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Original Research Article

A COMPREHENSIVE ANALYSIS OF CLINICAL CHARACTERISTICS, MICROBIAL PROFILE, PROGNOSTIC INDICATORS, AND TREATMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ACUTE PYELONEPHRITIS

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Abstract

Background: Pyelonephritis is frequently linked to diabetes mellitus, serving as a common cause. Poor outcomes are associated with both emphysematous pyelonephritis (EPN) and non-emphysematous pyelonephritis (NEPN). This study was conducted to examine the clinical characteristics, microbiological profile, prognostic factors, and treatment outcomes of pyelonephritis specifically in diabetic patients.

Methods: Acute pyelonephritis is considered present when a patient experiences fever with chills, rigors, flank pain, nausea, and vomiting. A diagnosis is confirmed through USG and KUB studies showing an enlarged kidney, collection presence, and perinephric fat stranding. Urine samples are collected through midstream voiding, catheterization, or suprapubic needle aspiration. A positive urine culture indicates $>10^5$ CFU/ml of bacteria. Glycemic control is classified as good (HbA1c <7%), moderate (HbA1c 7-7.5%), or poor (HbA1c >7.5%). Emphysematous pyelonephritis classification is based on CT scan findings.

Results: In a study of 40 patients with acute pyelonephritis and type 2 diabetes, 80% had non-emphysematous pyelonephritis (NEPN) and 20% had emphysematous pyelonephritis (EPN). Over 75% in both groups experienced loin pain, a hallmark of acute pyelonephritis. Burning micturition affected 75% of EPN and 28.12% of NEPN patients. Less than 15% reported decreased urine output and vomiting in both groups. The NEPN group had significantly lower rates of burning micturition, possibly indicating a link to pyelonephritis severity. In EPN patients, 75% had normal CECT KUB findings, with 50% of abnormalities falling into Class 3A. Approximately 50% of both groups were treated without IV antibiotics, with conservative management dominating. Other interventions, including DJ stents, antifungals, hemodialysis, percutaneous nephrolithotomy, and ureteroscopy with stenting, were also employed.

Conclusion: Diagnosing emphysematous pyelonephritis (EPN) in diabetic patients with pyelonephritis symptoms, particularly with poorly controlled blood sugars, requires a high suspicion index and early imaging. Most affected individuals are aged 51-70 years. Cases of both non-emphysematous (NEPN) and EPN are predominantly associated with gram-negative bacteria. EPN patients in Class I-IIIA respond well to antibiotics or additional percutaneous drainage (PCN), while Class IIIB and Class IV cases may require nephrectomy.

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Keywords: Diabetes Mellitus, Emphysematous Pyelonephritis, Nonemphysematous Pyelonephritis.

INTRODUCTION

Pyelonephritis is frequently associated with diabetes mellitus, with diabetic patients experiencing a higher incidence than non-diabetic patients. Patients with diabetes are more prone to bilateral pyelonephritis, which increases the risk of developing severe infections and complications. [1] In a recent community-based study, urinary tract infections (UTIs) ranked second, followed by lower respiratory tract infections, among older individuals with diabetes, with incidences of 51.4 and 147.9 per 1000 person-years for men and women, respectively. [2] The spectrum of involvement varies from lower urinary tract colonization to cystitis, pyelonephritis, and renal or perirenal abscesses. Diabetic patients exhibit a higher incidence of acute pyelonephritis than non-diabetic patients, although specific studies on this aspect are lacking. [3] The presentation of pyelonephritis in diabetics can manifest as either emphysematous or non-emphysematous pyelonephritis. Emphysematous pyelonephritis (EPN) is a rare and serious condition characterized by necrotizing infection of the renal parenchyma in the presence of gas in renal tissues. EPN is primarily triggered by poorly controlled blood sugar levels and urinary tract obstructions. The prevalence of diabetes among patients with EPN ranges from 53% to 90%. [4] Current treatment involves parenteral antibiotics with options for percutaneous or open surgical drainage and/or nephrectomy. However, there is no consensus on whether antibiotics alone are sufficient or if and when surgical intervention, particularly nephrectomy, is necessary. Non-emphysematous pyelonephritis (NEPN) is a prevalent urinary tract infection in individuals with diabetes. In a study that analyzed 223 patients with NEPN, only 14 had diabetes mellitus (DM). The findings indicated that 26% of cases had risk factors for NEPN and 9.4% experienced renal failure during the illness. [5] Moreover, diabetics face an increased risk of bilateral pyelonephritis, leading to more severe infections and complications, including a higher likelihood of acute kidney injury due to UTI, compared to non-diabetics. [6] Despite the absence of extensive studies focusing on the clinical and microbial profiles and treatment outcomes of diabetic patients with both non-emphysematous pyelonephritis (NEPN) and Emphysematous Pyelonephritis (EPN), this prospective observational study was conducted to address this gap. This study aimed to assess the clinical features, microbial profiles, and treatment outcomes of NEPN and EPN in patients with diabetes.

