Original Article

Emphysematous pyelonephritis: Does a standard management algorithm and a prognostic scoring model optimize patient outcomes?

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Abstract

Objective: The objective of the study is to analyze the risk factors determining the outcomes of patients with emphysematous pyelonephritis (EPN) by the adoption of a standardized management algorithm as well as to develop a prognostic scoring model to risk stratify these patients.

Materials and Methods: The hospital records of 72 consecutive patients with EPN from February 2012 to January 2018 were retrospectively reviewed. Demographic, clinicoradiographic, and laboratory characteristics were recorded. Patients were managed with a standard management protocol and based on outcomes divided into three groups. Group I survived with conservative management, Group II survived after emergency nephrectomy, and Group III expired. The risk factors for nephrectomy and mortality were analyzed.

Results: The mean age was 53 years. Male to female ratio was 4:5. There were 61 (84.7%), 4 (5.6%), and 7 (10%) patients in Groups I, II, and III, respectively. Diabetes mellitus was the most common comorbidity detected in 62 (86%) of patients. Type II EPN was the most common radiological presentation observed in 32 (44%) patients. Overall survival rate was 90%, and kidney salvage rate was 80%. *Escherichia coli* was the most common organism isolated. Thirty-two (45%) patients exhibited resistance to third-generation cephalosporin antibiotics. Thrombocytopenia, low body mass index (BMI), presence of >2 comorbidities, high total leukocyte count (TLC), and hypoalbuminemia were significantly associated with mortality. On adoption of the prognostic scoring system, mortality rates according to the risk subgroups were as follows: favorable - 0%, intermediate - 19%, and poor - 100%.

Conclusion: Conservative management adopting appropriate algorithm reduces mortality and avoids unnecessary emergency nephrectomies. Thrombocytopenia, low BMI, presence of >2 comorbidities, high TLC, and hypoalbuminemia were significantly associated with mortality.

Keywords: Algorithm for the management of emphysematous pyelonephritis, emphysematous pyelonephritis, prognostic scoring of emphysematous pyelonephritis

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INTRODUCTION

Emphysematous pyelonephritis (EPN) is a urologic emergency, defined as a necrotizing life-threatening infection of renal parenchyma caused by gas-forming bacteria.[1] It is not primarily a renal disease, but a complication of uncontrolled comorbidities such as diabetes mellitus (DM), immunosuppression, and urinary tract obstruction.[2,3] EPN has a female: male preponderance of 4:1 with a median age of 57 (range 24–83) years.[4,5] The conventional approach including open drainage and emergency nephrectomy (EN) was associated with more than 40% mortality.[6] Recently published systematic review and meta-analysis have reported an overall mortality rate of 18% in EPN patients.[7]

Percutaneous drainage (PCD) with medical management, followed by delayed nephrectomy in case of the nonfunctioning kidney is presently the preferred treatment modality and has established as the gold standard for the management of EPN.[4,8] Third-generation cephalosporins, aminoglycosides, and fluoroquinolones are presently administered as the first-line antibiotics in the management of these patients. The development of resistance to commonly used antimicrobials has an adverse impact on the outcomes of these patients[9] Still, treatment protocols vary across the institutions, and there is no well-defined management algorithm which can guide the treating physician in the management of these patients.[4,10] Although a number of case series has been published in literature in the past four decades, there is a wide variation in the risk factor assessment and reported mortality primarily due to the small sample size.[11-13] Hence, the objective of the present study is to analyze the risk factors and develop a novel prognostic scoring system to better help the physicians to prognosticate the outcomes of EPN patients in a larger cohort, especially in the present era of widespread antibiotic resistance. Furthermore, the present study would like to analyze the feasibility of adopting a well-designed algorithm in the management of these patients to deliver an optimal care.

MATERIALS AND METHODS

Seventy-two consecutive patients with a diagnosis of EPN who were managed in the Department of Urology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, from February 2012 to January 2018 were included in the present study. The study was conducted retrospectively by analyzing the data of the patients from a prospectively maintained database after obtaining institute ethical committee clearance. Based on the noncontrast computed tomography of kidney, ureter, and bladder findings, patients were classified according to Huang and Tseng Classification.[14] Class 1 – gas in the collecting system only; Class 2 – gas in the renal parenchyma without extension to the extrarenal space; Class 3A – extension of gas or abscess to the perinephric space; Class 3B – extension of gas or abscess to the pararenal space; and Class 4 – bilateral EPN or a solitary kidney with EPN. All patients were managed according to our departmental management algorithm, as depicted in Figure 1.

