Original Article

What is the prognosis of emphysematous pyelonephritis associated with extended-spectrum beta-lactamases producing microorganisms?

José Iván Robles-Torres, Marco Alberto Ocaña-Munguía,
José Gustavo Arrambide-Herrera,
Adrián Mauricio Martínez-Fernández, Rodrigo Romero-Mata,
Lauro Salvador Gómez-Guerra*

Urology Department, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

Abstract *Objective:* To describe the microbiological characteristics in emphysematous pyelonephritis (EPN), demonstrate the frequency of extended-spectrum beta-lactamase (ESBL) microorganisms, and determine if these microorganisms are associated with the prognosis of patients with EPN.

Methods: We conducted a retrospective study in patients with a diagnosis of EPN in a tertiary care hospital of the northeast region of Mexico during the period from January 2011 to January 2016. Clinical variables were analyzed to determine association with the presence of ESBL-producing microorganisms. Statistical significance was set with $p < 0.05$.

Results: A total of 63 patients were included; 55 (87.3%) of them were females, with a median age of 55 (interquartile range: 45—65) years. Conservative management was indicated in 38.1%; 42.9% were treated with ureteral stent; 12.7% with open or percutaneous drainage; 15.8% with early nephrectomy; and 9.5% with delayed nephrectomy. Reported mortality was 13 (20.6%) cases; 23 (36.5%) cases required admission to the intensive care unit. The most frequent microorganism isolated was *Escherichia coli* ($n = 34$, 53.9%). ESBL microorganisms were found in 31.7% of the population. No significant association of ESBL was found with admission to the intensive care unit, or with increased mortality.

Conclusions: To our knowledge, this is the first study that evaluates ESBL microorganisms as a prognostic factor in EPN. Risk factors associated with a poor prognosis in patients with EPN

---

* Corresponding author.
  E-mail address: laurogomez@hotmail.com (L.S. Gómez-Guerra).
  Peer review under responsibility of Tongji University.

have been described. The microbiological factors, specifically ESBL-producing bacteria, do not seem to influence in the prognosis of these patients.

1. Introduction

Emphysematous pyelonephritis (EPN) is defined as an acute, necrotizing, and severe infection of the renal parenchyma and surrounding tissues, mainly characterized by the presence of gas in the parenchyma, collecting system, perinephric and paranephric tissue [1—4]. It is associated with a high mortality rate, which ranges between 15% and 75% [5]. Risk factors associated with EPN were well described, diabetes mellitus being the most common implicated [6]. Four main factors involved in the pathogenesis of the disease were well described: Infection caused by gas-forming bacteria, chronically elevated glucose levels, alteration in the perfusion of peripheral tissues, and defects in the immune response [7].

Gram-negative enteric facultative anaerobic microorganisms mainly cause this condition. The most common causative microorganism reported in EPN is *Escherichia coli* (*E.coli*) in 60%—70% of the cases. The presence of Enterobacteriaceae, such as *E. coli*, *Klebsiella pneumoniae* and *Proteus* spp., under relative anaerobic conditions induces mixed acid fermentation of glucose, being this process the main pathway of gas formation in EPN [8].

The emergence of uropathogens resistant to first line antibiotic treatments is a serious problem in healthcare systems. An increase has recently been observed in extended-spectrum beta-lactamase (ESBL) producing microorganisms in urinary tract infections. The production of ESBL confers to the bacteria a natural resistance to penicillins, cephalosporins, and aztreonam, limiting the therapeutic options for these infections [9]. Recent literature has focused on determining prognostic factors in EPN [6,10]; however, none of them considered the microbiological factors as predictors of clinical responses or outcomes. Until the date, the prevalence of ESBL-producing microorganisms and their clinical implication in EPN have not been described.

The aim of this study is to describe the microbiological characteristics, demonstrate the frequency of ESBL microorganisms, and determine if these microorganisms have a relationship with the prognosis of patients with EPN.

