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RISK FACTORS FOR FEVER AND SEPSIS AFTER PERCUTANEOUS NEPHROLITHOTOMY: A SINGLE-CENTRE CROSS-SECTIONAL STUDY IN PAKISTAN

Muhammad Waqas[1] , Akhtar Nawaz[2], Siddiq Akbar[1], Muhammad Saad Hamid[1], Shabeer Ahmad[3], Sulaiman Shah[1]

1. Postgraduate Resident, Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan.

2. Associate Professor, Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan.

3. Postgraduate Resident, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.

Corresponding Email: Nawaz157@gmail.com

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ABSTRACT

BACKGROUND: Percutaneous nephrolithotomy (PCNL) is a preferred treatment option for large and complex renal calculi. However, infectious complications such as postoperative fever and sepsis remain clinically significant. The pathogenesis is multifactorial, which involves patient, stone, and operative factors. Reported rates differ widely, and local data from Pakistan is limited. Identifying risk factors could improve perioperative management and reduce morbidity.

OBJECTIVE: :: To determine the frequency of postoperative fever and sepsis after percutaneous nephrolithotomy (PCNL) and to identify associated preoperative and intraoperative risk factors.

METHODOLOGY: This study was conducted at the Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, from January 15 to September 30, 2025. A total of 110 adult patients undergoing PCNL were enrolled. Data was collected and analysed using SPSS version 23. A p-value <0.05 was considered statistically significant.

RESULTS: The median age of the study participants was 38 years (IQR: 20), with 58.2% being male and 41.8% female. Postoperative fever (temperature ≥38°C within 7 days) occurred in 38 patients (34.5%), while sepsis, defined according to SIRS criteria, was observed in 6 patients (5.5%). On forward-stepwise multivariable analysis, staghorn calculi (OR 8.95; 95% CI 1.64–48.88; p=0.011) and partial staghorn calculi (OR 4.64; 95% CI 1.16–18.52; p=0.030) remained independent predictors of postoperative fever. Obesity was also associated with fever (OR 44.4; 95% CI 1.70–1164; p=0.023); however, the wide confidence interval reflects statistical imprecision due to the small number of obese patients, and this finding should be interpreted cautiously. Longer operative time was significantly associated with both fever (p=0.034) and sepsis (p=0.002) on univariate analysis.

CONCLUSION; Staghorn and partial staghorn calculi were independent predictors of postoperative fever following PCNL. Prolonged operative time correlates with both fever and sepsis on univariate analysis. Recognizing risk factors allows clinicians to tailor perioperative care and enhance postoperative monitoring, potentially reducing complications.

KEYWORDS:Fever, Sepsis, PCNL (Percutaneous Nephrolithotomy), Risk factors, Pakistan

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INTRODUCTION

Kidney stones affect approximately 10.1% of the people worldwide, which may lead to pain, haematuria, chronic kidney disease and end-stage renal disease. [1] For large (≥2 cm) and complex stones, percutaneous nephrolithotomy (PCNL) has become a preferred surgical option. [2] Compared to open and laparoscopic procedures, PCNL offers several advantages, including less trauma, reduced bleeding risk, better stone removal efficiency, less postoperative pain and faster recovery. [3] However, the complications remain a concern. These include bleeding, urine leak, fever, sepsis, renal dysfunction, injuries to the diaphragm, pleura, surrounding organs, or intestines, and in rare cases, death of a patient. [4] Among complications, postoperative fever occurs in about 9.5% of the cases, while sepsis affects about 4.5%. [5]

