

**Original Research Article**

# A clinical study of emphysematous pyelonephritis

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## Abstract

**Background:** 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.

**Aim:** To study the clinical features, radiological classification and risk factors assess the prognostic factors and to study different management modalities of Emphysematous pyelonephritis and their outcomes.

**Materials and methods:** It was prospective study done on 48 patients who were diagnosed to have Emphysematous pyelonephritis from various departments in Osmania General Hospital from October 2004 to October 2006 were included in the study. The diagnosis of EPN was confirmed by plain CT KUB scan.

**Results:** All the 48 patients with EPN had diabetes mellitus (DM). All the 48 patients had poorly controlled DM. Left kidney was involved in 54.1% and Right kidney in 37.5% of cases. 6.25% of cases had bilateral involvement. Fever (93%) and tachycardia (64.5%) were most common presentation in patients. Thrombocytopenia was seen in 50% of these patients and 12% of patients with thrombocytopenia required platelet transfusion. Shock during initial presentation was seen in 22.9% of patients. 16.6% of patients presented with altered sensorium. E.coli was grown in 78% of patients and klebsiella in 6% of patients. There were 6 patients with dry EPN and 42 patients with wet EPN. 41.6% of patients had Class 2 EPN (Commonest class in our study), 25% of patients had class 3A EPN, 22.9% had Class 1 EPN, 6.25 had Class 4 EPN. 15.63% of patients were treated conservatively with antibiotics according to culture and sensitivity. 78% of patients required minimally invasive intervention. Nephrectomy was done in 6% of patients. Mortality rate in our study was 8.3%.

**Conclusions:** 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.

## Key words

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Emphysematous pyelonephritis, Minimally invasive intervention, Nephrectomy.

## Introduction

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Emphysematous pyelonephritis (EPN) is a severe, necrotizing infection of kidney, due to gas forming organisms [1, 2]. EPN involves a spectrum of disease processes that results in the production of gas in the renal parenchyma. EPN predominantly affects female diabetics [2]. Presence of obstruction with infection in urinary tract, reduced host immunity is the other risk factors. Historically the prognosis in these patients has been poor with high mortality rate [2, 3]. The management was aggressive with percutaneous nephrostomy and nephrectomy being the primary modes of treatment. Patients with diabetes, both insulin dependent and non-insulin dependent forms, comprise around 90% of EPN cases. The remaining 10% of cases show some form of immunological impairment. The factors that predispose to EPN in persons with diabetes may include, poorly controlled diabetes, calculus disease, papillary necrosis, immunosuppression. EPN has also been reported in transplanted kidneys [1, 2]. Gas in the collecting system only, emphysematous pyelitis, should be considered a separate entity. It has got excellent prognosis and recovery with medical treatment only. By contrast EPN patients are at high risk of death whether treated medically, percutaneous drainage or nephrectomy. The most common organism in culture was Escherichia coli, next is Klebsiella followed by Proteus, Pseudomonas. Anaerobic organisms like Clostridium, Bacteroides fragilis, fungi including Candida and Aspergillus fumigatus have also been reported in culture. 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 [1].

## Materials and methods

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It was prospective study done on 48 patients who were diagnosed to have Emphysematous pyelonephritis from various departments in Osmania General Hospital from October 2004 to October 2006 were included in the study. The diagnosis of EPN was confirmed by plain CT KUB scan.

**Inclusion criteria:** Patients with acute sepsis and shock were resuscitated and given appropriate supportive therapy. Supported therapy included, treatment of comorbid conditions, like diabetes mellitus, hypertension, chronic kidney disease etc.

**Exclusion criteria:** History of recent urinary tract instrumentation, Urinary fistula and History of recent genitourinary trauma.

Prognostic factors were Glycemic control, Renal function, Serum albumin level, Platelet count, Shock on presentation, Level of consciousness on presentation.

Glycosylated hemoglobin was done for all the patients to know about their glycemic control. Glycosylated hemoglobin of more than 7% was defined as poor glycemic 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 hemodialysis during the course of treatment was considered as risk factor. Hypoalbuminemia was defined as, serum albumin 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, ceftriaxone 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, Hydroureteronephrosis, Sepsis and Significant renal and perinephric collection.

