DISSERTATION ON

A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS"** is a bonafide work done by **Dr.S.KARTHIKAA,** at Madras Medical College, Chennai in partial fulfilment of the university rules and regulations for award of M.D., Degree in General Medicine (Branch-I) under our guidance and supervision during the academic year 2016-2019.

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I, **Dr.S.KARTHIKAA,** solemnly declare that this dissertation entitled **"A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOMES IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS"** was done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai during 2016-2019 under the guidance and supervision of my chief **Prof.Dr.G.SUNDARAMURTHY, M.D.** This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree in General Medicine (Branch-I).

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ABBREVIATIONS

CAUTI	-	Catheter Associated Urinary Tract Infection
CECT	-	Contrast Enhanced Computed Tomography
DJ stent:	-	Double J stent
E.coli	-	Escherichia coli
EPN	-	Emphysematous Pyelonephritis
GSL	-	Glycosphingolipid
HD	-	Hemodialysis
IL	-	Interleukin
mOsm	-	milliOsmoles
NEPN	-	Non Emphysematous Pyelonephritis
PMN	-	Polymorphonuclear Neutrophils
PCN:	-	Percutaneous Nephrostomy
TLR	-	Toll-Like Receptor
UPEC	-	Uropathogenic Escherichia coli
URSL:	-	Ureteroscopic Lithotripsy
USG-KUB:	-	Ultrasonogram - Kidney Urinary Bladder
UTI	–	Urinary Tract Infection
U.urealyticum:	-	Ureaplasma urealyticum
VF	-	Virulence Factor
VUR	-	Vesico-ureteral Reflux
XGP	-	Xanthogranulomatous Pyelonephritis

TABLE OF CONTENTS

INTRODUCTION

Diabetes mellitus is a common cause of pyelonephritis. Patients with diabetes mellitus have an increased incidence of pyelonephritis compared to non-diabetics. Bilateral pyelonephritis is more common in diabetics, which predisposes them to more severe infections and greater complications. Pyelonephritis in diabetics can present as emphysematous or non-emphysematous pyelonephritis.

Non-emphysematous pyelonephritis is a common UTI encountered in diabetic patients; may present in patients with good control of blood sugars also. Emphysematous pyelonephritis is a necrotizing infection of the renal parenchyma with presence of gas in the renal parenchyma, collecting system and perinephric tissue. Prevalence of diabetes in patients with emphysematous pyelonephritis ranges from 53-90%. Conventional treatment of emphysematous pyelonephritis is parenteral antibiotics with percutaneous/ surgical drainage and nephrectomy. Emphysematous pyelonephritis results in high morbidity and mortality, particularly if blood sugars are poorly controlled and diagnosis and treatment is delayed.

A high index of suspicion and early imaging studies are required in diabetic patients presenting with pyelonephritis to diagnose emphysematous pyelonephritis, especially if blood sugars are poorly controlled.

AIMS AND OBJECTIVES

To analyse the clinical features, microbiological profile, prognostic factors and treatment outcome of acute pyelonephritis in Type 2 diabetes mellitus patients.

REVIEW OF THE LITERATURE

Urinary tract infections are due to invasion and multiplication of microorganisms especially bacteria in the urinary tract, leading on to a wide range of clinical syndromes:

–urethritis (inflammation of urethra),

-prostatitis (inflammation of prostate),

-cystitis (inflammation of bladder),

-epididymitis (inflammation of epididymis),

-acute and chronic pyelonephritis (inflammation of the kidneys).

Infection can spread to involve the surrounding tissues resulting in perinephric abscess and spread to the bloodstream.

The incidence of urinary tract infection is very common in women of reproductive age group. Around 10–20% of women will experience symptomatic urinary tract infection at least once in their lifetime. Adult men suffer from UTI less common than women but if present usually it is complicated and related to abnormalities of the urinary tract, rarely, some infections can occur spontaneously in otherwise healthy young men.

