Submitted Manuscript BJU

Title: Emphysematous Pyelonephritis Prognostic Scoring System and Risk Stratification - an Eleven-Year Prospective Study at a Tertiary Referral Centre

Introduction

Emphysematous pyelonephritis (EPN) is a life-threatening necrotizing infection of the kidney that results in the production and accumulation of gas within the renal pelvi-calyceal collecting system, renal parenchyma or the peri-nephric and para-nephric spaces [1,2,3]. The earliest case of gas-forming renal infection was reported in 1898 [4]. It took more than 6 decades for Schultz and Klorfein to coin the term Emphysematous pyelonephritis (EPN) to the condition that links gas formation in the kidney to acute renal infection [5].

EPN remains an important but neglected clinical issue worldwide and there have been limited published reports of the condition in the literature. A meta-analysis of 32 reports with a total of 628 patients found that the average mortality rate was 18% [6].

We conducted an 11 year prospective longitudinal clinical study of 131 patients with EPN presenting to a tertiary referral centre, (the largest series to date) to define pre-morbid, clinical, laboratory and imaging features and identify prognostic factors associated with morbidity and mortality, and develop an EPN prognostic scoring system.

Patients and methods

A total of 131 patients with EPN, who were admitted and treated in a tertiary care referral centre in South India, over an 11-year period between Jan 2009 and Dec 2019 were included in the study. A list of all prognostic factors was identified from a prospective institutional database containing all pre-defined prognostic variables. Demographic parameters including age, gender, duration of diabetes, laterality of the disease, level of consciousness (alert, disoriented, and unresponsive), and body mass index (BMI) were recorded. Biochemical parameters including total leukocyte counts (TLC), platelet counts, blood glucose, serum creatinine, serum electrolytes and serum albumin were documented.

Urine cultures were taken at the time of admission for all patients. Blood culture was done in all patients either at the time of admission or during the febrile episodes. Those patients who had a minimally invasive treatment also had the urine sent from the aspitrate from the pelvi-calyceal system.

A prognostic scoring system was devised based on these parameters studied. A total of 18 parameters that were either found significant in the present study (based on internal validation) or in previous published literature (though not found significant in the present study) were short-listed. Each parameter was given a score ranging from 0 to 2, with a minimum total score of 1 and a maximum total score of 26 (**Table 1**). A higher score was correlated with a poorer prognosis.

Further risk stratification of the lethality of the disease was performed based on a combined prognostic score. Those with a score of 1 to 8 were grouped under the very low-risk category. Low-risk groups had a score of 9 to 15, the intermediate group had a score of 16 to 20 and those with a score of more than 20 (high-risk group) carried a higher risk of succumbing to the disease. The maximum score that could be obtained was 26.

Classification and parameters

All patients in our study underwent non-contrast abdominal CT and were sub-classified based on the Huang and Tseng classification, who classified EPN based on the location and extent of gas within the kidneys [7]. Class 1 included gas in the pelvi-calyceal system with normal renal parenchyma; class 2 contained gas in the renal parenchyma without extension to the extra renal space; class 3A showed extension of gas or abscess beyond the renal capsule into the perinephric space, but contained within Gerota's Fascia; Class 3B – an extension of gas or abscess to the pararenal space and Class 4 – bilateral EPN or a solitary kidney with EPN.

Patients were subdivided into three groups: group 1 - patients who survived without any intervention; group 2 - those who survived with intervention, including double J stent insertion, percutaneous nephrostomy (PCN) insertion, percutaneous drainage tube (PCD) placement or haemodialysis; group 3 - those who succumbed to the disease, with or without intervention. In groups 2 and 3, the decision to perform stenting, PCN, PCD or nephrectomy was taken based on the severity of symptoms, the prognostic scoring, risk stratification and the treating urologist's

primary assessment of the patient at the time of admission. These procedures were done as early as the patients were fit enough to undergo the procedures.

Several biochemical parameters were included in this study to formulate a prognostic scoring system. We defined shock as a patient who presented to the Emergency Room (ER) with systolic blood pressure less than 90 mmHg [8]. A platelet count of less than 100 x 10^9/L was defined as thrombocytopenia and a serum albumin level of less than 25 grams/L was recorded as Hypoalbuminemia. Hyponatremia was defined as a critical value of less than 130 mmol/L. Patients with a Serum Creatinine of less than 159.12 µmol/L, although more than the normal level laboratory reference was considered to be within the acceptable limits. Those with serum creatinine levels of more than 159.12 µmol/L were considered to have a high creatinine level. Leucocytosis was defined as an absolute count of more than 11 x 10^3 cells/mm^3 and Leucocytopenia with a count of less than 4 x 10^3 cells/mm^3.

Statistical analysis

Data analysis was performed using IBM SPSS version 16 and STATA 14, p-value <0.05 was considered significant. Descriptive statistics such as mean (sd), frequency (percentage) were used. Chi-square test/Fishers exact test was employed to test the association between the categorical variables. Shapiro- Wilk test was used to assess the normality of data. For quantitative measurements, the Kruskal Wallis test was used to test the differences between the groups. A penalized simple and multiple logistic regressions were used to calculate the crude and adjusted odds ratio to determine the risk factor for survivors. A univariate analysis was performed based on the demographic, clinical and biochemical factors that caused EPN. Variables with a statistically significant value and a probable biological relationship to the dependent outcome variable were subjected to non-conditional multivariate analysis to identify independent factors that were significantly related to the presence or absence of mortality due to the disease. Mortality was the key parameter considered for both univariate and multivariate analysis.