#### **Minimal invasive procedures included**

- DJ stenting
- Ureteroscopy and DJ stenting
- Percutaneous nephrostomy
- Percutaneous drainage

DJ stenting was done under local anesthesia. We used 4.5 F DJ stent. DJ stenting with Ureteroscopy was done under spinal anesthesia. Percutaneous nephrostomy was also done under local anaesthesia, patient in prone position under Ultrasound or Fluoroscopic guidance. We used either 12 F or 14 F nephrostomy tube for drainage. Percutaneous drainage was done under Ultrasound guidance with the help of 18 G needle.

Repeat CT scans were performed only when the patients did not show improvement to conservative and minimally invasive procedures. DTP renogram was performed on these patients after 4 to 6 weeks to know about the function of the kidney.

#### **Results**

Of the 48 patients 18 were male and 30 were female. The male to female ratio was 3:5. 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**). All the 48

patients with EPN had diabetes mellitus (DM). All the 48 patients had poorly controlled DM. The mean HbA1c was 10.87. Left kidney was involved in 54.1% of patients and right kidney in 37.5% of cases. 8.3% of cases had bilateral involvement.

**Table - 1:** Demographic distribution.

Variable	No of patients	%
<b>Sex</b>		
Male	18	37.5
Female	30	62.5
<b>Co-morbid</b>		
Diabetes mellitus	48	100
Chronic kidney disease	8	16.66
<b>Side of involvement</b>		
Left	26	54.16
Right	18	37.5
Bilateral	4	8.3

**Table - 2:** Presenting feature and Risk factors associated in study.

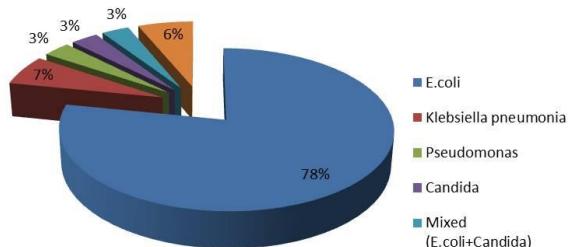
Presenting feature	No of patients	%
Fever	45	93.75
Tachycardia	31	64.58
Flank pain	34	70.83
Dysuria	13	27.08
Hypotension	16	33.33
Macroscopic hematuria	5	10.41
Altered sensorium	8	16.66
<b>Risk factors</b>		
Deranged renal parameters	35	72.9
Thrombocytopenia	24	50
Hypoalbuminemia	48	100
Shock	11	22.9
Altered sensorium	8	16.6
Poorly controlled DM	48	100
CKD	10	20.83

Fever (93.7%) and tachycardia (64.5%) were most common presentation in patients out of 48 patients. Thrombocytopenia was seen in 50% of these patients and 12% of patients with thrombocytopenia required platelet transfusion.

All 48 EPN had hypoalbuminemia. Shock during initial presentation was seen in 22.9% of patients. 16.6% of patients presented with altered sensorium (**Table – 2**).

Urine culture was sterile in 6.5% of patients. E.coli was grown in 78% of patients and klebsiella in 6% of patients. Pseudomonas was grown in 2 patients. Mixed growth (E.coli + Candida) was seen in one patient. Candida albicans was seen in one urine culture (**Figure – 1**).

**Figure - 1:** Urine culture results evaluated in study.



There were 6 patients with dry EPN and 42 patients with wet EPN. 41.6% of patients had Class 2 EPN (Commonest class in our study), 25% of patients had class 3A EPN, 22.9% had Class 1 EPN, 6.25 had Class 4 EPN (**Table – 3**).

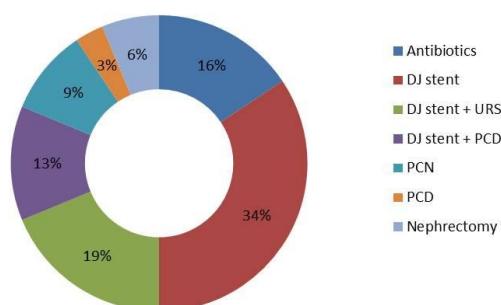
**Table - 3:** Type and EPN class and number of patients.

