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Emphysematous pyelonephritis (EPN): A prospective study on management modalities and outcome in a tertiary care hospital

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Abstract

Background: EPN was a rapidly progressive, fulminant, life threatening, necrotizing infection of kidneys and perinephric space. EPN was most commonly seen in patients with diabetes mellitus.

Aim and Objective: To study the clinical features, radiological classification, risk factors, Prognostic factors and management Modalities of Emphysematous pyelonephritis.

Methodology: 54 patients who were diagnosed to have Emphysematous pyelonephritis from various departments in Nizam's institute of medical sciences from December 2016 to November 2019 were included in the study. The diagnosis of EPN was confirmed by plain CT KUB scan.

Results: Of the 54 patients 16 were male and 38 were female. 40 patients with EPN had diabetes mellitus (DM). There was 4 patients who was diagnosed to have DM after admission. Left kidney involved in 51.80% (28) of patients. Right kidney in 37.03% (20) of cases. Out of 54 patients, 14 patients who were presented to us with EPN had a pre-existing CKD. Only 14 out of 54 patients with EPN had normal renal parameters. Thrombocytopenia was seen in 32 of these patients and 4 of patients with thrombocytopenia required platelet transfusion. Urine culture was sterile in 3 patients. E.coli was grown in 42 patients and klebsiella in 3 patients. There were 14 patients with dry EPN and 40 patients with wet EPN. 21.8% (12) patients has class 1 EPN. 43.75% (24) of patients had Class 2 EPN (Commonest class in our study), 25% (13) of patients had class 3A EPN, 3.1% (2) had class 3B EPN, 6.25% (3) has Class 4 EPN. The mean follow up was 8 months, ranging from 3 months to 24 months. 40 patients are under regular follow up.

Conclusion: Pre-existing CKD status, shock at presentation and altered sensorium are the poor prognostic factors in this study.

Keywords: Emphysematous pyelonephritis (EPN), klebsiella, thrombocytopenis, diabetes

Introduction

Emphysematous pyelonephritis (EPN) is a severe, necrotizing infection of kidney, due to gas forming organisms ^[1]. EPN involves a spectrum of disease processes that results in the production of gas in the renal parenchyma ^[2]. The gas can be focal or diffuse and can spread to the collecting system or track into the perinephric and paranephric spaces. EPN predominantly affects female diabetics ^[1]. Presence of obstruction with infection in urinary tract, reduced host immunity are the other risk factors. Historically the prognosis in these patients has been poor with high mortality rate ^[1, 3]. The management was aggressive with percutaneous nephrostomy and nephrectomy being the primary modes of treatment.

Recently with the advent of newer antimicrobials, which are highly effective against gas forming organisms and CT scan for early diagnosis there has been a changing trend towards conservative, minimally invasive modalities of management with a decrease in mortality rates and nephrectomies ^[4].

Aim and Objectives

To study

1. The clinical features, radiological classification and risk factors of - Emphysematous pyelonephritis
2. To assess the prognostic factors

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- To study different management modalities of Emphysematous pyelonephritis and their outcomes

Materials and Methods

Patient population

54 patients who were diagnosed to have Emphysematous pyelonephritis from various departments in Nizam's institute of medical sciences from December 2016 to November 2019 were included in the study. The diagnosis of EPN was confirmed by plain CT KUB scan. Patients who presented with acute sepsis and shock were resuscitated and given appropriate supportive therapy. Supported therapy included, treatment of co morbid conditions, like diabetes mellitus, hypertension, chronic kidney disease etc.

Exclusion criteria

- History of recent urinary tract instrumentation
- Urinary fistula
- History of recent genitourinary trauma

Prognostic factors

- Glycaemic control
- Renal function
- Serum albumin level
- Platelet count
- Shock on presentation
- Level of consciousness on presentation

Glycosylated haemoglobin was done for all the patients to know about their glycaemic control. Glycosylated haemoglobin of more than 7% was defined as poor glycaemic control. Acute renal impairment was defined as elevation of serum creatinine of more than 1.3 mg/dl. Presence of pre-existing CKD, need for haemodialysis during the course of treatment was considered as risk factor.

