

# Role of Minimally Invasive Urological Intervention in Acute Pyelonephritis - A Prospective Study

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## Abstract

**Introduction:** Acute Pyelonephritis (APN) is an acute bacterial infection of the renal pelvis and parenchyma. The clinical spectrum ranges from mild cystitis to severe Emphysematous Pyelonephritis where there is destruction of the parenchyma with gas formation.

**Aim:** To analyze factors determining need for Double J stenting in patients with Acute Pyelonephritis and also to study the clinical profile and predisposing factors associated with Acute Pyelonephritis.

**Materials and Methods:** A prospective study was conducted on 100 patients with pyelonephritis. These patients were subdivided into Group 1 (n=52, who had DJ stenting done) and Group 2 (n=48, who were conservatively managed).

**Statistical Analysis:** Descriptive statistics frequency analysis and percentage analysis were used for categorical variables and the mean and S.D. was used for continuous variables. To find the significance in categorical data Chi-square test and Fisher's exact test were used.

**Results:** Presence of turbid urine is one of the symptoms that needed DJ stenting. Patients with emphysematous pyelonephritis more often needed DJ stenting. Serum creatinine was initially high at presentation in most patients in both groups. However, in Group 2, all patients reached normal nadir levels with conservative management. In group 1, none of them had normal levels reached with conservative measures.

**Conclusions:** Factors that decided the final outcome included gross pyuria, significant fever spikes despite medication, persistent loin tenderness, persistently high total count despite medication, persistently high serum creatinine, thrombocytopenia, positive blood or urine culture and HbA1c > 9.2%. The presence of 2 or more of the above factors in a patient indicates need for stenting in APN cases.

**Key words:** Cystitis, Hydroureteronephrosis, Thrombocytopenia, Ureteric stent, Serum Creatinine

## INTRODUCTION

Acute pyelonephritis (APN) is an acute bacterial infection of the renal pelvis and parenchyma.<sup>[1]</sup> Majority of these infections are acquired by ascending infections from the lower urinary tract.<sup>[2]</sup> They may also be acquired by hematogenous route. Diabetes is a common predisposing

factor in these cases.<sup>[3]</sup> The clinical spectrum of APN may range from a very mild presentation which may mimic cystitis to a florid and severe infection in the form of emphysematous pyelonephritis where there is a destruction of the parenchyma with gas formation.<sup>[4]</sup>

These patients present with a definite set of symptoms and signs, with varying severity. Based on the severity and clinical condition of the patient, the decision of medication, stenting, or in rare cases nephrectomy, as a treatment option is taken. Nephrectomy is reserved for severe infections - emphysematous pyelonephritis with endotoxemia and with frank pus formation and parenchymal destruction. If the disease occurs bilaterally,

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care is taken for conservation of nephrons to prevent the patient from becoming anephric.

Patients with APN are primarily started on broad-spectrum antibiotics and response monitored.<sup>[5]</sup> If responding well, antibiotics continued and changed as per culture report and the patient recovers with conservative measures. If not responding, patients may require interventions in the form of Double J stenting (DJS) to drain the infection.<sup>[6]</sup> Although hydronephrosis may not be seen in these cases, it is proven that infection *per se* can lead to decreased or aperistalsis of the ureter and impede drainage or could be the presence of necrosed papilla causing obstruction.<sup>[7,8]</sup> These patients benefit from DJS.

Thus, conservative therapy is a first step modality of the treatment for these patients before subjecting them to DJS. However, this is a gray zone, with no definite protocol that helps decision-making easy for the treating doctor. The purpose of this study was to analyze the factors determining the need for DJS in patients with APN and also to study the clinical profile and predisposing factors associated with APN.