Results

Patient characteristics:

A total of 131 patients were included in the study. **Table 2** shows the clinical, epidemiological, and biochemical characteristics of the 3 groups. The average age was 57.4 years (mean +/- SD). Females were more commonly affected compared to males, with the female to male ratio being 1.5:1. Twenty patients (15.3%) developed bilateral disease. In the remaining patients, the left side was slightly more commonly involved (n=58) than the right (n=53), with the left to right ratio being 1.1:1. While the average BMI of all patients was 26.01, 6 out of 7 patients in group 3 fell in the obese range with a BMI of more than 30 (p =0.001). A tender loin with a palpable kidney was one of the clinical findings in acute EPN, seen in 28 patients in our study. A palpable tender kidney has been identified as one of the poor clinical prognostic parameters (p <0.001).

Of 131 patients, 102 patients were conscious on admission, 4 were admitted unresponsive and 25 were mildly disoriented. Three out of 4 unresponsive patients were in group 2. Shock at presentation was observed in 18 patients and 53 patients required intensive care. The presence of shock at initial admission indicates a poor prognosis and warrants immediate attention (p <0.001). Haemodialysis was required in 22 patients to stabilize before intervention (p <0.001). All 7 patients in group 3 needed haemodialysis to stabilize, of which two underwent emergency nephrectomy. Eventually, all 7 in group 3 died secondary to EPN.

Associated co-morbidities:

Diabetes mellitus constituted the single most commonly associated co-morbidity. Only ten patients were non-diabetics. Twenty-seven patients had blood glucose of less than 15.91 mmol/L with 57 patients having blood glucose levels of more than 26.52 mmol/L. All three groups had high average blood glucose at presentation (p-value was 0.632). Group 3 was found to have the highest blood glucose levels of 43.05 mmol/L. An HbA1C level of more than 7 was detected in a total of 107 patients. The average HbA1C levels were above 9 in all three groups, with a maximum of 10.3, noted in group 3 although there was no statistical difference between the three groups. The associated comorbidities included urolithiasis (n=6), coronary heart disease (n=7), a previous history of treated pyelonephritis (n=14), pre-existing chronic kidney disease (n=29), hypothyroidism (n=20 and

chronic alcoholism (n=2). However, no such significant associations of mortality were identified with comorbid illnesses or patient age, sex, or laterality of the EPN.

Haematology:

The mean total leukocyte count at the time of admission was 16.30 x 10^3 cells/ µl of blood. The absolute leukocyte count was higher in group 3 than in groups 1 and 2 and this value was found to be significant ($p<0.05$). Thrombocytopenia was observed in 60 patients. Although a degree of thrombocytopenia was observed in all three groups, there was a 100% association observed in group 3 with a mean platelet count of 47.02 x 10^3 cells/ µl of blood ($p<0.014$).

Biochemistry:

Hypoalbuminemia was noted in 42 patients, with all 6 patients in group 3 having a serum albumin level of less than 25 g/L. The overall average serum albumin level was 30.8 g/L, whilst the lowest values were observed in group 3 ($p=0.002$).

Hyponatremia on admission was another consistent biochemical abnormality recorded in our patients. The overall average serum sodium levels at presentation were above 130 mmol/L in groups 1 and 2, while in group 3 it was reduced to 122.2 mmol/L. Thrombocytopenia was observed in all 7 patients in group 3. Biochemical parameters including absolute leukocyte count, platelet counts, and serum creatinine after intervention also showed a significant difference between the three groups ($p<0.01$).

Microbiology and antibiotics:

The empirical antibiotic used was third-generation cephalosporins (Cefoperazone and Sulbactam combination), which were subsequently modified based on the urine and/or blood culture reports. However, this was not the uniform protocol followed in all patients. Those patients, who presented with shock, necessitating ICU admission and inotrope support, were either treated with Piperazilin-tazobactum or carbapenem antibiotics until the culture reports were obtained. **Table 3** illustrates the causative organisms isolated from the urine and blood cultures. The urine culture was positive in 77 patients, with Escherichia coli being the most common infective organism (n=58, 75.32%), followed by Candida albicans

in 11 patients. Gram-negative septicaemia due to Escherichia coli and Candida fungal septicaemia were the most common organisms seen in blood.

Imaging:

Table 4 illustrates the radiological classification of our patients in all 3 groups. Class 1 and 2 comprised the most common type of EPN (n=86), while class 3A and 3B together constituted 18 patients. Class 4 EPN was seen in 27 patients. The higher number of class 4 EPN was due to a higher number of bilateral cases. Most patients in groups 1 and 2 had class 1 or 2 diseases, while all 7 patients in group 3 had either class 3B or 4 diseases ($p<0.001$).

