

# Predictors of Renal Recovery among Patients of Obstructive Urolithiasis with Renal Failure- A Prospective Observational Study

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## ABSTRACT

**Introduction:** Timely intervention in patients of obstructive uropathy secondary to renal and/or ureteric stones can reduce the morbidity and mortality in such patients.

**Aim:** To determine the factors predicting recovery in patients of urinary stones and obstructive uropathy.

**Materials and Methods:** This prospective observational study was conducted at Shri Mahant Indresh Hospital, Dehradun, Uttarakhand, India, between December 2018 and June 2020. All patients with renal failure (serum creatinine >1.5 mg/dL) secondary to urinary stones presenting to the Emergency Department were included in the study. Baseline demographic data, clinical, haematological, biochemical and microbiological parameters were recorded at presentation and after Double J Stent (DJS) insertion at postintervention day 1, 3 and 7. Total 40 patients were divided into two groups i.e., recovered (n=25) and non recovered (n=15) groups. Receiver Operating Characteristic (ROC) curves were used to obtain optimal threshold duration of illness, the values of serum creatinine, serum urea, haemoglobin and serum potassium, and time to nadir creatinine for predicting renal recovery. The graphs were made using both Microsoft Excel and SPSS software.

**Results:** Out of total 40 patients, 29 were males and 11 were females. The mean duration of symptoms in the recovered and non recovered groups was 4.64 and 15.53 days, respectively (p=0.001). Thirteen out of 15 patients (86.6%) in the non recovered group and 10 out of 25 (40%) in the recovered group had pre-existing co-morbidities (p=0.004). Postobstructive diuresis was present in 84% patients in the recovered and 46.6% in the non recovered group (p=0.016). The nadir serum creatinine level was 1.26 mg/dL in recovered as compared to 6.08 mg/dL in the non recovered patients (p=0.001). The ROC curves were plotted for various parameters in order to find the prognostic accuracy in predicting recovery. The best criteria were symptom duration ≤6 days, serum creatinine at presentation ≤6.2 mg/dL, serum potassium ≤5.5 mg/dL, and haemoglobin level >9.4 g/dL.

**Conclusion:** Short duration of symptoms (≤6 days), lower serum creatinine levels (≤6.2 mg/dL), lower serum potassium levels (≤5.5 mg/dL), and higher haemoglobin level (>9.4 g/dL) were found to predict a greater chance of recovery. These factors can help in formulating treatment protocols for early intervention leading to a better prognosis in this subgroup of patients.

**Keywords:** Kidney stones, Predictive factors, Renal insufficiency

## INTRODUCTION

Renal stones have been a well-known entity for centuries, and the mention of renal stones can be found in early Egyptian and Indian literature dating back more than a thousand years. Nephrolithiasis is a common systemic disorder associated with both Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD).

In India, urolithiasis affects about 2 million people every year [1]. A population based study conducted in northern India reported that the lifetime prevalence (95% CI) of urinary stones was 7.9% (5.7-10.8) [2]. Amongst the patients presenting with urolithiasis, approximately 37% patients have bilateral renal stone disease [3]. Obstructive uropathy is one of the most common urological emergencies with an overall incidence of 20% [4]. Timely surgical decompression in the form of either a percutaneous nephrostomy or an indwelling JJ stent has been shown to decrease the mortality from 19.2 to 8.8% [5].

Various studies have attempted to identify factors predicting renal recovery in patients with obstructive uropathy [6-8]. Except for the recently published study by Sharma G et al., no other study has endeavoured to assess the factors comprehensively [8]. Therefore, this study was undertaken to ascertain the factors predicting recovery in a comprehensive and prospective manner in patients of obstructive uropathy secondary to urinary stones. Timely intervention in these patients would go a long way in reducing the associated short-term and long-term morbidity, mortality and medical expenses.

## MATERIALS AND METHODS

A prospective, hospital-based, observational study was conducted at Shri Mahant Indresh Hospital, Dehradun, Uttarakhand, India, between December 2018 and June 2020. All patients presenting to the Emergency Department and fulfilling the study criteria were enrolled for the study. Renal failure was defined as serum creatinine level >1.5 mg/dL for the purposes of the study [9]. The ethical clearance was obtained from the Institutional Ethics Committee (SGRR/IEC/4419) and written informed consent was taken from the patients.