2. Patients and methods

We conducted a retrospective study in patients with a diagnosis of EPN in a tertiary care hospital of the northeast region of Mexico during the period from January 2011 to January 2016. Approval by the medical ethics committee with registration code UR18-00008 (approved by the Ethics and Research Committee of the School of Medicine, Universidad Autónoma de Nuevo León, Mexico) was obtained. Patients with a diagnosis of EPN were included, as well as signs and symptoms compatible with upper urinary tract infection and clinical data of systemic inflammatory response.

Sociodemographic characteristics such as age, sex, and comorbidities were analyzed. Clinical presentation and laboratory parameters were collected at the time of admission to the emergency room, including complete blood count, urinalysis, urine culture, serum electrolytes, and blood chemistry. Leukocytosis was defined as leukocytes >11 000/μL, thrombocytopenia as platelet count <150 000/μL, renal failure with the presence of serum creatinine >1.2 mg/dL, and hypoalbuminemia as albumin <3.5 g/dL. The clinical outcomes were divided into those patients who survived without admission to the intensive care unit (ICU), and those who were admitted to the ICU during hospitalization. The criteria for admission to the ICU were patients who required advanced respiratory support, or patients who required support due to acute reversible organ failure. Huang and Tseng's classification [5] was used based on tomographic findings: Type 1—gas in the collecting system only; type 2—gas in the renal parenchyma without extension to the extrarenal space; type 3—extension of gas or abscess to the perirenal or pararenal space; and type 4—bilateral or solitary kidney with EPN. The quick Sepsis Related Organ Failure Assessment (qSOFA) score was determined upon arrival to the ER, which includes altered mental status, >22 breaths/min, and hypotension (systolic blood pressure <100 mmHg [1 mmHg=0.133 kPa]).

Therapeutic management was divided as follows: Conservative management (antibiotic therapy, fluid resuscitation, and metabolic control), urinary diversion with ureteral stent, percutaneous or open drainage, early nephrectomy, and delayed nephrectomy. Percutaneous drainage, with catheter placement was performed by the interventional radiology department. Delayed nephrectomy was performed in those cases in which conservative treatment, drainage, or urinary diversion were not effective based on the clinical and biochemical condition of the patient. Cases with insufficient medical records and absence of EPN demonstrated on computed tomography were excluded.

Urine cultures were analyzed. The microbiological identification was carried out by phenotypic method and biochemical system, following the guidelines of the Clinical and Laboratory Standards Institute [11]. Antibiotic resistance profile was determined by the microdilution plate method. The following antibiotics were included in the antibiotic profile: Levofloxacin, ciprofloxacin, nitrofurantoin, cefuroxime, ceftriaxone, ceftibuten, amikacin, gentamicin, ampicillin, amoxicillin/clavulanate, trimethoprim/sulfamethoxazole, colistin, fosfomycin, and meropenem. The production of ESBL was performed with the double disc sensitivity test.

Clinical variables were analyzed to determine association with the presence of ESBL-producing microorganisms. Statistical analysis was performed using SPSS Statistics version 24.0 (IBM Corp, Armonk, NY, USA). Categorical variables were analyzed using the Chi-square test and numerical variables with t-test. Statistical significance was set with $p < 0.05$.

3 Results

A total of 70 cases with a diagnosis of EPN were obtained during the period from January 2011 to January 2016. Seven cases were excluded due to insufficient medical records. We included 63 patients; 55 (87.3%) were females, and a median age of 55 (interquartile range: 45−65) years. The characteristics of the study population are shown in Table 1. The presence of flank pain was the most frequent symptom reported (79.3%), followed by hemodynamic instability (38.1%). The most frequent biochemical alteration was leukocytosis ($n = 41$, 65%). Diabetes mellitus (88.9%) and arterial hypertension (47.6%) were the most common comorbidities. The presence of urolithiasis was reported in 33.3%. A total of 28 (44.4%) cases reported a qSOFA ≥2 points on arrival to the ER. The Huang scale type 1 was reported in 34 (54.0%) cases, followed by type 4 in 12 (19.0%), type 3 (A and B) in 9 (14.3%) and less frequent type 2 with 8 (12.7%).