Figures 1 illustrates CT images from various classes of EPN. Of the 86 patients in Class 1 and 2, the majority of them improved with the insertion of a ureteric stent. Treatment with antibiotics alone was successful in 22 patients; the remaining patients required a double J stent placement and/or percutaneous nephrostomy (PCN) tube or percutaneous drainage tube (PCD) insertions. Seven patients died as a result of EPN, of which 2 died even before any attempt at surgical intervention (**Table 5**). About 75% of patients (n=98) had an overall hospital stay of 3 to 7 days. Two patients in group 3 expired within 12 hours of admission. The mean hospitalization time was 6.05 days (excluding the above 2 patients), with the maximum hospital stay of 20 days noted in a group 2 patient, who underwent nephrectomy for class 3b EPN.

Summary of Risk stratification:

To assess the lethality of EPN in our patients, risk stratification was performed based on the prognostic scoring system of Table 1. These patients were graded as very low risk, low risk, intermediate-risk, and high-risk categories. **Table 6** illustrates the summary of risk stratification based on the combined mean prognostic scoring points for each of the three groups separately. Group 1 had an average score of 10.59, group 2 scored 11.53, and group 3 had a score of 23. The overall average prognostic score in all 131 patients was 11.91. A higher prognostic score was seen to be associated with the mortality group. By risk stratification, both group 1 and 2 came under very low to low risk and intermediate category, while all patients in group 3 belonged to the high-risk category ($p<0.001$). All 7

patients in group 3 belonged to the high-risk category and eventually succumbed to EPN.

Univariate and multivariate analysis:

Using univariate analysis, 10 factors were identified to be significantly associated with the prognosis in patients with EPN (**Table 7**). These were body mass index, class of EPN, coagulation profile, palpable tender kidney, shock at presentation, need for haemodialysis, Serum sodium and albumin levels, level of consciousness, and need for ICU admission. In a multivariate analysis of these factors, none were found to be statistically significant (**Table 8**).

Discussion

The present study includes the largest number of EPN patients treated in a single centre. This is also to our knowledge the first study to provide an objective assessment of a prognostic scoring system along with a risk stratification model for patients diagnosed with EPN. Most patients had a significant improvement with medical management alone or by minimally invasive methods of intervention. The number of patients requiring emergency nephrectomy is considerably low in our study. The overall mortality from the disease is also <6%.

An underlying history of diabetes mellitus has been identified as a key prognostic indicator linked to the ultimate fate of patients presenting with EPN [9]. Although most commonly seen in patients with diabetes, EPN can also present in patients with urinary tract obstruction and immunocompromised status [10]. Historically the combination of diabetes and an obstructed upper urinary tract with EPN has been associated with a very high mortality rate, up to 71% [11]. Over the past 3 decades, various clinical, biochemical, and radiological parameters have been identified as major prognostic risk factors and the management of EPN has therefore improved significantly [12, 13]. A reduction in the mortality to 3-30% was also observed [14]. Because of the life-threatening behaviour and its strong association with diabetes mellitus, there appears to be a very narrow margin of error in treating such patients. Various studies in the past have documented the prognostic factors that alter the nature of the disease, the course of illness, and the ultimate outcome. Our study validated and performed an objective assessment

of those poor prognostic factors. We used our data to improve and refine the current scoring system for EPN [15]. Our study utilized a larger cohort to improve the scoring system by including risk stratification. Such measures may help us to effectively triage, segregate, and prognosticate all these patients into 4 groups which would help decide on the appropriate modality of treatment and supportive care. This is the first study to formulate a combined prognostic scoring/risk stratification system, by which we can assess the prognosis and stratify the risk of succumbing to this illness.

Diabetes mellitus appeared to be the most frequently associated risk factor in our patients. Of the 131, only 10 were non-diabetics. A high blood sugar level, immuno-compromised status, a high tissue sugar level, and glycosuria make the urinary tract more prone to infections [16]. The high tissue glucose content and gas production by the bacteria set up a conducive environment to produce carbon dioxide and hydrogen by fermentation of sugar for further enhanced growth of micro-organisms, which leads to renal parenchymal destruction and higher morbidity [17, 18].

Obesity and diabetes have also shown a strong association [19]. A higher BMI in turn has been found to have a significant correlation with poorer outcomes [20, 21, 22]. The BMI classification in our study was based on the WHO grading for the Asian population [23]. Over 85% in group 3 was associated with a BMI of more than 30 kg/m^2. In the literature, both very low BMI and high BMI are associated with a poorer prognosis. Jain et al, in their study on 72 patients with EPN, found a higher incidence of mortality in patients with low BMI [24]. However, Semins et al report a higher incidence of upper urinary tract infections in patients with a higher BMI. In their study on more than 95000 patients, they found a strong association of pyelonephritis with elevated BMI [25]. We observed a higher incidence of such infections in patients with a BMI of more than 25 kg/m^2 and 6 of the 7 patients in the mortality group were obese with a BMI of more than 30.

Thrombocytopenia was also associated with higher mortality. All patients in group 3 had a low platelet count, with a mean count of 47.02 x 10^9/L of blood. Many authors have identified thrombocytopenia as a strong prognostic factor for EPN [26, 27]. Aswathaman et al reported thrombocytopenia, hyponatremia altered

mental sensorium, and compromised renal function as poor prognostic factors. We found low serum albumin levels, low serum sodium level at presentation, high absolute leukocyte count, and a high HbA1C level to be strongly associated with a poorer prognosis [28].