Hypoalbuminemia was defined as, serum albumin less than 3.5 gm/dl. Thrombocytopenia was defined as platelet count less than 1.5 lakhs /cu mm. Shock was defined as systolic blood pressure less than 90 mm Hg. Altered sensorium was defined as a state of confusion or delirium, stupor or coma. All the patients were started on intravenous antibiotics, cefaperazone+sulbactam and aminoglycoside if the renal parameters are normal and then changed to culture specific antibiotics.

Conservative management included antibiotic therapy and supportive measures.

Indications for minimal invasive procedures

- Raising S. creatinine values
- Hydronephrosis
- Sepsis
- Significant renal and perinephric collection.

Minimal invasive procedures included

- DJ stenting
- Percutaneous nephrostomy
- Percutaneous drainage

DJ stenting was done under local anaesthesia. We used 5F, 26 cms DJ stent. Percutaneous nephrostomy was also done under local anaesthesia, patient in prone position under ultrasound/Fluoroscopic guidance. We used either 12F or 14F nephrostomy tube for drainage.

Percutaneous drainage was done under Ultrasound guidance with the help of 18 G needle. Repeat CT scans were performed to assess the improvement weekly till the patient is discharged. DTPA Renogram was performed after 4 to 6 weeks to know about the function of the kidney.

Indications for nephrectomy

- Not improving on minimal invasive treatment
- Non-functioning renal unit

Results and Observations

Of the 54 patients 16 were male and 38 were female. The male to female ratio was 4:7. The youngest patient was 34 years old and the oldest patient was 70 years old. The mean age group of presentation was 52.04.

Table 1: Sex distribution

Sex	No. of patients
Male	16
Female	38
Total	54

Co-Morbidities

40 patients with EPN had diabetes mellitus (DM). There was 4 patients who was diagnosed to have DM after admission. There were 4 patients with diabetic keto acidosis. All the 40 patients had poorly controlled DM. The mean HbA1c was 10.87

Table 2: Co-Morbidities

Co-morbid	Numbers
Diabetes mellitus	40
Chronic kidney disease	14

Table 3: Involvement of kidney

Left	Right	Bilateral
28	20	6

Left kidney involved in 51.80% (28) of patients. Right kidney in 37.03% (20) of cases. 11.1% (6) of cases had bilateral involvement.

Table 4: Presenting features

Presenting feature	No. of patients
Fever	40
Tachycardia	36
Flank pain	34
Dysuria	17
Hypotension	18
Macroscopic haematuria	14
Altered sensorium	16

Risk factors

Out of 54 patients, 14 patients who were presented to us with EPN had a pre-existing CKD. Only 14 out of 54 patients with EPN had normal renal parameters. Thrombocytopenia was seen in 32 of these patients and 4 of patients with thrombocytopenia required platelet transfusion. All 54 patients with EPN had hypoalbuminemia.

Shock during initial presentation was seen in 13 of patients. 16 of patients presented with altered sensorium.

Table 5: Risk factors

Risk factors	No. of patients
Deranged renal parameters	40
Thrombocytopenia	32
Hypoalbuminemia	54
Shock	13
Altered sensorium	16
Poorly controlled diabetes mellitus	40
CKD	14

Urine culture was sterile in 3 patients. E.coli was grown in 42 patients and klebsiella in 3 patients. Pseudomonas was grown in two patients. Mixed growth (E.coli+Candida) was seen in three patients. Candida albicans was seen in one patient.

Table 6: Urine cultures

Urine c/s	No. of patients
E.coli	42
Klebsiella pneumonia	3
Pseudomonas	2
Candida	1
Mixed (E.coli+Candida)	3
No growth	3
Total	54

There were 14 patients with dry EPN and 40 patients with wet EPN.

Table 7: No. of EPN patients

Type of EPN	No. of patients
Dry	14
Wet	40
Total	54

Table 8: EPN class and number of patients

Class of EPN	No. of patients
Class - 1	12 (21.8%)
Class - 2	24 (43.7%)
Class - 3 A	13 (25%)
Class - 3 B	2 (3.1%)
Class - 4	3 (6.2%)
Total	54

21.8% (12) patients has class 1 EPN. 43.75% (24) of patients had Class 2 EPN (Commonest class in our study), 25% (13) of patients had class 3A EPN, 3.1% (2) had class 3B EPN, 6.25% (3) has Class 4 EPN.

