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Prediction of Urosepsis after Percutaneous Nephrolithotomy using Neutrophil-Lymphocyte Ratio

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ABSTRACT

Introduction

Percutaneous nephrolithotomy (PCNL) is the preferred modality treatment for kidney stones >2 cm. Prediction of postoperative infection remains a major concern. The neutrophil-to-lymphocyte ratio (NLR) is an inexpensive and readily available marker of systemic inflammation and has shown potential in predicting infection and sepsis. This study aims to investigate the utility of preoperative NLR in predicting urosepsis following PCNL.

Methods

A prospective observational study was conducted on 86 patients undergoing PCNL at Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Nepal. Preoperative NLR was calculated from complete blood counts. Postoperative infectious outcomes were analyzed, logistic regression and receiver operating characteristic (ROC) curve analyses were performed to assess NLR's predictive value.

Results

Post-PCNL fever occurred in 43 patients (50%) and sepsis in 16 patients (18.6%). Patients with sepsis had significantly higher preoperative NLR (3.55 ± 2.25 vs. 1.82 ± 0.68, $p < 0.001$). An NLR cut-off of 1.86 predicted sepsis with area under curve (AUC) 0.829, 93.8% sensitivity and 68.6% specificity ($p < 0.001$). Higher risk of sepsis was seen in patients with chronic kidney disease (37.5%), preoperative percutaneous nephrostomy (46.7%), prior UTI admission (30.3%), staghorn stones (50%), longer operative time (99.69 ± 31.12 vs 78.26 ± 34.23 minutes).

Conclusion

Preoperative NLR may be a useful marker for identifying patients at increased risk of sepsis after PCNL, particularly in patients with complex stones and value >1.86. Further large-scale studies are needed to validate its role and compare it with other established biomarkers.

Keywords

Neutrophil-to-lymphocyte ratio; percutaneous nephrolithotomy; staghorn calculus; sepsis

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the preferred minimally invasive procedure for kidney stones larger than 2 cm, particularly for complex stones like staghorn calculi, due to its high stone clearance rate and faster recovery.[1,2] However, post-PCNL infections, ranging from mild fever to life-threatening urosepsis, remain a major concern. Urinary tract infections occur in up to 37% of cases, with urosepsis developing in 0.3% to 7.6%. Identifying risk factors preoperatively and detecting sepsis early can significantly reduce morbidity and mortality.[3–5]

While preoperative urine culture (UC) is commonly used for infection risk assessment, it is often unreliable, as 36.8% to 52.4% of patients who develop sepsis had negative UC results. This highlights the need for alternative biomarkers for more accurate risk prediction.[6,7] Biomarkers like procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6) have shown promise, but their routine use is limited.[8]

The neutrophil-to-lymphocyte ratio (NLR) is a simple, cost-effective inflammatory marker easily obtained from routine blood tests. Studies have demonstrated its predictive value in infections and prognosis, including sepsis risk in PCNL patients.[9–11] In 2016, Sen et al. identified NLR >2.5 as a strong predictor of post-PCNL sepsis.[12] Given its affordability and accessibility, NLR may serve as a useful biomarker for infection risk stratification. However, its predictive value in our clinical setting remains unexplored. This study aims to assess the role of NLR in predicting sepsis following PCNL.

METHODS

This cross-sectional prospective observational study was conducted from September, 2024 to February, 2025 at the Department of Urology & Kidney Transplant Surgery, Maharajgunj Medical Campus, Tribhuvan University, Nepal, following approval from the institutional ethical committee (Ref 206-081/082). Clinical data were collected from 115 patients, and after applying inclusion and exclusion criteria, 86 patients were enrolled in the study (Figure 1).

Exclusion criteria included patients younger than 18 years, those undergoing bilateral PCNL in the same session, individuals with hematological disorders (such as leukemia, thrombocytopenia, or hemophilia), abnormal renal anatomy (including horseshoe kidney, polycystic kidney, or ureteropelvic junction obstruction), patients on immunosuppressive therapy, and those undergoing a second-stage PCNL.