The demographic parameters such as age, gender, number of comorbidities, and body mass index (BMI) were recorded. Laboratory parameters included hemoglobin (HB), total leukocyte counts (TLC), platelet counts, blood glucose, serum creatinine, serum electrolytes, serum albumin level, urine, and exudate culture were documented. Based on the outcomes, the patients in our cohort were classified into three groups, namely Group 1 – Patients managed conservatively may or may not end up with elective nephrectomy; Group 2 – Patients survived with EN after initial PCD; and Group 3 – Patients who succumbed to their illness. The primary objective was to identify the risk factors associated with mortality in patients with EPN.

Based on the significant risk factors of our study and already been proven other poor-risk parameters in the previous multiple studies (even not significant in the present study),

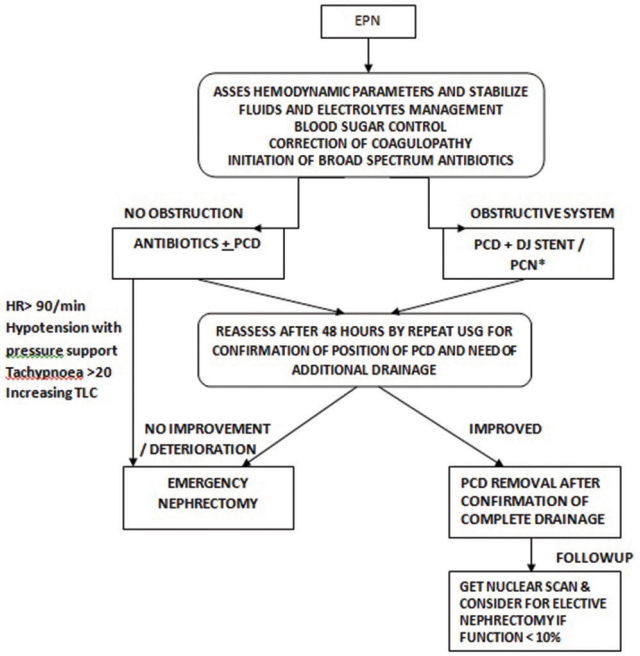

Figure 1: Algorithm for EPN management. *PCN: percutaneous nephrostomy, DJ stent = Double J stent, PCD: Percutaneous drainage (Insertion of pigtail catheter in renal parenchyma or perinephric space)

the authors derived a novel prognostic scoring system with a total score range from 0 to 10 [Table 1].

Statistical analysis

Continuous data were checked for normality by one-sample Kolmogorov–Smirnov test and expressed as mean with standard deviation or median with range. The comparison of the age, glucose level, HB, TLC, platelet count, creatinine, and BMI in relation to the categorical variables was carried out using independent Kruskal–Wallis test/analysis of variance. The association of outcome with categorical variables such as gender, laterality, and type of EPN was analyzed by Fisher's exact test. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0 (Armonk, NY, IBM Corp) at 5% level of significance, and $P < 0.05$ was considered as statistically significant.

RESULTS

The mean age of the patients in our cohort was 53 years. Male to female ratio was 4:5. Table 2 shows the baseline characteristics of the study population. DM was the most common comorbidity in 62 (86%) patients, followed by stone disease in 15 (21%). Three patients had both DM and stone disease.

Sixty-one (84.7%) patients were included in Group I, 4 (5.6%) patients in Group II, and 7 (9.7%) patients in Group III according to the predefined criteria. The presence of more than two comorbidities ($P < 0.001$), high TLC ($P = 0.036$), low BMI ($P = 0.015$), thrombocytopenia ($P = 0.046$), and hypoalbuminemia ($P = 0.001$) were significantly associated with mortality [Table 3].

Urine culture was positive in 52 (72%) and sterile in 20 (27%) patients. *Escherichia coli* was the most common organism isolated in 26 (36%) patients, *Klebsiella pneumoniae* in 21 (29%) whereas *Aspergillus* fungus grew in 5 (7%) patients. In the exudate culture, 39 (54%) patients exhibited *E. coli*, followed by *K. pneumoniae* in 21 (29%) patients, while 12 (16%) patients grew multiple organisms. *Aspergillus* was isolated in 2 (2%). Urine and exudate cultures showed similar characteristics in 28 (38%) patients while in the remainder 44 (62%) patients exhibited dissimilar organisms. On admission, the patients were empirically administered a combination of third-generation cephalosporin and aminoglycoside antibiotics, which was subsequently changed according to the culture report. Meropenem was the second most commonly used antibiotic followed by Piperacillin tazobactam. In 32 (45%) patients, the isolated organisms exhibited resistance to the third-generation cephalosporins.

