THE INCIDENCE OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME AND UROSEPSIS FOLLOWING RETROGRADE INTRARENAL SURGERY (RIRS) IN A TERTIARY CARE HOSPITAL OF KATHMANDU, NEPAL

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ABSTRACT

In recent years, the use of retrograde intra renal surgery (RIRS) for the management of nephrolithiasis is on the rise worldwide. It is commonly considered a safe procedure with lesser complications. The current study aimed to study the incidence of systemic inflammatory response syndrome and urosepsis following retrograde intra renal surgery (RIRS). This is the retrospective observational study among 356 patients who underwent RIRS and 52 were readmitted as 36 developed SIRS and 16 developed urosepsis as a complication in last 5 years (July 1st 2016 –June 30th2021) in department of Urology of B&B hospital, Kathmandu. It is found that only post-operative urine culture had significant association with SIRS with p- value (< 0.00). There was no normality in the data so Mann Whitney U test was applied to test the significant difference in the median values of some quantitative variables between the SIRS and No SIRS group. There was significant difference between the median values of stone volume and duration of fragmentation with p values 0.001 and 0.002 respectively. There was no variables that was found to be associated with urosepsis.

KEYWORDS

Retrograde intrarenal surgery (RIRS), urosepsis, systemic inflammatory response syndrome (SIRS)

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INTRODUCTION

Nephrolithiasis is one of the most prevalent benign urological disease and accounts for a large number of hospital visits. The prevalence and incidence of renal calculi varies throughout the world and have changed in the last several decades, with prevalence of 7% to 13% in North America, 5%–9% in Europe and 1%–5% in Asia.[1] The different types of kidney stones are formed due to varying risk factors such as diet, prior personal and family history of stones, environmental factors, medications and the patient's medical history.[2] The recurrence of renal calculi is common, with an estimated 5-year recurrence rate of up to 30–50% and many studies demonstrated that the recurrence rate of urinary calculi in cured patients increased annually after the initial stone event. These suggests that calculi formation is a lifelong disease and should not only be treated but also be prevented.[3]

The surgical management of urinary-stone disease has marked transformation and due to recently developing technology, certain improvements have been ensured for kidney stone treatment in the field of urologic surgery in this past 20 years.[4] Shock Wave Lithotripsy (SWL), percutaneous nephrolithotomy (PNL), open surgery and recently retrograde intra-renal surgery (RIRS) are the different methods for the surgical management of kidney stones.[5]

One of the main methods used for renal stone removal is retrograde intrarenal surgery (RIRS) using a flexible ureterorenoscope with laser. It doesn't cause renal parenchymal injury and there is a decreased risk of bleeding. RIRS allows minimally invasive access to renal stones and achieves success not inferior to that of percutaneous approaches.[6] RIRS is regarded as a first-line alternative surgery for percutaneous nephrolithotomy and this method was first reported in 1964 by Marshall, who explored the ureter by using a 9F pediatric flexible cystoscope, without any working channel or active deflection.[7] With the growing enhancement of medical field and technologies, the use of RIRS has gradually expanded to kidney stones with a size of more than 2.0 cm or even more than 3.0 cm. RIRS is performed through natural orifice. It can reduce hospitalization time and the risk of bleeding.[8] RIRS has higher stone free rates and lower morbidity because of this it has become popular in the minimal invasive management of renal calculi, particularly for lower pole stones. The different advantages of RIRS such as similar success as other methods and lower complication rates along with the shorter hospitalization period, because of all these reasons currently this approach is being recommended as the primary treatment.[9]

One of the main reasons for the frequent use of RIRS is that it has a lower complication rate than PNL and a higher SFR than SWL. This method is increasingly used as there is an increase in the number of its indications and also the surgeons are gaining more experience in performing it.[10] Following RIRS different complications have been reported, including hematuria, pain, fever, infection, sepsis, kidney loss and mortality. Systemic inflammatory response syndrome (SIRS) following RIRS have not been fully elucidated whereas infection remains a major postoperative complication after RIRS, with incidence approaching 25%.[11]

This retrospective study aimed to explore the predictive factors for post-operative urosepsis and SIRS following RIRS.

