DOI: 10.7860/IJARS/2023/65811.2959

Original Article

Surgery Section

Evaluation of Risk Factors for Fever and Sepsis after Ureteroscopic Lithotripsy: A Prospective Observational Study

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ABSTRACT

Introduction: Ureteroscopic Lithotripsy (URS) is gaining popularity for the management of ureteral stones and even renal stones due to its high efficacy and minimal invasiveness. While this procedure is generally considered safe with a low complication rate, febrile Urinary Tract Infection (UTI) after URS is not rare.

Aim: The aim of the present study is to analyse the risk factors for sepsis and febrile UTI after URS.

Materials and Methods: A prospective observational study was conducted at a tertiary referral centre in Jaipur, Rajasthan, from July 1, 2021, to July 1, 2022. The study included 148 patients with obstructive ureteral stones who underwent Ureteroscopy and Laser Stone Lithotripsy (URSL). The patients were divided into two groups: Group-A consisted of patients who developed urosepsis and fever after URSL, and Group-B consisted of patients who underwent URSL without urosepsis. Various risk factors like history of Percutaneous Nephrolithotomy (PCNL), types and sizes of stones, stone locations, duration of operation, mean catheter removal time, and hospital stays were recorded and compared. Chi-square tests and multifactorial logistic regression analyses were used.

Results: The incidence of febrile UTI was 12.16% (18 out of 148 patients). The mean age was 42.2±7.2 years in the postoperative febrile group and 42.75±7.44 years in the postoperative non-febrile group. Statistically significant differences were observed between the groups in terms of stone size ($p<0.001$), duration of operation ($p<0.007$), stone number ($p=0.002$), and stone location ($p=0.013$), which consequently led to an increase in mean catheter removal time ($p<0.001$) and length of hospital stay ($p<0.001$).

Conclusion: The present study identified several notable risk factors associated with the development of fever and sepsis following URS. Identifying these factors enables healthcare providers to identify patients who may be at a higher risk of postoperative complications and implement appropriate preventive measures.

Keywords: Renal stones, Stone number, Stone size, Urinary tract infection

INTRODUCTION

Over the past several decades, the incidence and prevalence of Kidney Stone Disease (KSD) have increased [1-3]. Ethnicity, geographic origin, weather, as well as nutritional and behavioural variables including exercise, nutrition, and hydration, can all affect KSD [2,3]. Treatment options for kidney stones depend on their size and location and may include Shockwave Lithotripsy (SWL), URSL, and PCNL [2,3]. URSL has become a more popular method for treating upper urinary tract stones since the ureteroscope's diameter was reduced and other device advancements were made. However, a URSL procedure can be complicated by postoperative febrile UTI with substantial consequences. Sugihara T et al., reported that 2.39% of 12,372 patients who underwent URSL experienced significant complications, such as septic shock [4].

Recent research indicates that the total complication rate for ureteroscopic surgeries ranges from 9% to 25% [5-9]. Although ureteroscopic treatments can cause UTIs, ureteral injuries, haematuria, and postoperative renal colic, UTI is one of the most prevalent consequences [5-7,10,11]. In endoscopic surgery, preventive antibiotics are frequently used to avoid procedure-associated infections. Fluoroquinolones have historically been used as preventative antibiotics for URS; however, even with preventive antibiotics, UTIs are still common after surgical procedures. Nonetheless, a study has been conducted to analyse the pathogens of febrile UTI following URS [12].

The novelty of the present study lies in its prospective observational approach aimed at investigating the specific risk factors associated with the development of fever and sepsis following URS. This research contributes to the existing body of knowledge by providing a focused analysis of these particular postoperative complications, shedding light on their determinants, and potentially offering insights into preventive strategies and enhanced patient care. The study aimed to identify the features and risk factors of febrile UTI following URS.

MATERIALS AND METHODS

A prospective observational study was conducted at a tertiary referral centre in Jaipur, Rajasthan, from July 1, 2021, to July 1, 2022. The study obtained approval from the Institutional Review Board (MGMC&H/IEC/JPR/2022/942) and adhered to the principles of the Declaration of Helsinki.

Inclusion criteria:

- Patients aged 18 years and above.
- Patients scheduled for URS procedure for obstructive ureteral stones.
- Both genders.
- Patients willing to participate in the study and provide informed written consent.

Exclusion criteria:

- Patients below 18 years of age.
- Patients with a history of Chronic Kidney Disease (CKD) stage 3, 4, or 5.
- Patients with a known history of immunosuppression (e.g., HIV, organ transplant recipients, cancer chemotherapy).
- Pregnant individuals.
- Patients with a known history of bleeding disorders.