**Inclusion and Exclusion criteria:** Patients of renal and/or ureteric stones having associated renal failure (serum creatinine >1.5 mg/dL) were included in the study. Patients of renal and/or ureteric stones having normal renal function and who were unwilling to give consent for intervention and subsequent follow-up were excluded from the study.

Total 40 patients were included in the study and divided into two groups:

- **Recovered group (n=25):** Patients who attained the recovery criteria (defined as serum creatinine <1.5 mg/dL within the 7 day postprocedure period).
- **Non recovered group (n=15):** Patients with serum creatinine levels >1.5 mg/dL (did not fulfill the recovery criteria).

## Procedure

Baseline demographic data, clinical, haematological, biochemical and microbiological parameters were recorded. Clinical parameters

included flank pain, vomiting, fever, renal angle tenderness, history of oliguria or anuria and co-morbidities. Haematological and biochemical parameters included haemoglobin level, Total Leucocyte Count (TLC), serum sodium, potassium, urea and creatinine levels. Urine routine examination and cultures were done at presentation. Patients who presented with severe metabolic acidosis, fluid overload, and persistent hyperkalemia underwent emergency haemodialysis, in consultation with a nephrologist. Ultrasound and/or Computed Tomography of Kidneys, Ureters and Bladder (CT KUB) were done, and findings were recorded, mentioning the stone size, stone location and grade of hydronephrosis. Thereafter, patients underwent Double J Stent (DJS) insertion (unilateral or bilateral, depending on the clinical indication).

Clinical, biochemical, haematological, and microbiological investigations as defined above were reanalysed on day 1, day 3 and day 7 postprocedure to assess recovery, to correct metabolic and electrolyte abnormalities, and treat infection. Patients were classified into recovered and non recovered groups based on achieving/not achieving a nadir serum creatinine level of <1.5 mg/dL. Both the groups were analysed statistically in order to identify factors predicting recovery.

#### Data collection was done using semi-structured questionnaire containing three parts:

1. Socio-demographic and clinical datasheet to record patients' demographic data including name, gender, age, height, weight, and clinical data which included diagnosis, clinical history, course of illness, symptoms and co-morbidity.
2. Laboratory data and radiological parameters were recorded.
3. Follow-up case sheet: All the laboratory parameters were recorded at postintervention day 1, 3 and 7.

## STATISTICAL ANALYSIS

The data obtained were tabulated in Microsoft Excel version 16.0 and statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 software. The quantitative data were expressed as mean and standard deviation. The categorical data were expressed in proportion and percentages. Chi-square test was performed to compare the proportion in two groups with categorical variable. Independent t-test was performed to look for difference in means of the two groups with quantitative variable. A p-value <0.05 was considered to be statistically significant. Receiver Operating Characteristic (ROC) curves were used to obtain optimal threshold duration of illness, the values of serum creatinine, serum urea, haemoglobin and serum potassium, and time to nadir of creatinine for predicting renal recovery. The graphs were made using both Microsoft Excel and SPSS software. ROC curves were created using Medcalc software. Area Under Curve (AUC) >0.5 was considered significant.

## RESULTS

Forty patients were enrolled, out of which 29 were males and 11 were females. The two groups were then evaluated in terms of the variables enlisted in [Table/Fig-1].

Ten (90.9%) females and 15 (51.7%) males showed recovery. This association of gender with recovery was statistically significant (p=0.03). No statistical difference was found in the mean age in both the groups (p=0.064).

The mean duration of symptoms in the recovered and non recovered groups was 4.64 and 15.53 days respectively which was statistically significant (p=0.001).

A total of 28 patients needed haemodialysis at presentation, which included all 15 patients in the non recovered group. Thirteen patients (out of 25) in the recovered group also needed haemodialysis at presentation due to severe metabolic acidosis, fluid overload or persistent hyperkalemia. However, none of them required haemodialysis postintervention. On the other hand, all the