## MATERIALS AND METHODS

A total of 100 patients were recruited in the prospective study. Ethics committee clearance and permission from the institutional review board to carry out the study were obtained. Informed consent was taken from all the patients before including them in the study. These patients were subdivided into Group 1 (who had DJS done) and Group 2 (who were conservatively managed). All patients admitted with diagnosis of APN, including emphysematous pyelonephritis in the Department of Urology, Sri Ramachandra Medical College and Research Institute, from September 2015 to March 2017 were included in our study. Patients with pyonephrosis or perinephric abscess, who either needed percutaneous nephrostomy or an external drainage of the collection were excluded from our analysis group. All patients who presented to the hospital either in the outpatient department or in the emergency department with complaints of fever, chills, rigors, nausea, vomiting, and dysuria, were evaluated and imaging done as appropriate. If ultrasound proved bulky kidney or perinephric fat stranding or perinephric fluid collection, or if clinically strong suspicion of APN was present, a plain computed tomography (CT) KUB (with contrast enhanced, if the renal parameters were not raised) was done.

On admission, all history and previous hospital admissions and treatment history data were collected, including age, sex, duration of illness, duration and treatment of diabetic status, hypertensive history, previous kidney

disease, stone disease, or previous urological intervention and documented. Patients underwent complete physical examination including looking for a rise in body temperature, tachycardia, abdominal, or renal angle tenderness, and a baseline laboratory investigations including complete blood count (CBC), random blood sugar, total count, renal function test, serum electrolytes, hemoglobin A1c (HbA1c), urine routine microscopy, urine culture, blood culture, and sensitivity.

Patients were initially started on broad-spectrum antibiotics usually consisting of third-generation cephalosporins with or without aminoglycosides, which were then changed to culture-specific antibiotics subsequently as required.

Patients who responded well to medical treatment were continued with the same conservative treatment until full recovery. Those patients who did not respond in terms of persistent fever spikes, unexplained tachycardia, bothersome tenderness, grossly elevated total counts, and/or high serum creatinine values were deemed as non-responders and were subsequently switched over to the DJS group. On the other hand, if the patients presented with either a failed trial of conservative measure elsewhere, or if they had gross symptoms or clinical signs or parameters warranting emergency intervention, they were taken up in the stented group straightaway. The clinical and laboratory parameters which were significantly present in these non-responders were analyzed. Post-operative resolution of symptoms was monitored and documented.

## Statistical Analysis

Our study data were collected and variables categorized as parametric or non-parametric variables. To describe the data, descriptive statistical frequency analysis and percentage analysis were used for categorical variables, and the mean and standard deviation was used for continuous variables. To find the significant difference between the bivariate samples in independent groups, the unpaired sample *t*-test was used. To find the significance in categorical data, Chi-square test and Fisher's exact test were used.

## RESULTS

A total of 100 patients were analyzed in our study. Of those, 52 patients who underwent DJS were in Group 1 and the remaining 48 who were conservatively managed were in Group 2. Table 1 summarizes the demographic data of the patients studied. The mean age of patients in our study was 60 years. The youngest was 14 years and the oldest was 90 years. Females were slightly more commonly affected ( $n = 54$ ) by urinary tract infection (UTI) than

**Table 1: Demographic data of the all the 100 patients studied**

Demographic data	Group 1	Group 2
Median age	60	59
Sex		
Male (n=46)	24	22
Female (n=54)	30	24
Laterality		
Right	17	20
Left	20	26
Bilateral	15	2
Diabetes mellitus (%)	92	89
Mean HbA1c	10.2	7.3
Mean serum creatinine levels on admission	3.8	2.5
Mean nadir creatinine levels at discharge	1.4	1.2
Mean total count levels on admission	17758	16085
Mean total count levels at discharge	8594	8338
Associated comorbidities n (%)		
Chronic kidney disease	26 (25)	24 (25)
Coronary artery disease	50 (96)	6 (12.6)
Previous UTI	7 (13.5)	15 (31.3)
Previous endoscopic instrumentations	7 (13.5)	6 (12.5)