Management

15.63% of patients were treated conservatively with antibiotics according to culture and sensitivity. They did not require minimally invasive therapy also. 78% of patients required minimally invasive intervention. Nephrectomy was done in 6.25% of patients. Mortality rate in our study was 7.4%.

20 patients required cystoscopy during DJ stenting. Six patients required percutaneous drainage and DJ stenting. 16 patients had ureteric calculus and 6 patients had necrotic papilla causing obstruction. Ultrasound guided percutaneous drainage was done for peri-nephric collection in 6 patients. Percutaneous nephrostomy was done in ten patients. Of these more than one nephrostomy tube was required in 2 patients. We have used 12 F or 14 F nephrostomy tube for drainage. Nephrostomy was done, patient in prone position under Ultrasound or Fluoroscopic guidance.

Nephrectomy was done in four patients with class 3A EPN. One of these patients was treated for pyrexia of unknown origin, and genital herpes elsewhere, and she presented to us late. She underwent DJ stenting followed by percutaneous nephrostomy but her sepsis worsened in spite of treatment with culture specific antibiotics, so nephrectomy was done after few days of minimally invasive treatment.

The other 3 patients who underwent nephrectomy presented with left hydroureteronephrosis and perinephric collection. DJ stenting and PCN was done for this patient. They recovered well from the acute episode but had severe loin pain. DTPA after 6 weeks showed no function and we have done nephrectomy in the follow up.

Mortality occurred in 4 patients.

Table 9: Treatment

Treatment	No. of patients
Antibiotics	8
Cystoscopy + DJ stent	20
DJ stent + PCD	6
PCN	10
PCD	6
Nephrectomy	4
Total	54

Follow up

The mean follow up was 8 months, ranging from 3 months to 24 months. 40 patients are under regular follow up. 10 patients lost follow up after successful initial management. One patient had recurrent EPN on the same side after 3 months, which was again managed conservatively. Another patient had a non-emphysematous pyelonephritis after 7 months, he was also managed conservatively.

Out of 14 patients with pre-existing CKD, who had dialysis during the course of treatment, 10 patients became dialysis dependent. There were 3 patients who did not have pre-existing CKD, had raised serum creatinine values, had to undergo haemodialysis during treatment, one of these patients also became dialysis dependent.

DTPA Renogram was performed after 4 to 6 weeks. Patients with Class 1 and Class 2 EPN had a near normal GFR and did not have any reduction in renal function. Patients with Class 3 and Class 4 EPN had reduced function on the affected side. The mean relative function of the affected kidney was 39% (range 19% to 56%). Patient with recurrent EPN became dialysis dependent; he had a small contracted kidney on follow up with Ultrasound.

Discussion

Emphysematous pyelonephritis was described as a rare, life threatening UTI. In 2000, Huang and Tseng² studied 48 patients in 11 years with EPN, which was the largest reported group, with the disease. Karthikeyan *et al.*, reported 42 patients in 6 years. In our study we have 54 patients with EPN in 2 years though the incidence of EPN varies from region to region, there does not seem to be any racial prevalence. EPN has been reported in all the parts of the world. The incidence of EPN is on the higher side in India.

The mean age group of presentation, described by Wan^[3] and Karthikeyan *et al.*,^[3] in their study was 54.7 & 53.2 respectively. In our study, the mean age group of presentation of patients with EPN was 51.07. The youngest patient was 34 years old and the oldest patient was 71 years old.

EPN common in female patients. The male to female ratio in

Wan's study was 1:6. In our study male to female ratio was 4:7. The reason for EPN being more common in female sex may be due to the fact that UTI is more common in females.

Escherichia coli (*E. coli*) was the commonest organism seen in both Huang *et al.* and Wan *et al.* series 69 % & 58% respectively, followed by *Klebsiella pneumonia* 29 % and 24 % respectively. In our study *E. coli* was seen in 78% of the cases, followed by *klebsiella* in 6% of cases (table 4). *Pseudomonas* growth was seen two patients. *Candida Albicans* growth was seen in one patient.

Candida species causing EPN was reported by ShoKeir *et al.*,^[5] in 1998. They have also observed high mortality with *Candida* growth. But in our study, patient who had *Candida* growth, was managed with cystoscopy and DJ stenting.