Incidence of Urinary tract infection increases with age for both sexes. It is estimated that 10% of men and 20% of women over the age of 65 years would have asymptomatic bacteriuria. The diagnosis of urinary tract infection is relatively difficult in older people, who are more prone to have asymptomatic bacteriuria.

TABLE 1.1: Categories of UTI in adults

Acute uncomplicated cystitis in young women
Recurrent acute uncomplicated cystitis in young women
Acute uncomplicated pyelonephritis in young women
Acute uncomplicated cystitis in adults with a following condition suggesting possible occult renal or prostatic involvement but without other known complicating factors:
Male sex
Elderly
Pregnancy
Diabetes mellitus
Recent urinary tract instrumentation
Childhood urinary tract infection
Symptoms for more than 7 days at presentation
Complicated urinary tract infection*
Obstruction or other structural factor: urolithiasis, malignancies, ureteral and urethral strictures, bladder diverticula, renal cysts, fistulas, ileal conduits, other urinary diversions
Functional abnormality: neurogenic bladder, vesicoureteral reflux
Foreign bodies: indwelling catheter, ureteral stent, nephrostomy tube
Other conditions: renal failure, renal transplantation, immunosuppression, multidrug-resistant uropathogens, health care–associated (includes hospital-acquired/ nosocomial place) infection, prostatitis-related infection, upper tract infection in an adult other than a healthy young woman, other functional or anatomic abnormality of urinary tract)
Asymptomatic bacteriuria

UNCOMPLICATED UTI

Uncomplicated UTI occurs in healthy postmenopausal women who do not have genitourinary abnormalities and diabetic women without nephropathy or neurologic bladder impairment[40]. A urinary tract infection is usually manifested by a combination of clinical features and the presence of bacteriuria. In Asymptomatic bacteriuria, there will be presence of bacteriuria without clinical symptoms and signs[35].Symptomatic bacteriuria refers to the clinical symptoms and signs which have occurred due to the presence of bacteria in urine.

TABLE1.2: Risk factors for urinary tract infections

Female sex
Previous urinary tract infection
Sexual intercourse
Lack of circumcision (children and young adults)
Vesicoureteric reflux
Urologic instrumentation or surgery
Urethral catheterization
Urinary tract obstruction, including calculi, prostatic hypertrophy
Neurogenic bladder
Polycystic kidney disease
Renal transplantation
Lack of urination after intercourse
Spermicide use
Diaphragm use
Pregnancy
Lower socioeconomic group
Diabetes
Sickle cell trait in pregnancy
Human immunodeficiency virus with high viral load
Neurologic disease, eg, spinal cord injury
Older age
Estrogen deficiency (loss of vaginal lactobacilli)
Bladder prolapse

COMPLICATED UTI

Complicated UTI is an infection of the urinary tract in which the efficacy of antibiotics is reduced because of the presence of one or more of the following:

- Structural abnormalities of the urinary tract
- Functional abnormalities of the urinary tract
- Metabolic abnormalities predisposing to UTIs
- Unusual pathogens
- Recent antibiotic use
- Recent urinary tract instrumentation.[42]

Table1.3: Abnormalities of the urinary tract that may be associated with complicated UTI

ABNORMALITY	EXAMPLE
Obstruction	Pelvicalyceal junction obstruction, ureteric or urethral strictures, prostate hypertrophy, urolithiasis, tumor, extrinsic compression
Neurologic impairment	Neurogenic bladder
Urologic devices	Indwelling catheter, ureteric stent, nephrostomy tube
Urologic abnormalities	Vesicoureteral reflux, bladder diverticuli, cystoceles, urologic procedures, ileal conduit, augmented bladder, neobladder
Metabolic/congenital diseases	Nephrocalcinosis, medullary sponge kidney, urethral valves, polycystic kidneys
Immunologic impairment	Renal transplantation

ORGANISMS CAUSING UTI

The commonly encountered organisms are gram negative bacteria, few gram positive cocci. Unusual pathogens include mycobacteria, yeasts and fungi, and opportunistic pathogens like Corynebacterium urealyticum.

