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MANAGEMENT OF EMPHYSEMATOUS PYELONEPHRITIS: OUR EXPERIENCE

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ABSTRACT: BACKGROUND: Emphysematous pyelonephritis (EPN) is a rare, severe, acute, necrotizing infection of the renal parenchyma and perirenal tissues that is caused by gas-producing bacterial pathogens. **AIMS AND OBJECTIVES:** To present our experience and discuss the various management approaches for treating Emphysematous pyelonephritis. **MATERIALS AND METHODS:** A retrospective analysis of the hospital records was done. A total of thirty two patients with EPN were admitted in our hospital from October 2011 to November 2013. All the patients were managed conservatively. Follow-up ranged from three months to two years. **RESULTS:** Of the thirty two patients, seven belonged to class I, fourteen to class II, eight to class IIIA, one to class IIIB and two to the class IV. Thirty patients had history of fever, 24 had localized flank pain while 7 had dysuria, 8 had hypotension and 6 patients presented with altered sensorium. E. coli was the most common bacteria, which was isolated from urine in 78% of the patients. On the risk factor stratification, twelve patients had simultaneous presence of 2 or more risk factors (thrombocytopenia-19 patients; renal function impairment-29 patients; shock-8 patient; altered sensorium-6). All the patients were initially managed with aggressive fluid and electrolyte resuscitation, control of blood sugar levels, and broad spectrum antibiotics. Intervention, in the form of percutaneous drainage or DJ stenting, was done in Twenty five patients. Thus, the acute episode was managed with conservative and minimally invasive management strategies in all the patients; however, two patients of class IIIA underwent nephrectomy because of their delayed presentation and due to not recovering from sepsis in spite of percutaneous drainage. **CONCLUSIONS:** EPN is now being more readily diagnosed, at an early stage, making conservative and minimally invasive management of EPN a safe, effective, and feasible option.

KEYWORDS: Emphysematous pyelonephritis, Dj stenting, percutaneous drainage, percutaneous nephrostomy, nephrectomy.

INTRODUCTION: Emphysematous pyelonephritis (EPN) is a severe, acute 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 para-nephric spaces. EPN predominantly affects female diabetics.¹ Non-diabetic patients can also develop EPN, albeit rarely, with a less severe clinical course as compared to diabetics.² 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

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conservative, minimally invasive modalities of management with a decrease in mortality rates and nephrectomies.⁴

We, in this study, present the clinical details and outcome of 32 patients of EPN managed at our center and discuss their management and outcomes.

MATERIALS AND METHODS: Between October 2011 and November 2013, a total of 32 patients were admitted in our hospital with EPN. All the patients were studied with respect to the clinical features at presentation, laboratory variables included white blood cell count, platelet count, serum albumin, serum sodium, hemoglobin A1C (HbA1C), and serum creatinine, as well as the results of urinalysis and Blood and urine cultures, obtained at the initial presentation. Non contrast computerized tomography (NCCT) was done in all cases to confirm the diagnosis and for classification. All the patients were thoroughly investigated, and the risk factors (as proposed by Huang and Tseng) were evaluated. All the patients were initially managed by aggressive diabetic control, correction, and maintenance of fluid and hemodynamic status, renal replacement therapy for raised renal parameters and antibiotics. The patients were followed up for 3-24 months (mean 8 months).

EXCLUSION CRITERIA:

1. History of recent urinary tract instrumentation.
2. Urinary fistula.
3. History of recent genitourinary trauma.

PROGNOSTIC FACTORS: 1. Glycemic control, 2. Renal function, 3. Serum albumin level, 4. Platelet count, 5. Shock on presentation and 6. Level of consciousness on presentation.

Definitions: According to the classification system of Huang and Tseng 2 which is based on the extent of air seen on computed tomography (CT), the patients were divided into one of the following five EPN classifications:

- Class I: Gas in collecting system only
- Class II: Parenchymal gas only
- Class IIIA: Extension of gas into perinephric space
- Class IIIB: Extension of gas into pararenal space
- Class IV: EPN in solitary kidney, or bilateral disease.

Wan et al.⁵ classified the gas collection as type I or type II, on the basis of CT scans:

Type I: Renal necrosis with presence of gas but no fluid (Dry)

Type II: Parenchymal gas associated with fluid in renal parenchyma, perinephric space, or collecting system (Wet).

Conservative management included antibiotic therapy and supportive measures.

