EMPHYSEMATOUS PYELONEPHRITIS-THE ROLE OF RENAL CONSERVATION

Dissertation submitted for
M.Ch Higher Speciality Degree Examination

Branch IV – UROLOGY

DEPARTMENT OF UROLOGY
KILPAUK MEDICAL COLLEGE & HOSPITAL,
GOVT. ROYAPETTAH HOSPITAL
CHENNAI .

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI
AUGUST-2007

Certificate

This is to certify that this dissertation entitled **"Emphysematous pyelonephritis-The Role of Renal conservation"** is the bonafide work done by **Dr.A.V.Gokul** under our direct guidance and supervision in the Department of Urology, Kilpauk Medical College Hospital & Govt. Royapettah hospital, Chennai, **,** in fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University for the award **of M.Ch Higher Speciality degree, Branch IV – Urology** during this period of study from Aug 2004 - Aug 2007.

Prof.P.Vairavel MS,DGO,MCh
Professor and Head,
Department of Urology ,
Kilpauk Medical College ,
Chennai – 600010.

Prof.K.ThiyagarajanMS, MCh,DNB,
Professor,
Department of Urology,
Govt. Royapettah Hospital ,
Chennai – 600013.

Date :

Place : Chennai

Dr.M.Dhanapal MD., DM

The Dean,

Kilpauk Medical College and Hospital,

Chennai – 600010

Acknowledgements

I wish to express my heartfelt gratitude to **Prof. P. Vairavel** MS, DGO, MCh., Professor and Head of the Department of Urology, Kilpauk Medical College, **Prof. K. Thiyagarajan** MS, MCh, DNB., Professor of Urology, Govt. Royapettah Hospital and **Prof. M. G .Rajamanickam** MS; MCh, Retired Professor and Head of Department of Urology, Kilpauk Medical College & Govt. Royapettah Hospital for the invaluable encouragement, advice and support they have lent from the time of conception to the time of completion of this study.

I am deeply indebted to **Dr.Muthulatha, Dr.Ilangovan, Dr.Leela Krishna, Dr.Deepak, Dr.Jayaganesh, Dr.Sivasankar and Dr.Senthilvel** for all the encouragement and support they have given to me during my course

I also express my gratitude to all my colleagues in the Department of Urology, Kilpauk Medical College Hospital & Govt. Royapettah Hospital, Chennai, for all the help they have rendered during my entire course here.

A special mention to **Dr. Thangavel**, epidemiologist, Mediscan Systems who by his statistical prowess and enthusiastic support has made this study see the light of the day.

I would also like to express my gratitude to **Dr. M. Dhanapal** MD,DM , Dean, Kilpauk Medical College for all the help he has rendered during my course here.

Last, but not the least, I thank my **family members** and my **blessed teachers** right from my school days, whose unfailing love, prayers and dedication have always been my source of inspiration for all my endeavours.

I finally dedicate this work in the name of the **Almighty** to all my patients who have been and shall continue to be my greatest teachers.

Chennai

May 2007

INTRODUCTION

Emphysematous pyelonephritis was first reported by Kelly and MacCallum in 1898[1] and was considered to be rare. The term EPN was first used by Schultz and Klorfein [2] and is applied when gas is formed only in or around the kidney[3]. The lack of a strict definition of EPN has resulted in the use of multiplicity of terms, such as renal emphysema, pneumonephritis, pyelonephritis emphysematosa and pneumonephrogram. As suggested by Schultz and Klorfein, emphysematous pyelonephritis is the preferred designation[4].

Gas-forming bacteria using glucose as a substrate cause necrotizing lesions in infected tissue, especially in diabetic patients or those with an obstructive urinary tract infection. EPN can be complicated by acute sepsis, resulting in a poor prognosis. Thus the disease presents a urologic emergency[5]. It deserves special attention because of its life-threatening potential. Mortality

rates associated with Emphysematous pyelonephritis vary from 7 to 75% [6,7] .

It has generally been regarded as a rare infection in the earlier reports. However, with the more extensive use of ultrasonography and computed tomography in the evaluation of patients with features of sepsis or complicated urinary tract infection (UTI), more cases of Emphysematous pyelonephritis (EPN) are being recognized. Huang et al believe that EPN is not rare and should be considered an important clinical entity [8].

Traditional therapy for emphysematous pyelonephritis was nephrectomy or open surgical drainage and appropriate antibiotics[6]. Hudson et al first described fluoroscopic guided percutaneous drainage for the treatment of emphysematous pyelonephritis[9]. The definitive treatment is nephrectomy. In patients with a general condition that prevents them from tolerating general anesthesia, medical therapy consisting of intravenous antibiotics and glycemic control measures with or without percutaneous drainage is often applied. However this is a disease

that most commonly affects diabetics- a systemic disease with proven hazardous effect over the other uninvolved kidney in the long run. Moreover emphysematous pyelonephritis can be a bilateral problem in 10%[10] and can affect solitary kidneys. These are the instances when renal conservation becomes more preferable.

AIMS AND OBJECTIVES

1) To study the feasibility of renal conservation in emphysematous pyelonephritis.

2) To analyse the various prognostic factors that favour renal conservation in emphysematous pyelonephritis.

REVIEW OF LITERATURE

Definition:

Emphysematous pyelonephritis is a severe acute bacterial infection of the kidney characterized the presence of gas within the renal parenchyma, collecting system or perinephric tissue [6,11] .

Controversy still exists on whether distinguishing gas accumulation within the renal parenchyma from gas in the perinephric tissue is necessary.

Some investigators suggested that the term emphysematous pyelonephritis should be applied only to gas formed within the renal parenchyma, whereas most prefer to include both conditions under the same designation[6]. The latter definition is favoured because it includes all the possible manifestations of gas-forming acute renal infections [8].

Sites:

Gas-forming infections can develop anywhere in the upper or lower urinary tracts, as follows:

1. in the renal parenchyma (emphysematous nephritis)
2. calyx and pelvis (emphysematous pyelitis)
3. ureter(emphysematous ureteritis)
4. urinary bladder (emphysematous cystitis) [12].

Etiology:

Emphysematous pyelonephritis occurs almost exclusively in patients with diabetes mellitus(DM),but occasionally in patients without DM along with obstruction of the corresponding renoureteral unit [8,11,13,12].

In 1941 Gillies and Flocks stated that three factors are essential for spontaneous gas formation in the kidney:

1) Obstruction of the urinary tract

2) Uncontrolled diabetes mellitus

3) Gas producing organisms [6]

4) Defective immune system [6,14] .

Causative organisms:

The main causative organisms in EPN are those normally found in urinary and gastrointestinal tracts. In the study by Michaeli et al [6], Escherichia coli was the most common organism (71%). In 19% of the cases >1 organism was present. *Aerobacter aerogenes* and *Proteus mirabilis* were isolated in some patients. Whenever an organism was found in the kidney at operation it was identical to that found in urine culture. Anaerobic bacteria were grown only in 1 of 54 cases [6].In the study by Huang et al, pathogens was identified in 98% of cases. *E.coli* was the commonest organism isolated (69%), *K.pneumoniae* was the second (29%). Two patients out of 48 had *E.coli* infection mixed with *Streptococcus spp.* or *Proteus spp*. Anaerobic organisms were not obtained [8].Thus the most common organism grown is *E.coli* followed by *Klebsiella*. *Proteus, Pseudomonas, Aerobacter aerogenes ,Streptococcus* and rarely anaerobes, *Candida albicans* and *Cryptococcus* may be grown[15].

Role of diabetes mellitus:

EPN most commonly occurs in diabetics. Diabetic patients are compromised hosts and they have an impaired defense mechanism for bacterial infection[14].In Michaeli et al's study, diabetes mellitus occurred in 87 of the patients. Though it has long been postulated that EPN is found exclusively in uncontrolled diabetics, it has also been reported in non diabetics and diabetics with excellent diabetes control. In the non diabetic patients, EPN is almost always associated with ureteral obstruction[6]. It has been postulated that high tissue glucose levels provide the substrate for the organisms to produce carbon dioxide and hydrogen via the fermentation of sugar[6].

The role of obstruction

Obstruction was present only in 40% of patients of Michaeli et al [6]. He refutes the notion that obstruction of the

urinary tract is necessary for gas formation. However, most of the patients with bilateral EPN and EPN in solitary kidneys had urinary tract obstruction. In the non diabetic patient, EPN nearly always is associated with ureteral obstruction[6]. In Huang et al's study, 22% of diabetics and all the non diabetics (2 patients) had associated urinary tract obstruction. Urinary tract obstruction also occurred more frequently in the left kidney than the right one (64% vs 36%)[8].

Pathophysiology

It has been postulated that high tissue glucose levels provide the substrate for the organisms to produce carbon dioxide and hydrogen via the fermentation of sugar[6].

Two important features found commonly in EPN are severe necrotizing infection and impaired vascular supply manifested by intrarenal thrombi and renal infarctions. These findings support the theory of Schainuck and associates[16],

emphasizing the importance of impaired tissue and vascular response, which enables organisms capable of producing carbon dioxide to use necrotic tissue as a substrate for gas generation. Local factors (obstruction and diabetic glomerulopathy) and systemic factors (increased risk of infectious complications associated with diabetes mellitus) contribute to tissue and vascular damage. Accordingly, it is the impaired host response and not hyperglycemia per se that predisposes to gas production in necrotic tissue. It has been suggested that gas formation may not associated inevitably with infection. The impaired host response theory is a feasible explanation for the presence of EPN in patients without diabetes or, possibly, even in those without evidence of infection. In patients with diabetes mellitus and EPN both mechanisms (sugar fermentation and defective host response) may coexist and explain the origin of profuse gas production[6].

Mechanism of Gas Formation

The actual mechanism of gas formation is controversial. Growing organisms require a constant supply of metabolic energy. The bacteria obtain their energy through fermentation of glucose. This proceeds via the glycolytic (Embden-Meyerhof) pathway, by which two molecules of adenosine triphosphate (ATP) are produced, nicotinamide adenine dinucleotide (NAD+) is converted to nicotinamide adenine nucleotide dehydrogenase (NADH), and pyruvate is generated in the process as end product. A variety of pathways have evolved in the microorganism for the reoxidation of NADH by pyruvate or its derivative. These pathways include lactic fermentation (*streptococcus*, *lactobacillus*), Alcoholic fermentation (many Yeasts, a few bacteria), mixed acid (formic acid) fermentation (most *Enterobacteriaceae*), butyric fermentation (*Clostridium*), butanediol fermentation (*Enterobacter*) and propionic fermentation (*Propionibacterium*).The formate produced by *Enterobacteriaceae spp.* in mixed acid fermentation is

relatively stable in alkaline pH. However the fermentation reactions lead to the accumulation of acids and when the pH reaches 6 or below, a gas forming microorganism like *E.coli*, will form an enzyme, formic hydrogenylase, which converts formic acid into carbon dioxide and hydrogen. The production of hydrogen is the hallmark of mixed acid fermentation because none of the other 5 pathways listed would give rise to hydrogen gas as the end product. Considering the natural tendency for the gas composition of a gas bubble to equilibrate with the surrounding tissue, it is reasonable that the gas will contain reasonable amounts of nitrogen, as well as oxygen, carbon dioxide and hydrogen, trace amounts of ammonia and methane might arise from the fermentation of mixed amino acids that were produced by the degradation of the necrotic tissue[14]. Rarely butyric fermentation of glucose by anaerobes could contribute to the gas.

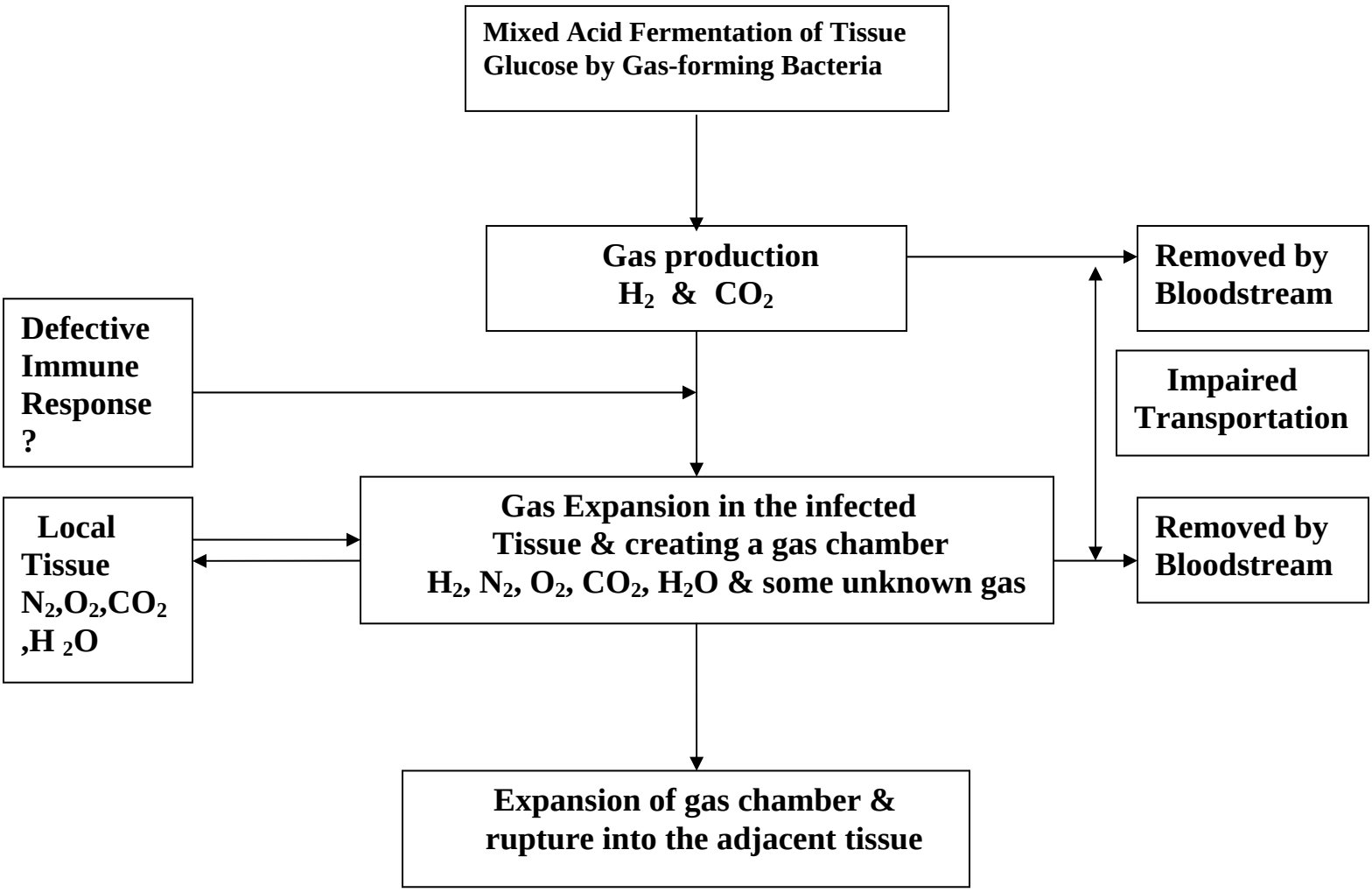
The mechanism of gas chamber(i.e, large gas bubbles) formation has been hypothesized as a series of increased gas production, impaired transportation of gas by vascular

compromise, creation of a gas chamber, equilibrium of gas chamber and tissue gas, and the expansion or collapse of the gas chamber.