Material and Methods

This cross-sectional study was conducted at the Departments of General Medicine and Urology at Deccan College of Medical Sciences (DCMS) and Owaisi Group of Hospitals, including Owaisi Hospital and Research Centre (OHRC) and Princess Esra Hospital (PEH) in Hyderabad. The study received institutional ethical approval as per the Helsinki Declaration for human research. Before participation, written consent was obtained from all study participants after providing a detailed explanation of the study's nature in the local language.

Inclusion Criteria

1. Individuals diagnosed with acute pyelonephritis (both emphysematous and non-emphysematous) and having type 2 diabetes mellitus.
2. Age >40 years
3. Males and females

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4. Voluntarily willing to participate in the study

Exclusion Criteria

1. Individuals with inflammatory conditions other than pyelonephritis,
2. History of trauma
3. Pregnancy
4. Malignancies
5. Other immunosuppressed conditions.

Acute pyelonephritis is considered present when a patient experiences fever with chills, rigors, flank pain, nausea, and vomiting. A diagnosis is confirmed through USG KUB studies showing an enlarged kidney, collection presence, and perinephric fat stranding. Urine samples are collected through midstream voiding, catheterization, or suprapubic needle aspiration. A positive urine culture indicates $>10^5$ CFU/ml of bacteria. Glycemic control is classified as good (HbA1c <7%), moderate (HbA1c 7-7.5%), or poor (HbA1c >7.5%). Emphysematous pyelonephritis classification is based on CT scan findings:
Class 1: Gas in the collecting system only
Class 2: Gas in the renal parenchyma without extension to the extra-renal space
Class 3A: Extension of gas or abscess to the perinephric space
Class 3B: Extension of gas or abscess to the pararenal space
Class 4: Bilateral EPN or solitary kidney with EPN.

Investigations included Complete Blood Count, urinalysis with culture and sensitivity, HbA1C, serum creatinine, fasting, and postprandial blood glucose levels, baseline ultrasound KUB, and CECT-KUB when necessary for suspected renal abscess or non-recovering pyelonephritis. Treatment involved antibiotic administration based on culture sensitivity reports. NEPN patients received parenteral antibiotics for 1 week followed by 2 weeks of oral antibiotics, while EPN patients were treated for at least 3 weeks. Fungal UTI patients were initially treated with fluconazole or amphotericin, adjusted based on culture sensitivity. Percutaneous drainage (PCD) was performed with a pigtail or percutaneous nephrostomy tube insertion into the pelvis or perirenal space, along with antibiotics. Nephrectomy was considered for the patient's refractory to antibiotics, PCN, and/or experiencing clinical deterioration. Patients were categorized into "good" and "poor" outcome groups based on successful antibiotic or PCN treatment versus nephrectomy or death.
Statistical analysis: All the available data was refined and uploaded to MS Excel Spreadsheet and analyzed by SPSS version 21 in Windows format. Continuous variables were represented as mean, standard deviation, and percentages. Categorical variables were calculated using the chi-square test and p-values of (<0.05) were considered as significant.

Results

A total of 40 cases were studied during the duration of the study. It included 25(62.5%) males and 15(37.5%) females. Table 1 shows that the majority of patients (65%) fall within the 41-60 age range, with the 51-60 group representing the largest proportion (40%). Decreasing representation in older age groups: The number of patients with both T2DM and APN steadily decreases with increasing age, with only 5% above 70 years old. The table does not show any cases in the age group below 40 years old. This suggests that individuals with T2DM are at a higher risk of developing APN in their middle age, particularly between 51 and 60 years old.

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The decreasing prevalence of APNs with T2DM in older age groups might be influenced by factors like declining immune function or changes in urinary tract physiology.