Table 1: Prognostic scoring system based on number of adverse factors

Risk factors	Present
Age >50 years	1
≥2 Comorbidities	1
TLC ≥12,000 or ≤4000	1
BMI ≥30 or ≤18	1
Platelets ≤100,000/mm^3	1
Serum creatinine ≥3	1
Albumin ≤2.5 g/dl	1
Grade of EPN II or III	1
Sodium ≤130	1
Multidrug resistance	1
Total score	10

EPN: Emphysematous pyelonephritis, TLC: Total leukocyte count, BMI: Body mass index

Table 2: Baseline characteristics of study population

Patients characterstics	Value
Total number of patients	72
Age in years (mean±SD)	53.33±10.77
Male:female ratio	32/40 (4:5)
Co-morbidities (%)	
DM	62 (86)
Hypertension	5
Pulmonary tuberculosis	1
Chronic kidney disease	5
Hypothyroidism	2
Chronic liver disease	1
Coronary artery disease	1
APLA syndrome	1
BMI in kg/m^2 (mean±SD)	24.21±3.4
Type of EPN (%)	
I	10 (13.9)
II	32 (44.4)
IIIa	15 (20.83)
IIIb	14 (19.44)
IV	1 (1.4)
Laterality (%)	
Right	33 (45.8)
Left	38 (52.8)
Bilateral	1 (1.4)
Stone disease	15 (20.8)

SD: Standard deviation, DM: Diabetes mellitus, BMI: Body mass index, EPN: Emphysematous pyelonephritis, APLA: Antiphospholipid antibody syndrome

Table 4 shows a comparison of parameters between the elective and EN patients. Among the 14 nephrectomies performed, 6 were emergency and 8 were elective. The indication for EN in our series was sepsis with progressive deterioration in the general condition in spite of PCD and intensive medical care. The mortality rate in EN group was 33% (2 patients died). However, no mortality was reported in elective nephrectomy group. The median follow-up of patients was 37 months (8–78 months).

On applying the prognostic scoring model, the patients were stratified into three risk categories-favorable (0–4), intermediate (5–7), and grave (8–10) [Table 5]. Among the 48 patients in the favorable risk group, 47 (98%) patients were successfully managed by PCD alone while 1 (2%)

Table 3: Comparison of parameters in different groups

Variables	Group I (%)	Group II (%)	Group III (%)	Significance
Total number of patients	61 (84.7)	4 (5.6)	7 (9.7)	
Age in years (SD)	52.43 (10.8)	58 (11.6)	58.57 (8.2)	0.245*
Female gender	32 (52.5)	4 (100)	4 (57)	0.217**
≥2 comorbidities	7 (11.5)	2 (50)	5 (71)	<0.001**
Mean glucose level in mg/dl (range)	273 (62-886)	335 (229-423)	389 (60-546)	0.992***
Right/left side	31/29 (1 bilateral)	0/4	2/5	0.226**
Mean hemoglobin in mg/dl (SD)	9.2 (1.8)	7.5 (1.7)	9.1 (1.8)	0.224*
Mean TLC count in/mm^3 (SD)	16594 (7137)	21027 (9244)	23447 (4564)	0.036*
Mean platelet counts in/mm^3 (range)	262×10^3 (47-808×10^3)	102.5×10^3 (55-582×10^3)	72×10^3 (58-360×10^3)	0.046***
Mean creatinine in mg/dl (range)	2.12 (0.7-10)	2.6 (1.6-11)	4.3 (2.56-7.7)	0.052***
Mean albumin in g/dl	2.9 (1.7-3.6)	2.7 (1.2-2.9)	2.2 (1.4-2.8)	0.001***
Mean BMI in kg/m^2 (SD)	24.6 (3.32)	22.33 (1.95)	21.12 (3)	0.015*
Stone disease	14 (23)	1 (25)	0	0.459**
Mean serum Na in mEq/L	131 (6.7)	129 (2.8)	131 (7.4)	0.837*
Mean serum K in mEq/L	4.4 (0.78)	4.6 (1.19)	4.6 (0.52)	0.739*
Type of EPN				
I	10 (16.4)	0	0	
II	28 (45.9)	0	4 (57)	0.276**
III	22 (36)	4 (100)	3 (43)	
IV	1 (1.6)	0	0	
Nephrectomy	8 (elective)	4 (emergency)	2 (emergency)	