The pathophysiology of the post-PCNL fever and sepsis is complex and multifactorial and includes the release of pro-inflammatory cytokines and chemokines,[6] ischemia-reperfusion injury and the body's reaction to blunt renal trauma. [7] Furthermore, fever often signals the onset of Systemic Inflammatory Response Syndrome (SIRS), and previous studies show that patients with postoperative fever face increased risk of SIRS. [8,9] A 2024 meta-analysis found that women undergoing PCNL develop postoperative fever more often than men, and among those with the postoperative fever, diabetes mellitus was present in 45.30% of the patients, hydronephrosis in 19.82%, staghorn stones in 10.48%, 24.78% had blood transfusions, and 17% had nephrostomy tubes or double-J stents. [5] Another study reported further risk factors for infectious complications, which included multiple puncture tracts, extended operative duration and presence of residual stones after the procedure. [10] Moreover, low body mass index (below 18.5 kg/m²) has also been found to have an increased risk of fever after PCNL. [11]

Recognizing the risk factors for postoperative fever after PCNL is essential to prevent SIRS and sepsis. In Pakistan, the reported incidence of fever after PCNL ranges from 2.2% to 7.7%, while sepsis has been documented in 4.2% to 10.2% of patients. [12,13]

However, the data reporting the risk factors for fever and sepsis following PCNL is still limited in the region, especially in the province of Khyber Pakhtunkhwa. Therefore, this study aimed to study the frequency of postoperative fever and sepsis and to identify associated risk factors of preoperative and intraoperative, to minimize intra and postoperative morbidity.

METHODOLOGY:

This cross-sectional descriptive study was conducted in the Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, from 15th January to 30th September, 2025.

Sample size was calculated using the OpenEpi Version 3 open-source calculator, based on an anticipated fever frequency of 7.7% derived from a previous study conducted in Rawalpindi, Pakistan, [12], with a 5% margin of error and 95% confidence level. The 7.7% figure from the 2016 study [12] was selected rather than the 5.9% reported in 2020 [13] to ensure an adequate number of fever events for analysis. Participants were recruited through non-probability convenience sampling.

Postoperative fever was defined as a body temperature of ≥38°C recorded at any time within seven days following the procedure. Sepsis was defined according to the Systemic Inflammatory Response Syndrome (SIRS) based criteria as suspected or documented infection in the presence of ≥2 of the following: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $PaCO_2$ <32 mmHg; and (4) white blood cell count >12,000/mm³, <4,000/mm³, or >10% immature (band) forms.

Inclusion criteria comprised patients aged ≥18 years of both genders who provided consent to participate. Exclusion criteria included patients with preoperative fever, active infection (raised white blood cell count or positive urine culture), history of allergic reactions to contrast media or anaesthetics used in PCNL, those who received blood transfusion before, during, or after the procedure, or those who declined participation. Patients with active infection received appropriate culture-directed antibiotic therapy and were scheduled for PCNL, the procedure only after documentation of sterile urine culture.

A data collection form was used to gather data from patient charts and direct interviews. Outcomes were recorded by monitoring patients for one week postoperatively through hospital follow-up visits and telephone calls. All patients received intravenous antibiotic prophylaxis with Cefoperazone–Sulbactam (2g) before the induction of general anaesthesia, in accordance with local institutional protocols. At the end of the procedure, a double-J ureteral stent was routinely inserted in all patients.

Data were analysed through IBM SPSS Statistics version 23. Quantitative variables were reported as mean and standard deviation for normally distributed data, and as median with interquartile range (IQR) for non-normally distributed data. Normality was checked using the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages. Associations between categorical variables were examined using the Chi-square test or Fisher's exact test, where appropriate, and the independent-sample t-test or Mann-Whitney U test was used for continuous variables. Multivariable binary logistic regression analysis was performed to identify independent predictors associated with the outcome variables. Variables with a p-value of less than 0.25 in univariate analysis were included in the multivariate model. The regression model was assessed for goodness of fit using the Hosmer-Lemeshow test, and results were presented as odds ratios (OR) with 95% confidence intervals (CI). Sepsis occurred in only six patients, giving <10 events per variable; therefore, multivariable logistic regression was not attempted. A p-value of less than 0.05 was considered statistically significant.