Table 1.4:[1]

Bacterial etiology of urinary tract infection

	%Uncomplicated	%Complicated[a]
Gram-negative		
E coli	70–95	21–54
P mirabilis	1–2	1–10
Klebsiella sp	1–2	2–17
Citrobacter sp	<1	5
Enterobacter sp	<1	2–10
P aeruginosa	<1	2–19
Other	<1	6–20
Gram-positive		
Coagulase-negative staphylococci	5–10[b]	1–4
Enterococci	1–2	1–23
Group B streptococci	<1	1–4
S aureus	<1	1–2
Other	<1	2

PYELONEPHRITIS

Pyelonephritis, from the Greek "pyelo" (pelvis), "nephros" (kidney), and "-itis" (inflammation), describes a severe infectious inflammatory disease of the renal parenchyma, calices, and pelvis that can be acute, recurrent, or chronic[33].Pyelonephritis is a less common manifestation of acute uncomplicated urinary tract infection than is cystitis. The ratio of pyelonephritis to cystitis episodes is reported to be 18:1 and 29:1 in women with recurrent infection[2].The highest incidence is among young women aged 20 to 30 years.

Pyelonephritis is associated with substantially greater morbidity, hospitalization is required for as many as 20% of affected non-pregnant women. Severe manifestations such as sepsis syndrome are uncommon. Acute

pyelonephritis complicates 1% to 2% of pregnancies, often occurring at the end of the second trimester or early in the third trimester. Preterm labour and delivery may occur and lead to poor foetal outcomes, as with any febrile illness in later pregnancy[3].Acute non-obstructive pyelonephritis is rarely a direct cause of renal failure. In the few reports of renal failure attributed to pyelonephritis, patients were elderly[4]or had comorbid conditions such as diabetes or HIV infection[5].

Acute pyelonephritis is typically a clinical diagnosis based on signs and symptoms of flank pain, tenderness, and fever with accompanying laboratory findings of leukocytosis, pyuria, positive urine culture, and occasionally bacteremia and hematuria. Most cases of acute pyelonephritis occur by the ascending route from the bladder and are caused by gram negative bacteria.