Type of EPN	No of patients	%
Dry	6	12.5
Wet	42	87.5
<b>Class of EPN</b>		
Class - 1	11	22.9
Class - 2	20	41.6
Class - 3 A	12	25
Class - 3 B	2	4.16
Class – 4	3	6.25
Total	48	100

16% 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% of patients. Mortality rate in our study was 8.3% (**Figure – 2**).

**Figure - 2:** Treatment modalities.



### Follow up

The mean follow up was 8 months, ranging from 3 months to 24 months. 28 patients are under regular follow up. 4 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 non-emphysematous pyelonephritis after 7 months, he was also managed conservatively.

### Discussion

Emphysematous pyelonephritis was described as a rare, life threatening UTI. In 2000, Huang and Tseng [2] studied 32 patients in 11 years with EPN, which was the largest reported group, with the disease. Karthikeyan, et al. [1] reported 42 patients in 6 years. In our study we have 48 patients with EPN in 3 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. [1] in their study was 54.7 and 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 was always common in

female patients. The male to female ratio in Wan's study was 1:6. In our study male to female ratio was 3:5. 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 most commonest organism seen in both Huang et al and Wan et al series 69% and 58% respectively, followed by Klebsiella pneumonia 29% and 24% respectively . In our study E.coli was grown in 78% of patients and klebsiella in 6% of patients. Pseudomonas was grown in 2 patients (**Figure – 1**). Pseudomonas growth was seen one patient. Candida Albicans growth was seen in one patient. Candida species causing EPN was reported by ShoKeir, et al. [4]. They have also observed high mortality with Candida growth. But in our study, patient who had Candida growth was managed with ureteroscopy 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 one patient. Both the patients had E.coli and candida growth. 10% Mixed growth of organisms have been observed in Sugandh shetty's [5] series. Rare organisms such as Clostridium species and Aspergillus famigatus was also reported by Alan and Richard, et al. [6]. There were two patients who had no growth in urine culture. Both 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. 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.

The total study group (number 48) was divided into two groups, Survivor (42 number) and Non survivor (number 6). The prognostic factors were studied in both the groups and their statistical significance identified (**Table – 4**).

**Table - 4:** Prognostic factors in survivor and non-survivor groups.

<b>Prognostic factor</b>	<b>Survivor group (42/48)</b>	<b>Non survivor group (6/48)</b>	<b>P value</b>
Thrombocytopenia	20	3	N.S
Hypoalbuminemia	32	5	N.S
Shock	7	3	0.0267
Altered sensorium	4	5	0.0026
Poorly controlled DM	35	5	N.S
CKD	7	5	0.0142

(N.S. - Not significant)

Shock (P- 0.0267), altered sensorium (P- 0.0026) and CKD (P- 0.0142) were statistically significant.

The Incidence of DM in Karthikeyan's [1], Huang's [2], Ali Nawaz khan [7], studies were 93%, 96%, 97% respectively. In our series all the 48 patients had DM. There were patients with both insulin dependent and non-insulin dependent DM. There was one patient for whom diabetes was diagnosed after admission. She was

diagnosed to have DM only, after the diagnosis of EPN.

There were 2 patients with diabetic ketoacidosis complicating EPN. Both these patients had to undergo hemodialysis, and had intensive care unit treatment. Sugandh shetty [5] in his series has reported high incidence of mortality in patients with DKA complicating EPN. Early hemodialysis of these 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 patients. 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 and class 4), whereas patients with HbA1c < 11.5 had class 1 and class 2 EPN. Higher the HbA1c, higher the class of EPN.

Patients with very high HbA1c also had problems like fourniers gangrene, diabetic foot, fungal maxillary sinusitis. They had a longer hospital stay and they required intensive care treatment also. Probably HbA1c may be a good prognostic marker in patients with EPN, however more studies are required to confirm this.

In Karthikeyan's [1] series, 8-10% of patients with EPN were non diabetic patients, but were immunocompromised. Patients with miliary tuberculosis, retroviral infection, radiation sickness, post renal transplant status are all at higher risk for EPN.