Four factors that may be involved in the pathogenesis of EPN include gas forming bacteria, high tissue glucose levels, impaired tissue perfusion, and a defective immune response. High tissue glucose levels in patients with DM may provide gas forming microbes with a microenvironment more favourable for their growth and rapid catabolism, which can cause the massive production of gas [14,17,18] . In case of urinary tract obstruction , the unrelieved obstruction and hydronephrosis may increase the pelvicalyceal pressure and compromise renal circulation, and result in impaired transportation of gas and subsequent creation of a gas chamber(ie, EPN)[8]. Yang and Shen[14] indicated that gas forming infection depends on rapid catabolism and impaired transport of end products at the site of inflammation. Local tissue damage caused by the gas forming bacteria, compounded by the diabetic microangiopathy, would perhaps markedly retard the transport of

catabolic end products away from the lesion and thereby result in the accumulation of gas. In the non-diabetic also, glucose may serve as the substrate for gas formation. In normal non-diabetics, around 20 mg% of glucose may be present and upto 60 mg% with acute or chronic renal disease. Subclinical glucosuria in renal infection may be enough to generate sufficient amounts of gas[12 to 36 cc of gas from 100 mg glucose at S.T.P] [2]. Gas in the urinary tract may originate from bacteria, a fistula between the urinary and gastrointestinal tracts or direct exposure to atmospheric air due to trauma or instrumentation [12].

Fig 1:Pathogenesis of emphysematous urinary tract infection[14]



PATHOLOGY

1) Severe acute and chronic necrotizing pyelonephritis and multiple cortical abscesses.

2) Papillary necrosis.

3) Acute inflammatory cell infiltration with focal necrosis and abscess formation.

4) Evidence of impairment of tissue circulation – infarction, vascular thrombosis, arteriosclerosis and glomerulosclerosis.

5) Features of diabetic nephropathy – Kimmelstiel-Wilson nodules, hyalinized arteriosclerosis and glomerulosclerosis.

The inflammatory findings are limited to the kidney in class 2 EPN, but extend to the perinephric areas in more severe cases.

CLASSIFICATION

Wan et al

Type I

Renal necrosis with either total absence of fluid content on CT or the presence of a streaky/mottled gas pattern demonstrated on radiograph or CT with lung window display.

Type II

Characterized either by the presence of renal/perirenal fluid in association with a bubbly/loculated gas pattern or by the presence of gas in the collecting system.

Type I emphysematous pyelonephritis is associated with more extensive parenchymal necrosis and a more fulminating clinical course than type II [7]

Huang et al Classification.

Class 1 – Gas in the collecting system only (Emphysematous pyelitis)

Class 2 – Gas in the renal parenchyma without extension into the extrarenal 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/Solitary kidney with EPN [8]

Michaeli et al classification

Stage I- Gas within the renal parenchyma or in the perinephric tissues.

Stage II- Presence of gas in the kidney and its surroundings.

Stage III- Extension of gas through Gerota's fascia or presence of bilateral EPN.

Mitra et al classified renal emphysema into two distinct entities and claimed that this classification had important prognostic and therapeutic implications.

1) **Emphysematous pyelitis** : A milder form with gas limited to the renal pelvicalyceal system. It is commonly associated with obstructive uropathy[6,19]. It responds well to conservative mode of therapy with or without a drainage procedure.
2) **Emphysematous pyelonephritis** : Gas extends further into the renal parenchyma, perinephric tissues and to retroperitoneum. It is a serious clinical condition with a high mortality and morbidity. In addition to medical treatment more aggressive surgical management viz., nephrectomy has been recommended to improve survival [15].

CLINICAL PRESENTATION

EPN presents mostly in adults [20].Juvenile diabetics do not appear to be at risk. Women are affected more often than men [21]. The usual clinical presentation is severe, acute pyelonephritis that fails to resolve during the first 3 days of treatment. In some

cases, a chronic infection precedes an acute attack. Almost all patients display the classic triad of fever, vomiting and flank pain[16]. Pneumaturia is absent unless the infection involves the collecting system. Results of urine cultures are invariably positive. Most frequently identified organism is E.coli; Klebsiella and Proteus are less common. Michaeli, in his review of 55 patients reported chills, fever(56%) , flank pain(48%) , Lethargy and confusion(24%) , Nausea and vomiting (16%), shock and coma(16%). Fever of unknown origin was the presenting feature in 18%. Pneumaturia was not very common. The average duration of symptoms before diagnosis was 21 days- the range being 0.5 to 240 days[6]. Huang et al reported fever in 79%, nausea/vomiting in 17% shock in 29%, altered consciousness in 19% and acute renal functional impairment in 35% of patients [8].

The incidence of diabetes was very high, 80%(Shokeir et al [12]), 96%(Huang et al [8]), and 87%(Michaeli et al [6]).

The side of involvement was predominantly left (60% in Shokeir et al's study[12] and 47% (Bum Soo Park et al)[5.].Bilateral presentation ranged from 5% [12] to 20% [22].

The most common localizing sign is costovertebral angle tenderness[5]. Leukocytosis is seen in about 67% and thrombocytopenia in 46%[8]. Patients may present in a state of medical emergency viz., diabetic ketoacidosis.

MICROBIOLOGY

The most common organism grown is E.coli (69% to 71%) followed by Klebsiella (29%)[8,6]. Bacteremia is found in almost half of all the cases and usually the same organisms are grown in urine , blood and tissue cultures[8,12]. More than one organism is isolated in around 19% of cases[6].

RADIOLOGY

The definitive modality of diagnosis of EPN is radiology. Radiology not only confirms the diagnosis, but also helps to classify EPN hence guiding the management and

prognostication of the disease. X-ray, USG and CT scan all help in the diagnosis. CT is the best modality for confirmation of the diagnosis. It defines the extent of gas dissemination very accurately and rapidly. It can precisely stage the gas distribution.

The USG [Ultrasonogram] helps in diagnosis of urinary tract obstruction, but may not be very sensitive to detect renal gas. USG demonstrates the intraparenchymal gas in the form of strong focal echoes[23,24]. USG is readily available, non invasive and cheap. The disadvantage is that it cannot measure the depth of gas collections and due to the dense echoes at the acoustic interface with total lack of penetration deep to the gas collections[3]. USG is less reliable in diagnosing this condition compared to CT scan.

Plain X-ray of the KUB region demonstrated gas in the region of the kidney and perirenal areas in 33% of cases. Infusion nephrotomography can be utilized to differentiate renal gas from overlying intestinal gas in equivocal cases[6]. IVU[Intravenous urogram] demonstrates non visualization in

around 45%. Even in those who showed excretion, majority showed a poor delineation. Due to the hazardous consequences of IV contrast on the kidneys in diabetics and due to the fact that not much information is provided by it (because the affected system is usually non functioning or poorly functioning) when compared to CT, its use should weighed judiciously. In addition to demonstrating renal gas, IVU may show other findings suggestive of renal inflammation like indistinct margins and mass effect[12]. Obstruction is demonstrated in around 25% of cases [21] and is better demonstrated by USG or retrograde pyelogram.

3 main patterns were described on X-rays by Langston and Pfister that had an apparent correlation with the stage of the disease. Diffuse mottling of the renal parenchyma, with radial distribution of the gas bubbles either along the pyramids or within the tubules was the earliest sign. Bubbly parenchyma surrounded by a crescent of gas is the manifestation of renal necrosis and this finding denotes further clinical deterioration. With extension

through the Gerota's fascia , gas can be seen in the retroperitoneum and may even extend upto the posterior thoracic wall[25].

Bum Soo Park et al found plain Xray KUB reliable as the initial modality for screening (picked up 50% of cases) and CT the most reliable modality for confirmation of the diagnosis (Diagnostic rate 100%) and for planning treatment. They consider USG unhelpful to locate renal gas[5].

MANAGEMENT

Patients with EPN are acutely ill and supportive measures should be rapid. Vigorous measures aimed at glycaemic control, maintenance of fluid balance and treatment of shock should be initiated as quickly as possible. Empirical broad spectrum antibiotics should be started when the diagnosis is suspected and the antibiotics can be tailored according to sensitivity once culture results are available. Obstruction, if present, should be relieved urgently.

According to Schultz and Klorfein, the disease is best treated by conventional medical methods and is not an indication of emergency surgery. They concluded that contralateral disease was often present and nephrectomy was unwarranted[2]. Joseph.B.Stokes JR[26], Dunn and Dewolf et al, in their study of 3 cases treated by nephrectomy[27] favoured an initial trial of conservative management with antibiotics. Their main concern was the possibility of recurrent disease in the contralateral kidney. Nephrectomy could be considered if the renal and perirenal gas or the toxic symptoms persist. They suggested that such patients be started on lifelong suppressive antibiotics and be followed up strictly. They concluded that medical management of EPN was preferable due to the high chances of the opposite kidney being involved, especially in diabetics. Avoidance of surgery, vigorous blood sugar control, appropriate antibiotics and relief of obstruction was rational.

Traditionally the consensus was that mere medical treatment was ineffective and prompt surgical drainage was

recommended and nephrectomy was often necessary. Mortality rate in patients who are treated only with antibiotics is 40%. Treatment is successful in 66% of patients who are treated with percutaneous nephrostomy and antibiotics, and in 90% of those with nephrectomy [28].Renal conservation has come into vogue for reasons already mentioned. The need to save the kidney in the setting of a high probability of the disease occuring in the opposite side later as well as the long term effects of diabetes on the opposite kidney. Patients presenting with synchronous bilateral disease as well as EPN affecting a solitary kidney present unenviable situations where renal conservation is highly desirable.

Huang et al[8] emphasized the importance of perinephric extension of gas. Even though the differences in clinical features among the 4 classes was not significant , there was a tendency towards higher mortality and failure of PCD from class 1 to 4. The best prognosis was enjoyed by class 1 patients. All of them survived with PCD and antibiotics with relief of obstruction whenever necessary. In class 2 also, all patients treated so, were

cured. For patients with extension of gas beyond renal parenchyma or bilateral EPN (class 3 and 4), 85% of patients with <2 risk factors (thrombocytopenia, acute renal functional impairment, disturbed consciousness and shock) successfully responded to PCD and antibiotics. The failure rate of conservative treatment (i.e., combined medical and minimally invasive treatment) was 15% for those with no or a single risk factor and 92% for those with 2 or more risk factors. In such cases, nephrectomy is expected to give the best management outcome. The advantages of PCD are that it drains the pus, releases the gas and hence the pressure to local circulation, provides pus that can be cultured and can help in further management and can provide increased rates of success in extensive EPN. They suggest PCD and antibiotics less extensive disease (class 1 & 2) and for extensive EPN with < 2 risk factors. This leads to a renal conservation in most of the cases. Nephrectomy provided the best treatment outcome for extensive EPN with fulminant course (2 or more risk factors). In managing class 4 EPN, bilateral PCD should be tried first. Emergency

nephrectomy carries a high risk in these patients. Nephrectomy should be done if PCD fails.

Poor glycaemic control was not a poor prognostic factor. Patients seen initially with organ systems dysfunction ran a rapid course with poor outcome. Severe proteinuria correlated with poor outcome and seemed to be a risk factor for extensive disease. The causes of severe proteinuria may be multifactorial with fever, underlying glomerulonephritis, and diabetic nephropathy may contribute.

Michaeli et al[6], in their review, state that attempts at renal conservation were often not successful. But even bilateral surgery was successful at times. The most important factor associated with survival was an approach combining medical and surgical treatment. They inferred that the most favourable outlook was presented by a patient receiving combined medical and surgical treatment for nonobstructive unilateral disease following a short interval of symptoms.