PATHOGENESIS

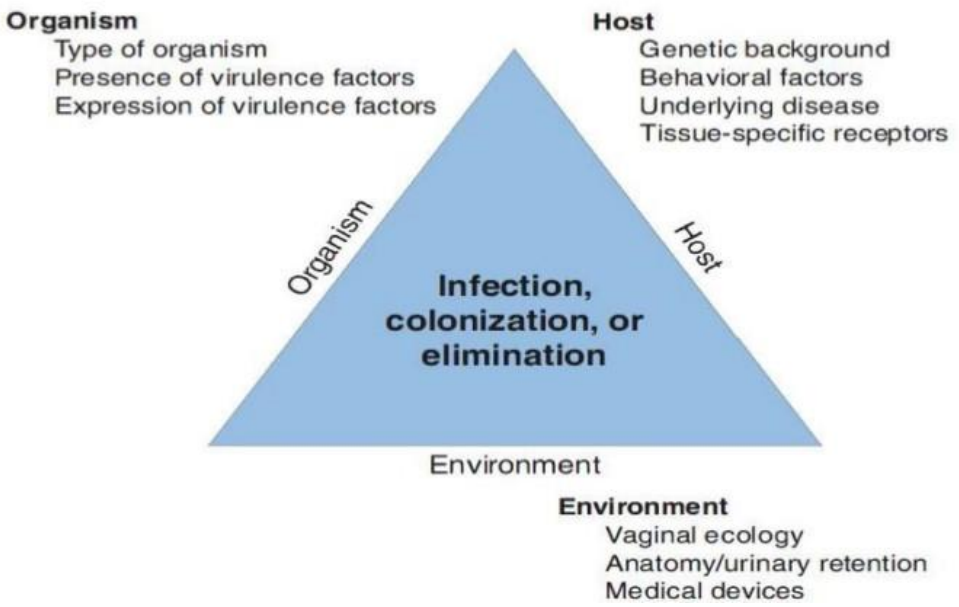


Fig.1.1.Etiopathogenesis of UTI

A familial susceptibility to pyelonephritis has been reported and attributed to polymorphisms with decreased expression of CXCR1, an IL-8 receptor[6]. Vesicoureteral reflux may contribute, although the ascent of the bacteria up the ureter also occurs in its absence. Vesicoureteral reflux is caused by the presence of adhesive P fimbria and powerful endotoxins that appear to inhibit ureteral peristalsis, thereby creating a functional obstruction.