Table 1: Showing the cases of Type 2 Diabetes Mellitus and Acute Pyelonephritis included in the study

Age group in Years	*Frequency*	*Percentage*
41 – 50	10	25.0
51 – 60	16	40.0
61 – 70	12	30.0
Above 70	2	5.0
Total	40	100.0

Table 2 shows that 50% of the patients reported no other comorbid conditions besides T2DM and APN. 25% of the patients have hypertension (HTN) in addition to T2DM and APN. Moderate prevalence of coronary artery disease: 20% of the patients have coronary artery disease (CAD) alongside T2DM and APN. Low prevalence of multiple comorbidities: Only 5% of the patients have a combination of HTN, CAD, and chronic kidney disease (CKD).

Table 2: Showing the existence of comorbidities cases of the study

Co-Morbidities	*Frequency*	*Percentage*
No	20	50.0
HTN	10	25.0
CAD	8	20.0
Multiple comorbidities (HTN/CAD/CKD combined)	2	5.0
Total	40	100.0

Out of the 40 patients admitted with acute pyelonephritis with type 2 diabetes mellitus, 32(80%) patients had NEPN and 8(20%) had EPN. Table 3 shows the distribution of fever duration among 40 patients with both T2DM and APN included in a study. It categorizes the number of days with fever and presents the frequency and percentage of patients within each category, separately for patients with and without EPN (presumably, elevated pyelonephritis nephritis score). Patients experienced fever for different periods, ranging from 4 to over 10 days. Similar distribution across EPN and NEPN groups: The percentage of patients in each fever duration category is relatively similar between those with and without EPN.

Table 3: Distribution of subjects of Type 2 Diabetes Mellitus and Acute Pyelonephritis included in the study

	Days		EPN	NEPN	Total
Fever Duration	4-7 days	Frequency	1	5	6
		Percentage	12.5%	15.65%	15.0%
	8 – 10 days	Frequency	3	10	13
		Percentage	37.5%	31.25%	32.5%
	> 10 days	Frequency	4	17	21
		Percentage	50.0%	53.13%	52.5%
Total		Frequency	8	32	40
		Percentage	100.0%	*100.0* %	*100.0*

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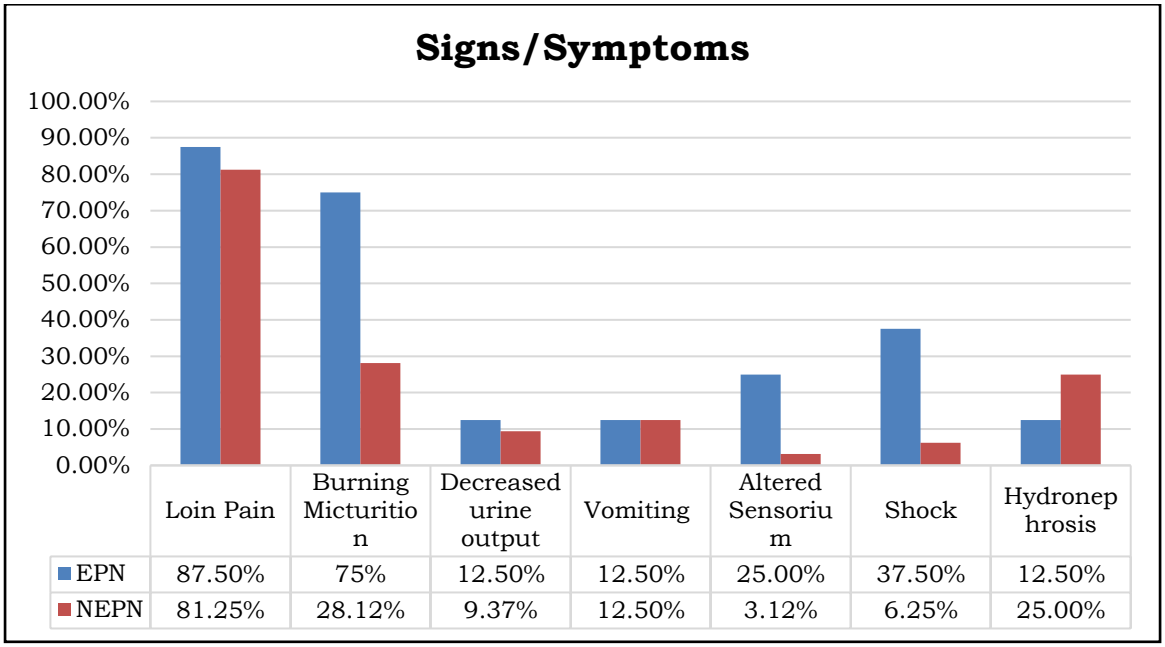
Majority with fever longer than 4 days: Over 80% of patients, regardless of EPN status, experienced fever for at least 8 days. Highest concentration in the >10 days category: Over half (52.5%) of all patients had fever for more than 10 days. Table 3 shows that fever duration in patients with both T2DM and APN tends to be longer, with most experiencing fevers lasting over 7 days. This might indicate the complex interplay of factors like immunosuppression in T2DM and bacterial infection in APN contributing to a protracted inflammatory response. Limited influence of EPN: The comparable distribution of fever duration across EPN and NEPN groups suggests that the severity of pyelonephritis nephritis may not significantly affect the overall length of fever in these patients.