MATERIALS AND METHODS

This is a retrospective observational study using non probability convenience method which was conducted among all the patients who underwent Retrograde intrarenal surgery(RIRS) for management of nephrolithiasis and who were readmitted for the complication of Urosepsis, Systemic inflammatory response syndrome (SIRS) following RIRS in last 5 years (July 1st 2016 –June 30th 2021) in department of Urology of B&B hospital, Kathmandu. During this period all patients who underwent RIRS for renal stone were included in this study. However, those patients in whom RIRS was converted to Mini PCNL were excluded in this study. The data was taken from the inpatient hospital registry which included general information (age, gender, BMI, comorbidities), pre and post-operative urine culture, stone characteristics (laterality of stone and location) and surgery-related information (operation time, complications).

Retrograde intrarenal surgery procedure: All RIRS procedures were performed under general anesthesia in the low dorsolithotomy position. As per our hospital microbial culture and sensitivity pattern, all patients were given single dose of Piperacillin – tazobactum 4.5gm IV were given as antibiotic prophylaxis at the time of induction of anesthesia.

Ureteroscopy was first performed using a semi-rigid 6.5/7-Fr ureteroscope (Karl Storz, Germany), with a flexible 0.035-inch guide wire inserted into the renal collecting system. A 9.5F ureteral access sheath (Cook

Medical, Bloomington, IN, USA) was then inserted into the proximal ureter along the guide wire under fluoroscopy guidance. A 7.5F flexible ureteroscope (PUSEN, China) was then advanced through the UAS. Stones were identified and fragmented by holmium: yttrium-aluminum garnet laser lithotripsy. Stones were dusted and later fragments were pop-dusted. A 6-Fr double-J ureteral stent was placed at the completion of surgery. Tablet Ciprofloxacin 500mg twice daily for five days in all patients who had undergone RIRS. Per oral analgesics were given on SOS basis.

The presence of post-operative fever was defined as a body temperature over 38°C within hospital stay that persisted for 48 h.[12,13] Based on previous consensus, SIRS was defined by 2 or more of following criteria: (1) body temperature less than 36°C or greater than 38°C, (2) heart rate greater than 90 beats per minute, (3) respiratory rate greater than 20 breaths per minute, and (4) white cell count >12,000/mm3 or <4000/mm3.[14] Patients who did not meet these criteria were included in the non-SIRS group.

The postoperative urinary tract infection was defined as incidence within the month of RIRS, temperature higher than 38.3 °C and positive results in urine or blood bacterial culture.

Statistical Analysis: The collected data were entered in Excel sheet and cleaned as per necessary. For the analysis of the data SPSS version 16 was used. Frequency and percentage were calculated for the categorical variables and median with inter quartile range was calculated for quantitative variables due to lack of normality in data set. To access the association between dependent and independent variables chi square test was applied. Continuity correction was applied as per necessary. Also, for the quantitative variables significance difference in median of the groups of the dependent variable was compared by using Mann Whitney-U test.

RESULTS

A total of 356 underwent RIRS in 5 years interval (July 1st 2016 –June 30th 2021) in which 52 were readmitted as 36 (10.1%) developed SIRS and 16 (4.4%) developed urosepsis as a complication respectively.

As shown in table 1, out of 356 patients, nearly two third (66.6%) of the patients were male and one third (33.4%) were female. The median age was 39 years with inter quartile range between 27 to 50 years, i.e. 50 percent of the patients were above the age 39 years and 50% below the age 39 years. Similarly, 50% of the patients were of the age between 27 years to 50 years and 25% of the patients were of age below 27 years and 25% were of the age above 50 years. Hence around 75% of the patients were of the age below 50 years. This result showed 60% of the patients had raised BMI and around one third have diabetes. Most of the patients had stone located in lower calyx followed by middle calyx.