INDICATIONS FOR MINIMAL INVASIVE PROCEDURES:

1. Raising s.creatinine values.
2. Hydroureteronephrosis.
3. Sepsis.
4. Significant renal and perinephric collection.

MINIMAL INVASIVE PROCEDURES INCLUDED:

1. DJ stenting.
2. Ureteroscopy and DJ stenting (URS+DJ stent).
3. Percutaneous nephrostomy (PCN).
4. Percutaneous drainage(PCD).

INDICATIONS FOR NEPHRECTOMY:

1. Not improving on minimal invasive treatment.
2. Non functioning kidneys.

RESULTS: Out of the 32 patients with EPN, 20 were females while 12 were males (Male: female; 3:5). Age range was 34-70 years with a mean age of 52 years. All patients were diabetic with raised blood sugar levels (Mean HbA1c was 10.87) at the time of admission due to poor diabetic control. Two patients had ureteral obstruction due to stone disease. The clinical presentation of the patients is given in Table 1. Pyuria was found in all the patients while leukocytosis was found in thirty (93.7%) patients. The urine of all the patients was submitted for culture and sensitivity testing. CT scan was performed for confirmation of the diagnosis as well as for classification. The distribution of the patients into various classes based on radiological investigation is given in Table 2. The representative images of patients with EPN are shown in Figures 1-4. On risk factor stratification (Table 3), as per the criteria proposed by Huang and Tseng, 12 patients had simultaneous presence of two or more risk factors (Thrombocytopenia- 19 patients; Renal Function Impairment- 29 patients; Shock- 8 patients).

Management strategies adopted in our Study: After admission, all the patients were initially managed by aggressive diabetic control, correction, and maintenance of fluid and hemodynamic status, and antibiotics. Initially, broad spectrum antibiotics were used. A combination of piperacillin and tazobactam was used as the first line antibiotic. Aminoglycosides were added in patients who had normal renal parameters while a quinolone was added in patients with deranged renal parameters (with dose adjustment). Antibiotics were changed in accordance with the sensitivity report when it was available. 15.63% of patients were treated conservatively with antibiotics only 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 9.3%. Table 4 Showing different management modalities in our study. Six patients required URS+DJ stenting. Two patients had ureteric calculus and four patients had necrosed papilla causing obstruction. Ultrasound guided PCD was done for peri- nephric collection in 1 patient. Four patients required PCD and DJ stenting. PCN was done in 3 patients. Of these more than one PCN tubes were required in 1 patient.

Nephrectomy was done in 2 patients with class 3A EPN. One of these patients underwent DJ stenting followed by PCN 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 patient who underwent nephrectomy presented with left hydronephrosis and perinephric

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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.

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. 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.

DISCUSSION: Emphysematous pyelonephritis (EPN) was described as a rare, life threatening UTI. Schultz and Klorfein first used the term EPN.⁶ The first case of EPN was reported by Kelly and Mac Cullen.^{6,7} EPN was described in patients with diabetes and poor socioeconomic status by Allen et al. But in our study there is no such difference in the incidence in relation to the economic status. EPN was always common in female patients. The male to female ratio in Wan's³ 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 commonest organism seen in both Huang et al¹ and Wan et al³ series 69 % & 58% respectively, followed by *Klebsiella* 29 % and 24 % respectively. In our study E.coli was seen in 78% of the cases, followed by *klebsiella* in 7% of cases as shown in table 5.

The total study group (number 32) was divided into two groups, Survivor (number 29) and Non survivor (number 3). The prognostic factors were studied in both the groups and their statistical significance identified as shown in Table 6. Shock (P- 0.0267), altered sensorium (P- 0.0026) and CKD (P- 0.0142) were statistically significant.

The Incidence of DM in Karthikeyan's⁴, Huang's¹, Ali Nawaz khan⁸, studies were 93%, 96%, 97% respectively. In our series all the 32 patients had DM. There were patients with both insulin dependent and non insulin dependent DM. HbA1c was estimated in all the 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 & class 4, where as patients with HbA1c < 11.5 had class 1 class 2 EPN. Higher the HbA1c, higher the class of EPN. Probably HbA1c may be a good prognostic marker in patients with EPN, however more studies are required to confirm this.

In Karthikeyan's⁴ 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 al² and karthikeyan et al⁴ reported high incidence of mortality, with EPN in transplant kidneys, due to immunosuppression. However there were no immunocompromised patients in our series of EPN.

Patients with preexisting 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 dialysis dependents as shown in Table 6.

Thrombocytopenia and altered sensorium, at the time of initial presentation were associated with poor prognosis.

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Thrombocytopenia was seen in 19 patients (59.38%) and 4 patients (12.5 %) with platelets less than 75000/cu mm required platelet transfusions. 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.