Figure 1 shows the percentage of patients with both T2DM and APN experiencing various symptoms, categorized by whether they have elevated pyelonephritis nephritis score (EPN) or not (NEPN). Over 75% of patients in both EPN and NEPN groups experience loin pain, a hallmark symptom of APN. Burning micturition is also relatively common, affecting 75% of EPN patients and 28.12% of NEPN patients. Decreased urine output and vomiting are reported by less than 15% of patients in both EPN and NEPN groups. the proportion of patients experiencing burning micturition is significantly lower in the NEPN group compared to the EPN group, suggesting its potential association with the severity of pyelonephritis nephritis. EPN score might influence symptom manifestation: The difference in burning micturition prevalence between EPN and NEPN groups suggests that a higher pyelonephritis nephritis score might be associated with more pronounced lower urinary tract symptoms.



	Loin Pain	Burning Micturition	Decreased urine output	Vomiting	Altered Sensorium	Shock	Hydronephrosis
EPN	87.50%	75%	12.50%	12.50%	25.00%	37.50%	12.50%
NEPN	81.25%	28.12%	9.37%	12.50%	3.12%	6.25%	25.00%

Figure 1: Table Showing the signs/symptoms of cases of Type 2 Diabetes Mellitus and Acute Pyelonephritis

A significantly higher proportion of EPN patients exhibit altered sensorium (25%) and shock (37.5%), indicating potential severe complications associated with their pyelonephritis. NEPN group: Notably lower percentages for these severe symptoms (3.12% and 6.25% respectively) suggest a milder presentation of APN. Hydronephrosis: Interestingly, the rate of this kidney obstruction appears higher in the NEPN group (25%) compared to the EPN group (12.5%).

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Table 4 shows the distribution of CECT KUB (Contrast-Enhanced Computed Tomography Kidney, ureter, and bladder) findings in 40 patients with both T2DM and APN, categorized by whether they have elevated pyelonephritis nephritis score (EPN) or not (NEPN). 75% of EPN patients had normal CECT KUB findings, while the remaining 25% exhibited various classifications and specific diagnoses. Among EPN patients with CECT KUB abnormalities, Class 3A appears to be the most frequent category (50%). The specific characteristics of this class are unclear from the provided information. Although less frequent, specific diagnoses like PUJ calculus and renal abscess are observed in both EPN and NEPN groups, highlighting the possibility of additional complexities contributing to APN in these patients.

Table 4: The distribution of cases CECT KUB of Type 2 Diabetes Mellitus and Acute Pyelonephritis

			EPN	NEPN	Total
CECT KUB	Class 1	Frequency	1	0	1
		Percentage	12.5%	0.00%	2.5%
	Class 2	Frequency	2	0	2
		Percentage	25.0%	0.00%	5.0%
	Class 3A	Frequency	1	0	1
		Percentage	50.0%	0.00%	2.5%
	Class 3B	Frequency	1	0	1
		Percentage	12.5%	0.00%	2.5%
	Class 4	Frequency	1	0	1
		Percentage	12.5%	0.00%	2.5%
	ND	Frequency	2	29	31
		Percentage	25.0%	90.62%	77.5%
	PUJ Calculus 2x1 cm	Frequency	0	1	1
		Percentage	0.00%	3.12%	2.5%
	PUJ Calculus 2x2 cm	Frequency	0	1	1
		Percentage	0.00%	3.12%	2.5%
	RT Renal Abscess (2x2 cm)	Frequency	0	1	1
		Percentage	0.00%	3.12%	2.5%
Total		Frequency	8	32	40
		Percentage	100.0%	100.0%	*101.0*