Wan et al described two classes of EPN[7]. The dry type (type 1) was associated with destruction of parenchyma, absence of fluid collection and streaky or mottled gas presented a fulminant course with a mortality rate of 69%. Type 2 had renal or perinephric fluid collection with bubbly or loculated gas and was associated with a mortality rate of 18%. This difference was probably due to immune compromise and vascular insufficiency in the kidneys and immunodeficiency in the diabetics. They described serum creatinine > 1.4mg% was associated with a poor outcome.

In their study of 20 cases, Shokeir et al[12] conclude that nephrectomy should immediately follow aggressive resuscitation and diabetes control. Even if the patient begins to improve, delay of nephrectomy is inappropriate because it jeopardizes the chances for survival. With this protocol of treatment, survival rates reached 80%.

Stein et al, in their case report and review of literature[22], subdivided treatment of bilateral disease into three groups: (1) those managed with medical therapy alone (without

surgical intervention); (2) those managed with unilateral surgical intervention (incision and drainage and or nephrectomy) to one kidney; and (3) those managed with bilateral surgical intervention, (bilateral incision and drainage, ipsilateral nephrectomy, and contralateral incision and drainage, and bilateral nephrectomy) . They concluded that there appeared to be a survival advantage if bilateral surgical intervention is performed with the intent to spare some renal function in patients with bilateral emphysematous pyelonephritis. This may include bilateral incision and drainage if there is minimal bilateral intraparenchymal involvement of gas without evidence of perinephric or adjacent organ involvement. When one renal unit is more extensively involved with or without perinephric gas, ipsilateral nephrectomy with contralateral incision and drainage may be appropriate with close radiographic monitoring of the remaining kidney If there is no resolution of intraparenchymal gas or progression postoperatively, then nephrectomy of the solitary kidney may be indicated. Bilateral nephrectomy should be reserved for those individuals with severe

bilateral disease with extensive renal parenchymal and perinephric extension of gas, as this renders the patient anephric and dialysis dependent.However, the small number of cases in the study may be a limiting factor to draw conclusions. High thoracoabdominal incision was preferred by Stein et al. It provided them with maximum exposure, allowed quick intraperitoneal access to the renal vessels, which should be secured first.

Bum Soo Park et al[5] consider nephrectomy to be the most effective modality of treating EPN. They were for immediate nephrectomy and all supportive and resuscitative measures were to be carried concomitantly. Their indications for renal conservation (with PCD and antibiotics) were solitary kidney, poor general/medical condition rendering the patient unfit for surgery, inadequate contralateral kidney and bilateral disease. For nephrectomy, they preferred a 11th rib bed approach through the loin.

Hung et al [29] have noted anaerobic bacteria, B. fragilis as the causative organism in a case of EPN. Anaerobic

bacteria had never been found to be a causative pathogen except in one case with Clostridium[30]. They consider ascent and invasion of anaerobes indigenous to the lower urethra, or a spread from adjacent organs such as the bowel or uterus as the probable source. The presence of obstruction may reduce the oxygen tension and impair tissue immunity and might predispose to EPN[8]. Hence they recommend that empirical treatment should also cover anaerobes in obstruction-related EPN.

MATERIALS and METHODS

This was a prospective study conducted in Kilpauk Medical College in its constituent hospitals Kilpauk Medical College Hospital and Government Royapettah Hospital from September 2004 to April 2007.

Inclusion criteria

1) Patients with features of acute pyelonephritis with gas in the renal parenchyma and beyond it.

The symptoms were Fever, chills, loin pain, vomiting.

2) Patients admitted in the emergency, but subsequently evaluated and found to have gas in the renal parenchyma and beyond it with features of acute pyelonephritis

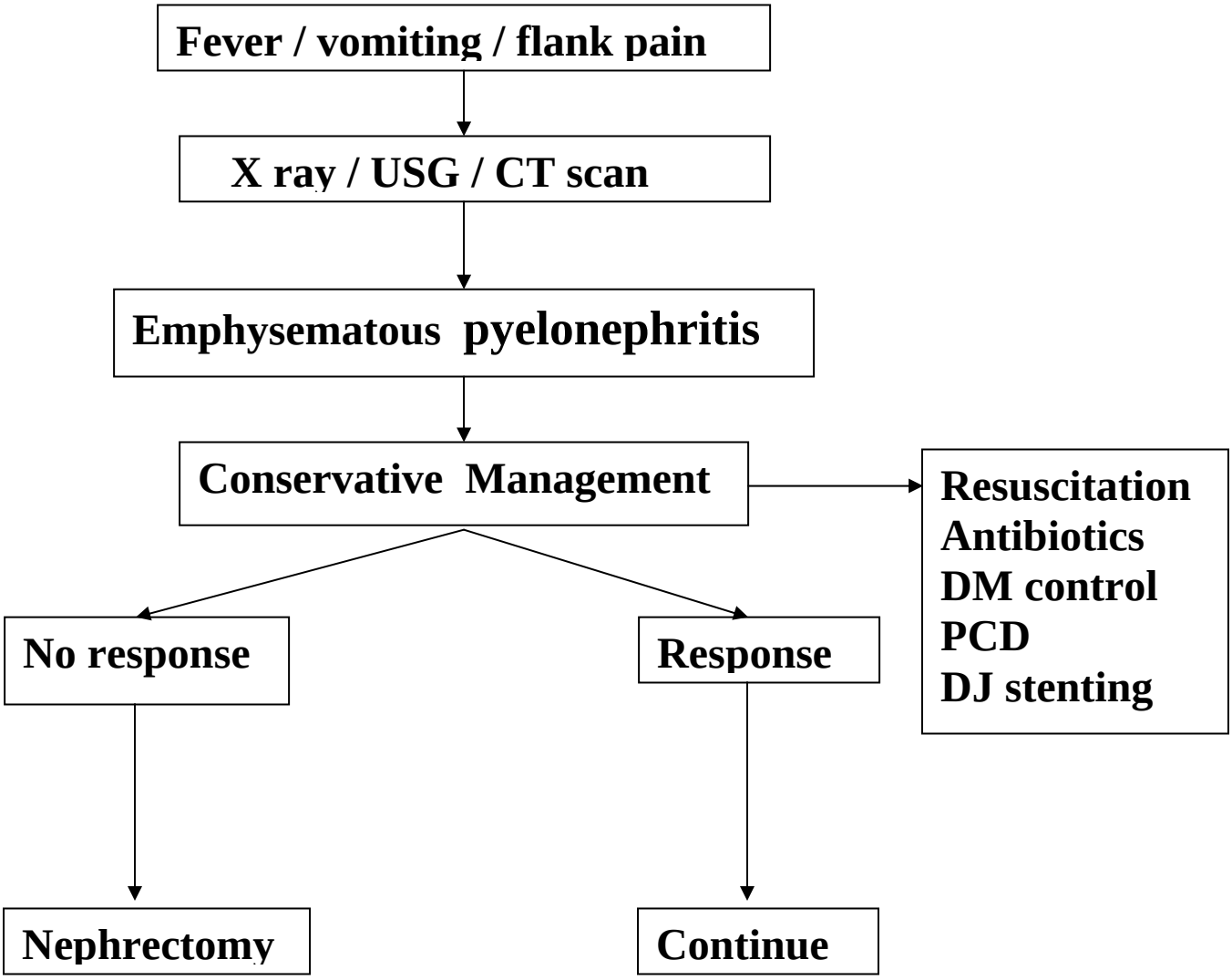
Exclusion criteria

1) Patients with features of acute pyelonephritis without gas in the renal parenchyma.

2) History of recent endoscopic or open interventions in the urinary tract.

3) History of recent catheterization.

Fig 2: Management protocol



All the patients who presented with fever, loin pain and vomiting underwent preliminary Xray KUB and USG abdomen. If findings suspicious of gas were present, they underwent CT KUB (with contrast enhancement if the renal parameters were not raised. Patients in whom gas could not be identified in either of these modalities underwent CT KUB based on clinical suspicion due to toxic clinical features. The patients were stratified based on Huang et al's CT classification[8].

On admission, baseline characteristics recorded included age, sex, history, duration of and treatment for diabetes mellitus, and duration of symptoms. The clinical features recorded included hemodynamic status, the degree of consciousness, hydration status. Blood glucose level, serum creatinine, blood urea, total and differential WBC counts, blood haemoglobin level and urine acetone were recorded on admission. A blood platelet count was done.

Shock was defined as systolic BP <90 mm Hg. Raised renal parameter was defined as serum creatinine > 1.5 mg%

or blood urea >40mg%. Altered consciousness was defined as patient in confusion, delirium, stupor or coma.

All patients were started on 3rd generation cephalosporins (cefotaxime, ceftriaxone or cefoperazone) and metrogyl. Aminoglycosides were added if renal parameters were normal. Antibiotics were later changed if necessary, based on culture and sensitivity. Vigorous resuscitation was carried out with hydration, correction of electrolyte imbalance if any and diabetes control measures was initiated with insulin in all the cases.

All patients were stratified to initially undergo conservative management with only antibiotics, antibiotics with PCD &/or DJ stenting. PCD was defined as percutaneous aspiration of pus and gas with/without percutaneous nephrostomy. PCN was done under USG guidance using a 8.5Fr single puncture nephrostomy catheter in prone, prone oblique or lateral positions via the flank taking care to avoid contamination of the peritoneum. Unsuccessful PCD was defined as progressive or persistent lesions on radiological studies with a clinical picture of unstable

hemodynamic status or prolonged fever after management. Our patients, depending on outcome, were stratified into the “good” and “poor” outcome groups. The “good” outcome group included patients treated with antibiotics only or PCD +/_ DJ stenting or DJ stenting only with antibiotics. The “poor” outcome group included patients who had unsuccessful PCD followed by nephrectomy or mortality.

Statistical analysis:

In the first step, descriptive analysis was done. Parametric variables such as age, disease duration, were expressed as mean and standard deviation and non-parametric variables such as sex, presence of diabetes mellitus, were expressed as proportions. They were presented in the form of tables and graphs.

In the second step bivariate analysis was done between outcome and various other independent factors. For non-parametric variables, chi square test was used and for parametric

variables student’s t test was used to assess the statistical significance.

The patients were stratified into 2 groups based on a cutoff value for serum creatinine, platelet count, and total count.The cutoff values were selected to be the upper limits of the normal. Chi square test was used to assess the statistical significance.

PROFORMA

Name Date of admission

IP no Date of discharge

Age

Sex

Complaints

Duration of symptoms

H/O DM (along with duration and treatment)

Clinical examination

Investigations at presentation

- Blood sugar
- Serum creatinine & Blood urea
- Total WBC count & hemoglobin
- Platelet count
- Urine acetone
- Urine culture & sensitivity

Blood culture

Mode of diagnosis

CT class

Presence of obstruction

Treatment category

Antibiotics used

Outcome

Number of days of hospital stay

RESULTS

Fig 3:Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age	25	38	82	55.12	9.71
Duration(days)	25	3	60	11.60	11.02
DM duration	20	3	27	9.50	5.65
Blood sugar	25	92	474	246.92	96.27
Se.Creatinine	25	0.6	4.3	1.84	1.04
Bl.Urea	24	15	116	52.54	25.80
Platelet	25	50000	220000	142400.00	44654.23
TC	24	6000	15600	10945.83	2963.98
HB	25	7.2	12.6	9.94	1.53
Hospital_stay	25	6	44	18.76	8.39

This table gives the descriptive statistics of the study population and their derived variables including the mean, standard deviation and maximum and minimum values.

Sample size:

Total number of patients included in this study was 25.

Age:

The mean age was 55.12 yrs with a standard deviation of 9.71.The youngest patient was 38 yrs and the oldest was 82 yrs old. Age was not significantly related to the outcomes in our study (p=0.094).

Sex:

62% of the total cases were males and 32% were females. There was no significant relationship between sex and outcomes (p=0.0607) (Fig 4).