Variables		Recovered N (%)	Non-recovered N (%)	p-value	Odds ratio (95%CI)
Gender	Female (11)	10 (90.9%)	1 (9.1%)	0.030	9.33 (1.05-82.62)
	Male (29)	15 (51.7%)	14 (48.3%)		
Duration of symptoms	≤7 days (26)	23 (88.5%)	3 (11.5%)	0.001	46 (6.74-313.9)
	>7 days (14)	2 (14.3%)	12 (85.7%)		
Anuria at presentation	No (16)	7 (43.7%)	9 (56.2%)	0.047	0.25 (0.06-1.00)
	Yes (24)	18 (75%)	6 (25%)		
Need for haemodialysis	No (12)	12 (100%)	0	0.02	0.035 (0.002-0.645)
	Yes (28)	13 (46.4%)	15 (53.6%)		
Blood parameters* (mean±SD)	Haemoglobin (g/dL)	11.31±2.07	8.92±2.15	0.001	
	Serum creatinine (mg/dL)	5.95±3.69	10.98±3.18	0.001	-
	Serum potassium (mg/dL)	4.72±0.80	5.34±1.08	0.04	-
	Nadir creatinine (mg/dL)	1.26±0.3	6.08±2.16	0.001	-
	Time taken to reach nadir creatinine (days)	5.16±2.07	5.93±1.83	0.24	-
	Percentage fall in creatinine (%)	70.39±18.02	44.33±22.01	0.001	-
Presence of co-morbidities	No (17)	15 (88.2%)	2 (11.8%)	0.004	9.75 (1.79-52.84)
	Yes (23)	10 (43.5%)	13 (56.5%)		
Radiology* (Mean±SD)	Largest stone diameter (mm)	16.21±6.93	16.36±10.13	0.96	-
Post obstructive diuresis	No (12)	4 (33.3%)	8 (66.7%)	0.016	0.16 (0.03-0.72)
	Yes (28)	21 (75%)	7 (25%)		

**[Table/Fig-1]:** Factors of renal recovery in the recovered and non-recovered groups. \*odds ratio was not calculated as data was quantitative (independent sample t-test was applied)

non recovered patients required haemodialysis subsequently. This was statistically significant (p=0.02).

Twenty four patients (18 in recovered and six in non recovered groups) were anuric upon presentation. Majority of these patients required haemodialysis support on presentation. Fourteen had bilateral hydronephrosis due to stone. The association of anuria with recovery rate was statistical significant (p=0.047).

Thirteen out of 15 patients in the non recovered group had pre-existing co-morbidities namely diabetes and hypertension, which are a leading cause of CKD (p=0.004, Chi-square test). The presence/absence of urinary tract infection was not a statistically significant parameter.

All patients with mild hydronephrosis, two-thirds with moderate hydronephrosis and none with gross hydronephrosis recovered. However, the association of degree of hydronephrosis with recovery could not be measured due to the absence of patients in mild hydronephrosis subgroup of non recovered and gross hydronephrosis subgroup of recovered patients.

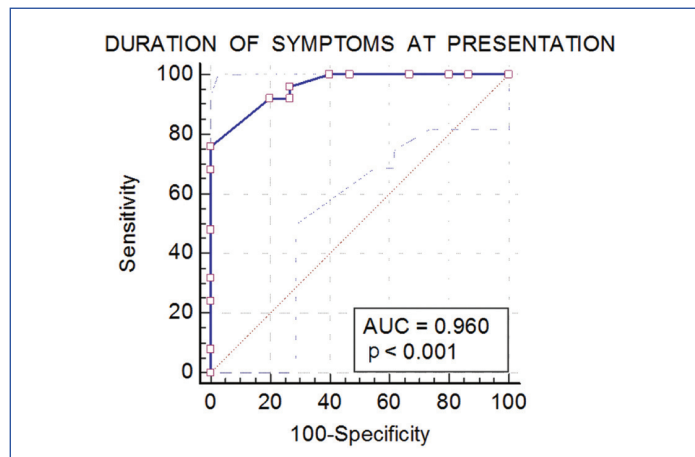
Postobstructive diuresis was present in 75% patients in the recovered and 25% in the non recovered group. This difference was statistically significant (p=0.016, Fisher's Exact test).

The patients who recovered had a higher mean haemoglobin level (11.31 g/dL) as compared to those who did not recover (8.92 g/dL). The mean serum potassium level was 5.34 mg/dL in the non recovered as compared to 4.72 mg/dL in the recovered groups. Similarly, the patients who did not recover had a higher serum creatinine level at presentation (10.98 mg/dL) as compared to the recovered patients (5.95 mg/dL). All these differences were found to be statistically significant (p=0.001, 0.04 and 0.001, respectively). However, the differences in mean TLC levels, serum sodium level

and largest stone diameter were not found to be statistically significant between the two groups.