*ANOVA test, **Fisher's exact test, ***Kruskal-Wallis test. ANOVA: Analysis of variance, SD: Standard deviation, BMI: Body mass index, EPN: Emphysematous pyelonephritis, TLC: Total leukocyte count

Table 4: Characteristics of elective and emergency nephrectomy patients

Parameters	Elective nephrectomy	Emergency nephrectomy
Total number of patients	8	6
Mortality (%)	0	2 (33)
Type of EPN		
I	1	0
II	3	2
III	4	4
IV	0	0
Urine culture	*E. coli* (4)	Candida (2)
	Sterile (3)	*E. coli* (1)
	E. coli + *Enterococcus* (1)	Sterile (3)
Exudate culture	*E. coli* (5)	*A. flavus* (2)
	Klebsiella (1)	Klebsiella (2)
	Sterile (2)	*E. coli* (1)
		E. coli + *Enterococcus* (2)

E. coli: *Escherichia coli*, *A. flavus*: *Aspergillus flavus*, EPN: Emphysematous pyelonephritis

Table 5: Prognostic scoring and outcome of patients

Score grading	Group I (%)	Group II (%)	Group III (%)	Total number of patients
Good (0-4)	47 (98)	1 (2)	0	48
Intermediate (5-7)	14 (66.6)	3 (14.2)	4 (19)	21
Poor (8-10)	0	0	3 (100)	3

patient required EN. There was no mortality in this group. Intermediate-risk group comprising 21 patients, 14 (66.6%) patients were salvaged with PCD while 3 (14.2%) survived after EN and mortality was encountered in 4 (19%) patients. In the poor risk group, all the 3 (100%) patients were expired.

DISCUSSION

The patients with EPN usually present in sepsis and need intensive care management. Like any other disease, the management of EPN can be guided by its associated factors. These factors can be modifiable or nonmodifiable and help us in triage. In our study, 61 (84.7%) patients were successfully managed by PCD alone, and only 4 (5.6%) required EN. The overall mortality rate was 9.7%, which is less than the other similar studies.[6-8] This reduction in mortality was achieved by following a standardized multidisciplinary approach and by avoiding aggressive surgical management whenever possible. There was no mortality in patients with Type I and IV EPN, while 4 (57%) and 3 (43%) patients with Type II and III EPN died. Since there was only one patient with Type IV EPN in our series, it is not possible to make a meaningful conclusion. Similarly, in Group II (patients requiring EN), all four patients had Type III EPN, even though the type of EPN was not a significant prognostic factor ($P = 0.276$).

In our series, DM was the most commonly associated comorbidity prevalent in 62 (86%) of patients. We observed that patients with >2 or more comorbidities had a significantly higher mortality risk. Among the 14 patients with >2 comorbidities, the mortality rate was 35.7%. Olvera-Posada *et al*.[15] observed that the severity of DM *per se* did not significantly correlate with the mortality. Hence, a combination of comorbidities is a poor prognostic

indicator rather than the severity of any single comorbidity. It has been further demonstrated that the chances of multiorgan dysfunction increases with the number of associated chronic comorbid conditions.[16]

Central obesity is well known to be associated with DM.[17] However, in our study, mean BMI of patients was 24.21 kg/m^2 and extremely low BMI was found to be significantly associated with mortality (P = 0.015). This observation can be explained by the fact that predominantly the patients with diabetes in the South Indian population have a low BMI.[18] On the contrary, Ramachandran *et al*.[19] demonstrated that in patients of EPN, high BMI was significantly associated with poor prognosis. Based on these, extremes of BMI can be considered as significant factors for mortality. For better interpretation, it is imperative to consider BMI along with other clinical features.

Moreover, in the mortality group, mean platelet counts and serum albumin level were 72,000/mm^3 and 2.2 g/dl, respectively. Thrombocytopenia (P = 0.046) and hypoalbuminemia (P = 0.001) were significantly associated with mortality. Surprisingly, patients with stone disease responded well to conservative management, and no mortality was reported in this group of patients.

Kapoor *et al*.[20] reported that thrombocytopenia, altered mental status, severe hyponatremia, and renal failure as poor prognostic factors similar to our study. However, the basis of serum creatinine cutoff of >2.5 mg/dl in their study was unclear. In our study, the mean creatinine was 3.06 mg/dl and this was not statistically significant parameter among groups (P = 0.052). However, clinically high serum creatinine was associated with mortality and median creatinine level in mortality group was 4.3 mg/dl.