Table 1: Clinical and demographic data of the patients

Variables	n	%
Sex		
Male	237	66.6
Female	119	33.4
Age (in years)		
≤20	23	6.5
21 to 40	175	49.2
41 to 60	131	36.8
60 Above	27	7.6
Median Age; 39 | IQ; 27 to 50		
BMI		
Normal (18.5 to 24.9)	145	40.7
Overweight (25 to 29.9)	210	59.0
Obese (30 and Above)	1	0.3
Median BMI; 25 | IQ; 25 to 26		
Smoking		
No	228	64.0
Yes	128	36.0
Diabetes		
No	259	72.8
Yes	97	27.2
Side		
Left	161	45.3
Right	134	37.7
Bilateral	61	17
Stone location		
Lower calyx	102	28.5
Middle calyx	49	13.8
Proxmial uretor	48	13.5
Upper calyx	33	9.3
Renal pelvis	31	8.7
Multiple	93	26.2

*multiple=stone occupying 2 or more of the renal pelvicalyceal system

Table 2: Association between SIRS and Selected variable				
Variables	**SIRS**		**Chi –square / Z -value**	**P-value**
	NO	**YES**		
Sex				
Male	214	23	0.130	0.719
Female	106	13		
Smoking				
No	205	23	0.000	0.984
Yes	115	13		
Diabetes				
No	235	24	0.748	0.387
Yes	85	12		
Prestented				
No	221	21	1.711	0.191
Yes	99	15		
Pre-operative urine culture				
Not Growth	314	28	30.280	0.000*
Organism isolated	6	8		
Post-operative urine culture				
Negative	304	36	1.254	0.263
Organism isolated	16	-		
UAS				
No	191	18	1.253	0.263
Yes	129	18		
Age (years)				
Median (Q_1 , Q_3)	38 (27, 50)	40(30 , 51)	0.508	0.611
BMI (kg/m^2)				
Median (Q_1 , Q_3)	25.3(24.2, 26.2)	25.4(24.5, 26.8)	0.771	0.441
Stone Volume (mm^3)				
Median (Q_1 , Q_3)	670 (580, 870)	830 (700, 1135)	3.319	0.001*
Duration of Fragmentation (min)				
Median (Q_1 , Q_3)	50(35, 65)	65(45, 80)	3.145	0.002*

(* indicates p-value less than 0.05 and significance of the test)

In table 2, to test the association between SIRS and different variables, chi square test was applied. It is found that only post-operative urine culture had significant association with SIRS with p- value (<0.00). As there was no normality in the data, Mann Whitney U test was applied to test the significant difference in the median values of some quantitative variables between the SIRS and no SIRS group. There was significant difference between the median value of stone volume and duration of fragmentation with p values 0.001 and 0.002, respectively. The median stone volume in no SIRS group was 670mm^3 with inter quartile range 580mm^3 to 870mm^3 whereas, it was 830mm^3 in the group with SIRS with inter quartile range 700mm^3 to 1135mm^3 i.e. there was significant difference in the stone volume in SIRS and no SRIS group. Also, 50% of the patients with no SIRS had stone volume between 580mm^3 to 870mm^3 whereas same percent of the patients with SIRS had stone volume between 700mm^3 to 1135mm^3. As the stone volume was significantly high in SIRS group the duration of fragmentation was also found to be high. The median duration of fragmentation in no SIRS group was 50 min

Table: 3 Association between urosepsis and selected variable				
Variables	**Urosepsis**		**Chi–square/ Z -value**	**P-value**
	NO	**YES**		
Sex				
Male	227	10	0.125	0.724
Female	113	6		
Smoking				
No	218	10	0.017	0.895
Yes	122	6		
Diabetes				
No	248	11	0.007	0.936
Yes	92	5		
Prestented				
No	232	10	0.231	0.631
Yes	108	6		
Pre-operative urine culture				
Not Growth	328	14	1.313	0.252
Organism isolated	12	2		
UAS				
No	201	8	0.524	0.469
Yes	139	8		
Age (years)				
Median (Q_1 , Q_3)	39 (27, 50)	35 (25 , 60)	0.347	0.729
BMI (kg/m^2)				
Median (Q_1 , Q_3)	25.3 (24.3, 26.3)	23.8 (23.0, 25.6)	2.270	0.023*
Stone Volume (mm^3)				
Median (Q_1 , Q_3)	690 (580, 890)	845 (610, 1055)	1.496	0.135
Duration of Fragmentation(min)				
Median (Q_1 , Q_3)	50 (35, 70)	52 (45, 82)	1.263	0.206