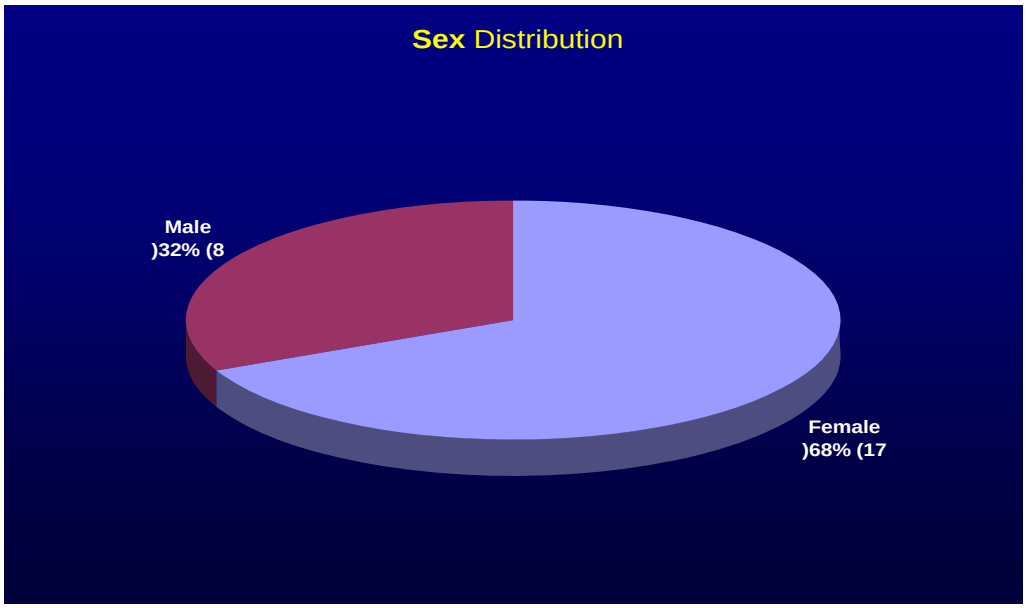


Figure 4: Sex distribution

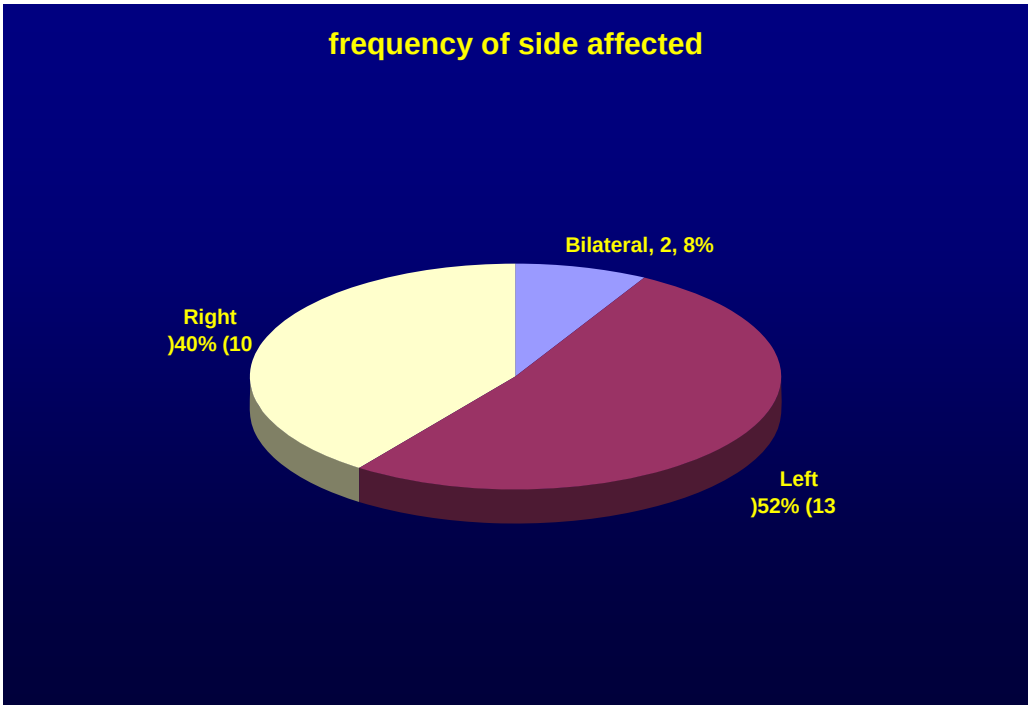


Figure 5: Frequency of side affected

Frequency of side affected:

The left kidney was affected in 52% of the cases, the right kidney in 40% of the cases and both kidneys in 8% cases. The relationship between the side of affection and outcomes were not statistically significant in our study (p=0.850) (Fig 5).

Associated diabetes mellitus :

88% of the patients were diabetic of which 8% were newly detected.12% of the patients were non diabetic. Diabetic status or the absence of it did not have a statistically significant relationship with the outcome (0.599) (Fig 6).

Treatment of diabetes mellitus :

Of the diabetics, 95% were on regular treatment.90% were on OHAs and 5% were on insulin . 5% of patients were on irregular treatment. Diabetic treatment and the mode of treatment did not reach statistical significance in our study (0.470) (Fig 7).

Symptoms :

The most common mode of presentation was fever & loin pain (14/25 ; 56%).Loin pain was the only presentation in 28% (7/25).

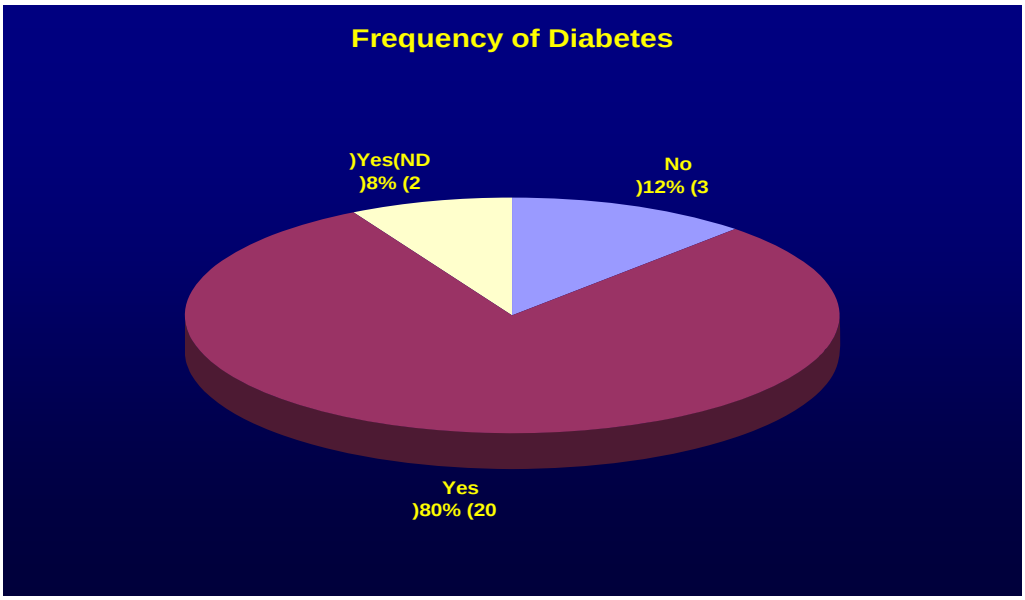


Figure 6: Frequency of diabetes

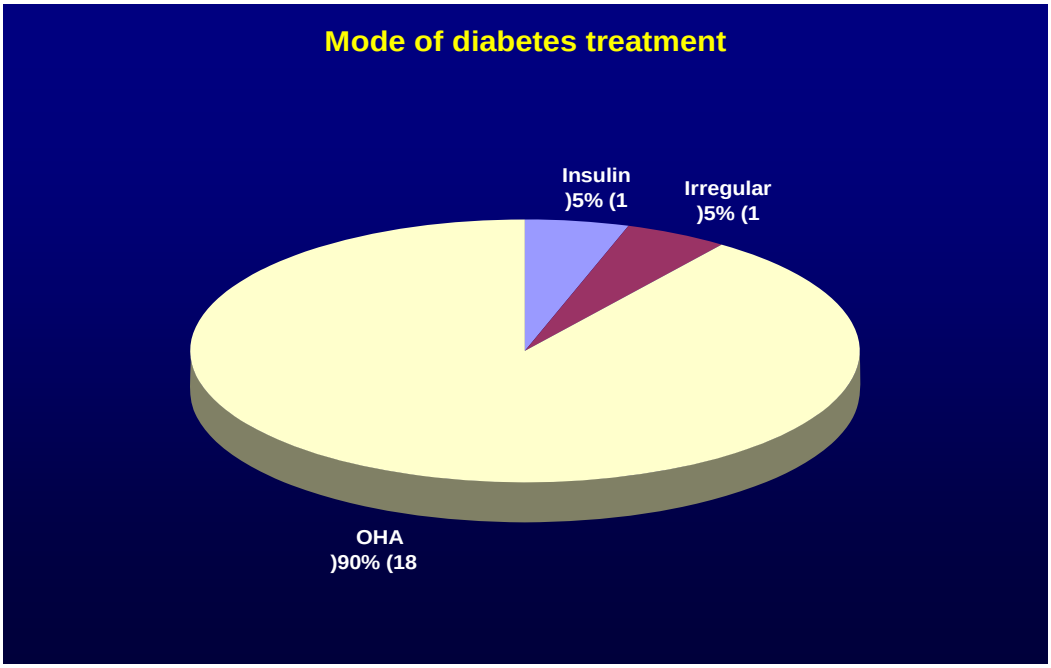


Figure 7: Mode of diabetes treatment

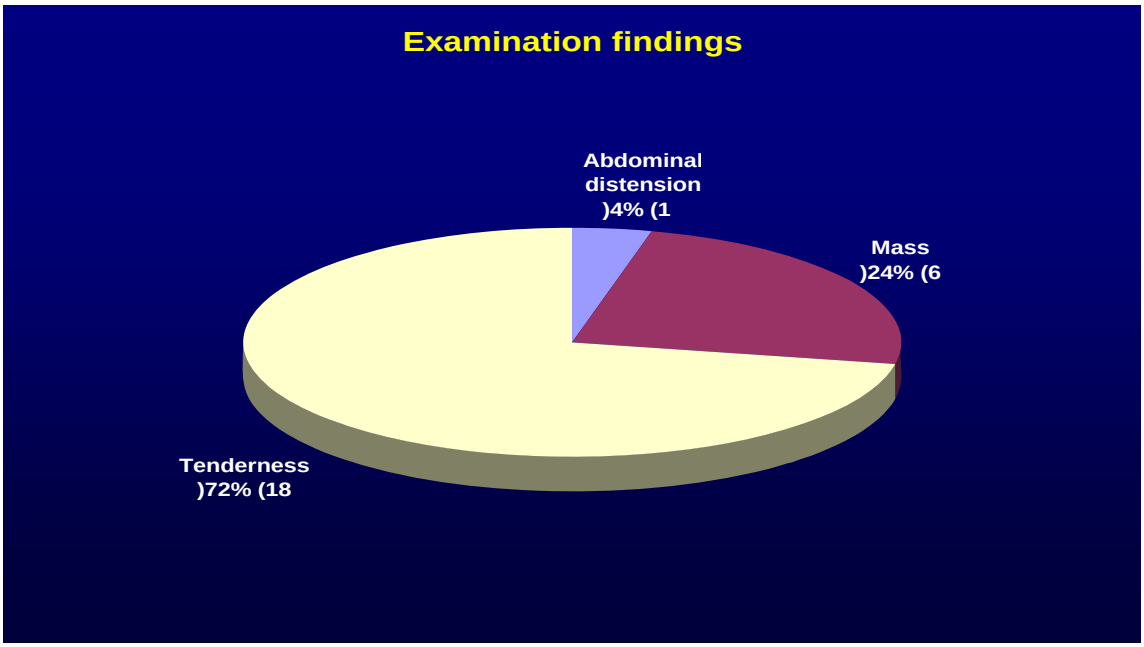


Figure 8: Examination findings

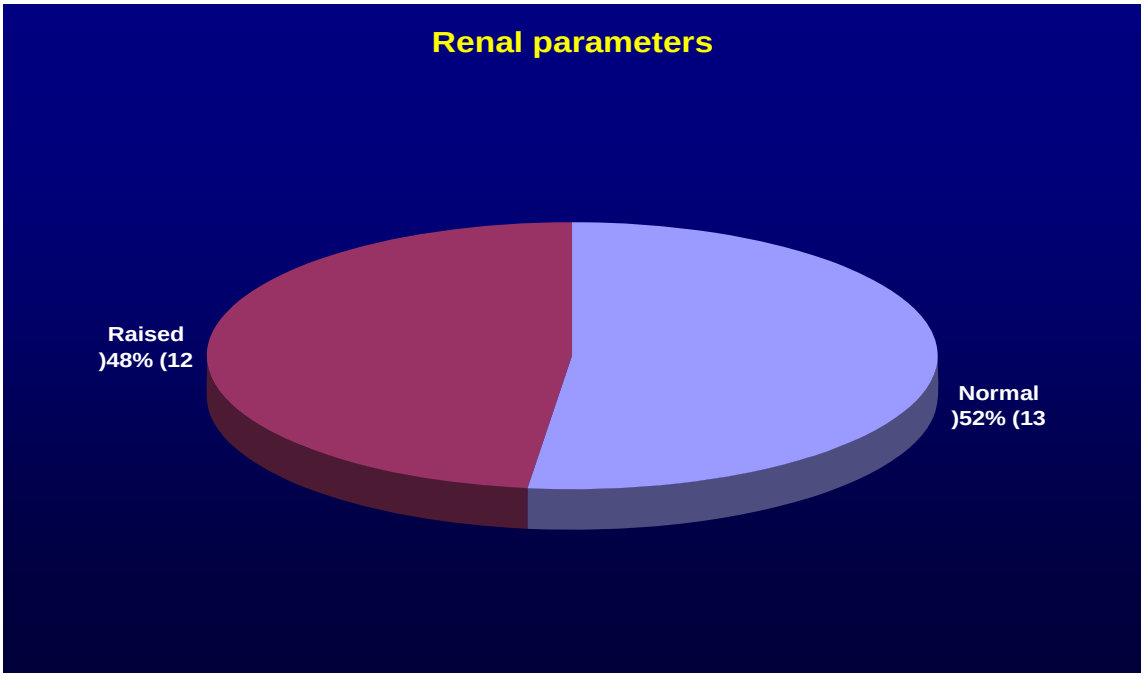


Figure 9: Renal parameters

Other modes of presentations like seizures, altered sensorium or vomiting constituted the rest (16%). Patient complaints were significantly related to the outcome (p=0.034).

Findings at clinical examination :

On clinical examination, the commonest finding was loin tenderness (72%). 24% presented with an abdominal mass and 4% with abdominal distension.

