hospital, Kolkata, West Bengal, India, from April 2023 and May 2025. Ethical clearance was obtained from the Institutional Ethics Committee (IEC Approval No. IPGMER/IEC/2023/487), and written informed consent was obtained from all participants.

Patients undergoing PCNL during the study period were screened. Only those with sterile midstream urine cultures were included,

allowing focused evaluation of SIRS risk factors unrelated to overt urinary tract infection.

Inclusion criteria: Adult patients undergoing PCNL with sterile preoperative urine culture were included.

Exclusion criteria: Patients with congenital urological anomalies, non-urinary sources of sepsis, severe immunosuppression, and those with long-term indwelling catheters, ureteric stents, or existing percutaneous nephrostomy drainage were excluded.

Sample size calculation: Based on Akdeniz E et al., reported 12.7% incidence of SIRS in patients undergoing PCNL with sterile urine cultures, and using the formula

Based on 12.7% incidence

The sample size was calculated using the formula

$$N = \frac{(1.96)^2 \times p \times q}{d^2},$$

where p = 0.127, q = 1 – p, and d = 0.049 (absolute precision of 4.9%) [9].

The minimum required sample size was 179, which was increased by 10% to account for potential dropouts, resulting in a final sample size of 197.

Study Procedure

Preoperative evaluation: All patients underwent comprehensive clinical and biochemical assessment, including complete blood count with measurement of haemoglobin levels, total leukocyte count, differential count, NLR, and PLR; serum creatinine estimation; CRP measurement; and urine microscopy and culture before surgery. Imaging evaluation was performed using ultrasonography and either Contrast-enhanced Computed Tomography (CECT) or intravenous pyelography to assess renal anatomy and stone characteristics. Stone size was calculated as the product of maximum length and width on imaging (cm^2). Inflammatory indices such as NLR and PLR were derived from the complete blood count.

Surgical Procedure: All PCNL procedures were performed under general anaesthesia following confirmation of sterile preoperative urine culture. Patients received prophylactic intravenous ceftriaxone (1 g) 30 minutes before incision. Key procedural steps included cystoscopic ureteric catheter placement in the lithotomy position, fluoroscopy-guided percutaneous renal access in the prone or supine position, tract dilation using 20-26 Fr Amplatz sheaths, and nephroscopy using 18 or 24 Fr rigid nephroscopes. Stone fragmentation was performed using pneumatic lithotripsy, and fragments were retrieved under direct vision. Antegrade ureteric stenting was routinely performed, while nephrostomy tubes were placed selectively.

Intraoperative Data Collection: Recorded intraoperative variables included the number of access tracts, operative duration (measured from renal puncture to nephrostomy placement), estimated blood loss, and stone clearance status, which was assessed nephroscopically and fluoroscopically as complete or incomplete.

Patients were monitored postoperatively for vital signs at 4-6-hour intervals. SIRS was defined according to the 2001 International Sepsis Definitions Conference criteria as the presence of at least two of the following [10]:

- Temperature >38.0°C or <36.0°C
- Heart rate >90 beats per minute
- Respiratory rate >20 breaths per minute
- White blood cell count >12,000/mm^3 or <4,000/mm^3

Group Division

Based on postoperative status, patients were divided into two groups:

- **Group I (SIRS group):** Patients fulfilling ≥2 criteria for SIRS
- **Group II (Non SIRS group):** Patients not meeting SIRS criteria

STATISTICAL ANALYSIS

Data were analysed using Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean±standard deviation or median with interquartile range, depending on data distribution. Group comparisons were performed using Student t-tests for continuous variables, and Chi-square test for categorical variables. Binary logistic regression analysis was used to identify independent predictors of postoperative SIRS, with results expressed as odds ratios and 95% confidence intervals. Receiver Operating Characteristic (ROC) curve analysis was performed to determine optimal cut-off values for key biomarkers. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant.

RESULTS

A total of 197 patients with sterile preoperative urine cultures underwent PCNL during the study period. Of these, 57 patients (28.9%) developed SIRS within 48 hours postoperatively, while 140 patients (71.1%) did not develop SIRS and served as the control group. Patients who developed SIRS were significantly older, with a mean age of 51.89±9.54 years compared to 48.75±11.27 years in the non SIRS group (p-value= 0.049) [Table/Fig-1].

Preoperative inflammatory markers demonstrated strong discriminatory ability, with significantly higher mean CRP levels in the SIRS group (7.4±3.9 mg/L vs. 2.9±2.1 mg/L; p-value <0.001). PLR (160.9±21.6 vs. 129.5±25.7; p-value <0.001) and NLR (3.8±1.1 vs. 2.4±0.8; p-value <0.001) were also significantly elevated in patients with SIRS.