Most of the recent studies have followed the radiological classification by Huang et al. In one of the largest meta-analyses on 175 patients from seven study cohorts, Falgas et al had classified EPN into two subtypes, namely type 1 and type 2, based on the presence or absence of fluid content in the kidney respectively [29]. They observed that patients with Type 1 EPN (renal parenchymal necrosis with the absence of fluid content or presence of a streaky/ mottled gas pattern), thrombocytopenia, bilateral involvement, hypotension, altered sensorium, and high serum creatinine levels were associated with fatal outcome. They also concluded that a conservative treatment alone had a higher fatal outcome and advised earlier intervention in the form of relieving the obstruction or nephrectomy. However, 22 patients in group 1 had received medical management with antibiotics and other supportive measures and recovered well. Supportive measures including nasal oxygen, intravenous fluids, inotropes, correction and optimization of electrolyte imbalance, appropriate antibiotics, and adequate glycaemic control are the pre-requisites for treating such patients with conservative measures. Moreover, the improved monitoring techniques and increased usage of higher generation antibiotics and antifungal agents have largely made conservative treatment a viable approach. Misgar et al stressed the need for maintaining a systolic blood pressure >100 mmHg, with good hydration and inotropes wherever needed [30]. Shock at presentation with a systolic pressure of less than 90 mmHg significantly increased the mortality rate [31]. Our observation was that 18 patients presented with shock and all 7 patients who died of the disease showed features of shock at presentation needing ICU care.

The presence of a tender kidney found during loin palpation indicates an acutely inflamed and enlarged kidney that needs a prompt decompression. Although most authors have discussed the need for either an internal or external diversion in such cases, there is no special mention of this particular clinical finding anywhere in the literature. We found that the presence of a palpable tender kidney is associated with a poorer prognosis requiring prompt treatment and intensive monitoring. Of

the 28 patients who presented with this clinical finding, 26 of them required intervention. The remaining 2 did not receive any intervention but required ICU care and monitoring. Seven eventually died of the disease. The threshold for intervention was very low in study patients who had a palpable tender kidney, reiterating the fact that in an acutely inflamed and palpable kidney with obstruction, especially in diabetic patients, immediate/early intervention may prove beneficial.

Until the late 1980s, EPN carried very high mortality of up to 40 to 50% and emergency nephrectomy was the accepted initial modality of treatment [32]. But with increased awareness amongst the urologists and physicians, with early diagnosis being made and with the use of minimally invasive interventional techniques available, such cases are being treated more conservatively, largely obviating the need for early nephrectomy [33]. Somani et al, in their evidence-based systematic review on 10 studies on 210 patients concluded that percutaneous drainage should be part of the initial management strategy in patients with EPN [34]. They also observed that medical management alone or emergency early nephrectomy carried much higher mortality than such minimally invasive approaches. In our cohort, 6 patients underwent early nephrectomy of which 5 needed ICU admission and PCN placement, 4 needed haemodialysis but 3 of them died of the disease. However, of the 7 patients who died of the disease, all 7 were in shock at presentation, needing ICU admission and haemodialysis. Five of them had a DJ stenting done. All 7 patients who died of EPN belonged to the high-risk category. None of the patients in the intermediate or low or very low-risk group succumbed to the illness. Similar prognostic scoring has been done by Jain et al, where 4 out of 7 patients who died belonged to the intermediate-risk category. We identified 10 clinical, radiological and biochemical parameters by univariate analysis to be significantly associated with the prognosis in each of the three groups. When each of the risk factors identified by univariate analysis was attributed equal significance, the trend analysis concluded that the risk of mortality was directly associated with the class of EPN ($p<0.001$) and the risk stratification by the prognostic scoring system ($p<0.001$). However, multivariate analysis showed that none of these factors independently influenced the ultimate outcome in such patients. Henceforth, the authors emphasize that the prognostic

assessment should be based not just on one independent factor, further reinforcing the need for a combined prognostic risk assessment scoring and a formal risk stratification, in order to make a better assessment of the ultimate outcome in patients with EPN. Jain et al also attempted to develop a prognostic scoring but did not perform a multivariate analysis [25].

To our knowledge, this study is the first and largest study to objectively assess the risk stratification in patients with EPN based on a combined prognostic scoring system. It is very important to follow up on the patients who were treated conservatively. Recurrent EPN is not very uncommon. Lu et al reported a recurrence in 8 out of 44 patients with EPN within 3 months of primary treatment [35]. However, in our study, we did not come across any patient with recurrent disease.

Limitations of our study

This study has limitations that are innate to many of the prospective studies performed for a longer duration. An absence of a uniform structured long term follow-up, lack of consensus amongst the treating physicians and urologists, absence of documentation of the split renal function using nuclear imaging in all patients are some of the limitations of the study. The lack of an external validation of the prognostic scoring system is another limitation of this study. Larger and prospective multi-institutional trials may be needed to further validate the study.