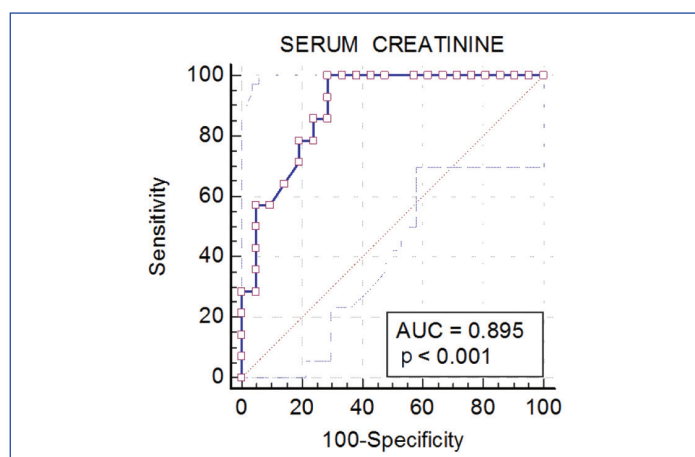
The nadir serum creatinine level was much lower (1.26 mg/dL) in recovered as compared to the non recovered patients (6.08 mg/dL). Similarly, the fall in serum creatinine levels in percentage terms was 70.39% in the recovered group versus 44.33% in the non recovered group. Both of these were statistically significant (p-value=0.001). The time taken to reach nadir creatinine level was slightly higher in the non recovered patients (5.93 days vs 5.16 days). This difference was not statistically significant.

Most of the patients in the study had bilateral ureteric stones (32.5%), followed by bilateral renal stones (17.5%). The other patients had unilateral stones in either of the locations. There was no statistically significant relation between stone location and recovery in the study (p=0.83).



Youden index	0.76
Area under curve	0.96 (0.845 to 0.997)
Associated criteria	≤6 days
95% Confidence interval	5.38-6.61
Sensitivity	76% (54.9-90.6)
Specificity	100% (78.2-100)
Significance level p (Area=0.5)	<0.001

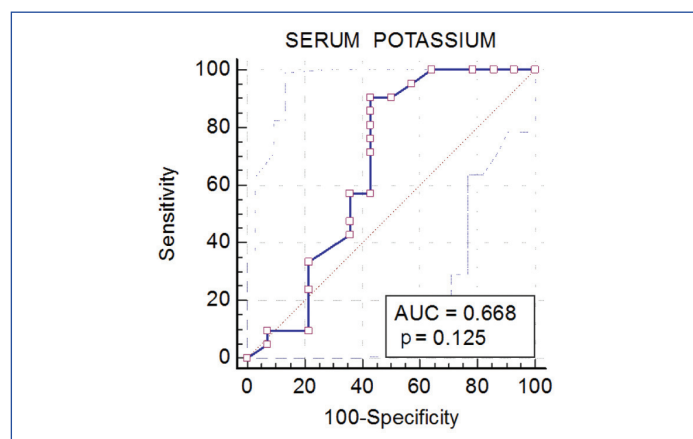
**[Table/Fig-2]:** The Receiver Operating Characteristic (ROC) curve showing prognostic accuracy of duration of symptoms with renal recovery.



Youden index	0.71
Area under curve	0.89 (0.845 to 0.997)
Associated criteria	≤6.2 mg/dL
95% Confidence interval	4.6-8
Sensitivity	71.43% (47.8-88.7)
Specificity	100% (76.8-100)
Significance level p (Area=0.5)	<0.001

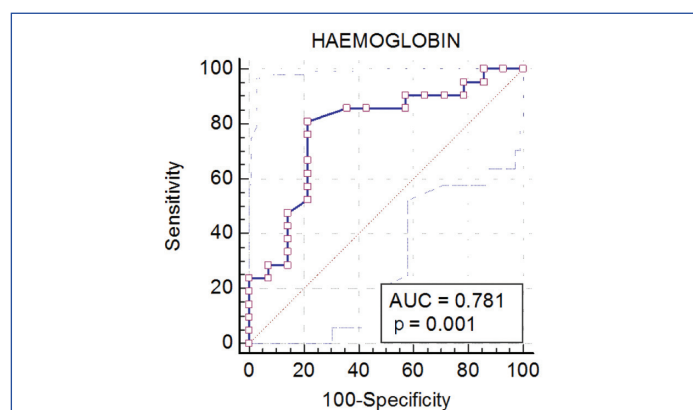
**[Table/Fig-3]:** The Receiver Operating Characteristic (ROC) curve showing prognostic accuracy of level of creatinine at presentation with renal recovery.