Majority of the patients with EPN are usually referred to our department after initial treatment in a primary and secondary health-care centers. As multiple studies suggest different prognostic factors, it is difficult for physician to properly prognosticate and manage this crucial emergency.[15,20-22] To overcome this, the authors have proposed a novel prognostic scoring system for the index patient to predict the outcomes in these vulnerable group of patients. The morbidity and mortality of the patients falling into the intermediate and grave prognostic risk groups is more than 50% in our series. We believe that this scoring system can help physicians to triage patients and refer patients who are expected to have poorer outcomes to tertiary care centers at the earliest.

Yu-Chuan Lu *et al*.[23] observed that *E. coli* was the most common causative organism in 49% of their patients, followed by *K. pneumoniae*. Overall, antimicrobial resistance rate was 79% for ampicillin, 22.7% for gentamicin, and 10.9% for third-generation cephalosporins. They had recommended third-generation cephalosporins as first-line treatment in their patients. Similarly, *E. coli* and *K. pneumoniae* were the most common causative organisms in our study. Interestingly, among the five (7%) patients, who grew fungus in urine culture, two patients had EN and two patients expired. Thirty-two (45%) patients of our series demonstrated resistance to third-generation cephalosporin. This is attributed to the fact that majority of patients were already treated with multiple antibiotics before being referred to our center. We believe that this unregulated antibiotic usage is one of the important reasons for the higher morbidity and mortality in our series and the authors strongly recommend for antibiotic stewardship which has not been adopted adequately in the developing countries. We recommend a combination of third-generation cephalosporin with aminoglycoside as a first line of treatment and administer carbapenem with aminoglycoside only when a patient has already been on a cephalosporin medication. We also observed that 44 (61%) patients had different organisms grown in urine and exudate culture. It could possibly because of urinary tract obstruction of affected kidney owing to papillary necrosis.

Falagas *et al*.[24] in their systematic review, and meta-analysis concluded that conservative management alone, bilateral EPN, Type I EPN, thrombocytopenia were associated with increased mortality. Moreover, hypotension, altered mental status, elevated serum creatinine may influence the patient outcomes, however, with limited evidence.

Although PCD with conservative management has been the favored initial approach for EPN management, there is a widespread variation in the clinical practice worldwide. Furthermore, in a recent meta-analysis by Aboumarzouk *et al*., concluded that PCD and medical management were associated with a significantly lower mortality rate than EN, with an odds ratio for PCD versus EN of 3.13 (1.89–5.16; P < 0.001). Although some authors have described standard protocols to be adopted for the management of EPN patients, still there are some pertinent question remain unanswered.[25,26] This includes management strategies in different clinical scenarios, when and how to reassess patients and how to follow these patients once the emergency has been dealt with. In an attempt to answer these, the authors have designed a standard algorithm which has been adopted in all the patients in our hospital. Patients with Grade I EPN

were managed with antibiotics followed by double J (DJ) stenting or percutaneous nephrostomy (PCN) if needed after stabilization. We advocate DJ stenting or PCN along with PCD in patients with EPN who present with hydroureteronephrosis and/or perinephric collection. PCD is the insertion of pigtail catheter in the air cavity. It is required in a patient with Grade II or III EPN with at least >3 cm renal parenchymal collection. It is mandatory to reassess these patients at 48 h by ultrasonography, as this period is the critical determinant of outcome. We consider EN in nonresponders or who deteriorate at this time frame. We also emphasize follow-up with radionuclide scan and consideration of nephrectomy if the differential function is <10% as poorly functioning kidney is always a source of recurrent pyelonephritis and urinary tract infection. The authors would like to suggest that there is no ambiguity in patient care by the adoption of this protocol.

To the best of our knowledge, this is the first study which has explored the feasibility of a scoring system to prognosticate EPN patients in a large cohort followed by the management of disease according to algorithm. The limitations of the study include retrospective study design and nonapplicability of multivariate analysis due to a limited number of patients in each arm. As this is an uncommon emergency condition with wide variations in management approaches, there is a need to perform a multi-institutional prospective study to validate our management algorithm and the scoring system which may help to us standardize the patient care to deliver optimal outcomes.