Conclusions

Our study highlights the need for an objective and qualitative assessment of the risk stratification in patients with EPN. A multi-disciplinary approach, a high index of clinical suspicion amongst treating physicians, an early accurate diagnosis, and usage of appropriate antibiotics, identifying the poor prognostic factors using the validated scoring system, risk stratification and initiation of prompt and appropriate treatment would make EPN a fully curable condition with less morbidity and mortality.

Conflicts of Interest: All authors have an interest in urological infections

Acknowledgments: Sir Zumla is a co-PI of the Pan-African Network on Emerging and Re-emerging Infections (PANDORA-ID-NET) funded by the European and Developing Countries Clinical Trials Partnership the EU Horizon 2020 Framework Programme for Research and Innovation. AZ is a National Institutes of Health Research senior investigator. All authors declare no conflicts of interest.
Financial support: No grant funding

Ethics and IRB: This study was approved by the Ethics review board of the Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India.

References

1. Pontin AR, Barnes RD, Joffe J and Kahn D: Emphysematous pyelonephritis in diabetic patients. Br J Urol 1995; 75: 71.
2. Michaeli J, Mogle P, Perlberg S, Heiman S and Caine M: Emphysematous pyelonephritis. J Urol 1984; 131: 203.
3. Nashi N, Pandya G. Images of the month 5: Emphysematous pyelonephritis: not your garden-variety pyelonephritis. Clin Med (Lond). 2019 Sep;19(5):421-422.
4. Huang Kelly HA, MacCallum WG: Pneumaturia. JAMA 1898, 31:375-381.
5. Schultz EH, Klorfein EH: Emphysematous pyelonephritis. J Urol 1962, 87:762-6.
6. Aboumarzouk OM, Hughes O, Narahari K, Coulthard R, Kynaston H, Chlosta P, Somani B. Emphysematous pyelonephritis: Time for a management plan with an evidence-based approach. Arab J Urol. 2014 Jun;12(2):106-15.
7. Huang JJ, Tseng CC. Emphysematous pyelonephritis: Clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med 2000;160:797-805.
8. Haider AA, Azim A, Rhee P, Kulvatunyou N, Ibraheem K, Tang A, O'Keeffe T, Iftikhar H, Vercruysse G, Joseph B. Substituting systolic blood pressure with shock index in the National Trauma Triage Protocol. J Trauma Acute Care Surg. 2016 Dec;81(6):1136-1141.
9. Abdul-Halim H, Kehinde EO, Abdeen S, LashinI, Al-Hunayan AA, Al-Awadi KA. Severe emphysematous pyelonephritis in diabetic patients: diagnosis and aspects of surgical management. Urol Int. 2005;75(2):123-8.

10. Dubey IB, Agrawal V, Jain BK, Prasad D. Emphysematous pyelonephritis in a non-diabetic patient with non-obstructed kidney: an unknown entity. Saudi J Kidney Dis Transpl. 2013 Jan;24(1):97-9.
11. Costas S. Renal and perirenal emphysema. Br J Urol. 1972 Jun;44(3):311-9.
12. Kapoor R, Muruganandham K, Gulia AK, Singla M, Agrawal S, Mandhani A, Ansari MS, Srivastava A. Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis. BJU Int. 2010 Apr;105(7):986-9.
13. Aswathaman K, Gopalakrishnan G, Gnanaraj L, Chacko NK, Kekre NS, Devasia A. Emphysematous pyelonephritis: outcome of conservative management. Urology. 2008 Jun;71(6):1007-9.
14. Karthikeyan VS, Manohar CMS, Mallya A, Keshavamurthy R, Kamath AJ. Clinical profile and successful outcomes of conservative and minimally invasive treatment of emphysematous pyelonephritis. Cent European J Urol. 2018;71(2):228-233.
15. Prakash JVS, Tamil Muthu M, Balaji AR, Vetrichandar S, Arasi KV, et al. (2019) A Novel Prognostic Scoring System for Emphysematous Pyelonephritis. J Urol Ren Dis 04: 1170. DOI: 10.29011/2575-7903.001170
16. Ahlering TE, Boyd SD, Hamilton CL et al. Emphysematous pyelonephritis: a 5-year experience with 13 patients. J. Urol. 1985; 134: 1086–8.
17. Khaira A, Gupta A, Rana DS, Gupta A, Bhalla A, Khullar D. Retrospective analysis of clinical profile, prognostic factors and outcomes of 19 patients of emphysematous pyelonephritis. Int. Urol. Nephrol. 2009; 41: 959–66.
18. Kamath SU, Patil B, Shelke U, Patwardhan SK. Comparing diabetic and nondiabetic emphysematous pyelonephritis and evaluating predictors of mortality. Saudi J Kidney Dis Transpl. 2019 Nov-Dec;30(6):1266-1275.
19. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes MetabSyndrObes 2014;7:587-91.
20. Ramachandran A, Snehalatha C, Shyamala P, Vijay V, Viswanathan M. High prevalence of NIDDM and IGT in an elderly south indian population with low rates of obesity. Diabetes Care 1994;17:1190-2.
21. Julka S. Genitourinary infection in diabetes. Indian J EndocrinolMetab. 2013 Oct;17(Suppl 1):S83-7.
22. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J EndocrinolMetab. 2012 Mar;16Suppl 1:S27-36.