To identify independent predictors of post-PCNL SIRS, all relevant clinical, laboratory, and operative variables were initially subjected to univariate logistic regression. Variables showing a p-value <0.1 were then included in a multivariate logistic regression model using a stepwise selection method. The final model identified seven independent predictors of SIRS, with excellent discrimination

Category	Parameters	SIRS group (n=57)	Non SIRS group (n=140)	p-value
Demographics	**Age (years)**, (Mean±SD)*	51.89±9.54	48.75±11.27	0.049
	Gender, n (%)#			0.516
	Male	31 (54.4)	69 (49.3)	
	Female	26 (45.6)	71 (50.7)	
	Religion, n (%)#			0.751
	Hindu	40 (70.2)	95 (67.9)	
	Muslim	17 (29.8)	45 (32.1)	
Co-morbidity	Diabetes mellitus, n (%)#	36 (63.2)	16 (11.4)	<0.001
Preoperative biochemistry	Serum creatinine (mg/dL), (Mean±SD)*	0.99±0.25	1.01±0.31	0.619
	Pyuria (>5 WBC/hpf), n (%)#	30 (52.6)	68 (48.6)	0.605
Imaging findings	Hydronephrosis present, n (%)#	35 (61.4)	80 (57.1)	0.582
Stone characteristics	Stone size (cm), (Mean±SD)*	3.55±0.84	2.60±0.70	<0.001
	Staghorn/partial staghorn calculus, n (%)#	34 (59.6)	43 (30.7)	<0.001

Operative variables	Multiple access tracts, n (%)#	47 (82.5)	48 (34.3)	<0.001
	Operative duration (minutes), (Mean±SD)*	112.28±19.53	79.36±17.59	<0.001
	Haemoglobin drop (g/dL), (Mean±SD)*	1.84±0.33	1.65±0.28	<0.001
	Blood transfusion required, n (%)#	19 (33.3)	12 (8.6)	<0.001
	Incomplete stone clearance, n (%)#	26 (45.6)	49 (35.0)	0.164

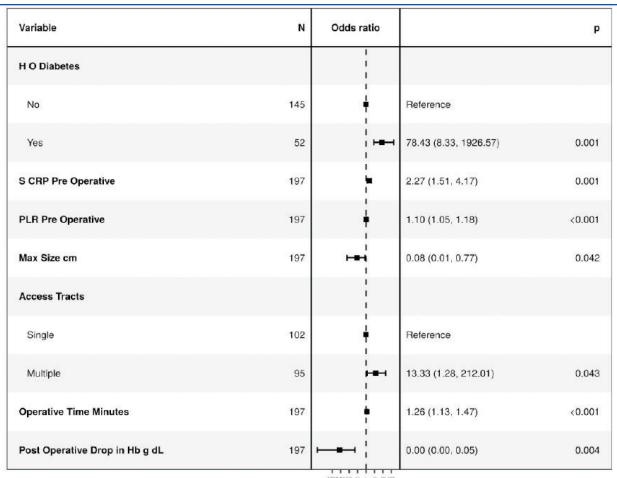
[Table/Fig-1]: Comparison of clinical, sociodemographic, biochemical, and operative parameters between SIRS and non SIRS groups.
Values are expressed as mean±standard deviation or number (percentage). * Student's t-test was used for comparison of continuous variables. # Chi-square test was used for comparison of categorical variables, as appropriate; CRP: C-reactive protein; PLR: Platelet-to-lymphocyte ratio; NLR: Neutrophil-to-lymphocyte ratio; WBC: White blood cells; hpf: high-power field.

(AUC=0.989), calibration (Hosmer–Lemeshow p-value=1.000), and pseudo-R^2 of 0.81 [Table/Fig-2]. In the adjusted model, haemoglobin decrease demonstrated a significant inverse association with SIRS (adjusted OR=0.02, 95% CI: 0.01–0.05; p-value=0.004), indicating reduced odds after adjustment for confounders.

Predictor variables	Univariate OR (95% CI), p-value	Multivariate OR (95% CI), p-value
Diabetes mellitus (Yes vs No)	13.29 (6.42-28.84), <0.001	78.43 (8.33-1926.57), 0.001
Serum CRP (per mg/L)	1.56 (1.38-1.80), <0.001	2.27 (1.51-4.17), 0.001
PLR (per unit increase)	1.05 (1.04-1.07), <0.001	1.10 (1.05-1.18), 0.001
Operative duration (per minute)	1.09 (1.07-1.12), <0.001	1.26 (1.13-1.47), <0.001
Stone size (per cm)	5.14 (3.07-9.50), <0.001	0.08 (0.01-0.77), 0.042
Access tracts (Multiple vs Single)	9.01 (4.34-20.35), <0.001	13.33 (1.28-212.01), 0.043
Haemoglobin drop (per g/dL)	7.50 (2.72-21.88), <0.001	0.02 (0.01-0.05), 0.004

[Table/Fig-2]: Univariate and multivariate logistic regression analysis of predictors of post-PCNL SIRS.

