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Risk Factors of Post PCNL Systemic Inflamatory Response Syndrome (SIRS)

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ABSTRACT

Background: urolithiasis is one of the most common benign urologic diseases, with a nearly 10% of lifetime incidence. In addition, the prevalence of urolithiasis has been rising through the decade worldwide.
Objective: To determine the parameters and contributing factors that are associated with SIRS following PCNL.
Materials and Methods: an observational retrospective case control study, the medical records of all patients who underwent PCNL for renal stones in-between 10/2017 and 4/2019 (320 patients) at Al-Hussein and Sayed Galal, Al-Azhar University Hospitals had been reviewed. The demographic and perioperative data of these patients had been collected.
Results: the study comprised 307 patients, the mean age of the studied patients was 40.9±15.8 years (range: 2.5 to 70 years). The mean BMI was 26±3 (range: 18 to 35). There were 193(62.9%) males and 114(37.1%) females. Twenty two patients had bilateral renal stone. In 170(55%) cases the targeted stone was in left side and the rest was in the right one. Forty eight (15.6%) cases developed SIRS post-operative. The age, gender, residual stones, hepatitis and diabetes were found to be independent risk factors for SIRS.
Conclusions: good preoperative assessment and strict control of DM and haptic diseases before the procedure, try to render the patient stone free intraoperative as much we can and strict follow up to these categories of patients postoperatively to detect inflammatory response and infectious complications as early as possible.
Keywords: SIRS, infectious complications, percutaneous nephrolithotomy.

INTRODUCTION

Urolithiasis is one of the most common benign urologic diseases, with a nearly 10% of lifetime incidence [(1)]. In addition, the prevalence of urolithiasis has been rising through the decade worldwide [(2)]**.** In the United States, the prevalence rate increased from 3.8% in the 1970s to 8.8% in the 2000s [(3)].

Percutaneous nephrolithotomy (PCNL) is the standard treatment for large renal stones >2 cm and staghorn calculi. It is less traumatic and quicker recovery compared with open surgery. In addition, PCNL has a higher rate of stone clearance than extracorporeal shock wave lithotripsy [(4)]**.** However, relatively higher perioperative complication rates were also reported; including fever (10.8%), blood transfusion (7%), thoracic complications (1.5%), sepsis (0.5%), embolization (0.4%), organ injury (0.4%), and urinoma (0.2%) [(5)]**.**

The rate of complications in PCNL can vary according to the complexity of stone disease as well as patient and procedure-related factors. Complication rates reported by various studies ranged from 3% to 83% [(6)]**.** Postoperative fever is a frequent occurrence with reported rates between 15% and 30% [(7)]**.** While urosepsis has been reported to occur in 0.9–4.7% of PCNL procedures [(8)]**.**

There are predictive tables and scoring systems to predict stone clearance, but there is limited literature on the prediction of complications during PCNL. Duration of procedure, bacterial load in the urine, severity of obstruction, and presence of infected stone directly affect the incidence of febrile urinary tract infection (UTI) and/or urosepsis [(9)]**.**

Infection remains a serious event as sepsis is the leading cause of perioperative mortality[(10)]**.** With sepsis established as an important complication of PCNL, focus has shifted to trying to predict its occurrence based on risk factors. There have been numerous studies investigating potential risk factors for the development of postoperative infectious complications in PCNL patients[(10)].

The following terms were identified according to the census statement published by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) in 2001[(11)]:
SIRS Criteria of two or more of the following:
(1) Body temperature >38°C or < 36∘C;
(2) Heart rate >90 bpm;
(3) Respiratory rate >20 breaths/min or PaCO2 <32mmHg;
(4) White blood cell count >12,000 cells/μL or <4,000 cells/μ.

SIRS describe the inflammatory process, independent of cause based on a combination of vital signs and blood work[(12)].
(1) Infection: Pathological process caused by invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic micro-organisms.
(2) Sepsis: Clinical syndrome defined by the presence of both SIRS and infection.

Historically, clinicians assume that blood cultures are required for the diagnosis of sepsis. In theory, sepsis may occur in the absence of bacteremia, and therefore blood cultures are not included in the definition of sepsis. Further, bacteremia is a poor indicator for sepsis because blood cultures are negative in up to 30% of cases of septic shock [(12)].

Hence, there is intense need to evaluate patient, stone and procedure-related factors in details as there are limited studies on this issue in literature. Current study was aimed to determine predictors of systemic inflammatory response syndrome following PCNL.

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AIM OF THE WORK

To determine the parameters and contributing factors that are associated with SIRS following PCNL.