Ethical approval with reference no. IREC No. 372 was obtained from the Institutional Review and Ethical Committee of the Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan.

RESULTS

The study included 110 participants, with a median age of 38 years (IQR: 20). 40.9% (n = 45) were aged 18–35 years, 39.1% (n = 43) were 36–50 years, 15.5% (n = 17) were 51–65 years, and 4.5% (n = 5) were older than 65 years. Males comprised 58.2% (n=64) and females 41.8% (n=46). The majority of the study participants had a normal BMI (53.6%, n=59); however, 35.5% (n=39) were overweight. Underweight and obese individuals each comprised 5.5% of the study sample (n=6 each). Congenital renal anomalies were identified in 4 patients (3.6%), including horseshoe kidney in 3 patients (2.7%) and crossed-fused renal ectopia in 1 patient (0.9%).

Hypertension was the most common comorbidity, present in 24 patients (21.8%), followed by diabetes mellitus in 16 (14.5%), chronic kidney disease in 11 (10.0%), and coronary artery disease in 7 (6.4%). A history of previous PCNL was recorded in 24 patients (21.8%), extracorporeal shock wave lithotripsy (ESWL) in 39 (35.5%), and open renal surgery in 19 patients (17.3%). Non-staghorn stones were observed in the majority of cases (80.0%, n = 88), while staghorn and partial staghorn stones were seen in 9 (8.2%) and 13 (11.8%) patients, respectively. Hydronephrosis was absent in 56.4% (n=62), with mild, moderate, and gross hydronephrosis observed in 25.5% (n=28), 16.4% (n=18), and 1.8% (n=2), respectively. At the time of surgery, 23 patients (20.9%) had a pre-placed double-J stent or percutaneous nephrostomy tube, and a nephrostomy tube was inserted intraoperatively in 29 patients (26.4%). Right-sided PCNL was performed in 58.2% (n=64) and left-sided in 41.8% (n=46). Single-tract access was used in 80.9% (n=89), multiple tracts in 19.1% (n=21). The duration of operation ranged from 80 to 140 minutes, with a median of 100 minutes (IQR: 30 minutes). Stone size

ranged from 16–55 mm (median = 22.5 mm, IQR = 6.3 mm). Complete stone clearance was achieved in 68.2% (n=75), with residual fragments in 31.8% (n=35). Postoperative fever occurred in 38 patients (34.5%), while sepsis was documented in 6 patients (5.5%).

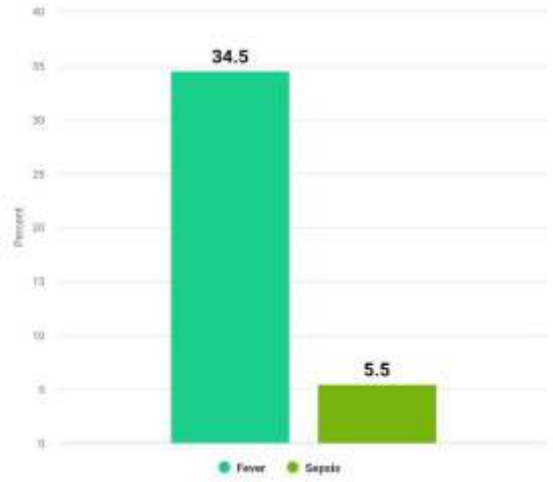

Figure 1: Incidence of Postoperative Fever and Sepsis Following PCNL (n = 110)

Postoperative fever showed statistically significant associations with several variables. BMI was significantly associated with fever (p=0.012), occurring most frequently in obese patients (83.3%, n=5/6) and overweight individuals (43.6%, n=17). Stone burden was also significantly associated with fever (p=0.003), with the highest incidence in patients with staghorn stones (77.8%, n=7/9). Additional significant associations were found with diabetes mellitus (p=0.011), history of open renal surgery (p=0.019), prior double-J stent or percutaneous nephrostomy placement (p=0.013), and hydronephrosis (p=0.012). In contrast, postoperative sepsis showed no significant association with the categorical variables (all p>0.05), as shown in Table 1.