The ROC curves were plotted for various parameters in order to find the prognostic accuracy in predicting recovery. For duration of symptoms [Table/Fig-2], the best criteria was found to be ≤6 days (95% CI: 5.38-6.61) with sensitivity of 76% (54.9-90.6) and specificity of 100% (78.2-100). The chances of recovery were statistically better at or below this cut-off level. Similarly, the absence of co-morbidity had a sensitivity of 64% (42.5-82) and specificity of 86.67% (59.5-98.3) in predicting the chances of recovery. On plotting the ROC curve for serum creatinine at presentation [Table/Fig-3], the best criteria found was ≤6.2 mg/dL (95% CI: 4.6-8) with a sensitivity of 71.43% (47.8-88.7) and specificity of 100% (76.8-100). Below this cut-off, the chances of recovery were statistically better. Similarly, the serum potassium level of ≤5.5 mg/dL was found to be statistically significant [Table/Fig-4] in predicting recovery (95% CI: 4.88-6.1) with a sensitivity of 90.48% (69.6-98.8) and specificity of 57.14% (28.9-82.3). A haemoglobin level of >9.4 g/dL (95% CI: 8.4-10.39) at presentation was associated with recovery with a sensitivity of 80.95% (58.1-94.6) and specificity of 78.57% (49.2-95.3) [Table/Fig-5].



Youden index	0.47
Area under curve	0.668 (0.489 to 0.818)
Associated criteria	≤5.5 mg/dL
95% Confidence interval	4.88-6.1
Sensitivity	90.48% (69.6-98.8)
Specificity	57.14% (28.9-82.3)
Significance level p (Area=0.5)	0.12

**[Table/Fig-4]:** The Receptor Operating Characteristic (ROC) curve showing prognostic accuracy of level of serum potassium at presentation with renal recovery.



Youden index	0.59
Area under curve	0.78 (0.609 to 0.902)
Associated criteria	>9.4 g/dL
95% Confidence interval	8.40-10.39
Sensitivity	80.95% (58.1-94.6)
Specificity	78.57% (49.2-95.3)
Significance level p (Area=0.5)	<0.001

**[Table/Fig-5]:** The Receptor Operating Characteristic (ROC) curve showing prognostic accuracy of level of haemoglobin at presentation with renal recovery.

## DISCUSSION

Urolithiasis is one of the common causes of renal failure in India. Renal failure secondary to obstructive urolithiasis has varied clinical outcomes depending on the type and timing of surgical intervention [10]. Early relief of obstruction can cure renal failure due to post renal etiology or stabilise renal function compatible with a comfortable life [11]. Various factors can affect the recovery of renal function after the relief of obstruction, like patient age, duration and degree of obstruction, and renal failure. Other confounding factors like the presence of infection and co-morbidities also play a role in recovery.

Double J Stents (DJS) and Percutaneous Nephrostomies (PCN) have been used for urinary diversion to relieve obstruction with equivalent outcomes [12]. The authors preferred DJS in the present study because of the advantages of internal drainage leading to better patient compliance and a readily available operation theatre for endourological procedures. Moreover, dependence on interventional radiologist and ultrasound machine, to place a PCN, was obviated.

Serum creatinine level was used as the parameter for renal recovery in our study. In order to have two groups for comparison we used a nadir serum creatinine level of 1.5 mg/dL to define renal recovery [9]. Degree and duration of renal damage was assessed by duration of symptoms, presence of anuria, need for haemodialysis, and haemoglobin and serum creatinine level at presentation, presence of hyperkalemia, stone size, and degree of hydronephrosis. Rate of renal recovery was assessed by the nadir creatinine level, time taken to reach nadir level, percentage fall in serum creatinine, presence of postobstructive diuresis and need for subsequent haemodialysis.