Renal parameters:

12 out of 25 patients (48%) had raised renal parameters.The rest (52%) had normal renal parameters. The mean serum creatinine value in the good outcome group was 1.547 with a S.D(standard deviation) of 0.786 and in the poor outcome group was 2.450 with a s.d of 1.290.The blood urea values in the good outcome group was 46.412 +/- 22.875 and in the poor outcome group was 67.429 +/- 28.136. The relationship of serum creatinine value with the outcome reached statistical significance (p=0.040), but not that of blood urea (p=0.068).(Fig 9)

Shock at presentation :

6 out of the total 25 patients (24%) presented with shock. The relationship of shock with the outcome was statistically significant (p=0.002). (Fig 10)

Mental status on presentation:

84% patients presented in normal mental status while 16% had altered mental status on presentation. Out of 4 patients with altered mental status, 3 were in the poor outcome group.Thus, altered mental status had a statistically significant relationship with the outcome(p=0.044). (Fig 11)

Blood sugar :

In the present study,the blood sugar value associated with a good outcome was 234.059 +/- 85.003 and the value associated with poor outcome was 274.250+/- 118.353. Blood sugar values at presentation did not show any statistically significant correlation with the outcome (0.341).

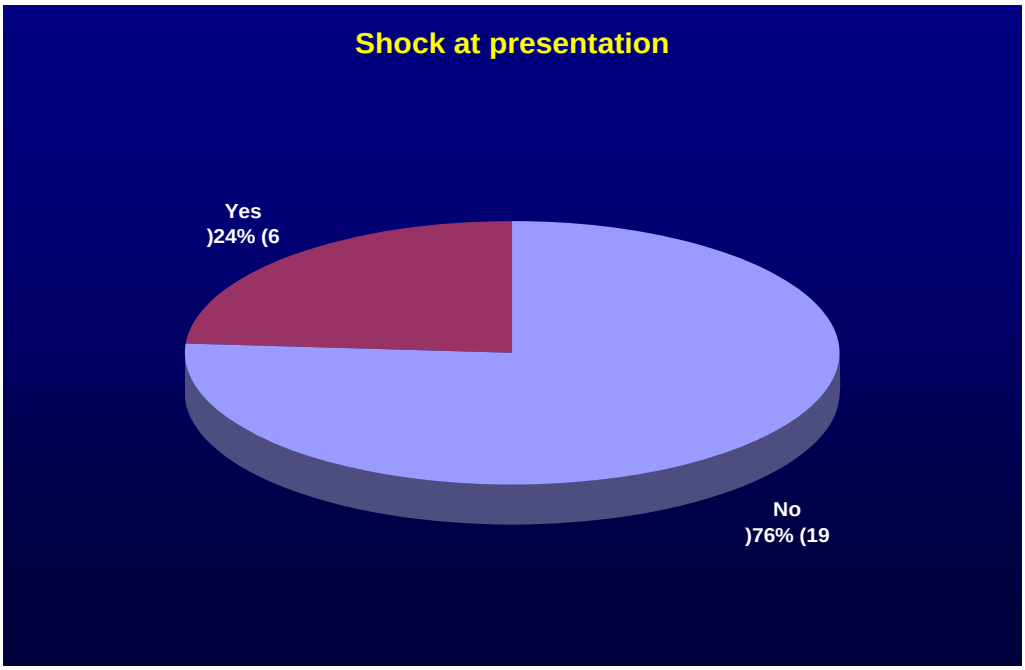


Figure 10: Shock at presentation

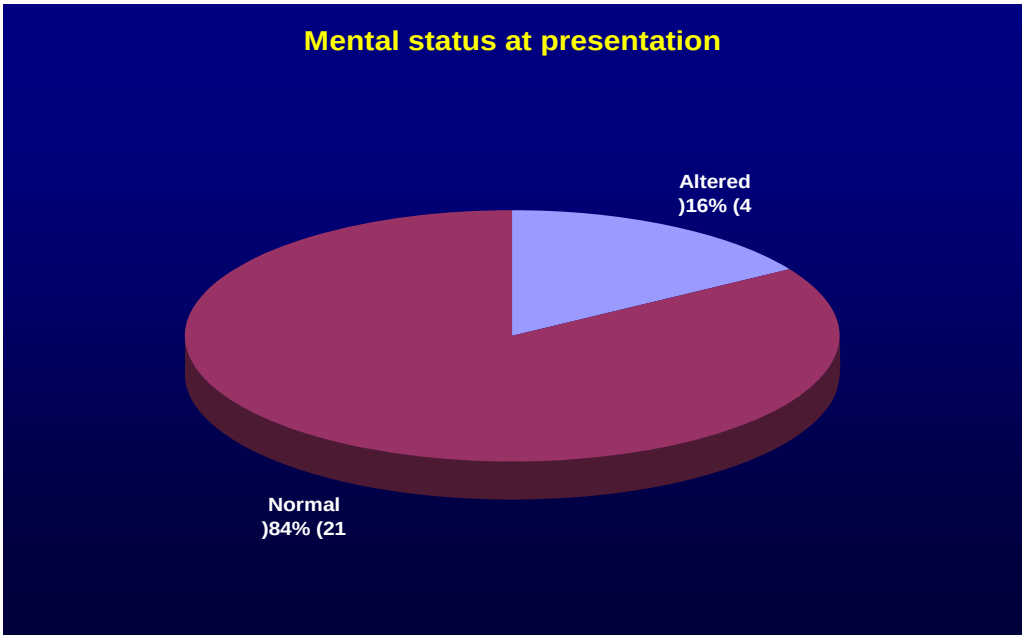


Figure 11: Mental status at presentation

Platelet count:

In the present study, the mean platelet count was 142400 with a S.D of 44654.23. Patients with a good outcome were associated with a mean platelet count of 157058.824 with a S.D of 34957.958. Poor outcome was associated with mean platelet count of 111250 with a S.D of 49117.207.The correlation between platelet counts and outcome was significant (p=0.013). The patients were further stratified into two groups based on whether the platelet count was above or below 120000/cmm. In the below 120000/cmm group, 5/12 were associated with a good outcome and 7/12 were associated with a poor outcome. In the above 120000/cmm group, 12/13 were associated with a good outcome and 1/13 were associated with a poor outcome. This reached statistical significance with a p value of 0.007.

Total count:

The mean total count (TC) in the present study was 10945.83 with a S.D of 2963.98.When correlated with the outcomes, the mean TC in the poor outcome group was 14114.286 with a S.D of

1193.634 and in the good outcome group was 9641.176 with a S>D of 2427.720. The correlation between blood TC and outcomes was statistically significant (p=0.000). When patients were further stratified based on whether their total count was above or below 10000/cmm, all patients in the below 10000/cmm group were associated with a good outcome. In the above 10000/cmm group, 6/14 were associated with a good outcome and 8/14 were associated with poor outcome. This association reached statistical significance (p=0.002).

Blood Haemoglobin (Hb):

In the present study, the mean Hb value was 9.94 with a S.D of 1.53. In good outcome patients, the Hb was 10.282 +/- 1.606. In the poor outcome group, the Hb was 9.200 +/- 1.116. There was no statistically significant correlation between the Hb value and the outcomes (p=0.100).

DKA at presentation:

2 patients (8%) were in DKA at presentation. No statistically significant correlation was found between DKA at presentation and outcome (p=0.569) (Fig 12).

CT classification:

The following was the distribution of the patients[8].

Class 1 – 4% (1 patient)

Class 2 – 44% (11 patients)

Class 3A- 24% (6 patients)

Class 3B- 16% (4 patients)

Class 4-12% (3 patients)

There was no correlation made out between CT class and the outcome (p=0.115) (Fig 13).

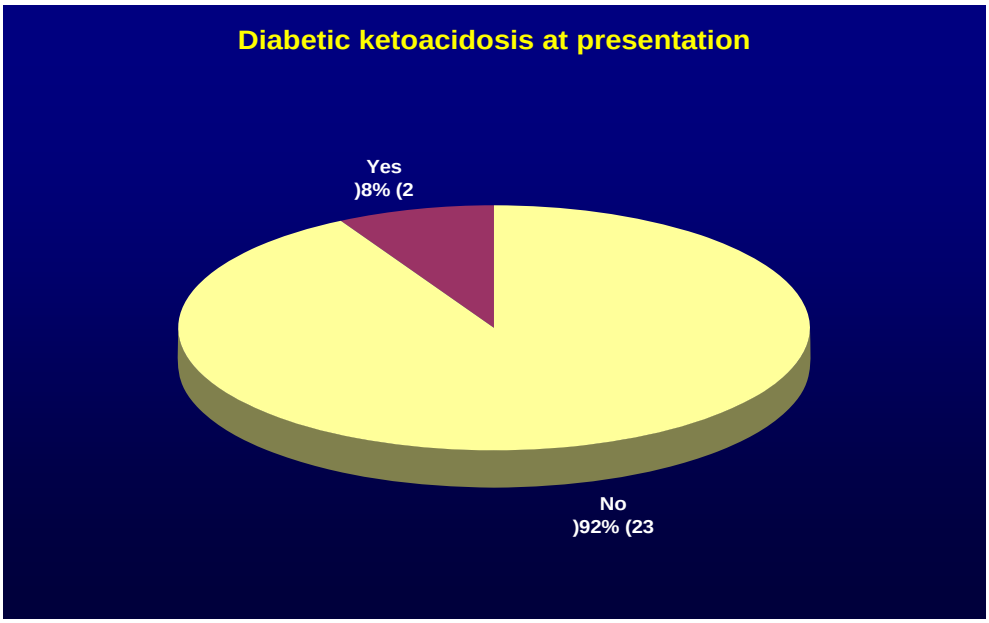


Figure 12: Diabetes ketoacidosis at presentation

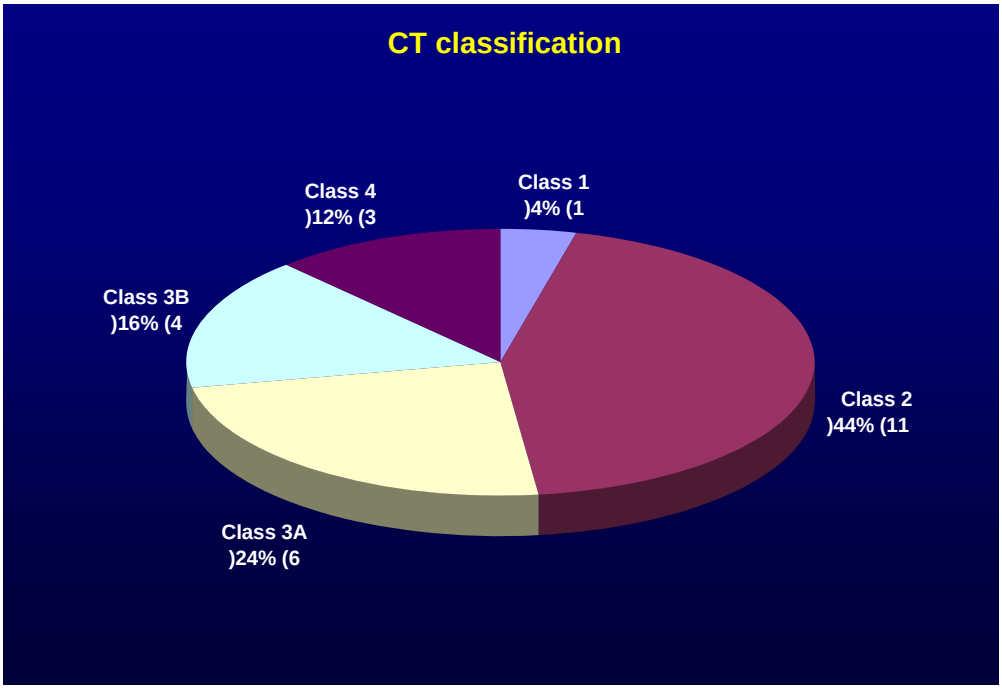


Figure 13: CT classification

Modes of treatment:

Antibiotics only was used in 12% of patients. DJ stenting was the only modality in 24% of the patients and PCD only in 52%. PCD was combined with DJ stenting in 12% of patients.The mode of treatment was not significantly related to the outcome (p=0.192).

Results of urine culture:

The commonest organism grown in urine culture was E.coli (72%).E.coli with Proteus was grown in 4%, and other organisms (Klebsiella, Proteus) in 24%.Urine culture result did not correlate with the outcome (p=0.435) (Fig 14).

Results of blood culture:

Blood cultures were positive in 40% of the cases.Of the 10 patients with a positive blood culture, 6 had poor outcome.The relationship between blood culture positivity and outcome reached statistical significance (p=0.014). (Fig 15)

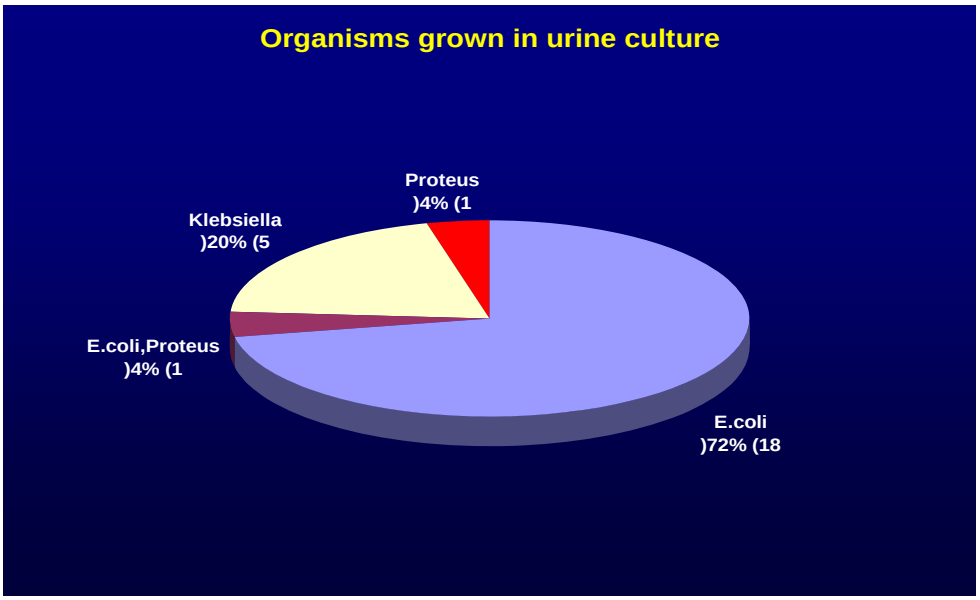


Figure 14: Organisms grown in urine culture

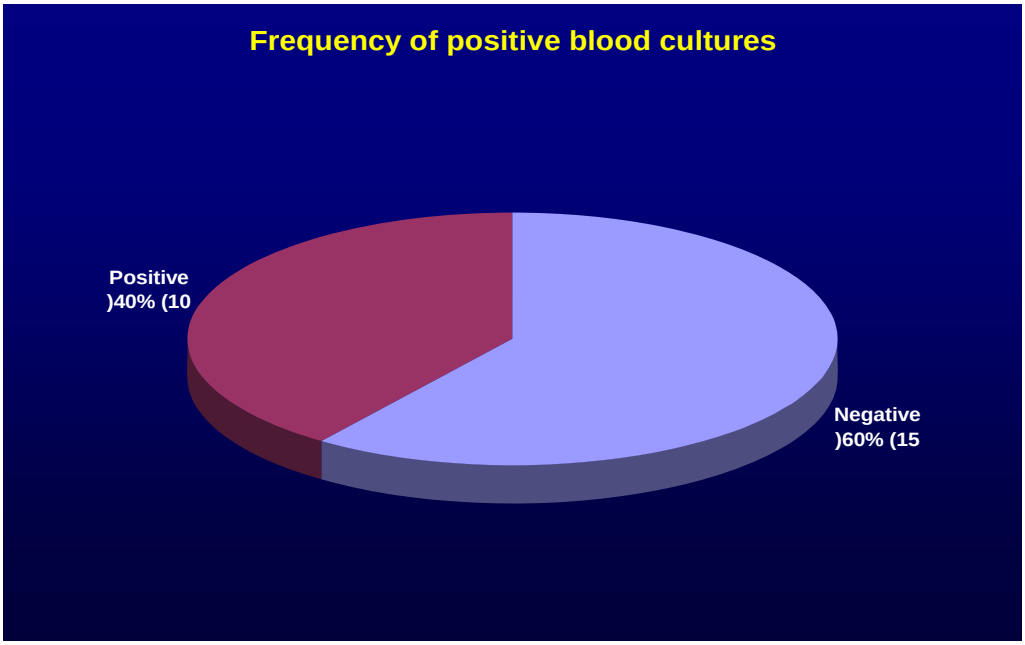


Figure 15: Frequency of positive blood cultures

Presence of obstruction:

In the present study, urinary tract obstruction was present in 68% of patients. 32% patients did not have associated obstruction.Of the 8 patients who had associated urinary tract obstruction, all the 8 were associated with good outcome. Of the 17 patients with no associated obstruction, 52.94% (9/17) had a good outcome and 47.05% (8/17) had a poor outcome. Thus the relationship between obstruction and outcomes was statistically significant (p=0.019). This implies that presence of obstruction when relieved would assist renal conservation.

Type of outcome:

68% patients (17/25) had a good outcome in the form of renal conservation. 32% patients (8/25) had a poor outcome as indicated by the loss of the renal unit (Fig 17).

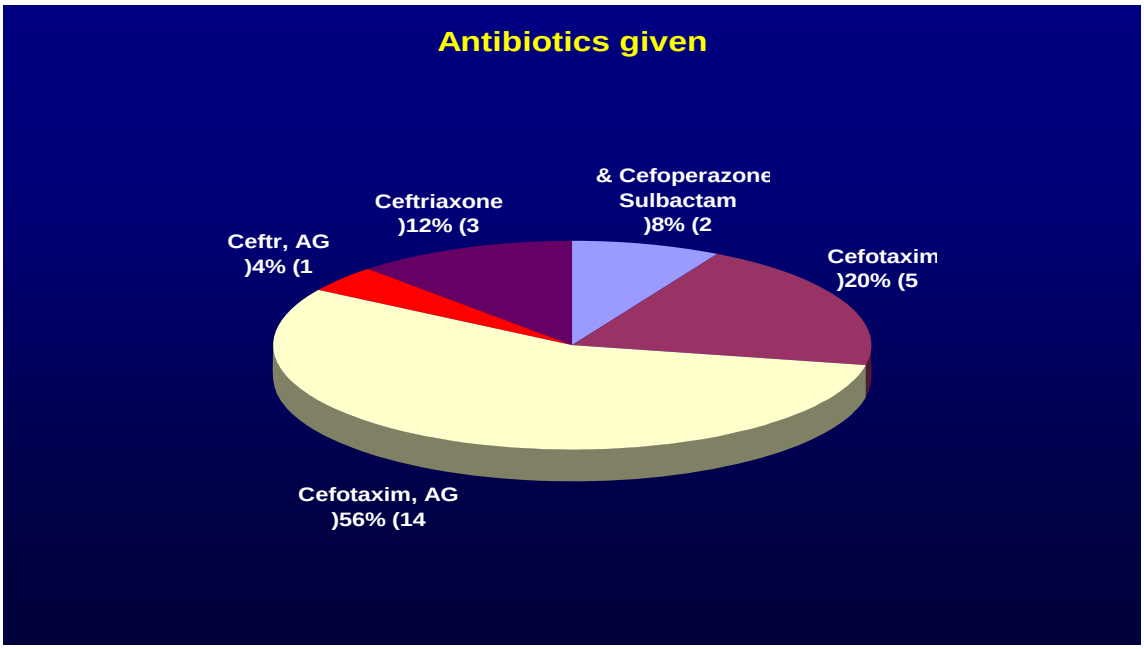


Figure 16: Antibiotics used.

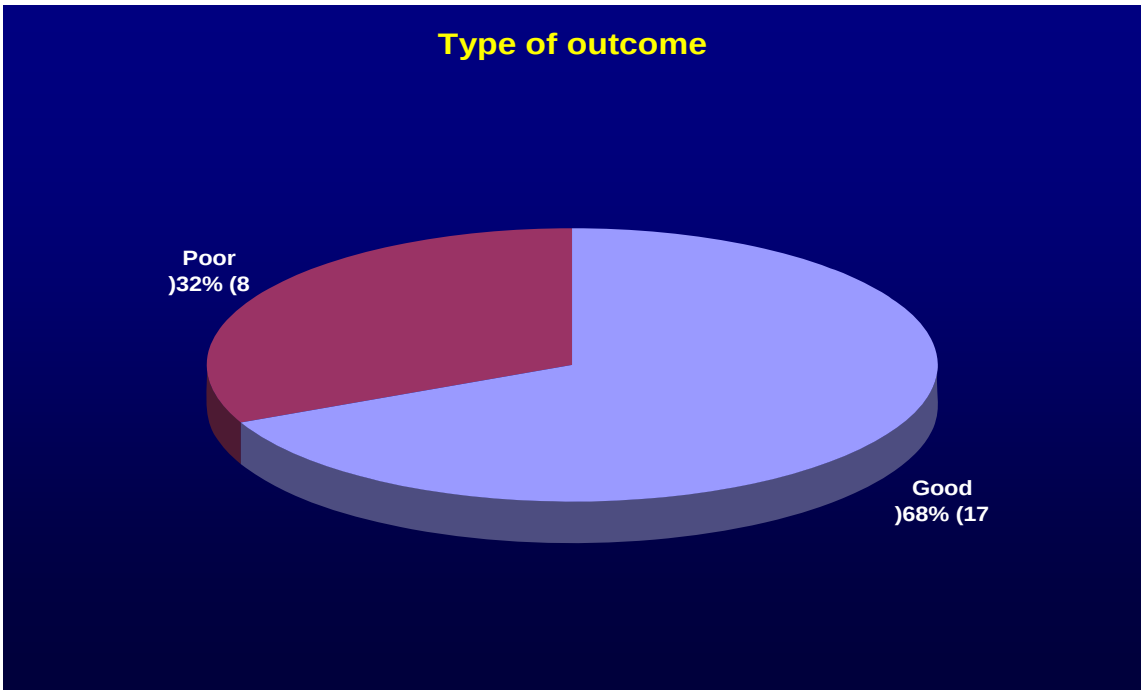


Figure 17: Type of outcome

DISCUSSION

25 patients were included prospectively during the study period. The results of the present study were analysed and compared with other studies.

Sl. No	Study	Design	Sample	Finding
1.	Huang et al[8]	Prospective	48	Class 1 or 2 & class 3 or 4 with <2 risk factors-conservation Others-nephrectomy
2.	Michaeli et al[6]	Retrospective	54	Resuscitation, early antibiotics, relief of obstruction & early nephrectomy.
3.	Shokeir et al[12]	Retrospective	20	Nephrectomy
4.	Bum Soo Park Et al[5]	Retrospective	17	Conservation in selected cases
5.	Chen et al[23]	Retrospective	25	Antibiotics with CT guided drainage
6.	Wan et al [19]	Retrospective	38	Predictors of high risk – S.Creatinine & Platelet count
7.	Present study	prospective	25	Conservation feasible. Predictors of poor outcome identified.

Fig 18: Comparative study

Age: Mean age in the present study is 55.12 yrs which is comparable with other studies [3,5, 6, 7, 8, 12] .

Sex distribution: In our study, there was a female predominance, which is seen in other studies also.

Side of involvement: In the present study, there was a predominance of left over the right side. In other studies also, a similar female predominance is seen.

Presenting complaints: The predominant mode of presentation in the present study was fever associated with loin pain. This is similar to other studies.[8,12].

Duration of symptoms before presentation: The mean duration of symptoms before presentation was 11.60 days in our study. In Chen et al's study [3], it was 18 +/- 8.64 days[3]. In our study, the

mean duration of symptoms before presentation in the good outcome group was 12.294 days and in the poor outcome group was 10.125 days. In comparison, in Huang et al's study, the duration of symptoms prior to diagnosis in the good outcome group was 8.2 days and in the poor outcome group was 6.1 days [8].

Presence of Diabetes mellitus: DM was present in 88% of patients in our study which correlates well with the studies of Chen et al [3] and Shokeir et al [12].The prevalence of DM in Huang et al's study was 96% [8].

Presence of shock: In the present study,5/8 (62.5%) of the patients in poor outcome group presented with shock and 1/17 (5.88%) of the patients in good outcome group presented with shock .In comparison, in Huang et al's study 56% in the poor outcome group and 17% of patients in the good outcome group presented with shock [8].

Altered mental status at presentation: In the present study, 3/8 (37.5%) of the patients in poor outcome group presented with altered mental status and 1/17 (5.88%) of the patients in good outcome group presented with altered mental status. In comparison, in Huang et al's study 50% in the poor outcome group and 3% of patients in the good outcome group presented with altered mental status [8].

Altered renal parameters: In the present study, the mean serum creatinine in patients with good outcome was 1.547+/-0.786 . The mean serum creatinine in patients with poor outcome was2.450+/-1.290.This reached statistical significance (p=0.040). Then the patients were stratified based on a cut off of serum creatinine(1.5mg/dl) and patients analysed with regards to the outcome. In the <1.5mg/dl group, 10/12 patients fell under the good outcome and 2/12 patients fell under the poor outcome group. In the >1.5mg/dl group, 7/13 fell under the good outcome and 6/13

patients fell under the poor outcome group. This was statistically not significant (p=0.114).

Only when cutoff value of serum creatinine was fixed at 1.4mg%, it reached near statistical significance with a p value of 0.054.

Management and outcome according to radiological classes: In the present study, 100% of patients in class 1(1/1) had a good outcome which is comparable with the Huang et al study[8].In class 2, 90.90% patients(10/11) had a good outcome and 9.09% patients(1/11) had a poor outcome. This is comparable with the Huang et al study[8]. In class 3A, 50% patients (3/6) had a good outcome and 50% patients (3/6) had a poor outcome. In comparison, in the Huang et al study[8], there was a 100% poor outcome. In class 3B, 25% patients (1/4) had a good outcome and 75% patients(3/4) had a poor outcome. In comparison, in the Huang et al study[8], there was a 49% poor outcome. In class 4, 66.66% patients (2/3) had a good outcome and 33.33%

patients(1/3) had a poor outcome. In comparison, in the Huang et al study[8], there was a 75% poor outcome.

Management and outcome

In the present study, use of antibiotics only was associated with a good outcome in 33.33% and a poor outcome in 66.66% patients, while in Huang et al's study, it was associated in 60% and 0% with good and poor outcomes respectively[8].

The use of PCD only was associated with a good outcome in 61.53% and a poor outcome in 38.46% patients, while in Huang et al's study, it was associated in 66% and 20% with good and poor outcomes respectively[8].

In the present study, PCD with DJ stenting was associated with a good outcome in 66.66% and a poor outcome in 33.33% patients. In patients treated with DJ stenting only, there was a 100% successful outcome.