Table 1: Association of Clinical Variables with Postoperative Fever and Sepsis (n = 110)

Variable		Total N	Fever present N (%)	p-value	Sepsis present N (%)	p-value
Age groups (years)	18 - 35	45	14 (31.1)	0.540	1 (2.2)	0.374
	36 - 50	43	18 (41.9)		3 (7.0)	
	51 - 65	17	4 (23.5)		2 (11.8)	
	>65	5	2 (40.0)		0 (0.0)	
Gender	Male	64	23 (35.9)	0.717	4 (6.3)	1.000
	Female	46	15 (32.6)		2 (4.3)	
BMI	Under weight	6	1 (16.7)	**0.012**	0 (0.0)	0.613
	Normal	59	15 (25.4)		3 (5.1)	
	Over weight	39	17 (43.6)		2 (5.1)	
	Obese	6	5 (83.3)		1 (16.7)	
Associated comorbidities	Hypertension	24	11 (45.8)	0.188	1 (4.2)	1.000
	Diabetes mellitus	16	10 (62.5)	**0.011**	1 (6.3)	1.000
	Coronary artery disease	7	3 (42.9)	0.691	0 (0.0)	1.000
	Chronic kidney disease	11	4 (36.4)	1.000	2 (18.2)	0.110
History of PCNL		24	9 (37.5)	0.731	1 (4.2)	1.000
History of ESWL		39	15 (38.5	0.522	3 (7.7)	0.664
History of open surgery		19	11 (57.9)	**0.019**	1 (5.3)	1.000
Stone burden	Staghorn	9	7 (77.8)	**0.003**	0 (0.0)	0.747
	Partial staghorn	13	7 (53.8)		1 (7.7)	
	Non staghorn	88	24 (27.3)		5 (5.7)	

Degree of Hydronephrosis	None	62	17 (27.4)	**0.012**	2 (3.2)	0.186
	Mild	28	8 (28.6)		4 (14.3)	
	Moderate	18	12 (67.7)		0 (0.0)	
	Gross	2	1 (50.0)		0 (0.0)	
Laterality	Right	64	19 (29.7)	0.206	3 (4.7)	0.693
	Left	46	19 (41.3)		3 (6.5)	
Tract	Single	89	30 (33.7)	0.704	3 (3.4)	0.083
	Multiple	21	8 (38.1)		3 (14.3)	
Presence of prior DJS / PCN		23	13 (56.5)	**0.013**	1 (4.3)	1.000
Nephrostomy tube		29	8 (27.6)	0.358	1 (3.4)	1.000
Residual stones (>4mm)		35	13 (37.1)	0.696	0 (0.0)	0.174

In the present study, operative time was significantly associated with postoperative fever, as indicated by the Mann–Whitney test (U = 1038.0, p = 0.034), with a higher mean rank in patients who developed fever (64.18) compared to those who did not (50.92), suggesting that longer procedures were linked to an increased risk of fever. In contrast, no significant association was observed between stone size and postoperative fever (U = 1284.5, p = 0.599). Postoperative sepsis was also significantly associated with longer operative time, as demonstrated by the Mann-Whitney test (U = 296.5, p = 0.002), with a mean rank of 93.08 in the sepsis group versus 53.33 in the non-sepsis group. Although patients with sepsis had higher stone size ranks (mean rank = 76.92) than those without sepsis (54.26), the difference did not reach statistical significance (U = 86.5, p = 0.090), as shown in Table 2.

