

# The Evaluation of Biochemical and Microbiological Parameters in the Diagnosis of Emphysematous Pyelonephritis

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*Emphysematous pyelonephritis (EPN) is a severe, necrotizing infection of the renal parenchyma, produced by gas-forming Gram-negative bacilli. Even though only few cases are reported in the literature, the disease is not so rare and can become life-threatening if the diagnose is not quick and the therapeutic measures efficient. The biochemical analysis are the first line diagnostic, indicating the severity of the infection. The aim of our study was to evaluate the importance of biochemical parameters, as first line diagnosis and also of the microbiological parameters, as etiologic diagnosis, in severe renal infections produced by gas forming bacilli mainly in diabetic patients, predominantly women, with obstructive nephrolithiasis.*

*Keywords: emphysematous pyelonephritis, diabetes mellitus, urinary infection*

The severe kidney infections are: pyelonephritis, pyonephritis and pyonephrosis. All these clinical forms of renal diseases are the subject of a noisy clinical picture, with fever and abdominal symptoms, ranging from mild abdominal pain to septic shock [1]. Emphysematous pyelonephritis (EPN) is a rare form of pyelonephritis, an acute necrotizing infection with gas, limited in the collecting system, renal parenchyma or extending to the perinephric and pararenal space, caused by Gram-negative, gas-forming bacilli, (*E. coli*, *Klebsiella*, *Proteus*, *Pseudomonas* spp are the most commonly reported etiological agents) [2]. When the patient has a severe urinary infection, with noisy clinical symptoms (fever and abdominal pain), we have to take into discussion the diagnosis of EPN mainly if the patient has major risk factors associated: diabetes mellitus, urinary obstruction and is of female gender.

First line diagnosis relies on biochemical parameters: acute inflammatory tests for the diagnosis of acute, severe infection, biochemical tests for the evaluation of the general condition of the patient and microbiological tests in order to find the etiology of the infection. But in order to differentiate EPN from other similar, more common renal infections, an ultrasound and a CT scan examination is needed [3]. The ultrasound can help in diagnosing urinary retention and lithiasic obstruction, but it has proven ineffective in showing gas production in the renal parenchyma. The CT scan is the gold standard method for the diagnosis of EPN because it is capable of locating areas of gas production and dead tissue [4, 25, 26].

When the patient has a clinical severe renal disease, we have to take into discussion the possibility of an EPN diagnosis and pay attention to the biochemical tests telling much about inflammation, unbalanced diabetes and renal failure. The microbiological tests are used to confirm the etiology. All these parameters must be followed during the evolution of the disease.

Since early 1900s, antibiotics have been used in infectious diseases, the most of them being used to treat infections in humans and animals. Sometimes the medical antibiotherapy is enough to treat the infection, at other times urgent nephrectomy is the solution to avoid a life-threatening general sepsis. EPN is considered a major urological emergency in order to avoid high morbidity and mortality [5].

## Experimental part

This retrospective study was performed at the Academic Emergency Hospital Urology Department, Sibiu, România, between the 1st of January 2012 and the 31st of december 2016 and included all the patients admitted in the hospital with the diagnosis of severe kidney infection. We found 189 patients with this diagnose and we analyzed their laboratory tests (biochemistry and microbiological tests). We also checked their radiological investigations and we divided the patients with pyelonephritis, pyonephrosis and pyonephritis.

We further considered only the 121 patients with the diagnosis of pyelonephritis and looked for those with EPN, as a form of pyelonephritis.

We analyzed all the significant biochemical parameters, recorded in the patients files (number of leucocytes, number of trombocytes, C-Reactive Protein, urea, creatinine, glucose and glicated hemoglobin) and also the microbiological parameters (uroculture, hemoculture).

All these parameters were tested in the Clinical Laboratory of our hospital and because the hospital has a centralized electronic system, we could see the last 5 years results of all our patients.

The ultrasound investigation helped us in diagnosing urinary retention and obstruction and the CT scan confirmed the gas infiltration of the renal parenchyma, collecting system, or perinephric tissue [26].

## Results and discussions

After performing laboratory tests and radiological investigations we diagnosed 121 out of 189 patients (64%) with pyelonephritis, 59 out of 189 patients (31%) with pyonephrosis and 9 out of 189 patients (5%) with pyonephritis, all being complications of preexisting renoureteral stones.

Because diabetes mellitus is a well known risk factor for EPN [6] we attentively looked for those with renal infection and diabetes and we found 49 out of 189 (25%) patients with this association. Among the 121 patients with pyelonephritis, only 8 patients (6.6%) developed EPN. All the 8 patients with EPN were diabetic and had urolithiasis, 6 of them with obstruction. The median age was 59 years and the sex distribution was 6 females versus 2 males.

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### 189 Severe Kidney Infections

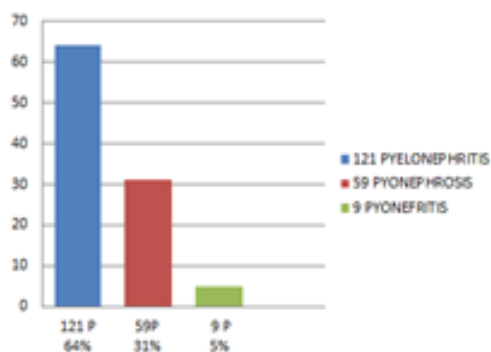


Fig.1. Patients with the diagnosis of Severe Kidney Infection

### UROCULTURE 121 – PYELONEPHRITIS

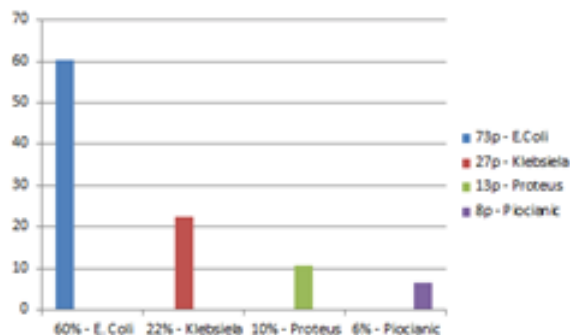


Fig. 2. Etiology agents in pyelonephritis

Biochemical analytes	Patients							
	F	F	F	F	F	F	M	M
Leukocytosis (mmc)	18325	21335	19650	25587	21453	19155	22318	26311
Platelets (mmc)	53000	45000	82000	68000	55000	60000	56000	87000
Urea (mg/dl)	69.0	74.4	59.9	86.4	81.5	59.6	103.5	61.1
Creatinine (mg/dl)	1.86	2.31	1.77	2.67	3.11	1.48	3.25	1.87
Glucose (mg/dl)	269.0	186.6	178.8	218.8	175.9	165.3	196.3	168.4
HbA1c (%)	8.5	7.8	7.4	8.1	6.9	7.0	8.6	7.7

**Table 1**  
PATIENTS WITH  
EPN-BIOCHEMICAL  
PARAMETRS

We analyzed the following biochemical analytes: number of leucocytes, number of platelets, C-Reactive Protein (CRP), urea, serum creatinine, glucose, glycosylated hemoglobin and microbiological tests: uroculture and hemoculture.

Analyzing the biochemical parameters of the 121 patients with pyelonephritis, we found leucocytosis, thrombocytopenia, modified urea and creatinine, increased CRP, increased glucose and increased glycosylated hemoglobin. There was no difference between the mean values of these biochemical analytes in the patients with pyelonephritis and emphysematous pyelonephritis.

We analyzed the urocultures of all the 121 patients with pyelonephritis and we found *E. coli* positive in 73 patients (60.3%) of the urocultures, *Klebsiella* spp in 27 patients (22.3%) and other Gram negative bacilli: *Proteus* in 13 patients (10.8%), *Pseudomonas* in 8 patients (6.6%) of the urocultures. There was no significant difference in the etiology of the urinary tract infection between the patients with pyelonephritis and emphysematous pyelonephritis.

Studying the hemocultures of the 121 patients with pyelonephritis we found 25 out of 121 patients (20%) positive with *E. coli*.

In our study all the 8 patients with EPN were diabetic patients, but not all the diabetic patients involved in the study developed EPN.

Urolithiasis was an associated pathology in all the 8 patients with EPN.

All EPN patients received antibiotic therapy and 2 of them required percutaneous drainage because of advanced disease. Despite of the intensive treatment 2 of the 8 patients died.

Emphysematous pyelonephritis was first described in 1898 and since then the number of reported cases was not very big [7-12]. In the USA, in a busy urologic department, only 1-2 cases were encountered per year [13]. In our experience we had approximately the same incidence (8 patients in 5 years). However, a study made by Al-Geizawi et al. in 2010 [14] concluded that EPN is vastly underreported.