Urine cultures: In the present study, E.coli was grown in 72% of patients and Klebsiella pneumoniae in 20% of patients. In

comparison, in the study of Bum Soo Park et al, 52% grew E.coli and 24% grew Klebsiella pneumoniae.In their study, 24% did not show any growth in the urine[5].

Blood cultures: In the present study, blood cultures were positive in 40% of patients. This compares well with Wan et al's study[7] in which 42.10% had positive blood cultures but is much less than in Bum Soo Park et al's study[5] in which 59% had positive blood cultures.

Obstruction: In the present study, obstruction was present in 32% of patients. In this group, when obstruction was relieved, there was a 100% association with good outcome. In the good outcome group, 47.05% patients had associated obstruction.This contrasts with Huang et al's study in which good outcome group was associated with obstruction in 25% patients only[8].

Platelet count: In the present study, 29.41% of the patients in the good outcome group and 87.5% patients in the poor outcome group had thrombocytopenia (platelet count < 120000). This is comparable to the study by Huang et al[8], in which, 28% in the good outcome group and 81% in the poor outcome group were associated with a platelet count of < 120000. This relationship reached statistical significance in both the present and Huang et al's study[8].

Total count: In the present study, the TC in good outcome group was 9641.17 +/- 2427.72 and in the poor outcome group was 14114.28 +/- 1193.634. In comparison, in the study by Wan et al[7], the TC in survivors was 13904 +/- 6568 and in nonsurvivors was 15500 +/- 6601.

SUMMARY

Of the total 25 patients included in the study the following were the findings.

- Emphysematous pyelonephritis is commoner in the females.
- There is a slight predominance of the left over the right side.
- The most common presenting symptoms were fever and loin pain.
- Emphysematous pyelonephritis predominantly affects the diabetics.
- Patients can present in the emergency with unrelated clinical features.
- Even though USG and Xray KUB can help in diagnosis, the most helpful is CT KUB.
- There is a high incidence of positive urine culture – the most common organism being *E.coli spp*.

- When blood cultures are positive, the organisms grown are the same as in urine cultures.
- When there is an underlying urinary tract obstruction, relief of the obstruction assists renal conservation.
- Various treatment modalities like antibiotics, PCD, DJ stenting either alone or in combination make renal conservation feasible in 68% of patients.
- Clinical factors like shock or altered mental status at presentation, absence of associated urinary tract obstruction, laboratory parameters like raised serum creatinine, raised TC, positive blood cultures, reduced platelet counts are all significant factors in determining the outcome during attempted renal conservation.

CONCLUSIONS

1) There is a definite role for renal conservation in properly selected patients of emphysematous pyelonephritis.

2) The following factors at presentation could tilt the balance towards nephrectomy in conservatively managed cases of emphysematous pyelonephritis

- Shock
- Altered mental status
- Raised serum creatinine
- Total count >10000/cmm
- Platelet count < 120000/cmm
- Positive blood cultures
- Absence of urinary tract obstruction.

PHOTOGRAPHS

Fig 19: Xray KUB showing gas in Lt renal area

Fig 20: Xray KUB showing gas in Lt renal area

Fig 21: USG KUB

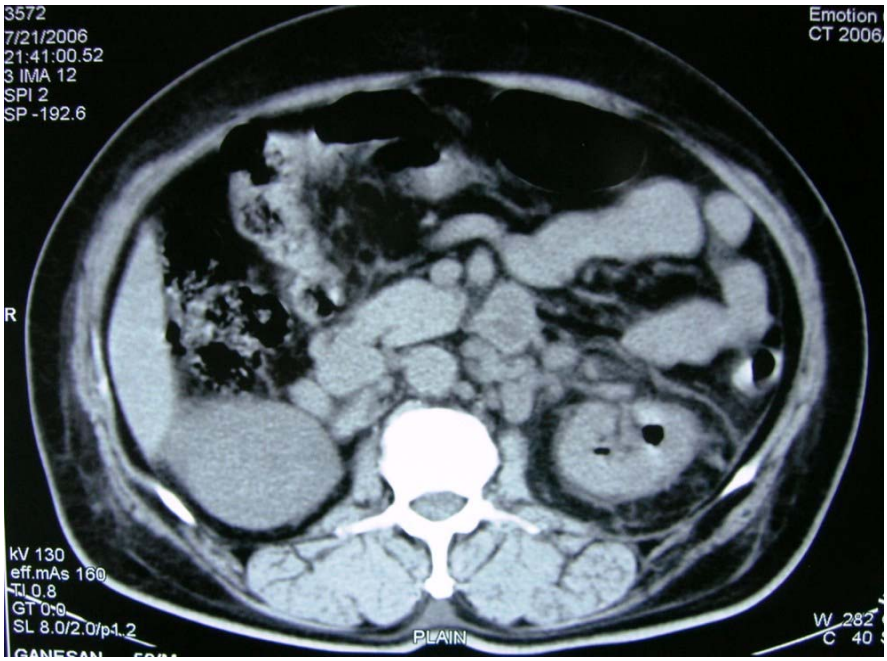


Fig 22: CT KUB Class 2 EPN

Fig 23: CT KUB Class 3A EPN

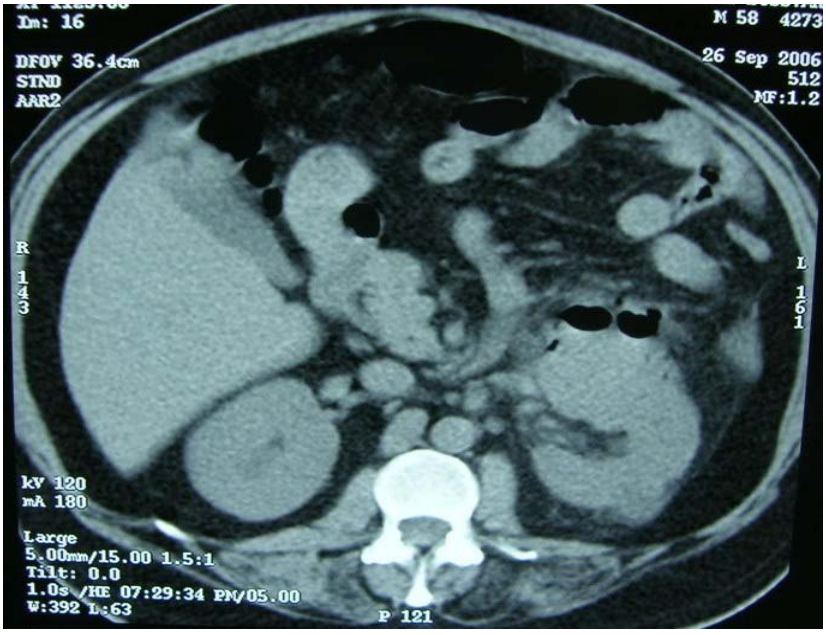


Fig 24: CT KUB Class 3B EPN

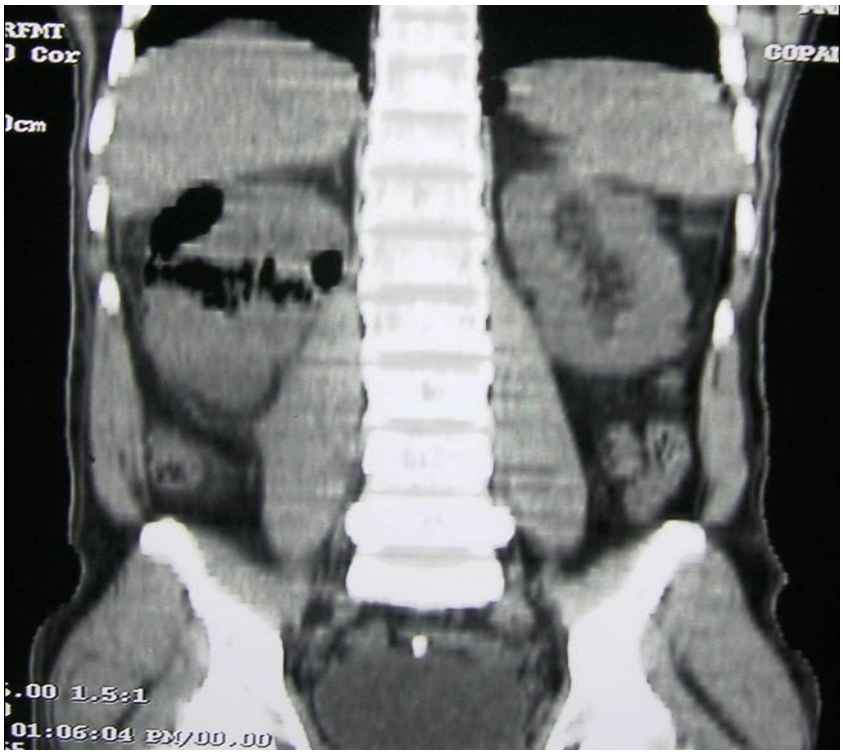


Fig 25: CT KUB-reconstructed image

Fig 26: Retrieved necrosed renal papilla

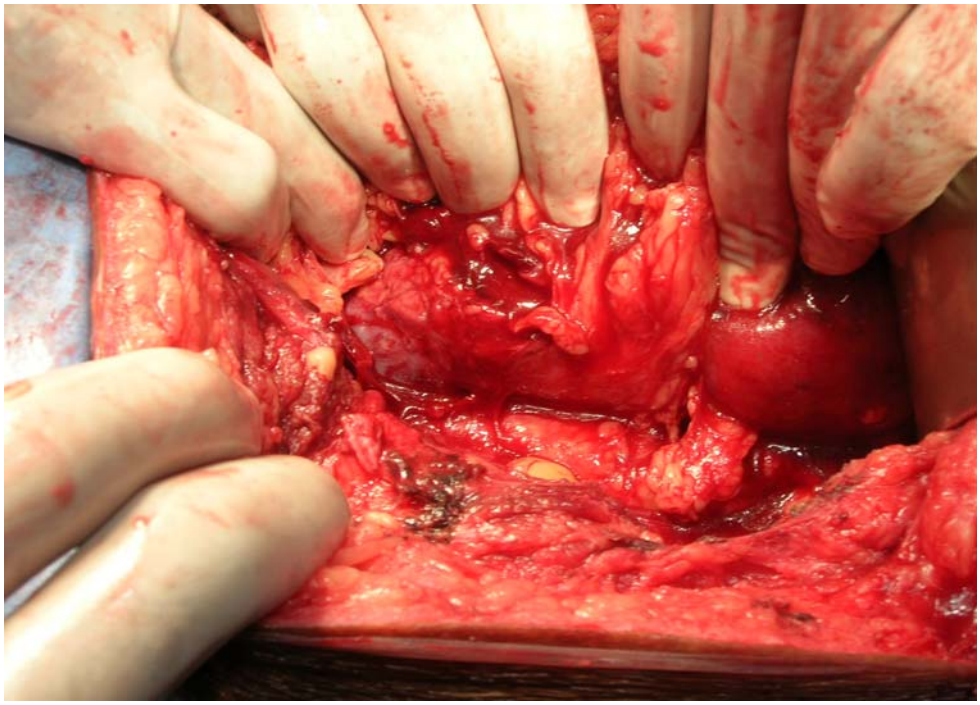


Fig 27: Nephrectomy in progress

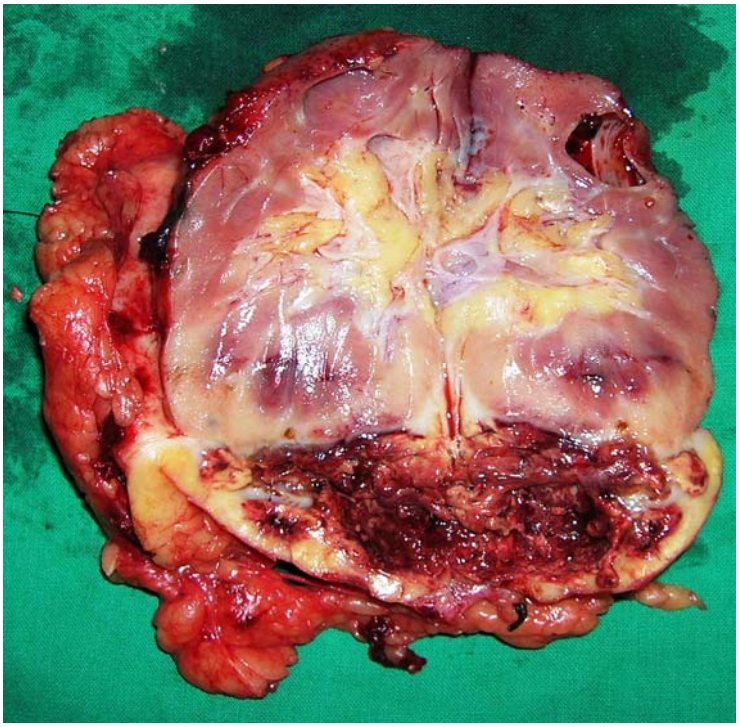


Fig 28: Cut section of left kidney post nephrectomy

ABBREVIATIONS

DM : Diabetes mellitus

UTI : Urinary tract infection

EPN : Emphysematous pyelonephritis

E.coli : Escherichia coli

K.pneumoniae : Klebsiella pneumoniae

B.fragilis : Bacteroides fragilis

ATP : Adenosine tri phosphate

NAD : Nicotinamide adenine dinucleotide

USG : Ultrasonogram

CT scan: Computerised Tomographic scan

IVU : Intravenous urogram

SD : Standard deviation

TC : Total count

Hb : Haemoglobin

BIBLIOGRAPHY

1. Kelly.H.A, Macallum.W.G. Pneumaturia.*JAMA.* 1898; 31: 375-81.

2.E.H.Schultz jr & Elliot.H.Klorfein: Emphysematous Pyelonephritis. *Journal of Urology.* June 1962; Vol 87, No 9: 762-765.