Alan, et al. [6] and karthikeyan, et al. [1] reported high incidence of mortality, with EPN in transplant kidneys, due to immunosuppression. However there were no immunocompromised patients in our series of EPN. Proteinuria was used as a prognostic factor in Wan [3] and Huang [2] 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 48 patients. Serum albumin did not have any significance with outcome.

There were 8 patients with Pre-existing CKD who presented with EPN. Presence of CKD and the need for hemodialysis (H.D.) during the course of treatment was considered as a risk factor. All these 8 patients were not dialysis

dependent before the EPN. They all required H.D during treatment. Their renal function deteriorated after EPN. 7 patients with pre-existing CKD became dialysis dependent.

Patients with pre-existing CKD, and patients who required hemodialysis 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 24 patients (50%) 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.

8 patients (16.6%) had altered sensorium, all these patients had a higher class of EPN (class 3 and class 4). 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 significant.

Altered sensorium was not seen in class 1 EPN, was seen in class 3 and class 4 EPN. There were 6 patients with dry type of EPN, (**Table - 2**) all the 8 patients had altered sensorium on presentation. Altered sensorium was seen in 8 patients, out of 8, seven 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, Suganatha shetty's [5] 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 12 patients with more than two risk factors, and 10 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 patients with three and four risk factors. Both these patients who underwent nephrectomy, presented to us late, so the diagnosis of EPN was made late. This clearly shows that patients with more than two risk 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 6 (12.5%) patients with type 1 EPN. Of the three deaths in our study two patients were of Type1 (dry type) EPN. They had a fulminant course, required intensive care monitoring. They had multiple risk factors.

In karthikeyan [1] series patients with type 1 EPN required emergency nephrectomy. Alan, et al. [6] 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 87% of patients with type 2 EPN. Nephrectomy was done in one patient others were managed conservatively and with minimally invasive treatments. In our series we had one mortality in Type 2 EPN.

Emphysematous pyelitis, Class 1 EPN was seen in 22.9% of patients. Class 1 EPN was described as benign by Karthikeyan, et al. as it had an excellent prognosis with antibiotic treatment alone, especially in the absence of obstruction. Two of our patients with Class 1 EPN were managed conservatively with antibiotics according to culture and sensitivity. Five patients required DJ stenting as they had obstruction and dilated kidneys.

41.6% of patients were under Class 2 EPN, this was the most common class in our study. Three of class 2 EPN patients were managed conservatively with antibiotics. 11 patients required DJ stenting and ureteroscopy to relieve distal obstruction. Patients with class 1 and class 2 EPN had a good outcome. The affected kidneys had normal GFR and function.

We had 12 patients (25%) in Class 3A EPN. four patients in class 3A required nephrectomy, both these patient 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 but she did not improve, so nephrectomy was done after one week. Though she had only three risk factors, nephrectomy was done because she was not improving from sepsis.

The other patient who underwent nephrectomy presented with left hydroureteronephrosis 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. Two patients with class 3A EPN, (wet type) had perinephric collections one of them required DJ stenting plus percutaneous drainage of abscess cavity, and the other patient required percutaneous nephrostomy. Early surgical intervention, for class 3 EPN, in the form of PCN/PCD was found beneficial in Karthikeyans group.

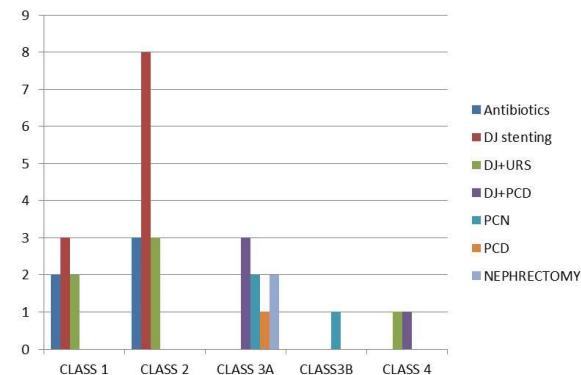
One patient had Class 3B EPN. He had large collection beyond gerotas fascia, Presented late with sepsis. PCN was done for this patient and two tubes were required. He didn't improve and ultimately died. In JJ Huang, et al. [2] series 4 mortalities were there in this class. He mentioned that high chance of PCD failure rate in class 3B, so nephrectomy should be considered.