The forest plot demonstrates the magnitude and direction of effect for each independent predictor, with diabetes mellitus, CRP, PLR, and prolonged operative duration emerging as the most influential contributors [Table/Fig-3].



[Table/Fig-3]: Forest plot of adjusted odds ratios for predictors of SIRS.

To further evaluate the diagnostic performance of individual predictors of post-PCNL SIRS, ROC analysis demonstrated that CRP ≥ 5.9 mg/L showed excellent diagnostic performance, with high specificity (91.4%), overall accuracy (84.3%), and the highest odds ratio among all parameters [Table/Fig-4].

Univariate logistic regression analysis demonstrated that several clinical, biochemical, stone-related, and intraoperative variables were significantly associated with the development of post-PCNL SIRS. Among sociodemographic factors, increasing age showed a modest but statistically significant association with SIRS, while gender and religion were not significant predictors. Diabetes mellitus emerged as a strong risk factor, with patients having markedly higher odds of developing SIRS. Preoperative inflammatory markers, including CRP, PLR, and NLR, were all significantly associated with increased SIRS risk [Table/Fig-5].

Each panel displays the corresponding area under the curve and overall performance trends, highlighting CRP and operative duration as the dominant predictors of SIRS [Table/Fig-6].

DISCUSSION

The present study highlights key clinical and procedural determinants of SIRS following PCNL.

Although patients in the SIRS group had a higher mean age, the strength of this association was reduced on non parametric analysis. Age-related immunosenescence, characterised by reduced neutrophil function, impaired T-cell proliferation, and diminished mucosal defence, represents a plausible biological explanation. Previous studies by Koras O et al., and He Z et al., have similarly identified age as an independent risk factor, suggesting a consistent age-related gradient [11,12].

Diabetes mellitus emerged as a strong independent predictor of SIRS. The immunological consequences of diabetes, including neutrophil dysfunction, cytokine imbalance, and microvascular compromise, have been well documented by Wei W et al., Murtha MJ et al., and Youssef LA and Spitalnik SL [13-15]. In addition, hyperglycaemia promotes uropathogen colonisation and biofilm formation, further emphasising the importance of strict glycemic control and intensified prophylactic strategies in diabetic patients [13,14].

Stone burden, encompassing both size and morphological complexity, was another critical determinant. Patients who developed SIRS had significantly larger stones, and multivariate analysis confirmed stone size as an independent predictor. Similar findings have been reported by He Z et al., and Lan S et al., who attributed the increased infectious risk to complex calyceal involvement, longer operative duration, and elevated intrarenal pressure [12,16]. These observations support the use of staged procedures, suction-assisted techniques, and individualised surgical planning in patients with a high stone burden.

Inflammatory biomarkers, including CRP, PLR, and NLR, demonstrated strong predictive value. The results are consistent with the findings of He Z et al., [12]. PLR and NLR reflect thrombocytosis and lymphopenia, respectively, both of which are hallmarks of an exaggerated systemic inflammatory response. Prior reports by Koras O et al., Rashid AO et al., and Amier Y et al., [11,17,18] similarly support the utility of these markers as inexpensive and readily available tools for risk stratification.

Prolonged operative duration showed a significant independent association with SIRS. As noted by He Z et al., extended operative time is associated with greater renal parenchymal trauma and sustained irrigation pressures, which may facilitate endotoxin translocation [12]. Operative duration therefore represents a practical intraoperative indicator for heightened postoperative surveillance and early intervention. The inverse association observed for haemoglobin decrease in the adjusted model may reflect collinearity with operative duration and access complexity rather than a true protective effect.

Parameters (Cut-off)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Odds Ratio (95% CI)	p- value
Age ≥ 41 years	91.2	22.9	32.5	86.5	42.6	3.08 (1.13–8.37)	0.022
Stone Size ≥ 2.9 cm	84.2	65.0	49.5	91.0	70.6	9.90 (4.49–21.87)	<0.001
CRP ≥ 5.9 mg/L	66.7	91.4	76.0	87.1	84.3	21.33 (9.51–47.88)	<0.001
PLR ≥ 142.24	87.7	70.0	54.3	93.3	75.1	16.67 (6.99–39.77)	<0.001
NLR ≥ 2.64	66.7	78.6	55.9	85.3	75.1	7.33 (3.70–14.52)	<0.001
Operative duration ≥ 100 minutes	80.7	82.9	65.7	91.3	82.2	20.21 (9.16–44.59)	<0.001
Haemoglobin drop ≥ 1.8 g/dL	57.9	71.4	45.2	80.6	67.5	3.44 (1.81–6.53)	<0.001

[Table/Fig-4]: ROC-based diagnostic performance of study parameters in predicting SIRS.