3. Ming-Tan Chen, Chun Nung Huang, Yi Her Chou et al. Percutaneous Drainage in the treatment of Emphysematous Pyelonephritis: 10 Year Experience. *Journal of Urology.* May 1997; Vol 157: 1569-1573.

4. Tang.H.J, Li CM, Yen MY, Chen YS, Wann SR, Lin HH et al . Clinical characteristics of Emphysematous pyelonephritis. *J Microbiol Immune Infect.* 2001; 34: 125-30.

5. Bum Soo Park ,Sunju Lee ,Youn Wha Kim et al.Outcome of Nephrectomy & Kidney Preserving Procedures for the treatment of

Emphysematous Pyelonephritis. *Scandinavian Journal of Urology & Nephrology*. 2006 ; 40: 332-338.

6. J.Michaeli, P.Mogle, S.Perlberg, S.Heiman & M.Caine. Emphysematous Pyelonephritis. *Journal of Urology*. Feb 1984; Vol 131: 203-208.

7. Yuang Ling Wan, Sing Kai Lo, Michael.J.Bullard. Predictors of Outcome in Emphysematous Pyelonephritis. *Journal of Urology*. Feb 1998; Vol 159: 369-373.

8. Jeng-Jong Huang, Ching-Chung Tseng. Emphysematous Pyelonephritis: Clinicoradiological Classification, Management, Prognosis & Pathogenesis. *Arch Int Med 2000.* Mar 27; vol 160: 797-805.

9.M'Liss.A.Hudson,Philip.J.Weyman,Andrew.H.Vandervliet & William.J.Catalona. Emphysematous pyelonephritis: Succesful management by Percutaneous drainage. *Journal of Urology*. Oct 1986; Vol 136: 884-886.

10.Zabbo.A, Montie.J.E, Popowniak.KL, Weinstein.AJ. Bilateral Emphysematous Pyelonephritis. *Urology*. 1985; 25: 293-6.

11.Ahlering.T.E, Boyd.S.D, Hamilton.C.l, Bragin.S.D, Chandrasoma.P.J. Emphysematous Pyelonephritis-A 5 year Experience with 13 patients. *Journal of Urology*. 1985; 134: 1086.

12.Ahmed.A.Shokeir, Mohd El Azab, Tarek-Mohsen & Tarek El Diasty. Emphysematous Pyelonephritis: A 15 Year Experience with 20 Cases. *Urology*. 1997; 49(3): 343-346.

13.Pontin.A.R, Barnes.R.D, Joffe.J, Kahn.D. Emphysematous Pyelonephritis in diabetic patients. British *Journal of Urology*. 1995: 75: 71-74.

14.Jeng Jong Huang, Kuan Wen Chen, Mirns Kuhn Ruaan. Mixed Acid Fermentation of glucose as a mechanism of emphysematous Urinary tract infection. *Journal of Urology*. July 1991; Vol 146: 148-151.

15.C.S.Mitra, S.Chakravarthy. Spectrum of Renal Emphysema. *Indian Journal of Nephrology*. 2001; 11: 53-57.

16.Schainuck.L.I, Cutler.R.E et al. *Amer.J.Med*. 1968; 44: 134.

17.Kuang Wen Chen, Jeng Jong Huang, Ming Howu et al. Gas in Hepatic veins: A Rare & Critical Presentation of Emphysematous Pyelonephritis. *Journal of Urology*. Jan 1994; Vol 151: 125-126.

18.Yang.W.H & Shen.N.C. Gas forming infections of the urinary Tract-An Investigation of Fermentation as a mechanism. *Journal of Urology*. 1990; 143: (960).

19.Costas.S. Renal and perirenal emphysema. British *Journal of Urology*. 1972; 44: 311.

20.Hawes.S, Whigham.T, Ehrmann.S et al. Emphysematous Pyelonephritis. *Infect Surg*. 1983; 2: 191.

21.Anthony.J.Schaeffer.MD. Infections of the urinary tract.Campbell's Urology 8th edn: 556-558.

22.John.P.Stein, Aaron Spitz, Donald.A.Elmajian et al. *Urology*. 1996; 47(1): (129-134).

23.Brenbridge.AN, Buschi.AJ, Cochrane.JA et al. Renal emphysema of the transplanted kidney:Sonographic appearance. *Am J Roentgenology*. 1979; 132: 656.

24.Conrad.MR, Bragman.R, Kilman.WJ. *Am J Roentgenology*. 1979; 132: 395.

25.Langston.C.S, Pfister.R.C. Renal emphysema-A case report and review of the literature. *Am J Roentgenology*. 1970; 110: 778.

26.Joseph.B.Stokes jr. Emphysematous Pyelonephritis. *Journal of Urology*.July 1966; Vol 96: 6-11.

27. Stephen.R.Dunn, William.Dewolf & Ricardo Gonzalez. Emphysematous Pyelonephritis: Report of 3cases treated by Nephrectomy. *Journal of Urology*. Sep 1975; Vol 114: 348-350.

28.Asgari.S.A. Successful Medical Treatment of Emphysematous Pyelonephritis. *Urology Journal(UNRC/IUA).* 2004; Vol 1, No 4: 282-283.

29.Hung Wei Liao, Tso Hsiao, Ke Hsun Lin, Hsin Hung Lin et al. Emphysematous Pyelonephritis caused by Bacteroides fragilis. *Nephrology Dialysis transplantation*. (2005); 20: 2575-2577.

30.Christensen.J, Bistrup.C.Case report: Emphysematous Pyelonephritis caused by Clostridium septicum and complicated by a mycotic aneurysm. *Br J Radiol*. 1993; 66: 842-843.

31. L.D.Wheeler. Cystitis Emphysematosa: Case Report. *Journal of Urology*. Jan 1954; Vol 71, No 1: 43-48.

32.Alfred.E.Turman & Charles Rutherford. Emphysematous Pyelonephritis with perinephric gas. *Journal of Urology*. Vol 105; Feb 1971: 165-170.

33.John.G.Moseley. A Case of Emphysematous Pyelonephritis. *British journal of Surgery*. June 1973; Vol 60, No 6: 495-496.

34.A.R.Pontin, R.D.Barnes, J.Joffe & D.Kahn . Emphysematous Pyelonephritis in Diabetic patients. *British Journal of Urology*. 1995; 75: 71-74.

35.Stephen.D.Mcmurray, Friedrich.C.Luft, Douglas.R.Maxwell & Stuart.A.Kleit. Emphysematous Pyelonephritis. *Journal of Urology*. May 1976; Vol 115: 604-605.

36.Craig.A.Carris & Joseph.D.Schmidt. Emphysematous Pyelonephritis: Single case report . *Journal of Urology*. Sep 1977; Vol 118: 457-459.

37.Sang Eun Lee, duck Ki Yoon & Young Kyoon Kim. Emphysematous Pyelonephritis .*Journal of Urology*. Dec 1977; Vol 118: 916-918.

38.A.Philip Depauw & Gilbert Ross jr. Emphysematous Pyelonephritis in a solitary kidney. *Journal of Urology*. May 1981; Vol 125: 734-736.

39.James.R.Johnson, Robert.C.Ireton & Benjamin.A.Lipsky. Emphysematous Pyelonephritis caused by Candida albicans. *Journal of Urology*. July 1986; Vol 136: 80-82.

40.Cheng Keng Chuang, Ming Kuen Lai, Phei Lang Chang et al. Xanthogranulomatous Pyelonephritis-Experience in 36 cases. *Journal of Urology*. Feb 1992; Vol 147: 333-336.

41.Charles.D.Best, Martha.K.Terris, J.Ronald Tacker & Jeffrey.H.Reese. Clinical & Radiological Findings in Patients with Gas Forming Renal Abscess treated conservatively. *Journal of Urology*. Oct 1999;Vol 162: 1273-1276.

42.Emmanuel Schenkman & Peter Auriemme. Bilateral Emphysematous Pyelonephritis with Autosomal Dominant

Polycystic Kidney disease. *Journal of Urology*.May 1998; Vol 159: 1633-1634.

43.Lucio.P.Fernandes , M.Jaffer Sajwany , A.Derweesh. Emphysematous Pyelonephritis & Cystitis associated with Bilateral Pelviureteric Junction Obstruction: A Case Report. *Journal of Paediatric Surgery*. May 1998; Vol 33, no 5: 739-740.

44.Venkataraman Ramanathan, Peter.T.Nguyen, Peter Van Nguyen, Ahmed Khan & Daniel Musher. Successful management of Recurrent Emphysematous Pyelonephritis . *Urology*. 67(3); 2006: (623e11-623e13).

45.L.A.Langdale, C.l.Rice, N.Brown. Emphysematous Pyelonephritis in a Xanthogranulomatous Kidney-an unusual cause of Pneumoperitoneum. *Archives of Surgery* .Mar 1988; Vol 123: No 3.

46.T.G.Sean, S.Seshadri, K.Saravu. Emphysematous Pyelonephritis. *JAPI*. 2002; 50: 1413-1415.

47.G.Donovan, H.Logan & D.Angus. Emphysematous Pyelonephritis:Diagnosis by ultrasound. *British Journal of Urology:* (213-214).

48.B.N.Shah & J.W.Fowler. Emphysematous Pyelonephritis. *British Journal of Urology:* (548-549).

49.K.B.H.Kou, H.S.Lam, S.H.Lee. Emphysematous Pyelonephritis: Drainage or Nephrectomy. *British Journal of Urology*. 1993; 71: (609-611).

50.J.corr,M.Gleeson, G,Wilson, & R.Grainger. Percutaneous Management of Emphysematous Pyelonephritis.*British journal of Urology*. (487-488).

51.Shehatto, N.Z.Al Awadhi, & S.Ghazah. Emphysematous Pyelonephritis:Surgical implications. *British Journal of Urology* 1990 ;66, 572-574.

52. Cheng Wang, Chin Chung Tseng, Rong Reuhan et al. ouble cancers of the Kidney & Ureter Complicated with Emphysematous Pyelonephritis within the Parenchyma of the renal tumor.

Scandinavian Journal of Urology & Nephrology. 1999; 33: (420-22).

53.Kenneth.L.Janson, James.A.Roberts, Stanley.R.Levine & Russel.H.Clark.Non Invasive Localisation of Urinary Tract Infection:Clincal Investigations & Experience. *Journal of Urology*, Sep 1983, Vol 130; 488-492.

54.Masayuki Tsugaya, Noriaki Hirao, Hiroshi sakagami et al.Computerised tomography in Acute Pyelonephritis:The Clinical Correlation. *Journal of Urology.*Sep 1990;Vol 144:611-613.

55.M.Ahmed, K.V.Dakshinamurthy.Emphysematous Renal Tract Disease due to aspergillus fumigatus. *JAPI* .June 2004 ,Vol 52 ;495-497.

56.James.A.Roberts.Management of Pyelonephritis & upper urinary Tract infection.*Urologic Clinics of North America*, Nov 1999, Vol 26 ;No 4 ,753-763.

57.Karthikeyan.A, Kumar.S, Ganesh.G. Emphysematous Pyelonephritis.*IJU*, 2005 ,Vol 21,issue 2 ,(118-119).

58. Guillermo Flores, Haiko Nellen, Francisco Magaña and Juan Calleja. Acute bilateral emphysematous pyelonephritis successfully
managed by medical therapy alone: A case report and review of the Literature.. *BMC Nephrology* 2002, 3:4

59.Asymptomatic Bacteriuria in patients with Diabetes-Enemy or Innocent Visitor.*NEJM*,Nov 2002, Vol 347,No 20;1617.

60.S.Bhadada, K.S.S.Reddy, A.Bhansali, P.Dutta, C.Sridhar, N.Khandelwal. Co-occurrence of Emphysematous Cystitis & Emphysematous myositis in Type 2 Diabetes.*JAPI,* Sep 2005,Vol 53; 821-823.

61.Ingrid Prkacin, Branko Novak, Dinko Skagro, et al. Emphysematous Pyelonephritis in a patient with Impaired Glucose Tolerance.*Diabetologica Croatica* 2001,30-3;(97-100).

62.Catherine Roy, Dominique.d.Pfleger, Christine.M.Tuchmann et al.Emphysematous Pyelitis-Findings in 5 Patients.*Radiology* 2001; 218: 647-650.

63.E.Grayson, Robert.m.Abbott, Angela.D.Levy, Paul.M.Shermac. Emphysematous Infections of the Abdomen & Pelvis-A Pictorial Review. *Radiographics* 2002; 22; 543-561.

64.Charles.S.Langston, Richard.C.Pfister. Renal Emphysema-A Case Report & Review of Literature. *Journal of Urology*, Dec 1970; Vol 110, No 4: 778-786.

65.M.Muttarak, W.Na Chiang Mai. Clinics in Diagnostic Imaging.*Singapore Medical Journal 2004*, Vol 45(7) ; 340.

66. Sugandh Shetty. Emphysematous Pyelonephritis; eMedicine from webMD.

67.Man YL, Lee TY, Bullard MJ, Tsai CC. Acute gas-producing bacterial renal infection: correlation between imaging findings and clinical outcome. *Radiology.*

*1996;*198:433-8.

68.Shahatto N, al Awadhi NZ, and Ghazali S: Emphysematous pyelonephritis: surgical implications. Br J Uro166: 572-574, 1990.