Multiple Fungal balls were removed. She was treated with intravenous anti-fungal agents, and she had a complete recovery. Mixed growth was seen in 3 patients. Both the patients had *E. coli* and *candida* growth. 10% Mixed growth of organisms have been observed in Sugandh shetty's⁶ series. Rare organisms such as *Clostridium* species and *Aspergillus famigatus* was also reported by Alan and Richard *et al.*^[2].

There were three patients who had no growth in urine culture. All these patients were treated elsewhere with antibiotics, and then referred here for EPN treatment. Blood cultures were positive in 30% of cases in Karthikeyan's series^[4]. In our patients, blood culture was positive in 25% of patients, two of them had *klebsiella* growth, rest of the patients had *E. coli* growth. All these patients who had a positive blood culture had a severe degree of sepsis and class 3A EPN.

Table 10: Prognostic factors in survivor and non-survivor groups

Prognostic factor	Survivor group (50)	Non-survivor group (4)	P value
Thrombocytopenia	28	4	N.S
Hypoalbuminemia	50	4	N.S
Shock	10	3	0.0267
Altered sensorium	12	4	0.0026
Poorly controlled DM	36	4	N.S
CKD	10	4	0.0142

The total study group (number 54) was divided into two groups, Survivor (number 50) and Non survivor (number 4). The prognostic factors were studied in both the groups and their statistical significance identified. Shock ($P=0.0267$), altered sensorium ($P=0.0026$) and CKD ($P=0.0142$) were statistically significant.

The Incidence of DM in Karthikeyan's^[4], Huang's¹ studies were 93% & 96%, respectively. In our series 40 patients had DM. There were patients with both insulin dependent and non-insulin dependent DM. There were 4 patients for whom diabetes was diagnosed after admission. They were diagnosed to have DM only, after the diagnosis of EPN.

There were 4 patients with diabetic ketoacidosis complicating EPN. These patients had to undergo haemodialysis, and had intensive care unit treatment. Suganadh Shetty^[6] in his series has reported high incidence of mortality in patients with DKA complicating EPN. Early haemodialysis of CKD patients with sepsis and severe acidosis, may probably prevent mortality. In karthikeyan's^[1] study the duration of diabetes was used as a prognostic factor, and he concluded that duration of diabetes had no correlation with the severity and prognosis of EPN.

HbA1c was estimated in all the patient. The mean HbA1c in our series was 10.87, this clearly shows the poor diabetic control of patients. Patients with a very high HbA1c > 11.5 % had a higher

class of EPN (class 3 & class 4), whereas patients with HbA1c < 11.5 had class 1 & class 2 EPN. Higher the HbA1c, higher the class of EPN.

In Karthikeyan's^[1] series, 8-10% of patients with EPN were non-diabetic patients, but were immune compromised. Patients with miliary tuberculosis, retroviral infection, radiation sickness, post renal transplant status are all at higher risk for EPN. Alen *et al.*^[2] and karthikeyan *et al.*^[1] reported high incidence of mortality, with EPN in transplant kidneys, due to immunosuppression. However, there were no immune compromised patients in our series of EPN.

Proteinuria was used as a prognostic factor in Wan^[3] and Huan^[1] series. But proteinuria did not have any significance with the outcome and with the class of EPN, so we decided to use S. Albumin levels as a prognostic factor and S. albumin status was estimated in all the patients. S.albumin level was low in 54 patients. Serum albumin did not have any significance with outcome.

There were 14 patients with Pre-existing CKD who presented with EPN. Presence of CKD and the need for haemodialysis (H.D.) during the course of treatment was considered as a risk factor. All these patients were not dialysis dependent before the EPN. They all required H.D during treatment. Their renal function deteriorated after EPN. 10 patients with pre-existing CKD became dialysis dependent. 14 (25.9%) of our patients had normal serum creatinine values. 14 patients (25.9%) of our patients had pre-existing CKD, 26 patients (48.1%) had raised serum creatinine values during EPN. In this group, 4 patients (15%) required haemodialysis during treatment for EPN, one patient in this group also became dialysis dependent.

Table 11: CKD risk factors

CKD risk factor	No. of patients	H.D. during treatment	H.D. dependent
Pre-existing CKD	14	14	10
No pre-existing CKD	40	4	1

Patients with pre-existing CKD, and patients who required haemodialysis during the course of treatment had a poor prognosis. Though they were managed conservatively with minimally invasive procedures, the outcome was poor, they became dialyses dependent.