Conservative management was indicated in 24 (38.1%) patients; 27 (42.9%) cases were treated with ureteral stent; 8 (12.7%) patients were managed with open/percutaneous drainage; 10 (15.8%) cases underwent early nephrectomy; and 6 (9.5%) patients were treated with delayed nephrectomy. Eight patients received more than one treatment due to refractory condition. Four patients were initially treated with a ureteral stent and then underwent nephrectomy after 72 h without improvement. One patient started with conservative management and then underwent percutaneous drainage. Two patients started with percutaneous drainage and then underwent nephrectomy. One patient started with placement of a ureteral stent and later underwent percutaneous drainage. The reported mortality was 20.6% (13/63); 36.5% (23/63) cases required admission to the ICU. In urine cultures, the most frequent microorganism reported was E. coli ($n = 34$, 53.9%), followed by Klebsiella spp. ($n = 9$, 14.3%), and Candida spp. ($n = 8$, 12.7%). Sterile cultures were reported in 14.3%. ESBL production was found in 31.7% of the population. E. coli ESBL was reported in 22.2% (14/63) strains and K. spp. ESBL in 9.5% (6/63).

Levofloxacin, ciprofloxacin, cefuroxime, cefotaxime, ceftriaxone, ceftibuten, gentamicin, ampicillin, amoxicillin/clavulanate, and trimethoprim/sulfamethoxazole demonstrated the highest resistance (>50%) among the antibiotics evaluated. Colistin, fosfomycin, and meropenem were the antibiotics with the highest susceptibility (Table 2).

We analyzed the association of ESBL microorganisms with clinical variables. The presence of these microorganisms was associated with leukocytosis (<11 000/μL; $p = 0.024$, odds ratio = 4.486) in univariate analysis. No significant association of ESBL microorganisms was found with admission to the ICU, or with increased mortality.

Table 1 Population sociodemographics, clinical, and microbiological characteristics in emphysematous pyelonephritis ($n = 63$).

Variable	Result
Demographic	
Age, median (IQR), year	55 (45−65)
Female, n (%), year	55 (87.3)
Clinical presentation, n (%)	
Hemodynamic instability[a]	24 (38.1)
Fever (>38.3 °C)	23 (36.5)
Flank pain	50 (79.4)
Biochemistry, n (%)	
Leukocytosis (>11 000/μL)	41 (65.1)
Thrombocytopenia (<150 000/μL)	15 (23.8)
Renal failure (serum creatinine >1.2 mg/dL)	36 (57.1)
Hypoalbuminemia (<3.5 g/dL)	34 (54.0)
qSOFA (≥2 points), n (%)	28 (44.4)
Comorbidities, n (%)	
Diabetes mellitus	56 (88.9)
Arterial hypertension	30 (47.6)
Chronic kidney disease	17 (27.0)
Hydronephrosis	23 (36.5)
Urolithiasis	21 (33.3)
Previous antibiotic[b]	34 (54.0)
Urine culture pathogens, n (%)	
E. coli	20 (31.7)
E. coli ESBL	14 (22.2)
Sterile culture	9 (14.3)
Candida spp.	8 (12.7)
Klebsiella spp. ESBL	6 (9.5)
Klebsiella spp.	3 (4.8)
Others[c]	3 (4.8)
Huang scale, n (%)	
Type 1	34 (54.0)
Type 2	8 (12.7)
Type 3 (A and B)	9 (14.3)
Type 4	12 (19.0)
Therapeutic management[d], n (%)	
Conservative	24 (38.1)
Ureteral stent	27 (42.9)
Percutaneous or open drainage	8 (12.7)
Early nephrectomy	10 (15.9)
Delayed nephrectomy	6 (9.5)
Clinical outcome, n (%)	
Mortality	13 (20.6)
Intensive care unit	23 (36.5)

IQR, interquartile range; ESBL, extended-spectrum beta-lactamases; E. coli, Escherichia coli.
[a] Systolic pressure <90 mmHg.
[b] Antibiotic in the last 3 months.
[c] Morganella morganii (1), Enterobacter cloacae (1), and Streptococcus agalactiae (1).
[d] Eight patients received more than one therapy in refractory cases (see results for details).