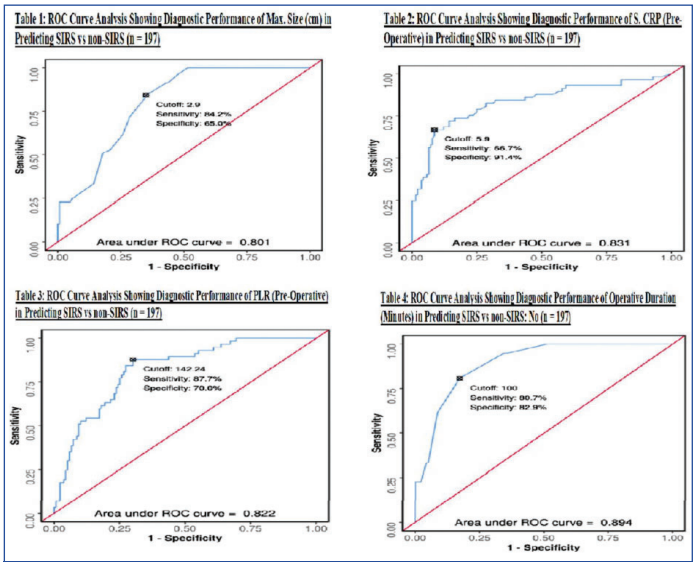
Variables	Odds ratio (95% CI)	p-value	Significance
Sociodemographic variables			
Age (per year)*	1.03 (1.00-1.06)	0.049	Significant
Gender (Male vs Female)#	1.22 (0.66-2.25)	0.516	Not significant
Religion (Hindu vs Muslim)#	1.11 (0.58-2.13)	0.751	Not significant
Co-morbidity			
Diabetes mellitus (Yes vs No)#	13.29 (6.42-28.84)	<0.001	Significant
Preoperative variables			
Serum creatinine (per mg/dL)*	0.91 (0.54-1.52)	0.619	Not significant
Pyuria (>5 WBC/hpf)#	1.17 (0.64–2.14)	0.605	Not significant
Hydronephrosis (Present vs Absent)#	1.19 (0.66-2.13)	0.582	Not significant
C-Reactive Protein (CRP) (per mg/L)*	1.56 (1.38-1.80)	<0.001	Significant
Platelet-to-Lymphocyte Ratio (PLR) (per unit)*	1.05 (1.04-1.07)	<0.001	Significant
Neutrophil-To-Lymphocyte Ratio (NLR) (per unit)*	1.41 (1.18-1.69)	<0.001	Significant
Stone-related variables			
Stone size (per cm)*	5.14 (3.07-9.50)	<0.001	Significant
Staghorn/partial staghorn calculus#	3.29 (1.69-6.40)	<0.001	Significant
Intraoperative variables			
Multiple access tracts (Yes vs No)#	9.01 (4.34-20.35)	<0.001	Significant
Operative duration (per minute)*	1.09 (1.07-1.12)	<0.001	Significant
Haemoglobin decrease (per g/dL)*	7.50 (2.72-21.88)	<0.001	Significant
Blood transfusion required (Yes vs No)#	5.48 (2.37-12.67)	<0.001	Significant
Nephrostomy tube placement#	0.91 (0.49-1.71)	0.734	Not significant
Incomplete stone clearance#	1.55 (0.83-2.89)	0.164	Not significant

[Table/Fig-5]: Univariate logistic regression analysis of variables associated with Post-PCNL SIRS.

Taken together, these results indicate that a combination of systemic inflammatory biomarkers, stone-related burden, and intraoperative complexity serves as a robust predictor of SIRS, even in patients with sterile preoperative urine cultures.

Limitation(s)

Being a single-centre study, the findings may have limited generalisability. SIRS was used as the primary outcome measure, which may not always correspond to true infection and can be influenced by factors such as inadequate pain control or the use of beta-blockers. In addition, intraoperative stone cultures and intrarenal pressure measurements were not assessed, both of



[Table/Fig-6]: Individual ROC curves for key predictors of SIRS.

which are recognised contributors to postoperative inflammatory responses. Finally, the absence of external validation of the predictive model highlights the need for future multicenter studies.

CONCLUSION(S)

Systemic Inflammatory Response Syndrome following PCNL is a significant postoperative complication that may occur even in patients with sterile preoperative urine cultures. Among these variables, diabetes mellitus, CRP, and operative duration emerged as the strongest independent significant predictors. These findings emphasise the need to move beyond reliance on urine culture status alone toward a more comprehensive evaluation of patient physiology and procedural complexity. Early identification of high-risk individuals using simple clinical and laboratory parameters may facilitate timely intervention, informed surgical planning, and ultimately improved outcomes following PCNL.

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