Preoperative laboratory evaluations included urine analysis, midstream urine culture, complete blood count, and renal function test, all conducted within one week prior to surgery. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing absolute neutrophil count by lymphocyte count available from the performed complete blood count. Renal stones were assessed preoperatively using computed tomography. Patients with positive urine culture (>100,000 CFU/mL) received targeted antibiotic therapy for at least seven days before surgery. For those with history of positive urine culture and a nephrostomy tube, intravenous antibiotics were initiated one day before surgery, guided by prior sensitivity results, and continued postoperatively. Patients with negative urine culture received intravenous Ceftriaxone 1 gram at the time of induction for general anesthesia and continued postoperatively.

Stone complexity was categorized according to the Guy's stone score[13], while stone size was determined by measuring its longest diameter and perpendicular width. In cases of multiple stones, the largest stone's dimension was recorded. Preoperative patient demographics and stone characteristics were documented. Operative time

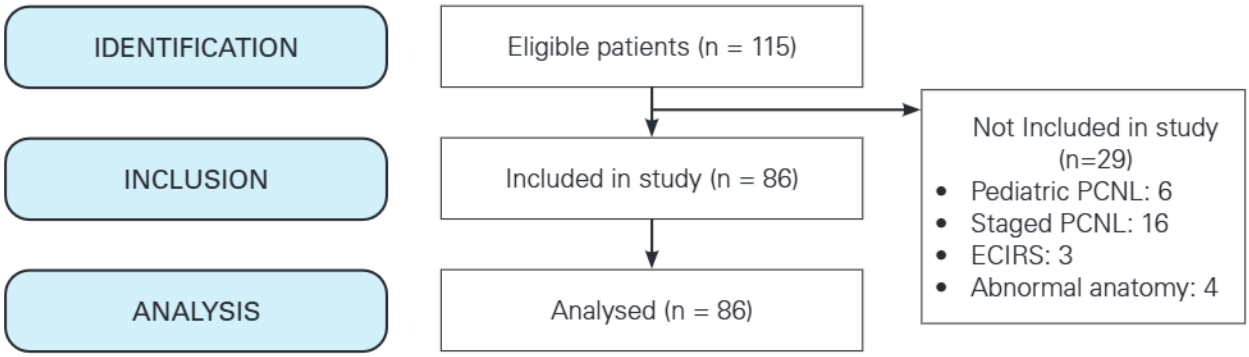

Figure 1. *STROBE chart*

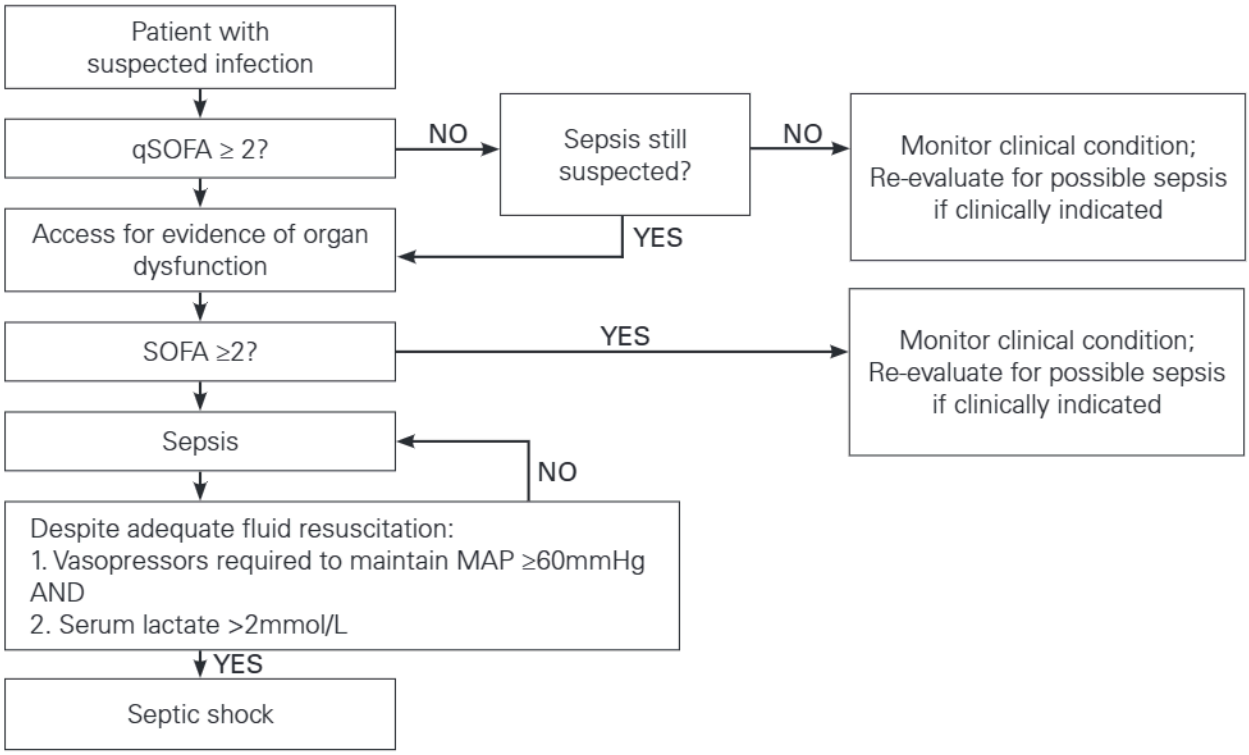

Figure 2. *Postoperative infection management*

was defined as the duration from the start of cystoscopy to the placement of a double-J (DJ) stent.

All patients underwent supine mini-PCNL in the Galdakao-modified supine Valdivia position. Intraoperative details, including procedure duration, stone clearance status, and complications such as bleeding, were recorded. Postoperative follow-up focused on detecting infective complications based on the Sepsis-3 guidelines[3,14] and sepsis was diagnosed if Sequential Organ Failure Assessment (SOFA) score of ≥2. (Figure 2)