PATIENTS AND METHODS

It was an observational retrospective case control study. The medical records of all patients who underwent PCNL for renal stones in-between 10/2017 and 4/2019 (320 subject) at Al-Hussein and Sayed Galal, Al-Azhar University Hospitals had been reviewed. **The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.**

Detailed patients' demographics, pre-operative laboratory, clinical and radiologic information and procedure parameters had been collected, including: The age and gender of our subjects, Associated medical co-morbidities, Laboratory data.

Stone characteristics including: size, site, number, density, laterality of stone and the presence of hydronephrosis.

History of previous procedures done before on the same kidney was inquired about.

Intra-operative data had been collected including: Type of anesthesia, Position.

Time of surgery:

1. Number of punctures.
2. Blood transfusion.
3. Type of stenting.
4. Post-operative parameters had been collected including.
5. Vital data.
6. Residual stone (yes/no).
7. Perioperative complications.

Also, the results of any post-operative laboratory investigations performed after surgery as urinalysis, CBC, liver function, and renal function tests had been determined.

All patients were categorized into two groups according to postoperative systemic inflammatory response syndrome (SIRS). Data were analyzed and factors predicting post-PCNL SIRS or fever will be determined.

SIRS criteria are identified according to the census statement published by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) in 2001 (two or more of the following) [13]**:**

(1) Body temperature > 38°C or < 36°C;
(2) Heart rate > 90 bpm;
(3) Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg;
(4) White blood cell count > 12,000 cells/μL or < 4,000 cells/μ.

RESULTS

Out of 320 subjects who underwent PCNL between 10/2017 till 4/2019 at the targeted hospitals, 307 were eligible for study. Thirteen patients were excluded owing to known data collection error.

The mean age of the studied 307 patients was 40.9±15.8 years (range: 2.5 to 70 years). The mean BMI was 26±3 (range: 18 to 35) (table **1**). There were 193 (62.9%) males and 114 (37.1%) females.

The main presenting symptom was renal pain in all patients. 104 (33.9%) patients had a history of previous renal stone procedure on the targeted side. The most common associated medical comorbidities were DM (17.6%), hypertension (16%) and chronic liver disease (7.2%).

The mean pre-operative serum creatinine was 1.03±0.28 mg/dL (range: 0.56 to 2 mg/dL). The mean pre-operative hemoglobin (Hb) level was 13.11±1.55 gm/dL (range: 9.2 to 16.80 gm/dL). The mean of WBCs count was $7*10^3$±1.94 /microliter (ranging from 3.2 to 13.1).

According to our study protocol, all patients had normal pre-operative coagulation profile, with no active UTI as evaluated clinically and by urine analysis and culture results.

Twenty-two patients had bilateral renal stone. In 170(55%) cases the targeted stone was in left side and the rest was in the right one.

Most of patients (191 patients 69.4%) had single renal stone 57 patients (17.6%) had two renal stones, 62 patients (20.2%) had 3 or more multiple renal stones. The mean stone size was 30.2±2.4 (range: 10.00 to 46.00 mm). As evaluated by abdominal X-ray KUB, most of patients (75.3%) had radio-opaque stone(s). The mean stone radio-density, as evaluated by NCCT (in HU), was 1026.56±427.91 (range: 500 to 1600). In patients with multiple stones with different radio-density, the mean HU was calculated and reported.

The majority of the stones were located in the renal pelvis 149 case 48.5%. While lower calyceal stones were in 55 cases 17.9%.

Forty eight (15.6%) cases developed postoperative SIRS.

The mean age in the group of cases that did not develop systemic inflammatory response syndrome (group 1) was (39.1±15.8) while in the group of cases that developed SIRS (group 2) was (50.7±11.4), which was statistically significant.

The mean of BMI in (group 1) was (26±3) while in (group 2) was (26±4), which was statistically insignificant.

In (group 1) 103 cases were females and 156 cases were males, while in (group 2) 11 cases were females and 37 were males, which was statistically significant.

In (group 1) 38 cases were hypertensive and 221 case were not, while in (group 2) 11 cases were hypertensive and 37 cases were not, which was statistically insignificant.

In (group 1) 34 cases were diabetic while 225 cases were not while in (group 2) 20 cases were diabetic and 28 were not, which was statistically significant.

In (group 1) only 4 cases were cardiac patients and the rest were not.While there are no cardiac patients among the (group 2), which was statistically insignificant.

In (group 1) 10 cases had a hepatic disease and 249 did not, while in (group 2) 12 cases had a hepatic disease and 36 did not, which was statistically

significant. There was no significant difference between the 2 groups as regard to stone size and the density of the stone. 162 cases in (group 1) had a single stone, 46 cases had 2 stones and 51 cases had multiple stones. While in (group 2) 29 cases had a single stone, 8 had two stones, and 11 cases had multiple stones. Thus, the stone number was insignificant.