Thrombocytopenia and altered sensorium, at the time of initial presentation were associated with poor prognosis'. Thrombocytopenia was seen in 32 patients (59.25%) and 6 patients (12.5 %) with platelets less than 75000/cu mm required platelet transfusions. There was one patient with a platelet count of 40,000/cu mm during presentation. She died in the intensive care unit few hours after admission. One of those patients who underwent nephrectomy also had thrombocytopenia during initial presentation.

16 patients (29.65%) had altered sensorium, all these patients had a higher class of EPN (class3 & class4). Patients who presented with thrombocytopenia required minimally invasive intervention for their recovery. They also required intensive care management, and had a longer hospital stay.

Majority of patients with platelets less than 1 lakh were in class 3 and class 4. Patients who had platelet count less than 1 lakh also had poor outcome, which was statistically significance.

Altered sensorium was not seen in class 1 EPN, was seen in class 3 and class 4 EPN. There were 14 patients with dry type of EPN, (Table 7) all the patients had altered sensorium on presentation.

Altered sensorium was seen in 16 patients, out of 16, 15 patients

were in class 3 and class 4 EPN. Presence of altered sensorium in higher class of EPN was significant. Similar observation was seen in Huang's, Sukanatha shetty's series.

Patients with altered sensorium became dialysis dependent in Karthikeyan's study, and they required emergency nephrectomy in Huang's and Tseng's study, but in our series patients, with altered sensorium did not require emergency nephrectomy, and all patients were not dialysis dependent after the treatment.

Acute renal insufficiency, thrombocytopenia, altered sensorium were the poor prognostic factors proposed by Huang, Tseng, *et al.* in EPN. Presence of more than two risk factors was considered as poor prognosis. Patients with more than two risk factors required nephrectomy in Huang's series. Karthikeyan's observation was, patients with two or 'more risk factors, irrespective of class required surgical intervention'.

We had 20 patients with more than two risk factors, and 16 of them, were managed with minimally invasive procedures. Patients with four and five risk factors were also managed with minimally invasive interventions. Nephrectomy was done in 4 patients.

All these patients who underwent nephrectomy had non-functional renal unit on follow up DTPA renogram after 6 weeks. This clearly shows that patients with more than two risk factors can also be managed conservatively and early appropriate treatment will help to salvage the kidney.

Type 1 EPN, (dry type) was less common than the type 2 EPN. Both these types were analyzed in detail by Wan *et al.* Type 1 had a fulminant course with a high risk of mortality. In our series of EPN, we had 14 (25.9%) patients with type 1 EPN. Of the four deaths in our study three patients were of Type 1 (dry type) EPN. They had a fulminant course, required intensive care monitoring. They had multiple risk factors.

In karthikeyan's series patients with type 1 EPN required emergency nephrectomy. Alen *et al.* [7] have reported successful management of type 1 EPN with PCN, and said that early intervention in dry EPN will reduce the mortality rate, but the outcome with dry EPN was poor. The affected kidneys had a poor function in the follow up studies, probably because of the extensive parenchymal destruction associated with Type 1 EPN. Type 2 EPN (wet type) was more common type, and mortality rate was low. Parenchymal destruction was comparatively less in type 2. We had 74.07% (40) of patients with type 2 EPN. Patients were managed conservatively and with minimally invasive treatments. In our series we had one mortality in Type 2 EPN as patient presented with shock.

Table 12: Type of EPN

Type of EPN	Total no. of patients	No. of deaths
Type 1 (dry)	14 (25.9%)	3 (21.4%)
Type 2 (wet)	40 (74.07%)	1 (2.5%)

Type of EPN and their management

Emphysematous pyelonephritis, Class 1 EPN was seen in 21.8% of patients. Class 1 EPN was described as benign by Karthikeyan *et al.* [7] as it had an excellent prognosis with antibiotic treatment alone, especially in the absence of obstruction. 4 of our patients with Class 1 EPN were managed conservatively with antibiotics according to culture and sensitivity. 8 patients required DJ stenting as they had obstruction and hydronephrosis.