Altered sensorium was seen in 6 (18.75%) patients, out of 6, five patients were in class 3 and class 4 EPN. Altered sensorium was not seen in class 1 EPN. Presence of altered sensorium in higher class of EPN was significant. Similar observation was seen in Huang's, Suganatha shetty's⁹ series.

There were 4 patients with dry type of EPN, all the 4 patients had altered sensorium on presentation. 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.

Wan et al' Type 1 EPN, (dry type) was less common than the type 2 EPN (wet type), had a fulminant course with a high risk of mortality.

Emphysematous pyelitis, Class 1 EPN was seen in 21.8% 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. 5 patients required DJ stenting as they had obstruction and dilated kidneys.

43.75% of patients were under Class 2 EPN, this was the most common class in our study as shown in Table 7. 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 8 patients (25%) in Class 3A EPN. Two 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

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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, 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 gerotafascia, Presented late with sepsis. PCN was done for this patient and two tubes were required. He didn't improved and ultimately died. In J J Huang et al ¹ 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 two 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 ², 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. 3patients had renal calculus, 2 patients had ureteric calculus. Tanmaya Goel et al ¹⁰ 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, 8-12weeks later.

Tseng et al¹ 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.

In Karthikeyans 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. 20 (62.50%) patients in our series had HUN, DJ stenting was done in 11 patients (34.3%), ureteroscopy and DJ stenting were done in 6 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 9.3% (3 patients). In Karthikeyan's⁴ 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,¹¹ in his meta analysis 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 Karthikeyans⁴ series emergency nephrectomy was done in only one patient, others were managed with PCN and a

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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. EPN can be successfully treated with conservative and minimally invasive interventions, irrespective of class of EPN and the number of risk factors. URS 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.

Preexisting CKD status, shock at presentation and altered sensorium are the poor prognostic factors in this study.

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Clinical features at presentation	No. of patients
Fever	30
Tachycardia	26
Flank pain	24
Dysuria	7
Hypotension	8
Macroscopic hematuria	4
Altered sensorium	6

Table 1: Clinical features at presentation

EPN classification	No. of patients	Percentage
According to the Wan et al (n=32)		
Type I (Dry type)	4	12.5%
Type II (Wet type)	28	87.5%
According to Huang and Tseng (n=32)		
Class I	7	21.8%
Class II	14	43.7%
Class III A	8	25%
Class III B	1	3.1%
Class IV	2	6.2%

Table 2: Radiological classification of patients (n=32)

Risk factors	No. of patients
Deranged renal parameters	29
Thrombocytopenia	19
Hypoalbuminemia	32
Shock	8
Altered sensorium	6
Poorly controlled DM	32
CKD (chronic kidney disease)	8

Table 3: Risk factors in patients (Huang and Tseng)

Treatment	No. Patients
Antibiotics only	5
DJ stent	11
DJ stent + URS	6
DJ stent + PCD	4
PCN	3
PCD	1
Nephrectomy	2

Table 4: Different Management modalities (n=32).

DJstent=Double J stent, URS= ureterorenoscopy, PCD=percutaneous drainage, PCN= percutaneous nephrostomy

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Organism found in urine for c/s	No. Patients (n=32)
E.coli	25
Klebsiella pneumonia	2
Psuedomonas	1
Candida	1
Mixed (E.coli+Candida)	1
No growth	2

Table 5: Organisms found in Urine for Culture

CKD risk factor	No. of patients	H. D during treatment	H.D dependent
Pre-existing CKD	8	8	7
No Pre-existing CKD	24	3	1

Table 6: Hemodialysis (H.D) requirement during & after treatment of EPN in Patient's with or without Pre-existing CKD. CKD= chronic kidney disease

Class of EPN Treatment	Class I	Class II	Class IIIA	Class IIIB	Class IV
Antibiotics	2	3			
DJ stenting	3	8			
DJ+URS	2	3			1
DJ+PCD			3		1
PCN			2	1	
PCD			1		
Nephrectomy			2		

Table 7: Management modalities according to EPN class.

DJ+URS= Uteroscopy+dj stenting, DJ+PCD= dj stenting +percutaneous drainage, PCN= percutaneous nephrostomy, PCD= percutaneous drainage

Fig. 1: CT scan showing gas within the pelvis of Right kidney (Class IEPN).

Fig. 1

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Fig. 2: CT scan showing gas within the parenchyma of the left kidney (Class II EPN).

Fig. 2

Fig. 3: CT scan showing gas within the pelvis of Right kidney (Class III EPN).

Fig. 3

Fig. 4: Coronal view of CT scan showing gas within the renal parenchyma extending into the Right perinephric space and pararenal space (Class IIIB EPN).

Fig. 4

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