In (group 1) 133 cases had the targeted stone in left side and 126 cases was in the right side, while in (group 2) 37 cases had the targeted stone in the left side and 11 cases was in the right side. Thus, the laterality of the targeted stone was statistically significant.

In (group 1) 168 cases had some degree of hydronephrosis and 91 cases did not. While in (group 2) 40 cases had some degree of hydronephrosis and 8 cases did not. So, the presence of hydronephrosis was significant. But the table showed that the degree of hydronephrosis was insignificant) there was no significant difference between the 2 groups according to the time consumed during the tract formation and the whole operation.

Table (1): Stone number, laterality and the presence of hydronephrosis

		SIRS				
		No		Yes		
		Count	%	Count	%	p value
Stone Numbers	Single	162	84.8	29	15.2	0.876
	Two	46	85.2	8	14.8	
	3 or More	51	82.3	11	17.7	
Laterality	Left	133	78.2	37	21.8	**0.001**
	Right	126	92.0	11	8.0	
Hydro-nephrosis	No	91	91.9	8	8.1	**0.012**
	Yes	168	80.8	40	19.2	
Hydro-nephrosis	Marked	17	77.3	5	22.7	0.145
	Mild	116	78.4	32	21.6	
	Moderate	35	92.1	3	7.9	

SD=standard deviation

One case needed blood transfusion in (group 1) while in (group 2) 29 cases needed blood transfusion which was significant.

In the (group 1) 245 case needed only 1 tract formation for PCNL and 14 case needed 2 tracts while in (group 2) 28 case needed 1 tract and 20 case needed 2 tracts which was significant.

In (group 1) 36 cases needed a DJ fixation while in (group 2) 15 case needed DJ fixation, which was significant.

The intraoperative complications were presented in 40 cases in (group 1) and 16 case in (group 2) which was significant.

The presence of residual stone(s) was found in 68 cases in (group 1) while 27 cases in (group 2), which was significant.

Finally, there was no significant difference between the 2 groups according to the position of PCN, the fluid used for irrigation and the type of the anesthesia.

Logistic regression analysis of the obtained significant risk factors was done and as shown in table (**2**).

Gender (male/female): Male patients were 2.9 times more risky to develop SIRS than females.

Residual Stone (yes/no): patients who had residual stones were 7.2 times more risky to develop SIRS than those who didn't have it.

Hepatic (yes/no): patients who had hepatic disease were 13.2 times more risky to develop SIRS than those who did not have.

Diabetes mellitus (yes/no): diabetic patients were 10.5 times more risky to develop SIRS than those who did not have the disease

Age: with every increase in age by one year there is increase in development of SIRS by 1.1.

Table (2): Independent risk factors

	B	S.E.	P value	OR	95% CI. for OR	
					Lower	Upper
Age	0.068	0.02	0.001	1.1	1.03	1.112
Gender	1.067	0.453	0.018	2.9	1.2	7.0
DM	2.355	0.495	<0.001	10.5	4.0	27.8
Hepatic	2.577	0.619	<0.001	13.2	3.9	43.5
residual stone	1.981	0.453	<0.001	7.2	3.0	17.5
Constant	0.598	1.139	0.599	1.8		

B=Regression coefficients, SE=Standard error of the coefficient, OR=Odds Ratio, 95% CI for OR= 95% confidence interval for the =Odds Ratio. P-value≤0.05 is considered significant

Receiver operating characteristics analysis (ROC) was done for the age, the best cut off point was 49.5 with sensitivity 0.646 and specificity 0.73 the area under the curve was 0.712, p value was <0.001, confidence interval was 0.636 and 0.788 for lower and upper boundaries respectively (figure **1** and table **3**).

Table (3): ROC analysis of the age

Area	SE	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.712	0.039	<0.001	0.636	0.788