Statistical analysis was performed using SPSS version 26.0 (SPSS, Chicago, IL, USA), with statistical significance set at $p < 0.05$. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies or percentages. Univariate analysis was conducted to assess the relationship between sepsis and individual variables. Multivariable logistic regression analysis was then performed to determine the independent association between NLR and sepsis. The receiver operating characteristic (ROC) curve was plotted to evaluate NLR's predictive value for sepsis, with sensitivity and specificity assessed using the Youden index.

RESULTS

The baseline patient and stone characteristics for groups with and without sepsis are presented in Tables 1 and 2. Post-PCNL fever occurred in 43 patients (50%), and 16 patients (18.6%) developed sepsis.

Patients with chronic kidney disease (CKD) had greater chance of developing sepsis (6 patients, 37.5%). Also there was greater likelihood of sepsis with preoperative percutaneous nephrostomy (PCN) placement (7 patients, 46.7%) and in those with prior history of hospital admission for UTI (10 patients, 30.3%) The pre-operative neutrophil-to-lymphocyte ratio (NLR) was significantly higher (3.55 ± 2.25 vs. 1.82 ± 0.68, $p < 0.001$) in those who developed sepsis. (Table 1)

Complex stone with higher Guy's stone score ($p = 0.01$), staghorn calculus ($p<0.001$) and larger stone size (37.03 ± 18.48 mm vs. 26.77 ± 12.3 mm, $p = 0.009$) was also associated with increased risk of developing sepsis postoperatively. (Table 2)

All sepsis cases were managed with intravenous antibiotics based on culture sensitivity, while 3 patients (3.5%) required intensive care support, no deaths were reported. Sepsis significantly prolonged hospital stays (6.13 ± 1.46 days vs. 4.0 ± 1.39 days, $p < 0.001$). (Table 3)

Patients with complex stones, including those with a higher Guy's stone score and staghorn calculi had lower stone-free rate (14% vs. 86%, $p < 0.001$), significantly higher incidence of postoperative fever (74.4% vs. 25.6%, $p < 0.001$) and sepsis (67.4% vs. 32.6%, $p < 0.001$).

Multivariable logistic regression identified NLR as a significant independent predictor of sepsis (95% CI: 0.00 – 2.45, $p = 0.043$) (Table 4). Receiver