In this study based on the serum creatinine levels, we found increased creatinine levels in 7/8(87.5%) of EPN cases and 12/32(37.5%) of NEPN cases. Table 5 shows the distribution of microorganisms identified in urine cultures of 40 patients with both T2DM and APN, categorized by whether they have elevated pyelonephritis nephritis score (EPN) or not (NEPN). High prevalence of bacterial isolates: In both EPN and NEPN groups, bacterial pathogens were detected in the majority of patients (87.5% in EPN and 90.6% in NEPN). Dominant organism: E. coli: Escherichia coli (E. coli) was the most frequently isolated bacteria in both groups, representing 50% of cases in the EPN group and 56.25% in the NEPN group. Other identified organisms: Other bacteria identified include Acinetobacter, Klebsiella, Pseudomonas, and Candida species (albicans and non-albicans). Similar distribution across groups: The pattern of microbial presence and percentage occurrence is largely similar between EPN and NEPN groups, suggesting no significant influence of pyelonephritis severity score on the type of pathogens isolated. No growth in a small percentage: A small proportion of patients in both

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groups (12.5% in EPN and 9.38% in NEPN) did not show any bacterial growth in their urine cultures.

Table 5: The distribution of microorganisms identified in urine cultures

			EPN	NEPN
Urine culture for microorganisms	Acinetobacter	Frequency	1	3
		Percentage	12.5%	9.38%
	Candida albicans	Frequency	0	1
		Percentage	0.00%	3.12%
	Candida Non albicans	Frequency	0	1
		Percentage	0.00%	3.12%
	E coli	Frequency	4	18
		Percentage	50.0%	56.25%
	Klebsiella	Frequency	1	2
		Percentage	12.5%	0.00%
	No growth	Frequency	1	3
		Percentage	12.5%	938%
	Polymicrobial	Frequency	1	3
		Percentage	12.5%	9.38%
	Pseudomonas	Frequency	0	1
		Percentage	0.00%	3.12%
Total		Frequency	8	32
		Percentage	100.0%	100.0%

Table 6: Treatment strategies for the patients with both Type 2 Diabetes Mellitus (T2DM) and Acute Pyelonephritis (APN)

			EPN	NEPN
Treatment excluding IV antibiotics	DJ Stent RT	Frequency	0	3
		Percentage	0.00%	9.37
	DJ Stent LT	Frequency	0	2
		Percentage	0.00%	6.25
	Antifungals	Frequency	0	2
		Percentage	0.00%	6.25
	DJ Stent (B/L)	Frequency	0	1
		Percentage	0.00%	3.12
	HD	Frequency	0	2
		Percentage	0.00%	6.25
	N	Frequency	4	15
		Percentage	50.00%	46.88
	Nephrectomy (RT)	Frequency	1	0
		Percentage	12.5%	0.00
	PCN (LT)	Frequency	1	2
		Percentage	12.5%	6.25
	PCN (RT)	Frequency	2	3
		Percentage	25.0%	9.37
	URSL(LT)+DJ Stent	Frequency	0	1
		Percentage	0.00%	3.12
	URSL(RT)+DJ Stent	Frequency	0	1
		Percentage	0.00%	3.12
Total		Frequency	8	32
		Percentage	100.0%	100.0%

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Table 6 shows the distribution of non-intravenous antibiotic treatments administered to 40 patients with both Type 2 Diabetes Mellitus (T2DM) and Acute Pyelonephritis (APN), categorized by whether they have elevated pyelonephritis nephritis score (EPN) or not (NEPN). Majority treated without IV antibiotics: Approximately 50% of patients in both EPN and NEPN groups received only non-intravenous antibiotic treatments. While "N" representing conservative management dominates both groups, other interventions like DJ stents (various placements), antifungals, hemodialysis (HD), and per cutaneous nephrostomy (PCN), and ureteroscopy with stenting were also employed with varying frequencies as denoted in table 6. EPN group cases have undergone nephrectomy, suggesting potentially more severe cases requiring surgical intervention. The NEPN group shows higher utilization of DJ stents and antifungals. Among the 8 cases of EPN, 25% (2/8) resulted in fatalities, while 3.12% (1/32) of NEPN patients with altered sensorium levels experienced poor outcomes. This association was statistically significant, with a p-value of <0.01. Additionally, a poor outcome was associated with the presence of shock, and this association was statistically significant, with a p-value of <0.001.