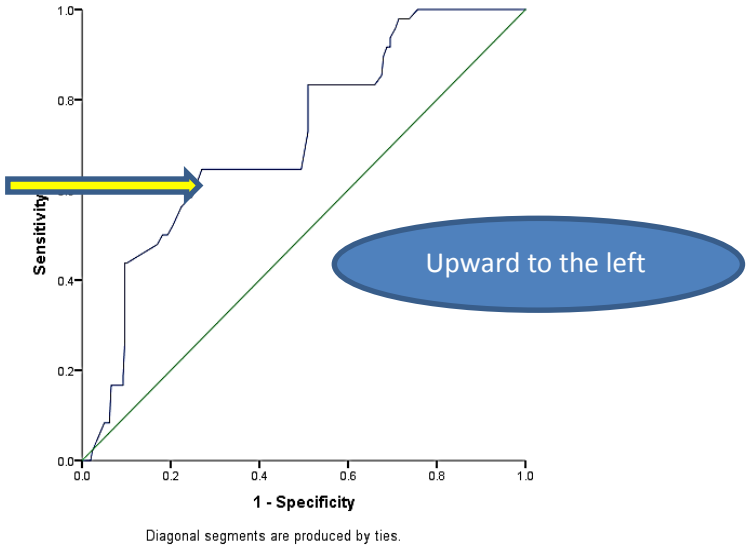

Figure (1): ROC analysis of the age

DISCUSSION

Sepsis is the leading cause of perioperative mortality[10]. With sepsis established as an important complication of PCNL, focus has shifted to trying to predict its occurrence based on risk factors. There have been numerous studies investigating potential risk factors for the development of postoperative infectious complications in PCNL patients[10].

Despite the fact that all patients in the current study received antibiotic prophylaxis, the rate of SIRS post PCNL was 15.6% (48 cases among 307) while in a large international cohort study done by the Clinical Research Office of the Endourological Society [CROES] including >5000 cases the presence of fever or SIRS was 10.5% (598 cases)[14].

In a study done by **Chen *et al.*[15]** the SIRS rate is 23.4%. And in another study done by **Kora*et al.*[16]** the SIRS rate was 27.4%.

In our study we found that Male patients were 2.9 times more risky to develop SIRS than females, however In a retrospective study including 117 case underwent PCNL done by **Sharifi *et al.*[17]**, the female gender was more liable to develop post PCNL fever.

in our study the age is significant risk factor after multivariate analysis (OR =1.1 i.e. with every increase in age by one year there is increase in development of SIRS by 1.1), while in a prospective study done by **Gonzalez-Ramirez *et al.*[18]** including 4456 cases the age was a significant risk factor with odds ratio 0.99 in the univariate analysis only.

It was reported in one study that BMI >18.5 kg/m2 was regarded as risk factor for post PCNL SIRS [19]. In the current study there was no significant difference between the BMI in both case and control group.

In **Gutierrez *et al.*[19]** study the presence of stag horn stone is significant risk factor (OR=1.88).

Also in a retrospective study done by **Chen *et al.*[15]** including 209 cases and in a prospective study done by **Mariappan *et al.*[20]**, including 132 cases they found that the stone size was a significant risk factor.

The impact of stone burden as a risk factor for post PCNL fever and SIRS is confirmed by several studies[21,22,23]. However, in our study there was no significant relation between the stone size and the development of post-operative SIRS.

Chen *et al.*[15] found that the presence of hydronephrosis was a significant risk factor.

In our study we found that the overall duration of the operative procedure has no association with post-operative SIRS, however.

The overall duration of the operative procedure was associated with postoperative infectious complications and SIRS in many studies. For example, in a retrospective analysis of 209 patients, **Chen *et al.*[15]** found that post-PCNL SIRS was associated with a longer mean operative time (132 min compared with 96 min in patients who did not experience SIRS), a difference that was statistically significant. Similarly, **Wang *et al.*[24]** demonstrated that operative time >90 min was strongly associated with occurrence of septic shock in their cohort of 420 patients. In our study we found that the multiple punctures during the procedure and the intraoperative blood transfusion both were significant in the univariate analysis while in the multivariate analysis were not, however in Chen et al 2008 study there was a significant relation between SIRS and both multiple punctures and blood transfusion. Post-operative DJ insertion is considered as risk factor for development SIRS post PCNL in many studies [17,21].

In our study 15(29.4%) of 51 patients who underwent DJ stenting during the procedure developed SIRS postoperatively which is significant in the unvariate analysis only while in the multivariate analysis was not.

In our study we found that patients who had residual stones were 7.2 times riskier to develop SIRS than those who didn't have it.

The contribution of residual stones to postoperative SIRS had been evaluated in two studies. **Gutierrez *et al.*[19]** found that the presence of residual stones was associated with increased likelihood of postoperative SIRS on univariate analysis.

CONCLUSION

We concluded that age, gender, residual stones, hepatitis and DM are independent risk factors for SIRS; intensive care should be taken when dealing with patients who have these risk factors. Good preoperative assessment and strict control of DM and haptic diseases before the procedure, try to render the patient stone free intraoperative as much as we can and strict follow up to these categories of patients postoperatively to detect inflammatory response and infectious complications as early as possible.

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