- Patients with severe comorbidities that might confound the outcomes (e.g., severe heart failure, advanced liver disease).
- Patients with contraindications to ureteroscopy or lithotripsy procedures.
- Patients who were unable to provide informed/written consent or follow-up.

With a 95% confidence interval, a 5% margin of error, a 10% population proportion, and a 7% dropout rate, a sample size of 148 patients was determined.

A total of 148 patients with obstructive ureteral stones requiring URSL were recruited. Patients who experienced urosepsis and fever after undergoing URSL for stone disease were compared with patients who underwent URSL surgery for stone disease without urosepsis and fever (Group B). Information on the patient's coexisting conditions, prior UTI history, prior endoscopic operations, preoperative urine culture, stone laterality, stone size, stone position, and operating time for infection both before and after surgery was collected during the study period.

Study Procedure

Prior to surgery, all patients undergoing URSL received preoperative antibiotic prophylaxis with an intravenous injection of ceftriaxone 1gm at night and one hour before the procedure. Under spinal anaesthesia, patients were positioned in lithotomy position, and a semi-rigid ureteroscope was introduced. A hydrophilic guidewire was inserted into the concerned ureter under fluoroscopic guidance. In cases of flexible URS, a 12/14-Fr ureteral access sheath was placed along the guidewire up to the proximal ureter. Stones were fragmented using a holmium laser lithotripter/pneumolithotripter. Small calculi fragments (<2 mm) were allowed for natural drainage, while larger fragments were removed using a tripronge forceps. Intraoperatively, a 5 Fr ureteral stent was placed, intraoperatively. A 14 Fr urethral catheter was placed at the end of the operation. The ureteral stent was removed three weeks after the URSL procedure. A basic X-ray of the kidney, ureter, and bladder was performed to detect any visible stones before the removal of the DJ stent.

A postoperative febrile UTI was defined as the presence of pyuria and a temperature greater than 38°C within one week of surgery, without any other organs showing signs of infection [12].

STATISTICAL ANALYSIS

Statistical analyses were performed using GraphPad Statistics version 3.0 software. Risk factors were compared and determinants influencing the incidence of infectious complications subsequent to URS were examined using Chi-square tests and multifactorial logistic regression analyses. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 148 patients were included in two different groups. The incidence of febrile UTI was 12.16% (18/148 patients). The mean age was 42.2±7.2 years in the postoperative febrile group and 42.75±7.44 years in the postoperative non-febrile group [Table/Fig-1].

The history of PCNL, URSL, cytolithotripsy, and ureteral D-J stenting was comparable in both groups and did not show statistical significance [Table/Fig-2]. However, there were significant differences in stone location (p=0.013), stone size (p<0.001), duration of operation (p<0.007), and stone number (p=0.002). These differences resulted in an increased mean catheter removal day time (p<0.001) and length of hospital stay (p<0.001) [Table/Fig-3].

Characteristics	Fever (18)	No fever (130)	p-value
Age	42.2±7.02	42.75±7.44	0.24
Gender			
Male	11 (61.11%)	87 (66.92%)	0.15
Female	7 (38.89%)	43 (33.08%)	
BMI (kg/m^2)	23.4±2.21	24.1±4.51	0.09

[Table/Fig-1]: Demographic data.
Means are compared by unpaired t-test, where areas % are compared by Chi-square test

n (%)	Fever (18)	No fever (130)	p-value
History of			
PCNL			
Positive	2 (11.11)	10 (7.69)	0.36
Negative	16 (88.89)	120 (92.30)	
URSL			
Positive	3 (16.67)	7 (5.38)	0.42
Negative	15 (83.33)	123 (94.62)	
Cytolithotripsy			
Positive	1 (5.56)	3 (2.31)	0.51
Negative	17 (94.44)	127 (97.69)	
Ureteral D-J stenting			
Positive	2 (11.11)	16 (12.31)	0.68
Negative	16 (88.89)	114 (87.69)	