23. WHO Expert Consultation: Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
24. Jain A, Manikandan R, Dorairajan LN, Sreenivasan SK, Bokka S. Emphysematous pyelonephritis: Does a standard management algorithm and a prognostic scoring model optimize patient outcomes? Urol Ann. 2019 Oct-Dec;11(4):414-420.
25. Semins MJ, Shore AD, Makary MA, Weiner J, Matlaga BR. The impact of obesity on urinary tract infection risk. Urology. 2012 Feb;79(2):266-9.
26. Kapoor R, Muruganandham K, Gulia AK, Singla M, Agrawal S, Mandhani A, et al. Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis. BJUInt 2010;105:986-9.
27. Kangjam SM, Irom KS, Khumallambam IS, Sinam RS. Role of Conservative Management in Emphysematous Pyelonephritis - A Retrospective Study. J Clin Diagn Res. 2015;9(11):PC09-PC11.
28. Aswathaman K, Gopalakrishnan G, Gnanaraj L, Chacko NK, Kekre NS, Devasia A. Emphysematous pyelonephritis: Outcome of conservative management. Urology 2008;71:1007-9.
29. Falagas ME, Alexiou VG, Giannopoulou KP, Siempos II. Risk factors for mortality in patients with emphysematous pyelonephritis: A meta-analysis. J Urol 2007;178:880-5.
30. Misgar RA, Mubarik I, Wani AI, Bashir MI, Ramzan M, Laway BA. Emphysematous pyelonephritis: A 10-year experience with 26 cases. Indian J Endocrinol Metab. 2016;20(4):475–480.
31. Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. BJU Int. 2011; 107: 1474-1478.
32. Shokeir AA, El-Azab M, Mohsen T, El-Diasty T. Emphysematous pyelonephritis: a 15-year experience with 20 cases. Urology. 1997 Mar;49(3):343-6.
33. Alsharif M, Mohammedkhalil A, Alsaywid B, Alhazmy A, Lamy S. Emphysematous pyelonephritis: Is nephrectomy warranted?.Urol Ann. 2015;7(4):494–498.
34. Somani BK, Nabi G, Thorpe P, et al. Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis? Evidence from a systematic review. J Urol. 2008;179(5):1844-1849.

35. Lu YC, Chiang BJ, Pong YH, Huang KH, Hsueh PR, Huang CY, et al. Predictors of failure of conservative treatment among patients with emphysematous pyelonephritis. BMC Infect Dis 2014;14:418.

Table 1: Prognostic scoring system

S. No	Parameters	Scoring		
		0	1	2
1	**Age (in years)**	< 40	40 - 59	60 and above
2	**Diabetes**	No		Yes
3	**Unilateral or bilateral**		Unilateral	Bilateral, Solitary Kidney
4	**Level of consciousness**	Alert	Disoriented	Unresponsive
5	**Class of EPN (Huang et al)**	1,2	3a, 3b	4
6	**Heart rate (per minute)**	50-90	<50, >90	
7	**Blood sugar (mmol/L)**	<9.99	9.99-16.65	> 16.65
8	**Serum Creatinine at presentation (μmol/L)**	<99.91	99.91-166.51	>166.51
9	**Urine culture**	Negative	Positive	
10	**Temperature (Centigrade)**	36 – 38	<36, > 38	
11	**Platelet count (10^9/L)**	>100	<100	
12	**Total count ($10^3/\mu L$)**	4 - 11	<4, >11	
13	**INR (International normalized ratio)**	<1.3	1.3-2.0	>2.0
14	**Palpable tender kidney**	No	Yes	
15	**Shock at presentation**	No	Yes	
16	**BMI**	19-30	<19, >30	
17	**Sodium at presentation (mmol/L)**	>130	<130	
18	**Serum Albumin (g/L)**	>25	<25	

Total Score: Minimum: 1 Maximum: 26.

Table 2: Demographic, clinical and biochemical characteristics of patients with EPN

Variables	**Group 1 (%)** (No surgical intervention)	**Group 2 (%)** (Surgical intervention)	**Group 3 (%)** (Mortality)	**p value**
Total no. of patients	n = 22	n = 102	n = 7	
Mean age	55.2+/-9.59	54.75+/-11.30	62.14+/-2.26	0.14
Female	14(63.63)	60(58.82)	5(71.42)	0.68
Male	8(36.36)	42(41.17)	2(28.57)	
Laterality L:R				
Unilateral	18 (81.81)	87 (85.29)	6 (85.71)	0.58
Bilateral	4 (18.18)	15 (14.70)	1(14.28)	
Right	11(50)	39(38.23)	3(50)	0.30
Left	7(31.81)	48(47.05)	3(50)	
Body mass index (BMI)	26.58+/-4.06	25.59+/-3.81	31.17+/-1.27	0.001
BMI > 30 (obese)	5 (22.72)	14 (13.72)	6 (85.71)	
Body temperature	38.85+/-1.46	38.82+/-1.31	40+/-0.59	0.54
Palpable tender kidney	2 (9.09)	19 (18.62)	7 (100)	<0.001
Shock at presentation	1 (4.54)	10 (9.80)	7 (100)	<0.001
Need ICU care	6 (27.27)	40 (39.21)	7 (100)	0.006
Need for Hemodialysis	2 (9.09)	13 (12.74)	7 (100)	<0.001
Comorbidities				
Diabetes mellitus*	20 (90.90)	94 (92.15)	7 (100)	0.63
Hypertension	12 (54.54)	45 (44.11)	3 (42.85)	0.85
Associated Illness (APN,CAD,CKD,COPD)	12 (54.54)	47 (46.07)	4 (57.14)	0.99
Level of Consciousness (Disoriented or Unresponsive)	5 (22.72)	20 (19.60)	5 (71.42)	0.05
Biochemical parameters				
Absolute Leucocyte count (10^3 cells/ microliter)	14.64+/-6.55	16.29+/-6.81	26.47+/-7.95	0.02