Table 2: Comparison of Operative Time and Stone Size by Fever and Sepsis Status (n = 110)

Variable	Group		Median	Mean Rank	P-value
Operative Time (minutes)	Fever	Yes	110.00	64.18	**0.034**
		No	100.00	50.92	
	Sepsis	Yes	135.00	93.08	**0.002**
		No	100.00	53.33	
Stone Size (mm)	Fever	Yes	22.00	57.70	0.599
		No	23.00	54.34	
	Sepsis	Yes	27.50	76.92	0.090
		No	22.00	54.26	

In view of the limited number of fever events (n = 38), including all candidate predictors in a single model would have violated the recommended threshold of ≥ 10 events per variable and risked severe over-fitting and unstable estimates. Therefore, we employed a forward stepwise (likelihood-ratio) procedure (entry $p < 0.05$, removal $p > 0.10$), which sequentially adds only those covariates that meaningfully improve model fit. In the multivariable forward likelihood-ratio model, three factors remained independently associated with fever. Staghorn stones increased the odds of fever almost nine-fold compared with non-staghorn stones (adjusted odds ratio [OR] = 8.95, 95 % CI 1.64–48.88; p = 0.011). Partial staghorn stones carried a fourfold risk relative to non-staghorn calculi (OR = 4.64, 95 % CI 1.16–18.52; p = 0.030). Obesity remained a significant predictor after adjustment (OR = 44.4, 95 % CI 1.70–1164; p = 0.023), whereas overweight and normal-weight individuals were not independently associated with fever (p > 0.10). The model showed good overall fit (Hosmer–Lemeshow $\chi^2 = 0.49$, df = 4, p = 0.975), explained 25 % of the variance (Nagelkerke $R^2 = 0.252$), and at a 0.50 cut-off correctly classified 81/110 patients, yielding overall accuracy 73.6 %, sensitivity 42.1 % (16/38), and specificity 90.3 % (65/72). The association between obesity and postoperative fever should be interpreted with considerable caution as this estimate was based on only six obese patients, five of whom developed fever, resulting in a very wide confidence interval and likely model instability. Therefore, this finding should be regarded as hypothesis-generating rather than definitive.

DISCUSSION

This study investigates risk factors for fever and sepsis following PCNL. A 2024 meta-analysis reported postoperative fever and sepsis prevalence rates of 9.5% and 4.5%, respectively. [5] Our study found higher incidence rates of fever (34.5%) and sepsis (5.5%). Comparative studies show varying results. A 2020 study in Islamabad reported fever in 3.7% of patients <60 years and 2.2% in those ≥60 years. [13] Kumar et al. (2019) found fever in 18.9% and sepsis in 2.6% of 201 patients. [14] The CROES global registry study by Gutierrez et al. Reported postoperative fever in 10.4% of 5,313 patients. [15] A 2016 Iraqi study documented fever and sepsis rates

of 28.33% and 5.0%, respectively. [16] The observed rates in our study exceed those reported in most comparative studies, with a notably higher fever rate of 34.5%, which may be attributed to the routine placement of DJ stents in all patients. Hence, comparison between stented and non-stented groups was not possible, and therefore, the independent effect of routine stenting on postoperative fever could not be evaluated.

In the present study, postoperative fever was significantly more common in patients with diabetes mellitus (62.5%, 10 of 16, p = 0.011), aligning with a 2024 meta-analysis[5] (45.3%, 53 of 117, p < 0.001). Although the meta-analysis identified female gender as a risk factor for fever (p =< 0.001), we did not observe a significant association with gender in our study (p = 0.717). Furthermore, significant associations were observed between postoperative fever and body mass index (p = 0.012), presence of staghorn calculi (p = 0.003), history of open renal surgery (p = 0.019), previous placement of a double J stent or percutaneous nephrostomy (p = 0.013), and hydronephrosis (p = 0.012). These associations were not identified in the 2024 meta-analysis.