43.75% of patients were under Class 2 EPN, this was the most common class in our study. Four of class 2 EPN patients were managed conservatively with antibiotics. 12 patients required DJ stenting.

Two patients required DJ stenting along with percutaneous drainage for perinephric collection. 6 patients underwent percutaneous nephrostomy as DJ stenting was not successful. Patients with class 1 and class 2 EPN had a good outcome. The affected kidneys had normal GFR and function.

We had 13 patients (25%) in Class 3A EPN. Two patients in class 3A required nephrectomy, both these patients presented to us late. The first patient was treated for pyrexia of unknown origin and genital herpes elsewhere, EPN was diagnosed later. PCN was done initially along with DJ stent. She improved but in follow up after 6 weeks with DTPA Reno gram renal unit was non-functional so nephrectomy was done.

The other patient who underwent nephrectomy presented with left hydronephrosis and perinephric collection. DJ stenting and PCN was done for this patient. She recovered well from the acute episode but had severe loin pain. DTPA after 6 weeks showed no function and we have done nephrectomy. Three patients with class 3A EPN, (wet type) had perinephric collections one of them required DJ stenting plus percutaneous drainage of abscess cavity, and the three patients required percutaneous nephrostomy. Early surgical intervention, for class 3 EPN, in the form of PCN/PCD was found beneficial which is also noted in Karthikeyan's group.

Two patients had Class 3B EPN. They had large collection beyond Gerota's fascia, Presented late with sepsis.

Table 13: EPN class and treatment modality

Class of EPN treatment	1	2	3A	3B	4
Antibiotics	4	4			
Cystoscopy + DJS	8	12			
DJS+PCD		2	3		1
PCN		6	3	1	
PCD			5		1
Nephrectomy			2	1	1

We have three patients with class 4 EPN. One of them was managed with DJ stenting and PCD. The other patient was treated with PCD. He had a solitary kidney, didn't improve with treatment and died. One patient who recovered from initial management underwent nephrectomy in follow-up. Class 4 EPN was described as life threatening, dangerous disease by Alen *et al.* [7] who had observed EPN in solitary kidneys and EPN in transplant kidneys in their series.

Management of EPN with calculus disease

Calculus disease with EPN was seen in 20 patients. Fifteen patients had renal calculus, five patients had ureteric calculus. Tanmaya Goel *et al.* [7] had a series of patients with calculus disease and EPN. Initial conservative management followed by treatment of stone disease at a later date were their recommendations. In our case, ten patients required cystoscopy and DJ stenting, as an emergency procedure. Nephrectomy was done for 2 patients who had renal calculus. Two other patients who had renal calculus with EPN were managed conservatively with PCN. PCNL was done after they recovered from EPN, eight to twelve weeks later [8-10].

In our group of patients DJ stenting was the treatment of choice, when a patient presented with HUN. 36 (66.67%) patients in our series had HUN, DJ stenting was done in 26 patients (48.1%). PCN was placed in 10 patients in whom stenting was not successful. DJ stenting and PCN was done to relieve obstruction either due to stone or necrotic papilla. All these patients improved dramatically after these minimally invasive procedures.

In our study, the mortality rate was 7.4% (four patients). In Karthikeyan's ^[1] series the mortality rate was 17%, and in Huang series 18.8% ^[2]. Emergency nephrectomy rate was 42% in Huang's series' and 3% in Karthikeyan's series. In our study, there were no emergency nephrectomies.

Conclusion

- Emphysematous pyelonephritis should be suspected in every diabetic patient, presenting with features of acute pyelonephritis.
- E. coli is the most common organism associated with EPN.
- Non-contrast CT scan is the imaging modality of choice for diagnosis of EPN.
- Emphysematous pyelonephritis can be successfully treated with conservative and minimally invasive interventions, irrespective of class of EPN and the number of risk factors.
- Cystoscopy and DJ stenting is the treatment of choice for patients with dilated pelvicalyceal system.
- Patients with extensive parenchymal involvement will benefit from PCN and PCD.
- Aggressive and early intervention will help to salvage the kidneys in class 3 and class 4 EPN.
- However, nephrectomy should be promptly attempted for patients not responding to conservative methods and patients with extensive, fulminant course of disease.
- Pre-existing CKD status, shock at presentation and altered sensorium are the poor prognostic factors in this study.

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Conflict of interest

None

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