CONCLUSION

Conservative management following an appropriate algorithm reduces mortality and avoids unnecessary emergency nephrectomies. Scoring system is not difficult to understand, easily applicable and guides in disease management even for the primary care physician. Although EPN is still a dreaded disease, multidisciplinary approach in a tertiary care center may help in optimizing these patients.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Michaeli J, Mogle P, Perlberg S, Heiman S, Caine M. Emphysematous pyelonephritis. J Urol 1984;131:203-8.
2. Schultz EH Jr., Klorfein EH. Emphysematous pyelonephritis. J Urol 1962;87:762-6.
3. Huang JJ, Chen KW, Ruaan MK. Mixed acid fermentation of glucose as a mechanism of emphysematous urinary tract infection. J Urol 1991;146:148-51.
4. Somani BK, Nabi G, Thorpe P, Hussey J, Cook J, N'Dow J. Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis? Evidence from a systematic review. J Urol 2008;179:1844-9.
5. El-Nahas AR, Shokeir AA, Eziyi AK, Barakat TS, Tijani KH, El-Diasty T, *et al*. Kidney preservation protocol for management of emphysematous pyelonephritis: Treatment modalities and follow-up. Arab J Urol 2011;9:185-9.
6. Ahlering TE, Boyd SD, Hamilton CL, Bragin SD, Chandrasoma PT, Lieskovsky G, *et al*. Emphysematous pyelonephritis: A 5-year experience with 13 patients. J Urol 1985;134:1086-8.
7. Aboumarzouk OM, Hughes O, Narahari K, Coulthard R, Kynaston H, Chlosta P, *et al*. Emphysematous pyelonephritis: Time for a management plan with an evidence-based approach. Arab J Urol 2014;12:106-15.
8. Pontin AR, Barnes RD. Current management of emphysematous pyelonephritis. Nat Rev Urol 2009;6:272-9.
9. Lau SM, Peng MY, Chang FY. Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection. J Microbiol Immunol Infect 2004;37:185-91.
10. Lin YC, Lin YC, Lin HD, Lin LY. Risk factors of renal failure and severe complications in patients with emphysematous pyelonephritis-a single-center 15-year experience. Am J Med Sci 2012;343:186-91.
11. Menif E, Nouira K, Baccar S, Nouira Y, Mouelhi M, Horchani A, *et al*. Emphysematous pyelonephritis: Report of 3 cases. Ann Urol (Paris) 2001;35:97-100.
12. Touiti D, Deligne E, Badet L, Colombel M, Martin X, Gelet A. Emphysematous pyelonephritis: Report of 3 cases. Prog Urol 2001;11:703-6.
13. Klein FA, Smith MJ, Vick CW 3rd, Schneider V. Emphysematous pyelonephritis: Diagnosis and treatment. South Med J 1986;79:41-6.
14. Huang JJ, Tseng CC. Emphysematous pyelonephritis: Clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med 2000;160:797-805.
15. Olvera-Posada D, Armengod-Fischer G, Vázquez-Lavista LG, Maldonado-Ávila M, Rosas-Nava E, Manzanilla-García H, *et al*. Emphysematous pyelonephritis: Multicenter clinical and therapeutic experience in Mexico. Urology 2014;83:1280-4.
16. Frey C, Zhou H, Harvey D, White RH. Co-morbidity is a strong predictor of early death and multi-organ system failure among patients with acute pancreatitis. J Gastrointest Surg 2007;11:733-42.
17. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes Metab Syndr Obes 2014;7:587-91.
18. Sokhal AK, Kumar M, Purkait B, Jhanwar A, Singh K, Bansal A, *et al*. Emphysematous pyelonephritis: Changing trend of clinical spectrum, pathogenesis, management and outcome. Turk J Urol 2017;43:202-9.
19. 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.
20. 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. BJU Int 2010;105:986-9.
21. 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.
22. Aswathaman K, Gopalakrishnan G, Gnanaraj L, Chacko NK, Kekre NS, Devasia A. Emphysematous pyelonephritis: Outcome of conservative management. Urology 2008;71:1007-9.
23. Lu YC, Hong JH, Chiang BJ, Pong YH, Hsueh PR, Huang CY, *et al*. Recommended initial antimicrobial therapy for emphysematous

pyelonephritis: 51 cases and 14-year-experience of a tertiary referral center. Medicine (Baltimore) 2016;95:e3573.
24. 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.
25. Aboumarzouk OM, Hughes O, Narahari K, Coulthard R, Kynaston H, Chlosta P, *et al*. Emphysematous pyelonephritis: Time for a management plan with an evidence-based approach. Arab J Urol 2014;12:106-15.
26. Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. BJU Int 2011;107:1474-8.