(* indicates p-value less than 0.05 and significance of the test)

The post-operative urine culture were positive of all the 16 urosepsis cases.

with inter quartile range 35 to 60 min whereas it took 65 min in SIRS group with inter quartile range 45 to 80 min. Age, sex, BMI, smoking habit, diabetes, prestented and post-operative urine culture were not found significantly associated with SIRS.

As shown in table 3, no variables were found to be associated with urosepsis whereas median BMI value was found to be significantly different in urosepsis and no urosepsis group. Other variables like age, sex, smoking, diabetes, stone volume, duration of fragmentation were not found to be associated with urosepsis.

DISCUSSION

In the study conducted by Koras O et al among 949 patients, the mean age ±SD was 47.2 ± 14.3 and median BMI was 26.7. The left kidney had more renal stone than right kidney and commonest site for stone location was renal pelvis.[15] Similarly, the study done by Senocak *et al*[16] among 492 patients, 43.7% of the patients were female and median age of patients was 42 years. The median BMI was 26.4 and 11.8% had diabetes. The commonest site for stone location was renal pelvis. In this study, out of 356 patients, 237 (66.6%) were male and 60%

of the patients had raised BMI. More than one third of the patients were found to be smoker and around one third had diabetes. Likewise, 161 (45.3%) of the patients had renal stone on left side and lower calyx was the commonest site of the stone location.

In the study conducted by Li *et al*,[17] among 484 patients, 66.9% were male and the median age among patients was 51 years. The pre-operative urine cultures was positive among 32.6%. The median surgical time for the RIRS procedure was 59 minutes. Post-operative fever was found in 59 patients (17.5%), and SIRS was found in 22 patients (6.5%). In the similar study conducted by Zhang *et al*[11] surgical times (p <0.001) and high stone burden (p <0.001) were found to be predictive for the occurrence of postoperative SIRS and the preoperative positive urine culture results, operative time, and stone size >20mm were significantly associated with the onset of SIRS (p=0.040, p=0.009, and p=0.001, respectively). In this study it is found that only post-operative urine culture had significant association with SIRS with p- value (<0.00). As there was no normality in the data, Mann Whitney U test was used to test the significant difference in the median values of some quantitative variables between the SIRS and No SIRS group. It showed significant difference between the median values of stone volume and duration of fragmentation with p values 0.001 and 0.002 respectively.

In the study conducted by Kim *et al*[6] among 150 patients, the mean patient age was 56.64±13.91 years, and both genders were evenly distributed (male 49.6% vs female 50.7%) and the mean BMI was 25.04±4.10. The preoperative pyuria was the only statistically significant predictive factor for postoperative febrile urinary tract infection (UTI). Gender, BMI, stone size, preoperative bacteriuria, operative time and operative techniques were not risk factors of febrile UTI. In the similar study conducted by Kazan *et al*,[18] UTI was seen in 20 (6.9%) out of 289 patients. Those patients had a higher rate of UTI history (55% vs 20.5%, p=0.000) and longer operative times (62.5 vs 60 min., p=0.008). In this study no variables were found to be associated with urosepsis whereas median BMI value is found significantly different in urosepsis and no urosepsis group. Other variables like age, sex, smoking, diabetes, stone volume, duration of fragmentation were not found to be associated with urosepsis.

In conclusion, the study showed that SIRS was more common than urosepsis after conducting RIRS for nephrolithiasis. The incidence of SIRS was 36 (10.1%) and urosepsis was 16 (4.4%) respectively as complications following RIRS. The post-operative urine culture had significant association with SIRS and also there was significant difference between the median value of stone volume and duration of fragmentation. None of the variables were found to be associated with urosepsis whereas median BMI value was found to be significantly different in urosepsis and no urosepsis group.

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