Blood Sugar at presentation (mmol/L)	15.279+/-7.316	15.927+/-6.772	20.818+/-3.483	0.04
HbA1C	9.16+/-2.12	9.27+/-2.67	10.28+/-1.81	0.72
Serum Creatinine on admission (µmol/L)	295.26+/-241.33	275.81+/-182.15	401.43+/-125.56	0.06
Serum Creatinine After intervention (µmol/L)	139.7 +/-66.3	127.32+/-71.62	253.77+/-107.87	0.001
INR	1.26+/-0.21	1.19+/-0.21	2.41+/-0.27	0.001
Serum Sodium level (mmol/L)	132.54+/-5.40	131+/-5.23	121.57+/-3.45	0.004
Serum Albumin (g/L)	30.1+/-6.30	31.3+/- 6.9	22.7+/- 1.1	0.002
Platelet count (10^9/L)	156.23+/-81.08	174.16+/-126.86	47.02+/-15.57	0.01
Urine C/S	11 (50)	61 (59.80)	5 (71.42)	0.77
Combined mean Prognostic score	10.59	11.53	23	

Table 3: Causative infective organisms in urine and blood culture

Causative infective organisms in urine and blood culture		
Urine culture (n=77)	**Blood cultures (n=31)**	**Total (n=108)**
Escherichia coli (n=58, 75.32%)	Escherichia coli (n=19, 61.29%)	Escherichia coli (n=77, 71.29%)
Candida albicans (n=11, 14.28%)	Candida albicans (n=09, 29.03%)	Candida albicans (n=20, 18.51%))
Klebsiella (n=5, 6.49%)	Klebsiella (n=2, 6.45%)	Klebsiella (n=7, 6.48%)
Enterobacter (n=1, 1.29%)	Enterobacter (n=1, 3.22%)	Enterobacter (n=2, 1.85%)
Acinetobacter (n=2, 2.59%)		Acinetobacter (n=2, 1.85%)

Table 4: Radiological classification of patients with EPN *(based on the Huang and Tseng classification)*

Class of EPN	Group 1 (%)	Group 2 (%)	Group 3 (%)	P value
Class 1 (n=45)	10 (22.2)	35 (77.8)	0	<0.001
Class 2 (n=41)	8 (19.5)	33 (80.5)	0	
Class 3A (n=10)	0	10 (100)	0	
Class 3B (n=8)	0	6 (75)	2 (25)	
Class 4 (n=27)	4 (14.8)	18 (66.7)	5 (18.5)	
Total (N=131)	22 (16.8)	102 (77.9)	7 (5.3)	

Table 5: Details of the surgical procedures performed

Procedures done	**Group 1 (%) (n = 22)**	**Group 2 (%) (n = 102)**	**Group 3 (%) (n = 7)**	**P value**
Supportive treatment only			2 (28.6)	
Antibiotics only	22 (100)	0	0	
DJ stenting only	0	91 (89.2)	1 (14.2)	<0.001
Percutaneous nephrostomy	0	19 (18.6)	3 (42.9)	0.075
Per cutaneous drainage tube	0	16 (15.6)	2 (28.6)	0.076
Early Nephrectomy	0	3 (2.9)	2 (28.6)	0.001
Mortality	0	0	7	<0.001

Table 6: Risk stratification based on prognostic scoring system

Risk of lethality	Group 1 (n=22)	Group 2 (n=102)	Group 3 (n=7)	Total (n=131)	P value
Very low	6	17	0	23	<0.001
Low	13	70	0	83	
Intermediate	3	15	0	18	
High	0	0	7	7	
Average Prognostic score	10.59	11.53	23	11.91	
Average risk score	1.86	1.98	4	2.61	

Table 7: Univariate analysis of the clinical and biochemical parameters of patients