A 2019 Indian study [14] identified several risk factors for postoperative fever following PCNL, including prolonged operative time over 90 minutes (p = 0.004), with 28.4% of such patients developing fever, prior renal surgery (p = 0.033), with 27.3% affected and residual calculi (p = 0.004), with a 40% incidence of fever. In comparison, our study also found a significant association between operative time and postoperative fever (p = 0.034), as well as with a history of open renal surgery (p = 0.019). However, unlike the Indian study, no significant link was observed between fever and residual stones. Additionally, while the Indian study reported a strong association between nephrostomy tube placement and postoperative sepsis (p < 0.001), our study did not demonstrate this relationship (p = 1.000).

A 2016 study from Iraq [16] found postoperative fever in 62.5% of diabetic patients (p = 0.001), aligning with our results. Stone burden showed a strong association with the postoperative fever, with 77.8% of participants with staghorn stones and 44.4% with partial staghorn stones developing fever (p = 0.001). Our data also revealed a similar trend (p = 0.003), with 77.8% patients with staghorn stones and 53.8% with partial staghorn stones developing fever. The Iraqi [16] study, moreover, reported a significant association between hydronephrosis and postoperative fever (p = 0.001), with fever in 27.8% of patients with moderate and 54.5% of patients with mild hydronephrosis (p = 0.001). Our findings also support this association (p = 0.012); however, we found the reverse distribution (p = 0.012), with postoperative fever occurring in 67.7% of moderate hydronephrosis cases, and only 28.6% with mild hydronephrosis cases had fever. While the Iraqi study identified significant associations with the number of tracts, operative time, stone size, and residual stones, our study only found the operative time finding (p = 0.002 in our study vs. p = 0.013 in Iraq study), and other variables showed no significant association in our study.[16]

By providing data from a tertiary care hospital, our study adds to the limited local evidence base. Furthermore, a prospective design reduced the recall bias and improved the accuracy of the data by following a seven-day postoperative follow-up period that allowed consistent assessment of fever and sepsis after the procedure. However, this study has its limitations, and as a single-centre study, the findings may not apply to other institutions or healthcare systems. The association between obesity and fever is particularly uncertain because of only six obese patients, and hence, the adjusted odds ratio (44.4; 95% CI 1.70–1164) has an extremely wide confidence interval that limits the interpretability. Similarly, the small number of sepsis cases (n=6) meant we lacked sufficient events-per-variable for stable multivariable logistic regression. Furthermore, although forward stepwise logistic regression was used to limit the overfitting given the moderate number of fever events (n=38), the stepwise selection methods remain methodologically controversial and may produce unstable models or biased p-value estimates; therefore, the multivariable findings should be interpreted with appropriate caution. Therefore, larger and multicenter studies are needed to validate these findings, which will provide more precise estimates of these associations.

CONCLUSION

In this single-centre study, staghorn and partial staghorn calculi were independent predictors of postoperative fever following percutaneous nephrolithotomy. Although obesity demonstrated statistical significance in the multivariable model, the association should be interpreted with caution due to the small number of obese patients and the resulting wide confidence interval, which limits the precision of the estimate. Prolonged operative time was significantly associated with both postoperative fever and sepsis on univariate analysis. The findings highlight the multifactorial nature of infectious complications following PCNL and the importance of both patient and procedure-related factors in influencing the outcomes. Careful perioperative risk stratification, optimization of modifiable risk factors and efforts to minimize operative duration may help reduce the postoperative morbidity. Larger, multicenter studies are warranted to validate these findings and provide more precise risk estimates.

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Key Contributions of the Authors	
Author Names	**Author Contributions**
Muhammad Waqas	A, B, C, D
Akhtar Nawaz	A, B, C, D
Muhammad Saad Hamid	B, C, D
Siddiq Akbar	B, C, D
Shabeer Ahmad	B, C, D
Sulaiman Shah	B, C, D

Key for Author Contributions:
A.Conception or Design
B.Acquisition, Analysis, or Interpretation of Data
C.Manuscript writing
D.Critical Review and approval
All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved