



Retrospective analysis of clinical profile, prognostic factors and outcomes of patients with emphysematous pyelonephritis

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ABSTRACT

Aim: To study the clinical profile, prognostic factors and outcome in patients with emphysematous pyelonephritis (EPN). **Methods:** All patients admitted with a diagnosis of EPN between the period from March 2014 to March 2017 were included in this retrospective study. **Results:** Overall 64 cases were included in this study out of which 49 were females, 15 were males. 43 (67.2%) cases had type 2 Diabetes Mellitus. E.coli (64.1%) was the commonest microorganism isolated in blood, urine and pus culture. Presence of shock, DIC, increased serum creatinine at the time of admission were identified as poor prognostic factors. Severe hypoalbuminemia, need for emergency dialysis and presence of polymicrobial infection were significantly associated with failure of conservative treatment. **Conclusion:** EPN requires special attention because of its life threatening complications mainly due to sepsis at the initial presentation, and outcome depends upon the clinical course and prognostic factors.

Keywords: Emphysematous pyelonephritis, diabetes mellitus, E.Coli, hypoalbuminemia, shock, DIC, prognostic factors, conservative treatment.

INTRODUCTION

Emphysematous pyelonephritis (EPN) is a urologic emergency characterized by acute necrotizing parenchymal and perirenal infection, caused by gas forming uropathogens^[1]. It commonly occurs in Diabetic patients in whom high tissue glucose levels provides substrate for microorganisms such as E.Coli, which produces carbon dioxide by sugar fermentation. (Schainuck et al,1968). In addition to diabetes many patients have associated urinary calculi,

urinary tract obstruction or papillary necrosis and significant functional renal impairment. Overall mortality has been reported to be 19% to 43% (Freiha et al, 1979). Women are more affected than men and almost all cases occur in adults. Clinical triad is fever, vomiting and flank pain^[2]. E.Coli is the most commonly identified organism in urine cultures. CT is the imaging of choice in defining the extent of emphysematous process and in guiding management. Most patients are septic and if the kidney is functioning, fluid resuscitation and broad spectrum antimicrobial therapy are essential^[3,4]. If a kidney is obstructed, catheter drainage may be instituted. Nephrectomy is reserved for patients in whom there is failure of medical treatment. This study is aimed at analysing the clinical profile, prognostic factors and outcomes of patients with EPN.

METHODS

This was a single centre study conducted in the Institute of Urology, Madras Medical College, Chennai. Patients with verified Inclusion criteria for Emphysematous Pyelonephritis and treated in the institution from March 2014 to March 2017 were included in the study. This was a retrospective study. Information on demographic profile, comorbid medical conditions, clinical profile, laboratory investigations, imaging findings, type of management and outcomes of patients were obtained from medical records. Clinical features included signs and symptoms at initial presentation and patients' haemodynamic status. The laboratory variables included elevated white blood cell count, thrombocytopenia, hypoalbuminemia, increased serum creatinine as well as urine, blood and pus culture at the initial presentation. Management modalities including conservative treatment like antibiotic therapy, need for haemodialysis, percutaneous drainage and DJ stenting and surgical management like nephrectomy were analysed and outcomes measured. Finally factors predictive of mortality and failure of conservative treatment were analysed.

DEFINITION

Thrombocytopenia is defined as platelet count less than 120,000/ml, serum hypoalbuminaemia as serum albumin less than 3gm/dl, shock as blood pressure of less than 90/70 mmHg and along with evidence of end organ damage, leucocytosis as more than $12 \times 10^9/L$, increased serum creatinine as $>0.3 \text{ mg/dl}$. Glycosylated haemoglobin A1 level more than 0.08 was defined as poor control of glucose level.

Class of disease (on basis of extent of air on CT scan)^[5]

- Class I : gas in the collecting system only
- Class II : gas in the renal parenchyma without extension to extra renal space
- Class IIIa : extension of gas or abscess to peri-nephric space
- Class IIIb : extension of gas or abscess to para-renal space
- Class IV : bilateral EPN or solitary kidney with EPN

STATISTICAL ANALYSIS

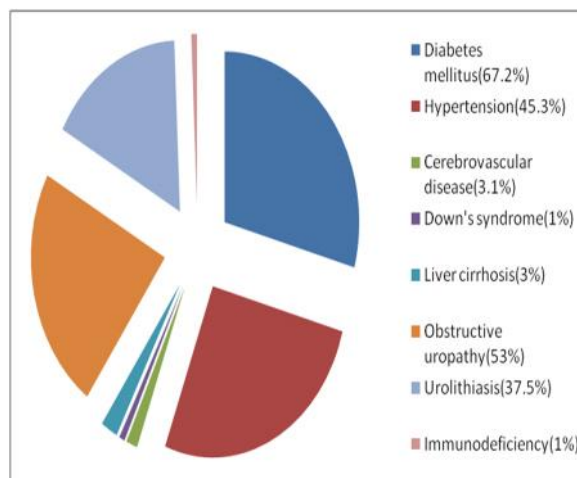
Quantitative variables were calculated as median while the categorical variables were calculated as frequencies and percentages. Chi-square and Fisher's exact test were used for comparing qualitative variables between the 2 groups. Wilcoxon test was used for comparing the quantitative variables between the 2 groups. A p-value of <0.05 was considered as significant.

RESULTS

Among the 64 subjects studied in this retrospective investigation, 15 were males (23.4%) and 49 were females (76.6%). The mean (standard deviation) age of the patients was 44.5 (10.2).

In this study among 64 cases, 43 (67.2%) were diagnosed with Type 2 diabetes mellitus and 34 (53.5%) patients had obstructive uropathy and 24 (37.5%) of the patients had urolithiasis as a comorbid condition. Other comorbid conditions observed were hypertension (29 patients; 45.3%), Cerebrovascular accidents (2 patients; 3.1%), Down's syndrome (1 patient; 1.6%), liver cirrhosis (3 patients; 4.7%) and immunodeficiency (1 patient; 1.6%) as in figure 1.

Figure 1: Distribution of various comorbidities in Emphysematous pyelonephritis



In this study, fever (51 patients; 79.7%) and flank pain (49 patients; 76.6%) were the commonest clinical presentation. Others presented as dysuria (46 patients; 71.8%), tenderness in loin (38 patients; 59.3%) and crepitus (11 patients; 17.1%). Shock was observed in nearly half of the patients (31 patients; 48.4%) as the initial clinical presentation and DIC in 11 patients (17.2%) and oliguria in 11 patients (17.1%).

Table 1: Clinical data and lab investigations of patients with Emphysematous pyelonephritis

Clinical Signs	Number of patients	Percentage (%)
Dysuria	46	71.8
Fever	51	79.7
Pain in loin region	49	76.6
Tenderness in loin	38	59.3
Crepitus	11	17.1
Shock	31	48.4
DIC	11	17.2
Oliguria	11	17.1
Leucocytosis	43	67.2
Thrombocytopenia	26	40.6
Hypoalbuminemia	38	59.3
Increased Serum creatinine	33	51.5

Among the laboratory investigations, leucocytosis was present in 43 patients (67.2%), thrombocytopenia was present in 26 patients (40.6%). Increased Serum creatinine was noticed in 33 patients (51.5%) and 38 (59.3%) patients had hypoalbuminemia at the initial presentation. Thirty six patients had class 1 EPN, 15 had class 2, 4 had class 3A, 4 had class 3B and 5 had class 4 stage based on CT imaging findings as in Table 1.

Escherichia coli were the predominant etiological agent isolated by culturing urine, blood or pus samples, present in 41 (64.1%) patients followed by Klebsiella pneumoniae (12 patients; 18.7%), Pseudomonas aeruginosa (6 patients; 9.4%) and Proteus mirabilis (5 patients; 7.8%). Monomicrobial infection was found in 56 patients (87.5%) and polymicrobial infections were found in 8 patients (12.5%). Urine cultures were positive in 51 patients (79.7%) and 34 patients (66.7%) had E. coli infections. Bacteremia occurred in 24 patients (37.5%), among them E. coli was noticed in 11 patients (45.8%). Cultures of wound pus were positive in 34 patients (53.1%), E. coli in 14 (41.2%), P. mirabilis in 9 (26.5%) and K. pneumoniae in 6 (17.6%).

Table 2: Bacterial isolates from various clinical specimens

Bacteria isolated	Clinical specimens (n=64)		
	Blood (n=24)	Urine (n=51)	Wound pus (n=34)
Escherichia coli	11 (45.9)	34 (65.4)	14 (41.2)
Klebsiella pneumoniae	6 (25)	7 (13.5)	6 (17.6)
Pseudomonas aeruginosa	5 (20.8)	7 (13.5)	3 (8.8)
Proteus mirabilis	2 (8.3)	4 (7.7)	9 (26.5)
Staphylococcus aureus	-	-	2 (5.9)

Third generation cephalosporins were most often prescribed initially to patients (47/64; 73.4%). The overall survival rate was 57/64 (89.06%). Conservative treatment was done in 61 patients of which 14 patients received antibiotics alone, out of which 11 recovered and 4 died. 44 patients were treated with Percutaneous Drainage (PCD) and antibiotics of which 33 patients recovered and 11 had failure of treatment. Among them 4 patients died and 7 had recurrent EPN within the next 3 months. Elective nephrectomy was done in those 7 patients. DJ stenting was done in 3 patients and the patients recovered successfully. Emergency nephrectomy was done in 3 patients and they had a successful outcome. The overall failure rate of conservative therapy was 14/61(22.95%).

Figure 2: Flowchart showing outcome of EPN

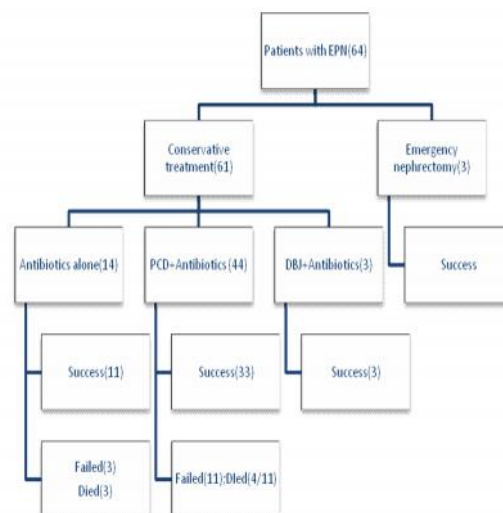


Table 3: Comparison of comorbidities, laboratory findings and clinical profile of patients with EPN.

Variable	Survivors (n=57)	Died (n=7)	P value
Comorbid condition			
Diabetes mellitus	37	6	0.01*
Hypertension	27	2	0.38
Prior cerebrovascular accident	2	0	1.0
Downs Syndrome	1	0	1.0
Liver cirrhosis	2	1	0.5
Obstructive uropathy	29	5	0.41
Urolithiasis	21	3	0.32
Laboratory findings			
Leucocyte	12.8	14.9	0.87
Platelet count	185	105	0.27
Thrombocytopenia	21	5	0.04*
Hypoalbuminemia	31	7	0.03*
HbA1C	33	5	0.67
Increased Serum Creatinine (>0.3mg/dl)	27	6	0.03*
Clinical profile			
DIC	5	6	0.01
Pyuria	30	4	0.7
Haematuria	27	5	0.16
Polymicrobial infection	1	7	0.002*
Shock	25	6	0.03*
Bacteremia	20	4	0.5
Inappropriate antibiotic therapy	11	6	0.04*
Haemodialysis	3	6	0.002*
Involved side of kidney	23	6	0.6

Table no. 4: Factors associated with failure of conservative treatment

Variable	Success group (n=47)	Failure group (n=14)	P value
Hypoalbuminemia (<3 mg/dl)	20	18	0.003*
Need for haemodialysis	2	7	0.03*
Polymicrobial infection	1	7	0.04*

Severe hypoalbuminemia (p=0.003), presence of polymicrobial infection (p=0.04) and the need for haemodialysis (p=0.03) at the initial presentation were significantly associated with failure of conservative treatment.

DISCUSSION

In our study, females (76.6%) were more commonly affected than males. This result is similar to that of other studies and might be due to increased susceptibility to urinary tract infections in females as evidenced in previous studies by Wan YL, Lee TY 1996, Pontin AR 97. Among the comorbid medical conditions analysed, Diabetes Mellitus was more commonly associated (67.2%). This is supported by previous studies such as Schainuck et al (1968), Ramachandran et al (2001), Dutta P et al (2007) which states that Emphysematous pyelonephritis is more common among patients with diabetes mellitus and also explains that high tissue glucose levels provides substrate for micro organisms. The mean age of the patients in our study was 44.5 ± 10 yrs which was evident that almost EPN exclusively occur in adults (Hawes et al,1983).