We have 3 patients with class 4 EPN. One of them was managed with DJ stenting and ureteroscopy. The other patient was treated with DJ stenting and PCD. He had a solitary kidney, didn't improved with treatment and died. Class 4 EPN was described as life threatening, dangerous disease by Alan, et al. [6], who had observed EPN in solitary kidneys and EPN in transplant kidneys in their series. Karthikeyan in his series of patients had mortality in class 4 EPN, in transplant kidney. EPN in transplant kidneys carries very high mortality due to the Immunosuppression whereas bilateral emphysematous pyelitis had good prognosis, and also had a good outcome.

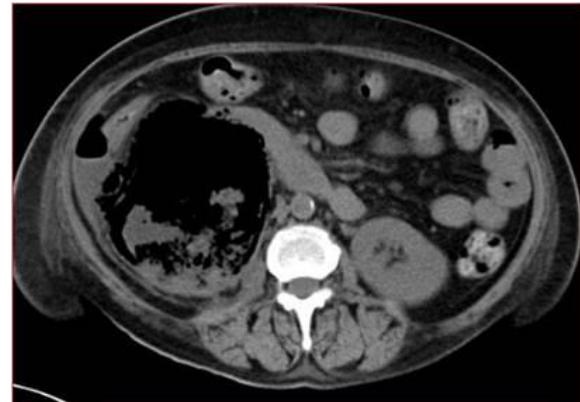
Calculus disease with EPN was seen in 5 patients. Three patients had renal calculus, two patients had ureteric calculus. Tanmaya Goel, et al. [8] had a series of patients with calculus disease and EPN. Initial conservative management followed by treatment of stone disease at a later date were their recommendations. In our case, two patients required ureteroscopy and DJ stenting, as an emergency procedure. Nephrectomy was done for 1 patient who had renal calculus. Two other patients who had renal calculus with EPN were

managed conservatively with DJ stenting, ESWL was done after they recovered from EPN, eight to twelve weeks later (**Figure – 3, 4, 5, 6, 7**).

**Figure - 3:** Treatment modality and EPN class.



**Figure – 4:** Class 3 EPN right kidney.



**Figure – 5:** Emphysematous pyelitis right kidney.



Tseng, et al. [2] had studied, host factors and the bacterial virulence factors predisposing to EPN. Necrosed papilla, ureteric calculus, sluggish ureteral peristalsis due to bacterial toxins and

sepsis were the common causes of HUN described by Tseng.

**Figure – 6:** Class 2 emphysematous pyelonephritis.



**Figure – 7:** X-ray KUB - Bilateral emphysematous pyelonephritis.



In Karthikeyan's [1] series patients with hydroureteronephrosis (HUN) required PCN, and antibiotic treatment. Few patients in Alan's series required PCD and also irrigation with 14 F pig tail catheters. In our group of patients DJ stenting was the treatment of choice, when a patient presented with HUN. 30 (62.50%) patients in our series had HUN, DJ stenting was done in 16 patients (34.3%), ureteroscopy and DJ stenting were done in 9 patients (18.7%). Ureteroscopy was done to relieve obstruction either due to stone or necrosed papilla. All these patients improved dramatically after these minimally invasive procedures.

In our study the mortality rate was 8.3% (4 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. Both the patients who underwent nephrectomy were managed initially with percutaneous nephrostomy. Nephrectomy was done only after a trial of minimally invasive therapy.

Chaung, et al. [9], in his metaanalysis has observed 42% mortality with emergency nephrectomy in EPN. Patients with extensive parenchymal involvement who were managed with single or multiple PCN, required elective nephrectomy later, the mortality in this group was only 8%. In Karthikeyans [1] series emergency nephrectomy was done in only one patient, others were managed with PCN and a functional study was performed to document renal function, and elective nephrectomy was done at a later date. He also observed reduced mortality rate with this initial conservative treatment. Our study also proves that, conservative management and early appropriate minimally invasive intervention in patients with EPN will reduce the mortality and morbidity.

## 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. Ureteroscopy 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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