HbA1c: Hemoglobin A1c, UTI: Urinary tract infection

**Table 2: Details of the symptomatology and clinical signs of the patients studied**

Features	Group 1	Group 2	P value
Symptoms (n=52+48=100)			
Fever	52	47	0.4800
Chills/rigor	52	5	<0.0001*
Loin pain	46	26	<0.0001*
Lower tract symptoms	30	22	0.3166
Nausea/vomiting	46	30	0.0043
Turbid urine	41	1	<0.0001*
Signs (n=52+48=100)			
Temperature>100 F	52	16	<0.0001*
Persistent tachycardia	52	28	<0.0001*
Palpable tender kidney	50	30	<0.0001*
Leukocytosis	41	36	0.6665
High serum creatinine (at presentation)	41	38	0.3747
Nadir creatinine reaching normal levels	0	38	<0.0001*
Thrombocytopenia (<1 lakh/cub mm)	46	10	<0.0001*
HbA1C levels>9.0	46	18	<0.0001*
Urine microscopy (n=52+48=100)			
Glycosuria	12	8	0.4628
Proteinuria	19	9	0.0736
Urine culture positivity (%)	32	8	<0.0001*
Blood culture positivity (%)	22	1	<0.0001*

Chi-square test done to find the significance in categorical data. Values marked \*indicates statistically significant value with P&lt;0.05. HbA1c: Hemoglobin A1c

men (n = 46). The left kidney was more affected than the right. Overall, 46% left sided, 37% right sided, and 17% were bilateral. Diabetes mellitus constituted the single most common associated condition that predisposed to APN. About 84% (n = 84) of our study population were diabetics. The distribution of diabetics in both the groups was almost identical. The other comorbidities such as chronic kidney disease and coronary artery disease were

more or less equal in both the groups. About 45 patients have had previous UTIs and 26 of them have had a history of previous endourological instrumentation.

Table 2 summarizes the symptomatology and clinical signs of the patients studied. The most common presenting complaints are fever with chills and rigors and loin pain. Nausea, vomiting, dysuria, and pyuria were the other common symptoms observed. From Table 2, it is well evident that if the patient has chills and rigor, nausea and vomiting, or severe loin pain, there is a higher chance that they need DJS. The presence of turbid urine is one of the symptoms that needed DJS, and the difference between the two groups was statistically significant. Similarly, the presence of palpable tender kidney with a high temperature of more than 100 F with persistent tachycardia also pointed toward a higher need for DJS. Moreover, leukocytosis was observed in both groups, and the difference was not statistically significant. Serum creatinine was initially high at presentation in most patients in both groups. However, in Group 2, all patients reached normal nadir levels with conservative management. In Group 1, none of them had normal levels reached with conservative measures. Thrombocytopenia was another significant finding that was more often associated in Group 1. The difference between the groups was statistically significant. Positive cultures in urine and blood were also significantly seen in Group 1 than the other group.

Table 3 summarizes the CT findings in both the groups. From Table 1 could infer that features of APN such as inflamed kidney with increased parenchymal thickness, perinephric, and periureteric stranding are seen in both the groups. Patients with emphysematous pyelonephritis more often needed DJS. However, associated stones and hydronephrosis were more commonly seen in Group 1 but with no statistically significant difference from the other group.

## DISCUSSION

Pyelonephritis describes a severe infectious and inflammatory disease of the renal parenchyma. The major causative pathogens of APN are Gram-negative bacteria.<sup>[9,10]</sup> *Escherichia coli* cause approximately 60–80% of uncomplicated infections.<sup>[11,12]</sup> Other Gram-negative pathogens include *Proteus mirabilis* as well as *Klebsiella*, *Enterobacter*, and *Pseudomonas* species. *P. mirabilis* does not commonly cause urinary tract infections in normal hosts but is frequently associated in patients with complicated UTIs. This is more prevalent in those who present with functional or anatomical abnormalities and in those with urolithiasis or a chronic indwelling urinary catheter.<sup>[13]</sup> In

**Table 3: Radiological findings in both the groups**

Demographic data	Group 1 (n=52)	Group 2 (n=48)	P value
Radiological findings (n=100)			
Acute pyelonephritis	40	42	0.2000
Emphysematous pyelonephritis	6	0	0.0274*
Associated stones	3	0	0.2436
Associated hydronephrosis	3	0	0.2436

Chi-square test done to find the significance in categorical data. Values marked \*indicates statistically significant value with  $P < 0.05$

older hospitalized patients, because of increased usage of catheters (portals to infection), Gram-negative organisms such as *P. mirabilis*, *Klebsiella*, *Serratia*, and *Pseudomonas* are more common etiologies.<sup>[14,15]</sup>

Pyelonephritis occurs predominantly in the diabetic population. The presence of glucose in urine is considered to enhance bacterial growth.<sup>[16]</sup> In our study, diabetes was an important prognostic factor. Although diabetes was commonly found in both groups, the levels of uncontrolled sugar were detrimental in deciding between two treatment modalities. The chances of a conservative medical treatment are inversely proportional to the blood sugar levels. Random blood sugar values were found to be variable with daily monitoring, but the HbA1c was found to be consistent with prognosis of the disease. Higher value of HbA1c (>9%) indicated lesser chance of resolution with medical management alone. In a retrospective study over 68 patients with pyelonephritis, the prevalence of diabetes was found to be as high as 36.8%.<sup>[17]</sup> In one of the largest prospective, observational, multicenter cohort studies of women with APN, involving 1062 women, Wie *et al.* concluded that diabetes mellitus constituted a major risk factor for early clinical failure of patients with community-onset APN.<sup>[18]</sup> In yet another retrospective chart review on 225 patients, Efstathiou *et al.* demonstrated that diabetes mellitus and immunosuppression lead to a prolonged hospital stay and a longer convalescence period.<sup>[19]</sup>

Emphysematous pyelonephritis is almost exclusively seen in diabetics with poorly controlled sugar levels. The high glucose levels in the tissue provide the gas-forming organisms a suitable environment for their rapid growth and rapid catabolism, which produces massive production of gases.<sup>[20,21]</sup> In cases with ureteric obstruction, hydronephrosis may increase the pelvicalyceal system pressures and compromise renal circulation and result in impaired transportation of gases and subsequent creation of gas chamber, compounded by diabetic nephropathy and result in further accumulation of gases in the pelvicalyceal system.

A report of fever and chills, flank pain, and irritative voiding symptoms (e.g, urgency, frequency, and dysuria)

in a female patient should prompt a workup. Other key symptoms include nausea or vomiting. The triad of flank pain, fever, and nausea and vomiting occurs much more often in patients with pyelonephritis than in those with cystitis.<sup>[22]</sup> Symptoms such as fever with chills and rigors, loin pain, and nausea were the predominantly common presenting complaints noted in our study. Between the groups, symptoms of fever, chills and rigors, nausea, and loin pain were constant in the stented group. These were similar to findings by Wie *et al.*<sup>[18]</sup>

Temperature >100.4°F (38.0°C) is a key finding supporting the diagnosis. In one study, temperature  $\geq 100^\circ\text{F}$  (37.8°C) was strongly correlated with APN.<sup>[23]</sup> All these three clinical signs were analyzed and found to be statistically significant. This indicates that the presence of fever spikes, tachycardia, and loin tenderness predisposed the patient to enter the stenting group.

Urinalysis shows pyuria, bacteriuria, and varying degrees of hematuria. Turbidity and proteinuria were more commonly seen in the stented group, with more number of normal test results being found in the non-stented group.

The commonly noted organism in culture was *E. coli*, noted in 25 cases. *Klebsiella* species noted in 4 patients, *Enterobacter* species in 2 patients, and *Candida* species in 1 patient. These were similar to results noted in Christopher *et al.*<sup>[24]</sup> In a total of 1062 women patients in study by Wie *et al.*, 784 (73.8%) gave positive urine cultures. *E. coli* was the most common pathogen (90.3% in 708 patients).

Bacteriuria was accompanied by bacteremia (with the same pathogen) in 60 men (58.8%) and 75 women (60.9%).<sup>[19]</sup> Blood cultures are indicated in all patients. Blood cultures are positive for the causative pathogen in approximately 10–20% of women with acute uncomplicated pyelonephritis. Blood C/S - shows the presence of blood culture being positive as a strong indicator of patient requiring stenting as a treatment option.

Other initial laboratory tests indicated in the initial workup are CBC, erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP). The CBC shows elevated



total leukocyte counts, decreased platelet counts, ESR elevation, and CRP elevation and all are in favor of acute inflammatory process in the system, helpful in diagnosis.

Total counts found to be one of the parameters reflecting the severity of infection in the blood. WBC counts of >20,000/cubic mm were significantly found to have early clinical failure after the treatment of pyelonephritis.<sup>[18]</sup> In our study, total count being elevated and persistently elevated despite medical management indicated need for DJS for better outcome. The falling trend of total counts was noted and documented and observed that patients with total count responding to medical therapy predominantly settled with medication alone and patients with total count not responding to medicines were candidates who required stenting for disease resolution.

The platelet count turned out to be a prognostic factor, with high levels signifying better recovery and lesser chance of need for DJS and lower platelet counts being clinically more toxic, requiring DJS. This was similar to the finding noted by Chung *et al.*<sup>[17]</sup>

The derangement of renal parameters was the most commonly noted laboratory finding. The trend of serum creatinine rise/fall was studied and was taken as a variable to be included in our study. The trend was found to be statistically significant and was similar to the results of Wie *et al.*<sup>[18]</sup>

Computerized tomography of kidney, ureter, and bladder gives excellent anatomic detail and helps us in clearly establishing the diagnosis. CT study can often be useful when patients are not responding to treatment as expected or after 72 h.<sup>[25,26]</sup> CT study with the presence of emphysematous pyelonephritis, stone, or Hydroureteronephrosis (HUN) was strong factors tilting treatment outcome toward DJS group.

The main goals of treatment are infection control and symptom reduction. The decision whether to treat the patient empirically, and whether to admit the patient for intravenous antibiotic treatment, should be based on the patient's symptoms and comorbidities.

The role for stenting in APN with obstruction due to necrosed papilla, turbid pus flakes or stone are straightforward. It is also accepted and recommended for DJS in pyelonephritis even in the absence of hydronephrosis, due to - ureteric dyskinesia. Infection *per se* can cause decreased ureteric mobility by two mechanisms - bacterial toxins acting directly on the ureteric smooth muscle and bacteria producing products - act on ureteral peristalsis mechanism.<sup>[27]</sup> These products

are – inflammatory exudates, histamine, serotonin, bradykinin, and prostaglandin.<sup>[28]</sup>

The highly statistically significant factors ( $P = 0.001$ ) in our study included gross pyuria, significant fever spikes despite medication, persistent tenderness, persistently high total count despite medication, persistently high serum creatinine, low platelet counts, positive blood culture, and HbA1c >9%. These factors were analyzed between the stented and the non-stented groups, and it was inferred that the presence of one factor made medical management a viable option. Patients with two or more of these factors make DJS the ideal treatment option. In our study, majority of the patients had more than five positive factors and hence carried a poorer outcome.

### Limitations of the Study

Most of the patients referred to our center had tried a conservative treatment elsewhere before being referred to us. Being a tertiary care referral hospital, many such patients were admitted in a critical stage, necessitating an early intervention. If the number of patients in each group was higher, interpretation of the data would have had much more relevance. Resistance to antibiotics was yet another major factor that tilted the balance toward early intervention. As most of the patients had received a variety of antibiotics before reaching our hospital, the urine culture done at our center had grown pan-resistant strains that prompted us to directly recruit the patients in Group 1.

### Future Recommendations

The physicians must be aware that pyelonephritis is a clinical condition that if diagnosed early and treated appropriately, can be fully treated. A study with more number of patients recruited in each arm would give us a much better data that could convince our statistical analysis in a better way. General practitioners and physicians must be forewarned about the possibility of pan-resistant organisms in cases of antibiotic abuse.

### CONCLUSIONS

A high index of clinical suspicion, identification of the unfavorable prognostic parameters, and an early intervention are required to achieve a better outcome in such patients. The presence of poor prognostic factors like gross pyuria, high temperature, persistent loin tenderness, persistently high total count, persistently high serum creatinine, thrombocytopenia, positive blood or urine culture, and HbA1c of more than 9% strongly suggest a need for a minimally invasive urological intervention. The presence of air in the parenchyma or the collecting system

or hydroureteronephrosis on CT imaging is an indication for DJS for disease resolution.

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