Having our own experience with this disease during the last 5 years, we wanted to compare our finding with the literature theories related to EPN.

The first step diagnosis relies on the biochemical tests about the inflammation status of the patients and about their general status. In our study we concluded that there

is no significant difference between the biochemical parameters of those with pyelonephritis and EPN and also no significant differences between the etiology of the common pyelonephritis and EPN. The conclusion of this finding is that there must be risk factors associated to the pyelonephritis in those persons who developed EPN.

The main risk factor, found in all our 8 patients with EPN, was diabetes. According to the literature EPN is strongly associated with diabetes mellitus, diabetes being present in 95% of the patients with EPN. [15]. Diabetes predisposes to urinary tract infections, but not all the diabetic persons develop EPN. The gas formation has no correlation to diabetes (the Gram negative bacilli are the etiology of gas formation), but diabetic microangiopathy may contribute to the slow transport of catabolic products and may lead to accumulation of gas [17, 18].

There are some other factors that predispose diabetes patients to EPN: uncontrolled diabetes and high levels of glycosylated hemoglobin [19]. In all our 8 EPN cases the diabetes was uncontrolled with high serum levels of glucose and with high levels of glycosylated hemoglobin. The literature says that only 72% of the patients have high levels of glycosylated hemoglobin [20].

Another major risk factor for EPN is the renal obstruction with lithiasis. The literature mentions that obstruction is the main cause of EPN in persons without diabetes [21]. In our study all the 8 diabetic patients developed the severe urinary infection on preexistent nephrolithiasis.

The 3rd major risk factor was gender. In our study, females were predominantly affected: 3 females vs 1 male. The literature says that affected females exceed the number of males in a report 4 females vs 1 male. [22] and others say 6 females vs 1 male [23].

The EPN prognosis can be determined according to the type of emphysematous pyelonephritis, 3 stages of gas spreading: Stage 1- Gas in the collecting system. Stage 2- Gas in <50% of renal parenchyma, with minimal spread to surrounding tissues and sepsis rapidly controlled. Stage 3- Gas in >50% of renal parenchyma, extensive spread of infection in perinephric area, or evidence of multi-organ failure, uncontrolled sepsis, or refractory shock [1, 14].

We had cases in all the 3 stages, but the 2 cases who died were in stage 3 (gas in >50% of renal parenchyma, extensive spread of infection in perinephric area, or evidence of multi-organ failure, uncontrolled sepsis, or refractory shock), so the mortality rate of stage 3 EPN was 100%. According to the literature the mortality rate in EPN stage 3. is 80% [14].

Other prognostic factors are serum creatinine and platelets count. Studies associate the mortality rate with high leucocytes number, high serum creatinine levels and low platelets number. [24]. All our patients had high numbers of leucocytes, variable levels of creatinine, all greater than 1.4 mg/dL and the platelets were under the normal range, but we could not correlate the values with the mortality rate, because we had only 2 patients who died, and statistically it is not relevant.

Because the treatment of EPN involves sometimes urgent nephrectomy, the literature analyzes the advantage of this treatment [18].

In our study all the 8 EPN patients had a surgical nephrectomy but it was life saving only in 6 patients, so the overall success of nephrectomy was 75%. Because 2 patients died, despite the energetic treatment, the mortality rate was 25%. Comparable results can be found in the literature there are: HuangJJ, Tseng CC, had 90% success after nephrectomy (9 from 10 patients) and the mortality rate was 18%. [1, 24, 25].

## Conclusions

Emphysematous pyelonephritis is a rare but severe kidney infection with acute necrosis in renal parenchyma and perirenal space. Infection is caused by gaseous uropathogens and requires early diagnosis and initiation of treatment. The risk factors for a renal infection to become EPN are: unbalanced diabetes, obstructive urolithiasis and female gender. Biochemical and microbiological tests: leucocytes, platelets, urea, serum creatinine, glucose, glycosylated hemoglobin, are the first line diagnosis. The prognostic factors related to diabetes and also those related to the general status of the patient, relies also on biochemical data. Severe prognosis factors are the modified values of serum creatinine (high) and number of platelets (low). Analyzing these cases we could compare our work to others and improve the knowledge concerning this life-threatening renal disease and recommend a more aggressive treatment.

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