Discussion

Diabetes mellitus (DM) is a prevalent risk factor for urinary tract infections (UTIs). Studies indicate that diabetics face an increased relative risk of UTI, ranging from 1.2 to 2.2 compared to nondiabetics. [7, 8] Among hospitalized patients with acute pyelonephritis, DM is identified as the predominant predisposing cause. [9] Additionally, the severity of UTIs is elevated in individuals with DM, leading to higher hospitalization rates compared to nondiabetics, with 3.4-24.1 times increase in diabetics. Pyelonephritis in DM often presents as bilateral and is associated with more significant complications. While urinary tract infections (UTIs) in diabetic individuals are typically more severe, the range of causative organisms for acute pyelonephritis is comparable to that in nondiabetics. In this study, Escherichia coli (E. coli) was identified in the urine culture of 55% of patients. Emphysematous pyelonephritis (EPN) is a severe and necrotizing renal infection that can lead to high morbidity and mortality, especially when diagnosis and subsequent interventions are delayed. This study found limited statistically significant differences in presenting clinical features between non-EPN and EPN cases. Diagnoses were often incidental, emphasizing the need for early imaging in diabetics with suspected acute pyelonephritis due to the significant differences in management approaches. EPN cases were confirmed through CT scans, known for their high sensitivity compared to other imaging modalities. [9] Approximately 50% of patients exhibited no comorbidities other than diabetes mellitus. Irrespective of EPN status, over 80% of patients endured fever for a minimum of 8 days. Notably, more than half (52.5%) of all patients experienced fever lasting beyond 10 days, with a concentration in this duration category. Loin pain, a hallmark symptom of APN, was observed in over 75% of patients across both EPN and NEPN groups. Burning micturition was relatively common, affecting 75% of EPN patients and 28.12% of NEPN patients. Both decreased urine output and vomiting were reported by less than 15% of patients in both EPN and NEPN groups. The optimal approach to managing EPN remains a subject of debate. Initial management involves fluid and electrolyte resuscitation, antibiotic administration, glycemic control, and relief of obstruction. Subsequently, the choice arises between continuing medical management alone or opting for percutaneous drainage (PCD) or surgical nephrectomy. While a few reports indicate success with medical therapy alone, it generally carries the highest mortality rates. [10-12] Consequently, surgical therapy was traditionally considered the gold standard for EPN treatment until the early 1990s. However, over the last two decades, PCD coupled with antibiotics has gained increasing

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recognition as an effective approach for managing EPN. In this study, DJ stents were placed in either the right (RT), left (LT), or both (B/L) kidneys to aid drainage. Hemodialysis (HD) was done for patients with severe kidney dysfunction. Per cutaneous nephrostomy (PCN) was done to remove kidney stones. Ureteroscopy with stenting was done to diagnose and treat ureteral obstruction, often with the placement of a stent. Nephrectomy: was performed in one of the cases EPN group, suggesting a more severe case requiring kidney removal. The poor outcomes of the present study could be explained by the presence of diabetes, bilateral pyelonephritis, and delayed institution of antibiotics. Mortality was reported in 25% and 3.12% of patients with EPN and NEPN respectively ($P = 0.03$). Poor outcomes were reported more often in EPN compared to NEPN.

Conclusion

Diagnosing emphysematous pyelonephritis (EPN) in diabetic patients with pyelonephritis symptoms, particularly with poorly controlled blood sugars, requires a high suspicion index and early imaging. Most affected individuals are aged 51-70 years. Cases of both non-emphysematous (NEPN) and EPN are predominantly associated with gram-negative bacteria. EPN patients in Class I-IIIA respond well to antibiotics or additional percutaneous drainage (PCN), while Class IIIB-IV cases may require nephrectomy. Altered sensorium and shock at presentation indicate a poor prognosis. Diabetic pyelonephritis can lead to renal failure and high mortality.

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