These microorganisms had no association with the extension of gas in the renal parenchyma classified by Huang scale (Table 3). Multivariate analysis showed no significant association of any of the variables studied (data not shown in Tables).

Table 2 Antimicrobial susceptibility rates of uropathogens in patients with emphysematous pyelonephritis ($n=46$[a]).

Antibiotic	Susceptibility, n (%)	Resistance, n (%)
Levofloxacin	23 (50.0)	23 (50.0)
Ciprofloxacin	17 (37.0)	29 (63.0)
Nitrofurantoin	32 (69.6)	14 (30.4)
Cefuroxime	11 (23.9)	35 (76.1)
Cefotaxime	14 (30.4)	32 (69.6)
Ceftriaxone	22 (47.8)	24 (52.2)
Ceftibuten	22 (47.8)	24 (52.2)
Amikacin	31 (67.4)	15 (32.6)
Gentamicin	22 (47.8)	24 (52.2)
Ampicillin	9 (19.6)	37 (80.4)
AMC	10 (21.7)	36 (78.3)
TMP/SMX	6 (13.0)	40 (87.0)
Colistin	44 (95.7)	2 (4.3)
Fosfomycin	37 (80.4)	9 (19.6)
Meropenem	42 (91.3)	4 (8.7)

AMC, amoxicillin/clavulanate; TMP/SMX, trimethoprim/sulfamethoxazole.

[a] Sterile cultures and Candida spp. strains were excluded. The strains analyzed were *E. coli* ($n=34$), *Klebsiella* spp. ($n=9$), *Morganella morganii* ($n=1$), *Enterobacter cloacae* ($n=1$), *Streptococcus agalactiae* ($n=1$).

4. Discussion

To our knowledge, our work represents the first study that evaluates ESBL-producing microorganisms in patients with EPN. Furthermore, it represents the most extensive cohort published in our country. As described in the literature, EPN was more frequent in women. The most frequent comorbidity was diabetes mellitus, reported in 69%–85% of the patients [12,13]. Overall mortality and ICU admission were 20.6% and 36.5%, respectively, similar to the mortality described, in other studies between 11% and 42% [6,10].

Like other genitourinary tract infections, *E. coli* is the most frequent microorganism reported in EPN [10,14,15]. It has been postulated that the mixed acid fermentation of glucose by Enterobacteriaceae (such as *E. coli*, *K. pneumoniae*, and *P.* spp.) under anaerobic conditions, is the main route of gas formation in EPN [7,8]. Tseng et al. [8] studied the virulence factors of *E. coli* associated with the formation of EPN and showed that the determinant gene for the specific uropathogenic protein called *usp* (a bacteriocin gene) was associated with the disease, and it was found in 93% with EPN, compared with 24% of the healthy patients. It is believed that bacteriocins (proteins produced by host bacteria that destroy competing bacteria) from EPN strains could help eliminate competing bacteria that colonize necrotic or petrous tissue [8,16]. Diabetes mellitus with poor glycemic control and obstructive uropathy with impaired renal circulation are some of the host factors that are most importantly associated with gas formation [17].

Various risk factors for increased mortality have been described in these patients. The classification proposed by Huang and Tseng et al. [5] showed that mortality from EPN increased as the disease spread. In addition, they demonstrated that the presence of thrombocytopenia, acute kidney injury, altered state of consciousness, and shock were factors associated with a worse prognosis. Kapoor et al. [18] established that hyponatremia, extensive destruction of the renal parenchyma (gas in >50%), and early nephrectomy (<1 week) were associated with higher mortality and ICU admission. Other risk factors described are multi-organ dysfunction, hyperglycemia, and leukocytosis [19]. Recently, Jain et al. [20] proposed a prognostic scoring based on the number of factors, including age (>50 years), comorbidities (>2), leukocytosis, body mass index (>30 kg/m^2 or <18 kg/m^2), thrombocytopenia, serum creatinine (>3 mg/dL), hypoalbuminemia, Huang scale II or III, hyponatremia, and multidrug resistance. Three prognostic groups were proposed: Good risk group (0–4 adverse factors) showed no mortality and only one needed emergency nephrectomy; intermediate risk group (5–7 adverse factors) reported a mortality rate of 19%, with the need of emergency nephrectomy in 14.2%; and poor risk group (8–10 adverse factors) showed a mortality of 100% [20]. They concluded that a combination of comorbidities and risk factors is an indicator of poor prognosis rather than the severity of any single comorbidity. This scoring system represents a helpful tool to evaluate and prioritize early management in those who are expected to have poor outcomes. In our population, hemodynamic instability, qSOFA≥2, hypoalbuminemia, Huang scale III, and early nephrectomy were associated with ICU admission. Huang scale IV and early nephrectomy were associated with mortality ($p<0.05$, data not shown in Tables), similar to previous studies [6,10,19,20].

Lu et al. [14] in their study demonstrated that resistance to third-generation cephalosporins, polymicrobial infections, and the use of previous antibiotic therapy were risk factors for mortality in this population. In addition, they determined that the presence of third-generation cephalosporins resistant microorganisms presented a higher frequency of disseminated intravascular coagulation and a higher requirement for hemodialysis [14]. Sterile urine cultures have been reported in 27% of urine cultures and dissimilar microorganisms between urine and exudate cultures in 62% of cases with EPN [20].

In a previous study carried out in our center, it was determined that the rate of ESBL-producing microorganisms in non-gas-forming urinary tract infections was 21.5%, compared to 31.7% reported in EPN in the present study. Third generation cephalosporins, fluoroquinolones [8], and carbapenemics were reported with higher resistance rates between patients with EPN compared to non-gas-forming infections [9].

Multiple diagnostic algorithms have been described, and they stipulated that the use of broad-spectrum antibiotics and early percutaneous drainage is currently the management of choice for EPN [8,20,21]. However, many of these studies do not consider antimicrobial resistance patterns. Lu et al. [14] proposed, based on their microbiological analysis and resistance rates, that these patients should be treated with at least with a third-generation cephalosporin, with or without an aminoglycoside, such as amikacin. Empirical carbapenem is recommended in patients with a history of previous hospitalization, use of antibiotics in the last year,

Table 3 Comparison of demographic, clinical and prognostic factors between patients with emphysematous pyelonephritis caused by ESBL-producing agents and non-ESBL agents ($n=63$).

Variable	ESBL, $n=20$ (31.7%)	non-ESBL, $n=43$ (68.3%)	p-Value	OR (95% CI)
Demographic				
Age, median (IQR), year	63.5 (51−67.5)	52 (44−61)	0.053	N/A
Female, n (%)	16 (80.0)	39 (90.7)	0.235	0.41 (0.091−1.844)
Clinical data, n (%)				
Hemodynamic instability[a]	6 (30.0)	18 (41.9)	0.367	0.595 (0.192−1.847)
Fever (>38.3 °C)	7 (35.0)	16 (37.2)	0.865	0.909 (0.300−2.75)
Flank pain	16 (80.0)	34 (79.1)	0.932	1.059 (0.283−3.960)
Biochemistry, n (%)				
Leukocytosis (>11 000/μL)	17 (85.0)	24 (55.8)	0.065	4.486 (1.143−17.602)
Thrombocytopenia (<150 000/μL)	4 (20.0)	11 (25.6)	0.628	0.727 (0.200−2.648)
Renal injury (creatinine >1.2 mg/dL)	11 (55.0)	25 (58.1)	0.815	0.880 (0.302−2.563)
Hypoalbuminemia (<3.5 g/dL)	9 (45.0)	25 (58.1)	0.330	0.589 (0.202−1.716)
qSOFA (≥2 points), n (%)	8 (40.0)	20 (46.5)	0.580	0.766 (0.261−2.250)
Comorbidities, n (%)				
Diabetes mellitus	17 (85.0)	39 (90.7)	0.503	0.581 (0.117−2.883)
Arterial hypertension	9 (45.0)	21 (48.8)	0.777	0.857 (0.296−2.486)
Chronic kidney disease	7 (35.0)	10 (23.3)	0.356	1.723 (0.539−5.503)
Hydronephrosis	8 (40.0)	15 (34.9)	0.695	1.244 (0.417−3.711)
Urolithiasis	6 (30.0)	15 (34.9)	0.702	0.800 (0.225−2.511)
Previous antibiotic[b]	9 (45.0)	25 (58.1)	0.330	0.589 (0.202−1.716)
Huang scale, n (%)				
Type 1	10 (50.0)	24 (55.8)	0.731	0.791 (0.273−2.292)
Type 2	1 (10.0)	7 (16.3)	0.206	0.270 (0.030−2.365)
Type 3 (A and B)	4 (20.0)	5 (11.6)	0.406	1.900 (0.450−8.008)
Type 4	5 (25.0)	7 (16.3)	0.446	1.714 (0.469−6.265)
Gas formation in kidney (>50% renal parenchyma), n (%)	9 (45.0)	12 (27.9)	0.180	2.114 (0.700−6.379)
Therapeutic management[c], n (%)				
Conservative	7 (35.0)	17 (39.5)	0.730	0.824 (0.273−2.483)
Ureteral stent	9 (45.0)	18 (41.9)	0.815	1.136 (0.390−3.310)
Percutaneous or open drainage	4 (20.0)	4 (9.3)	0.235	2.438 (0.542−10.958)
Early nephrectomy	1 (10.0)	9 (20.9)	0.103	0.198 (0.023−1.691)
Delayed nephrectomy	4 (20.0)	2 (4.7)	0.053	5.125 (0.853−20.788)
Clinical outcome, n (%)				
ICU	9 (45.0)	14 (32.6)	0.374	1.636 (0.550−4.866)
Mortality	6 (30.0)	7 (16.3)	0.228	2.143 (0.611−7.511)

IQR, interquartile range; ICU, intensive care unit; ESBL, extended-spectrum beta-lactamase; OR, odds ratio; CI, confidence interval; qSOFA, quick Sepsis Related Organ Failure Assessment; N/A, not applicable..

[a] Systolic pressure <90 mmHg.
[b] Antibiotic in the last 3 months.
[c] Eight patients received more than one therapy in refractory cases (see results for details).

and requiring hemodialysis. Furthermore, they suggested that the use of gentamicin and fluoroquinolones should be avoided due to the high rates of resistance reported in this population [14]. The previous recommendations do not seem to be adequate for our population, since it was demonstrated in a previous study that the resistance rate to third generation cephalosporins was higher (48%) [9], and increased to 52.1% in patients with EPN. In our population, empirical use of carbapenems seems to be the treatment of choice, adjusting the treatment according to the resistance profile as soon as the sensitivity patterns are available.

To our knowledge, this is the first study that evaluates the presence of ESBL microorganisms as a prognostic factor in EPN. Our analysis did not show increased mortality or the need for ICU admission in patients with an infection caused by ESBL-producing microorganism. It was found that patients with leukocytosis had ESBL bacteria more frequently in univariate analysis, but no significant association in multivariate analysis. These results suggest that a single variable does not have a significant impact in the outcomes of EPN, as proposed by Jain et al. [20].

There are limitations in our study. This is a retrospective analysis of a small population in a single center. A clonal study of the strains obtained was not carried out to determine if the strains were specific of our institution or the geographic area. Prospective multicenter studies with a greater number of cases are required to support the findings of our study.

5. Conclusions

Risk factors associated with a poor prognosis in patients with EPN have been described. The microbiological factors, specifically bacteria that produce ESBL, do not seem to have influence in the prognosis of these patients. However, the higher rates of antimicrobial resistance in this population must be considered when starting empirical antimicrobial treatment.

Author contributions

Study design: José Gustavo Arrambide-Herrera, José Iván Robles-Torres.
Data acquisition: Marco Alberto Ocaña-Munguía, Adrián Mauricio Martínez-Fernández.
Drafting of manuscript: José Iván Robles-Torres.
Critical revision of the manuscript: Rodrigo Romero-Mata, Lauro Salvador Gómez-Guerra.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

References

[1] Michaeli J, Mogle P, Perlberg S, Heiman S, Caine M. Emphysematous pyelonephritis. J Urol 1984;131:203—8.

[2] Pontin AR, Barnes RD, Joffe J, Kahn D. Emphysematous pyelonephritis in diabetic patients. Br J Urol 1995;75:71—4.

[3] Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. BJU Int 2011;107:1474—8.

[4] Kumar A, Turney JH, Brownjohn AM, McMahon MJ. Unusual bacterial infections of the urinary tract in diabetic patients—rare but frequently lethal. Nephrol Dial Transplant 2001;16:1062—5.

[5] Huang JJ, Tseng CC. Emphysematous pyelonephritis: Clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med 2000;160:797—805.

[6] 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.

[7] Huang JJ, Chen KW, Ruann MK. Mixed acid fermentation of glucose as a mechanism of emphysematous urinary tract infection. J Urol 1991;146:148—51.

[8] Tseng CC, Wu JJ, Wang MC, Hor LI, Ko YH, Huang JJ. Host and bacterial virulence factors predisposing to emphysematous pyelonephritis. Am J Kidney Dis 2005;46:432—9.

[9] Robles-Torres JI, Ocaa-Munguía MA, Madero-Morales PA, Ruíz-Galindo E, Gómez-Guerra L. Antimicrobial resistance and extended spectrum beta-lactamases in urinary tract infections: A serious problem in Northern Mexico. Urology 2020; 80:1—12.

[10] 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.

[11] Weinstein MP, Lewis II JS, Bobenchik AM, Campeau S, Cullen SK, Galas MF, et al. Performance standards for antimicrobial susceptibility testing. 31th ed. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 2021. p. 29—50.

[12] Aswathaman K, Gopalakrishnan G, Gnanaraj L, Chacko NK, Kekre NS, Devasia A, et al. Emphysematous pyelonephritis: Outcome of conservative management. Urology 2008;71: 1007—9.

[13] Somani BK, Nabi G, Thorpe P, Hussey J, Cook J, N'Dow J, et al. Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis? Evidence from a systematic review. J Urol 2008;179:1844—9.

[14] 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 2016;95:e3573. https://doi.org/10.1097/MD.0000000000003573.

[15] 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.

[16] Parret AH, De Mot R. Escherichia coli's uropathogenic-specific protein: A bacteriocin promoting infectivity? Microbiology 2002;148:1604—6.

[17] Tseng CC, Huang JJ, Ko WC, Yan JJ, Wu JJ. Decreased predominance of papG class II allele in *Escherichia coli* strains isolated from adults with acute pyelonephritis and urinary tract abnormalities. J Urol 2001;166:1643—6.

[18] 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.

[19] Olvera-Posada D, García-Mora A, Culebro-García C, Castillejos-Molina R, Sotomayor M, Feria-Bernal G, et al. Prognostic factors in emphysematous pyelonephritis. Actas Urol Esp 2013;37:228—32.

[20] 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;11:414—20.

[21] Kuzgunbay B, Turunc T, Tokmak N, Turunc T, Dirim A, Aygun C, et al. Tailored treatment approach for emphysematous pyelonephritis. Urol Int 2011;86:444—7.