[Table/Fig-2]: Risk factor including history of participants.
PCNL: Percutaneous nephrolithotomy; URSL: Ureterorenoscopic lithotripsy, data are compared by Chi-square test

n (%)	Fever (18)	No fever (130)	p-value
Diabetes			
Positive	4 (22.22%)	16 (12.31%)	0.64
Negative	14 (77.78%)	114 (87.69%)	
History of Pre-operative Urinary Tract Infection (UTI)			
Positive	3	15	0.24
Negative	15	115	
Stone location			
Distal ureter	11	81	0.013
Mid ureter	4	31	
Proximal ureter	3	18	
Stone number			
Single	14 (77.78)	122 (93.84)	0.002
Multiple	4 (22.22)	8 (6.15)	
Mean stone size mm	13.76±3.08	9.26±3.05	<0.001
Duration of operation			
≤1 hour	4 (22.22)	108 (83.08)	0.007
>1 hour	14 (77.78)	22 (16.92)	
Mean catheter removal day	3.84±1.11	2.01±0.89	0.019
Days of hospital stay	8.25±2.83	4.74±2.14	<0.001

[Table/Fig-3]: Risk factor for postoperative fever.
Data are compared by unpaired t-test, Chi-square test, and Multivariate analysis logistic regression

DISCUSSION

Out of 148 patients, 18 (12.16%) developed fever after the procedure. Sugihara T et al., reported that 2.39% of 12,372 URSL cases in Japan had serious complications, including febrile UTI [4]. Mitsuzuka K et al., unveiled an occurrence rate of 18.3% for febrile UTIs within their cohort. It is noteworthy that the present study deviates from their work primarily based on distinct inclusion criteria [13]. Specifically, their study encompassed individuals with preoperative pyuria, which potentially elucidates the elevated rate of febrile UTIs observed in their study. Their findings highlighted preoperative pyuria as a plausible risk factor for febrile UTIs. In the present investigation, patients with preoperative UTIs underwent intensified antibiotic treatment, providing rationale for the absence of pre-existing UTIs as a discernible risk factor. Conversely, the

study by Sohn DW et al., scrutinised a cohort of 531 patients who had undergone diagnostic ureteroscopy or URS [14]. Their findings indicated a lower incidence of infectious complications, specifically observing a 3.8% rate of febrile UTIs. This reduced occurrence in comparison to our study could potentially be ascribed to the incorporation of diagnostic ureteroscopy, a procedure associated with a diminished risk of infectious complications in contrast to lithotripsy interventions.

Female sex is considered a risk factor for the development of post-URSL fever in some studies [15], while others have not found a significant association [16]. In the current study, it was not identified as a risk factor (p=0.150). BMI >18.5 kg/m^2 was regarded as a risk factor for post-URSL fever [17], but no such association was found in the current study. The p-value for post-URSL fever and BMI was 0.09, indicating no statistically significant association, which is comparable to a Korean study [18]. Diabetes mellitus is regarded as a risk factor for fever post-URSL [18,19], but no such association was found in the current study. Several explanations have been proposed to explain the increased risk for infection, including glucosuria and impaired immune or leukocyte function [20,21].

Previous research [22-26] suggested a positive correlation between stone size, gravel content, stone retention likelihood, and heightened postoperative infection. Additionally, larger stones can potentially harm the kidney and renal pelvis mucosa during crushing, leading to vascular exposure, increased fluid absorption [27,28], and greater chance of bleeding. While past studies [29,30] suggested a strong link between stone size/quantity and infection/fever risk, the present study findings are consistent with them. Larger stones, due to the difficulty in traversing narrow channels, might necessitate extra access points, thereby prolonging operation time and increasing bleeding risk [31,32]. Furthermore, it is noteworthy that the study was conducted within a single medical centre. Given the potential variability in pathogen antibiotic resistance profiles across different centres, a subsequent multicentric study is warranted to establish more robust generalisability and comprehensiveness of the findings.

Limitation(s)

The study has a limited sample size. Additionally, the study did not include an analysis of the potential impact of irrigation pressure or volume. This omission was due to the lack of measurements regarding irrigation flow rate and renal pelvic pressure, as manual irrigation was used during URS. As a result, the assessment of irrigation flow pressure was not possible, which is a notable deficiency in the study's methodology.

CONCLUSION(S)

The prevalence of infectious complications following URS was associated with extended operative time, stone size, and stone number, which led to a significant increase in the length of hospital stay and catheter indwelling time. Further studies are warranted to reach a valid conclusion. It is the responsibility of the healthcare facility to develop policies and procedures and evidence-based guidelines for the reprocessing of all critical and semi-critical patient care items.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 05, 2023
- Manual Googling: Sep 14, 2023
- iThenticate Software: Sep 19, 2023 (17%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 04, 2023**
Date of Peer Review: **Aug 04, 2023**
Date of Acceptance: **Sep 20, 2023**
Date of Publishing: **Nov 01, 2023**