Table 1. Demographic characteristics of patients with and without sepsis

Variable Total (n=86)		Total (n=86)	Sepsis		p value
			Present (n=16)	Absent (n=70)	
Age		47.31 ± 13.69	48.31 ± 12.33	47.74 ± 14.14	0.68
Sex	Male	53 (61.6%)	11 (20.8%)	42 (79.2%)	
	Female	33 (38.4%)	5 (15.2%)	28 (84.8%)	0.52
Laterality	Left	44 (51.2%)	8 (18.2%)	36 (81.8%)	0.92
	Right	42 (48.8%)	8 (19%)	34 (81%)	
Diabetes Mellitus		18 (20%)	5 (27.8%)	13 (72.2%)	0.26
Hypertension		46 (53.5%)	11 (23.9%)	35 (76.1%)	0.18
Chronic Kidney Disease		16 (18.6%)	6 (37.5%)	10 (62.5%)	0.03
ASA	I	33 (38.4%)	5 (15.2%)	28 (84.8%)	0.272
	II	38 (44.2%)	6 (15.8%)	32 (84.2%)	
	III	15 (17.4%)	5 (33.3%)	10 (66.7%)	
NLR		2.15 ± 1.32	3.55 ± 2.25	1.82 ± 0.68	<0.001
Prior admission for UTI		33 (38.4%)	10 (30.3%)	23 (69.7%)	0.028
Pre-operative PCN placement		15 (17.4%)	7 (46.7%)	8 (53.3%)	0.002

Table 2. Stone characteristics of patients with and without sepsis

Stone characteristics	Total (n=86)	Sepsis		p value
		Present (n=16)	Absent (n=70)	
Guy's stone score				0.01
Grade 1	28 (32.6%)	2 (7.1%)	26 (92.9%)	
Grade 2	14 (16.3%)	0	14 (100%)	
Grade 3	22 (25.6%)	6 (27.3%)	16 (72.7%)	
Grade 4	22 (25.6%)	8 (36.4%)	14 (63.6%)	
Staghorn calculus	43 (50%)	14 (32.6%)	29 (67.4%)	<0.001
Stone size (Largest in mm)	28.68 ± 14.35	37.03 ± 18.48	26.77 ± 12.63	0.009
Hounsfield unit (HU)	11.87 ± 370.80	1251.13 ± 450.36	1173.23 ± 352.33	0.45

Table 3. Postoperative Outcomes of patients with and without sepsis

Outcomes	Total (n=86)	Sepsis		p value
		Present (n=16)	Absent (n=70)	
Operating time (minutes)	82.24 ± 34.53	99.69 ± 31.12	78.26 ± 34.23	0.024
Stone clearance	37 (43%)	3 (8.1%)	34 (91.9%)	0.03
Hospital stay (days)	4.40 ± 1.63	6.13 ± 1.46	4.00 ± 1.39	<0.001
Post-operative fever	43 (50%)			
Post-operative sepsis	16 (18.6%)			
Post-operative ICU stay	3 (3.5%)			

operating characteristic (ROC) analysis determined that a preoperative NLR cutoff of 1.86 could predict postoperative sepsis with 93.8% sensitivity and 68.6% specificity (AUC = 0.829, CI: 0.707–0.951, p < 0.001) (Figure 3).

DISCUSSION

Despite advancements in flexible ureteroscopic lithotripsy for treating upper urinary and renal stones, percutaneous nephrolithotomy (PCNL) remains irreplaceable in certain cases due to factors such as stone burden, complexity, and location.[15] While PCNL has a low complication rate with fever being the most commonly encountered infectious complication, occurring in 10–25% of cases, and is managed with a short course of intravenous antibiotics. However, severe infection leading to sepsis and septic shock, though rare, can have serious consequences.[12,16,17]

Elevated NLR has been associated with poor prognosis in various malignancies and is widely recognized as an infection marker in sepsis patients, correlating with disease severity.[12] Kidney stones trigger the release of inflammatory mediators, including IL-6, IL-7, IL-8, and TNF-α, resulting in an increased neutrophil count and weakens the immune system by reducing the cytolytic activity of lymphocytes, T cells, and natural killer cells, thereby intensifying the innate immune response and underlying inflammation, resulting in increased NLR.[12,18–20]

A study by Wu et al., (2023) highlighted that an increased NLR may indicate a persistent inflammatory response with findings aligning with few other studies by Sen et al., and Kriplani et al., for predicting sepsis and SIRS in post-PCNL.[12,17,20] Additionally, factors such as preoperative urine culture positivity, stone size, stone complexity, and operative duration were also identified as potential risk factors for sepsis.[12,17,21,22]

Despite its potential as a predictive marker, the role of the NLR in forecasting infectious complications post-PCNL has not been extensively studied. This research seeks to determine the value of preoperative NLR in predicting sepsis following PCNL. Although various cutoff values have been proposed, an optimal threshold remains unclear.[12,17,19,21,22]

A study by Sen et al. involving 487 PCNL patients established a significant correlation between preoperative NLR and postoperative sepsis, with a ROC curve analysis identifying a cutoff value of 2.50 for predicting SIRS/sepsis.[12] Similarly, Kriplani et al. conducted a retrospective study with 517 patients and found that preoperative NLR could serve as an early predictor of SIRS and sepsis, with cutoff values of 2.03 and 2.45, respectively.[17]

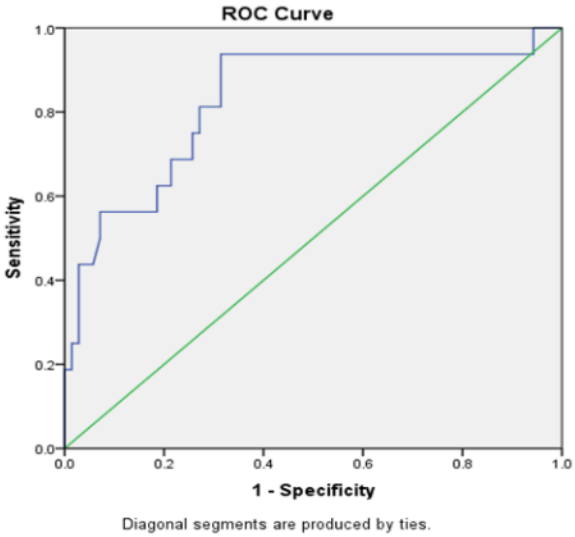

Figure 3. *Receiver operating characteristic (ROC) curve analysis results of NLR in predicting postoperative sepsis*

Other studies have suggested cutoff values ranging from 2.5 to 2.71.[21,22] However, our study identified a lower cutoff of 1.86, likely due to the greater heterogeneity of stone complexity in our sample.

Staghorn calculi and stones classified under higher grades of Guy's stone score are associated with lower stone clearance rates and increased infection risk. In our study, 50% of patients had staghorn calculi, a higher proportion compared to previous studies: Kriplani et al. (4.06%), Yousuf et al. (10.55%), and Yang et al. (6.9%). Staghorn stones are often colonized with bacteria, making complete preoperative urine sterilization challenging and thereby increasing the likelihood of postoperative sepsis.[17,21,22]

Our findings indicated that 50% of patients developed fever post-PCNL, while 18.6% experienced sepsis—higher than in previous studies. Kriplani et al. reported SIRS and sepsis rates of 10.8% and 1.5%, respectively; Sen et al. noted 18.7% SIRS and 5.1% sepsis; and Yousuf et al. documented a sepsis rate of 15.2%.[12,17,21] The increased sepsis rate in our study may be attributed to the inclusion of more complex stones, a greater proportion of cases with prior urinary tract infections (UTIs) with positive urine culture, as well as in patients with prior hardware placement such as nephrostomy tube.

Stone clearance in our study is 43%, lower than the 84.1–90% reported by the Clinical Research Office of the Endourological Society (CROES).[23] Clearance rate declined with increasing stone size. However, our clearance rate for non-staghorn calculi is 86%, aligning with the previous studies and reinforcing the impact of stone complexity on outcomes.

This study has several limitations. It is a single-center analysis with a limited sample size, and subgroup analyses were not performed to avoid unreliable conclusions. Additionally, we relied solely on NLR as an infection marker, without incorporating other biomarkers such as procalcitonin and C-reactive protein. Future large-scale, multicenter prospective studies incorporating multiple infection markers are needed to validate these findings.

CONCLUSION

Postoperative infection appears to be influenced by multiple factors and neutrophil-to-lymphocyte ratio (NLR) may serve as a useful, accessible and cost-effective indicator. Patients with NLR greater than 1.86 could benefit from closer postoperative monitoring to support early detection of infectious complications. However, further prospective studies are needed to validate these findings and to compare the predictive accuracy of NLR with other established biomarkers.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

- Robal Lacoul: Research concept, Research design, Literature review, Research experiment, Data collection, Data analysis, Statistical analysis, Manuscript preparation
- Manish Man Pradhan: Research concept, Research experiment, Statistical analysis, Manuscript preparation
- Suman Chapagain: Research concept, Research design, Data analysis
- Sujeet Poudyal: Literature review, Research experiment, Data collection
- Bhojraj Luitel: Research design, Data collection, Statistical analysis, Manuscript preparation
- Pawan Raj Chalise: Literature review, Data analysis, Statistical analysis, Manuscript preparation

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