Obstructive uropathy occurred in 53.5% of the patients in our study which was also a high comorbid condition but was associated with a poor outcome as supported in a study by Michaeli et al,1984 which stated that nonobstructive unilateral disease receiving combined medical and surgical treatment was associated with a favourable outcome rather than obstructive uropathy^[6]. This was in contrast to our study in which despite 53.5% of the patients are obstructive uropathy, the overall survival rate was 57/64(89.06%). The left kidney(29 patients;64.4%) was more affected than the right side which is supported by studies such as Evanoff 1983, Michaeli 2008, Ambarkhaira 2009.

The overall mortality in our study was 7/64 (10.93%) which was very lower than the previous studies which stated that the mortality range to be between 19-43% (Huang and Tseng 2000, Freiha et al,1979). The most commonest clinical presentation in our study was fever (79.7%) and flank pain (76.6%) as well evidenced in previous studies supported by Schainuck et al 1968, Jeng Jong Chin 2000. E coli was the commonest micro organism found in culture (41patients;64%).

Our findings were similar to the studies done by Ankur Gupta 2009, AhleringTE 1985, Schultz EH 1987, Tang et al 2013.

The commonest initial presentation was shock (48.45) and DIC(17.2%) in our study[7]. DIC, Pyuria, Haematuria, Shock, polymicrobial infection, bacteremia, inappropriate antibiotic therapy, need for haemodialysis, most commonest side involved in the kidney were considered in the clinical profile and analysed among survivors and non survivors. Presence of DIC (p=0.01), polymicrobial infection (p=0.002), shock (p=0.002),inappropriate antibiotic therapy (p=0.04), need for haemodialysis (p=0.002) were found as poor prognostic factors in our study [8]. This was supported by previous studies by Ambarkhaira 2009, Huang and Tseng 2000, Wan YL 2013, Dutta P et al 2000, Shokeir 2007, Baliga KV et al 2007, Menif E 2003. There was no significant difference between age, presence of comorbid condition other than diabetes, leucocyte count, platelet count, level of HbA1C, side of involved kidney, pyuria, haematuria, bacteremia in survivors and non survivors.

Serum creatinine more than 3mg/dl (p=0.03), thrombocytopenia (p=0.04), hypoalbuminemia (p=0.04) was significantly associated with mortality. Serum albumin is the most abundant protein in human plasma. Albumin synthesis is suppressed in response to inflammatory conditions, sepsis, trauma or after major surgery. Hypoalbuminemia and serum creatinine was found to be a strong predictor of increased mortality in our study. This supports that accelerated protein breakdown is a feature of metabolic alterations seen in patients with acute kidney injury. In the present study, severe hypoalbuminemia was significantly associated with failure of conservative treatment . Even in patients treated with PCD + antibiotics, failure rate was still significantly associated with severe hypoalbuminemia as in Table 4. Therefore patients with severe hypoalbuminemia had high risk of conservative treatment failure, going for further management like open drainage or repeated PCD and nephrectomy. However PCD with antibiotics is the initial management of choice in patients with severe hypoalbuminemia as it immediately reduces renal tissue pressure and decreases the mortality rate.

Failure of conservative treatment in our study was 22.95% (14/61) which was found to be less than previous studies done by Yu Chan Lu (33%), Somani BK (47%), Pontin AR (67%) and more than in the study done by Anglo JC et al 1997. Previous studies states that the medical treatment with antibiotics alone carries highest mortality (70-90%), Michaeli J 1984, Klein 1986, Kapoor 2010, Sheng WH 2002. Our study finding was only 3/14 (21%). Presence of diabetes (p=0.01) was significantly associated with increased mortality as well as with failure of conservative management (OR=1.32)^[9,10]. Microbial organisms cultured from urine, blood and pus includes E.Coli, Klebsiella pneumonia, Pseudomonas, Staphylococcus aureus^[11,12,13]. To conclude, appropriate antibiotic treatment along with early intervention reduces mortality overall^[13].

The limitations in our study were retrospective study design, single centre study, small sample size and lack of data regarding susceptibility rate of organisms to antibiotics. Results of the study should be interpreted with these limitations in the background.

CONCLUSION

Diabetes mellitus appears to be the most common risk factor for developing EPN. Severe hypoalbuminemia, need for emergency dialysis and presence of polymicrobial infection are significantly associated with failure of conservative treatment. Presence of shock, DIC, increased serum creatinine at the time of admission are identified as poor prognostic factors.

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