The duration of symptoms at the time of admission had significant relationship with recovery. The mean duration of symptoms in the recovered and non recovered groups was 4.64 and 15.53 days, respectively. The ROC curve showed a cut-off value of 6 days indicating the patients with more than 6 days symptom duration were prone to non recovery. Other studies have also reported a shorter symptom duration (of 25 days and 4 weeks respectively) to be a significant predictor of recovery [6,8]. The mean serum creatinine levels, haemoglobin levels, and potassium levels also indicate the duration and degree of renal dysfunction. All these parameters were significant in predicting recovery, with patients having higher haemoglobin and lower serum creatinine and potassium levels having better chances of recovery. On plotting the ROC curves, haemoglobin level of >9.4 g/dL, serum creatinine level of ≤6.2 mg/dL and potassium level of ≤5.5 mg/dL had the best prognostic value. Presence of post obstructive diuresis, lack of need of postprocedure haemodialysis, nadir serum creatinine, rate of fall of serum creatinine, indicate renal recovery. All these factors achieved statistical significance in predicting recovery. However, the time needed to reach nadir creatinine level did not reach statistical significance, probably because of a short follow-up time (7 days) in the current study.

Diabetes and hypertension are leading causes of CKD worldwide. Their presence significantly altered the course of recovery in our patients. The recovered group patients had the presence of co-morbidities in 10 out of 25 patients compared to 13 out of 15 in the non recovered group.

Rajadoss MP et al., have reported a symptom duration of ≤25 days, absence of hypertension, parenchymal thickness of >16.5 mm and haemoglobin level of <9.85 g/dL to be associated with good recovery on bivariate analysis [6]. Similarly, Harraz A et al., reported that serum creatinine at presentation, haemoglobin level episodes of previous obstructive uropathy and urine culture were independent predictors of the rate of renal recovery multivariate analysis [13]. In another recent study, patients with renal function recovery had significantly lower mean age (46.1 years vs 51.9 years), serum creatinine (7.7 mg/dL vs 10.3 mg/dL) and blood urea (150.1 mg/dL

vs 191.2 mg/dL) at presentation [8]. This study used age, haemoglobin level, duration of symptoms, presence of solitary functioning kidney, and venous blood pH level to construct a score which would predict renal recoverability.

Complicated urolithiasis caused by obstructive uropathy can lead to AKI and early decompression is recommended in such patients. The presence of infection has been associated with non recovery in many studies [9,14,15]. In the current study, more than half of the patients in both the groups had infection but did not reach statistical significance.

Various radiological factors like parenchymal thickness, degree of hydronephrosis, stone location and size have been studied for their association with likelihood of recovery. Renal cortical thickness was reported to predict renal function recoverability by Sasmol S et al., [16]. Long-standing obstruction can also lead to a greater degree of hydronephrosis. Statistically significant association between degree of hydronephrosis and failure rates of ureteric stenting have also been reported [17]. The authors also found that the majority of patients in the recovered group had mild to moderate hydronephrosis as compared to gross hydronephrosis in the non recovered group. Stone burden and location have been found to be significant predictors of recovery in many studies [9,14,18,19]. In the present study, stone size and location did not reach statistical significance in predicting recovery.

To the best of the authors' knowledge this is the most exhaustive prospective study to determine the prognostic factors of renal recovery in patients with renal failure secondary to obstructive uropathy. The authors studied a large number of clinical, biochemical and radiological parameters which are readily available in routine clinical settings to identify a few relevant good or bad prognostic markers in such cases. These factors can be applied in low-resource settings and accurate predictions can be made. Early decompression of these kidneys is recommended for better chances of restoration of renal function.

### Limitation(s)

The limitations of the study were small sample size and a short duration of follow-up. This was due to resource constraints and the onset of the pandemic during data collection. Further prospective studies and randomised trials with longer follow-up are needed for validation and generalisation of the study findings.

### CONCLUSION(S)

Short duration of symptoms (≤6 days), lower serum creatinine levels (≤6.2 mg/dL), lower serum potassium levels (≤5.5 mg/dL), and higher haemoglobin level (>9.4 g/dL) predict a greater chance of recovery with a high degree of accuracy in patients with obstructive urolithiasis and renal failure. Similarly, the presence of post obstructive diuresis, lack of need for postprocedure haemodialysis, rapid fall of serum creatinine also have significance in predicting renal recovery in such patients. Diabetes and hypertension, which are leading causes of CKD significantly altered the course of recovery in our patients.

High stone burden, high prevalence of diseases like diabetes and hypertension, coupled with associated complications like renal failure can lead to long hospital stays and high financial burden in a country with limited resources like India. The positive predictors in the present study can help in formulating treatment protocols for early intervention leading to a better prognosis in that subgroup of patients.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]

- Plagiarism X-checker: Mar 09, 2022
- Manual Googling: Jun 02, 2022
- iThenticate Software: Jun 06, 2022 (8%)

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