Feature	Odds Ratio (95% CI)	P
Level of consciousness	7.09 (1.41-35.48)	0.017
Class of EPN	38.12 (2.08- 697.39)	0.014
Coagulation abnormality (Deranged INR levels)	54.02 (2.93 - 994.68)	0.007
Body mass index	18.15 (2.8 - 117.71)	0.002
Palpable tender kidney	64.33 (3.48 - 1189.62)	0.005
Shock at presentation	145.74 (7.61 - 2790.03)	0.001
Need for ICU care	20.89 (1.15 - 379.88)	0.040
Need for hemodialysis	84.29 (4.52 - 1571.85)	0.003
Serum sodium levels	24.23 (1.33 - 441.18)	0.031
Serum albumin levels	30.71 (1.68 - 560.29)	0.021
Absolute leucocyte count	19.67 (0.28 - 1377.85)	0.169
Blood sugar at presentation	5.28 (0.28 - 98.03)	0.265
HbA1C	1.77 (0.36 - 8.66)	0.481
Serum creatinine on admission	1.03 (0.02 - 53.41)	0.988
Serum creatinine after intervention	2.19 (0.266 - 16.84)	0.478
Platelet count	15.19 (0.84 - 275.88)	0.066
Urine C/S	1.25 (0.25 - 6.12)	0.785
Blood sugar	2.79 (0.15 - 51.52)	0.490
Blood CS	0.53 (0.11 - 2.65)	0.442
Body temperature	4.64 (0.25 - 84.79)	0.301
Total leukocyte count	4.43 (0.24 - 81.11)	0.315

Table 8: Multivariate analysis of clinical and laboratory parameters

Feature	Adjusted Odds Ratio (95% CI)	P
Level of consciousness	5.88 (0.26 - 131.39)	0.263
Class of EPN	1.08 (0.02 - 42.24)	0.968

Coagulation abnormality (Deranged INR levels)	1.87 (0.10 - 34.74)	0.676
Body mass index	5.53 (0.22 - 137.24)	0.297
Palpable tender kidney	5.07 (0.37 - 68.86)	0.223
Shock at presentation	9.78 (0.09 - 1066.27)	0.341
Need for ICU care	0.97 (0.05 - 26.40)	0.988
Need for dialysis	0.56 (0.01 - 44.04)	0.795
Serum sodium levels	1.45 (0.04 - 55.97)	0.842
Serum albumin levels	4.32 (0.1 - 195.37)	0.452

Legends for images

Figure 1: CT findings of various types of EPN (class 1 to 3)

1a: Class 1 EPN with air in the renal pelvis with air-fluid level (blue arrow)

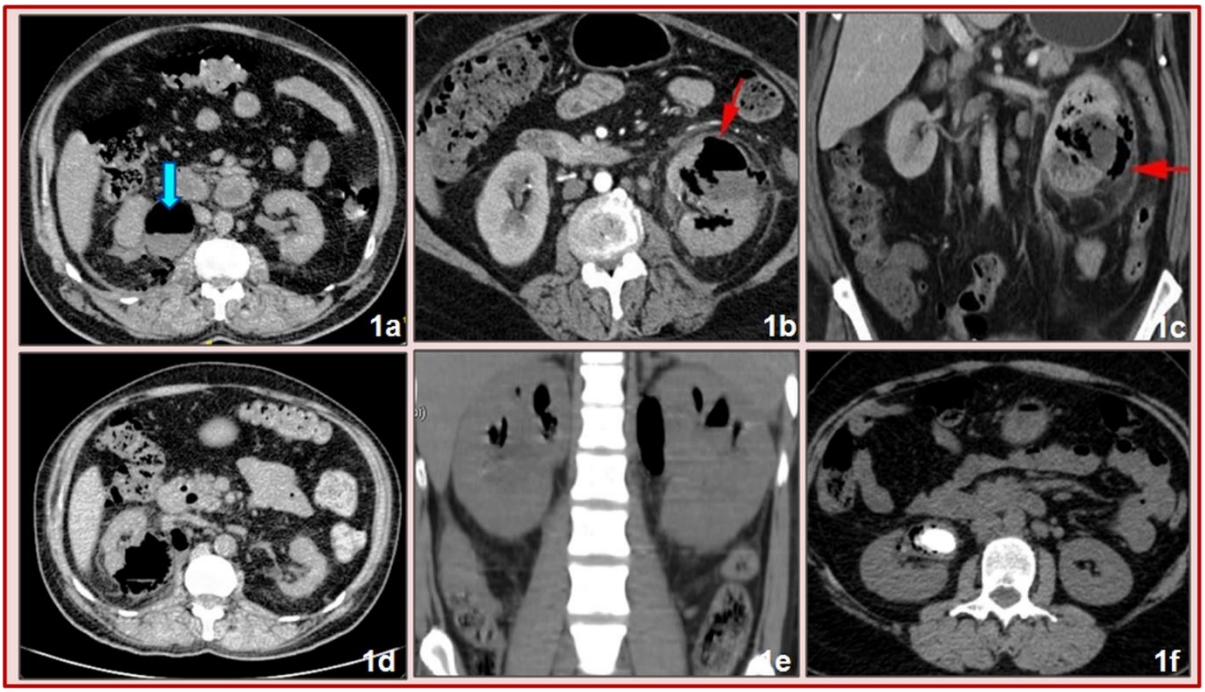
1b: Class 2 EPN with Gas in renal parenchyma (red arrow)

1c: Class 3 A EPN with gas in perinephric tissue (red arrow)

1d: Class 3B EPN with gas extending beyond Gerota's fascia.

1e: Class 4 EPN with bilateral air pockets in the parenchyma.

1f: Class 2 EPN with gas and stone in the right renal pelvis


1a
1b
1c
1d
1e
1f