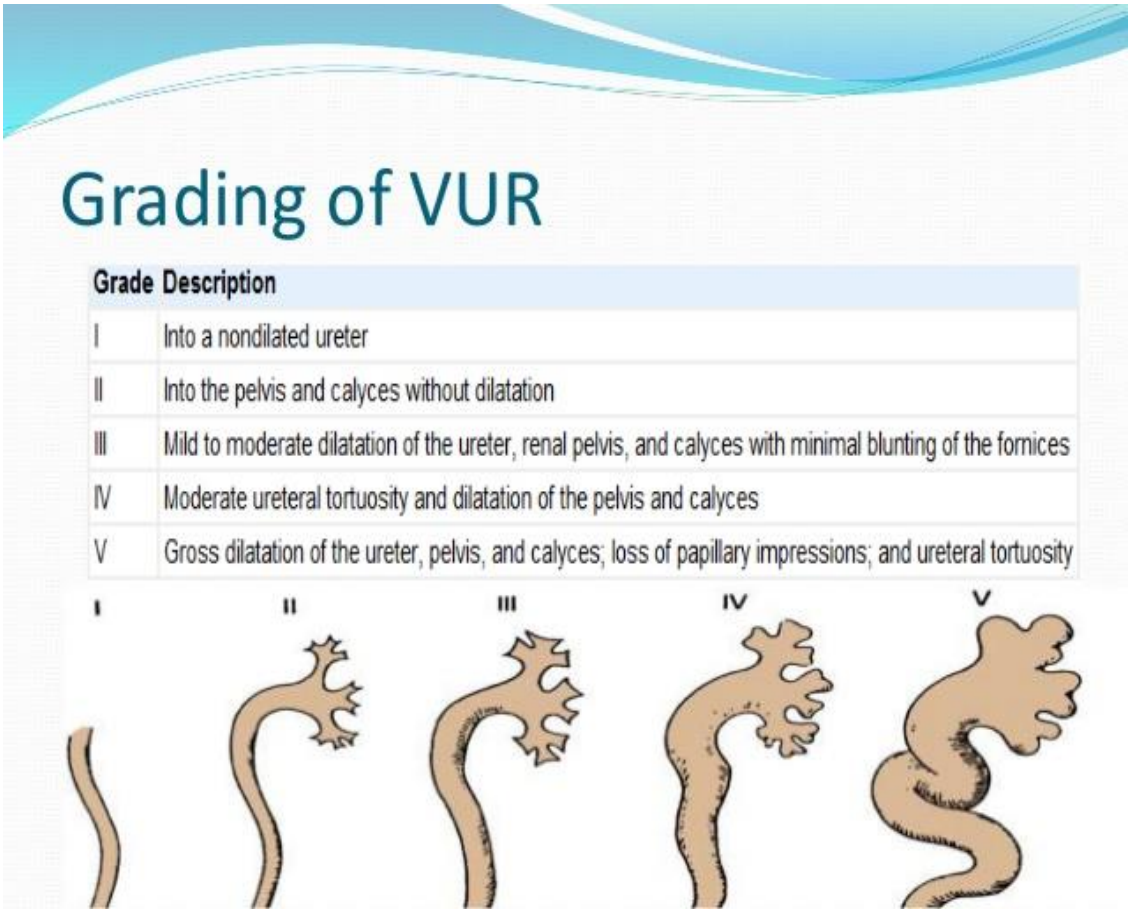


Fig.1.2.Grades of Vesico-ureteral reflux

E.coli is isolated in 85 to 90% of women who present with acute uncomplicated pyelonephritis[7].The gram-negative bacteria, most commonly *Escherichia coli*, are transported to renal pelvis, where intra-renal reflux occurs and the organisms traverse the calyceal system to the ducts and tubules within the renal pyramid. There is a leukocyte response to the bacteria within the

tubules. Enzyme release results in destruction of tubular cells with subsequent bacterial invasion of the interstitium. The resultant inflammatory response involves both the interstitium and tubules. From there, the infection progresses and it spreads throughout the pyramid and to the adjacent parenchyma. The inflammatory response leads to focal or more diffuse swelling of the kidney. Vasoconstriction of the involved arteries and arterioles is noted. Without adequate treatment, necrosis of the involved regions and microabscess formation occur. These microabscesses may coalesce into larger macroabscesses, which tend to be surrounded by a rim of granulation tissue. Perinephric abscess results from the rupture of an intra-renal abscess through the renal capsule or the leak from an infected and obstructed kidney (pyonephrosis). The overall distribution in the kidney is usually patchy or lobar, but sometimes it is diffuse. Subsequent scarring of the kidney after treatment reflects the magnitude of the infection and tissue destruction that occurred. Vesicoureteral reflux is most common in childhood but may occur in adults with lower urinary tract infections or neurogenic bladders. Hematogenous infection occurs initially in the cortex of the kidney. It eventually involves the medulla. It does not tend to be lobar or pyramidal in distribution. The areas of involvement are usually round, peripheral, and frequently multiple. These infections are usually caused by gram positive bacteria, such as *Staphylococcus aureus* and *Streptococcus* species.

Blood-borne infection is less common than ascending infections and is usually observed in intravenous drug abusers, immune compromised patients, or patients with a source of infection outside the kidney, such as heart valves or teeth. Most bacterial data are derived from research with *Escherichia coli,* which accounts for 70-90% of uncomplicated UTIs and 21-54% of complicated UTIs (i.e. UTIs that are secondary to anatomic or functional abnormalities that impair urinary tract drainage; are associated with metabolic disorders; or involve unusual pathogens). A subset of *E.coli,* the uropathogenic *E.coli* (UPEC), also termed extra-intestinal pathogenic *E.coli* (ExPEC), accounts for most clinical isolates from UTIs. UPEC derives commonly from the phylogenetic groups B2 and D, which express distinctive O, K, and H antigens. *UPEC* genes encode several postulated virulence factors (VFs), including adhesins, siderophores, protectins, and toxins, as well as having the metabolic advantage of synthesizing essential substances. Virulence factors such as adhesins have specific regions that attach to cell receptor epitopes in a lock-and-key fashion. Mannose-sensitive adhesins (usually type 1 fimbriae) are present on essentially all *E coli*. They contribute to colonization (e.g. bladder, gut, mouth, vagina) and possibly pathogenesis of infection; however, they also attach to polymorphonuclear neutrophils (PMNs), leading to bacterial clearance

Mannose-resistant adhesins permit the bacteria to attach to epithelial cells, thereby resisting the cleansing action of urine flow and bladder emptying. They also allow the bacteria to remain in close proximity to the epithelial cell, enhancing the activity of other VFs. The P fimbriae family of

adhesins is epidemiologically associated with prostatitis, pyelonephritis (70-90% of strains), and sepsis. This family of adhesins is associated with less than 20% of asymptomatic bacteriuria (ABU) strains. The FA/Dr family is associated with diarrhoea, UTI, and particularly pyelonephritis in pregnancy. The S/F1C family is associated with neonatal meningitis and UTI. Siderophores are involved in iron uptake, an essential element for bacteria, and possibly adhesion. Protectins and their contributions to virulence include the following:

- Lipopolysaccharide (LPS) coatings: resist phagocytosis
- Tra T and Iss: resist action of complement
- Omp T: cleave host defense proteins (eg, immunoglobulins)

Toxins, which affect various host cell functions, include the following:

- Alpha-hemolysin
- Cytotoxic necrotizing factor–1
- Cytolethal distending toxin
- Secreted autotransporter toxin

No single VF is sufficient or necessary to promote pathogenesis. Apparently, multiple VFs are necessary to ensure pathogenesis, although adhesins play an important role in epithelial attachment and inflammatory response. Evidence suggests that the pathogenesis of pyelonephritis takes a 2-step path. First, UPEC attaches to the epithelium and triggers an inflammatory response involving at least 2 receptors, glycosphingolipid (GSL) and Toll-like receptor 4 (TLR4). In the mouse model,

GSL is the primary receptor and TLR4 is recruited and is an important receptor for the release of chemokines[38]. When TLR4 is genetically absent, an asymptomatic carrier state develops in the infected mice. Second, as a result of the inflammatory response, chemokines (eg, interleukin-8 [IL-8], which is chemotactic for PMNs) are released and attach to the neutrophil-activating chemokine receptor 1 (CXCR1), allowing PMNs to cross the epithelial barrier into the urine. In children prone to pyelonephritis, for example, CXCR1 expression has been shown to be significantly lower than in control subjects. Several other host factors militate against symptomatic UTI[41]. Phagocytosis of bacteria in urine is maximized at pH 6.5-7.5 and osmolality of 485 mOsm; values deviating from these ranges lead to significantly reduced or absent phagocytosis. Other important factors are the flushing action of urine flow in the ureter and bladder, the inhibition of attachment of type 1 fimbriae *E coli* to uroepithelial cells by tubular cell–secreted Tamm-Horsfall protein, and the inhibition of attachment by some surface mucopolysaccharides on the uroepithelial cells[39].

OBSTRUCTION

Obstruction is the most important factor. It negates the flushing effect of urine flow; allows urine to pool (urinary stasis), providing bacteria a medium in which to multiply; and changes intrarenal blood flow, affecting neutrophil delivery. Obstruction may be extrinsic or intrinsic. Extrinsic obstruction occurs with chronic constipation (particularly in children), prostatic

swelling/mass (eg, hypertrophy, infection, cancer), and retroperitoneal mass. Intrinsic obstruction occurs with bladder outlet obstruction, cystocele, fungus ball, papillary necrosis, stricture, and urinary stones. With increasing size of stone, the probability of stone passage decreases while the probability of obstruction increases. Nonetheless, stones as small as 2 mm have resulted in obstruction, while 8-mm stones have occasionally passed spontaneously[36].

Infectious stones, urease stones, or triple-phosphate stones composed of magnesium ammonium phosphate or struvite and apatite account for 10-15% of all urinary stones. They develop secondary to the action of urea-splitting organisms and can grow rapidly and branch out (ie, staghorn calculi).Infectious stones, urease stones, or triple-phosphate stones composed of magnesium ammonium phosphate or struvite and apatite account for 10-15% of all urinary stones. They develop secondary to the action of urea-splitting organisms and can grow rapidly and branch out (ie, staghorn calculi).If left untreated, staghorn calculi will destroy the kidney and may cause the death of the patient. Complications include azotemia, hydropyonephrosis, perinephric abscess, pyelonephritis (severe or end-stage), sepsis, and xanthogranulomatous pyelonephritis. Incomplete bladder emptying may be related to medication (eg, anticholinergics).

The spermicide nonoxynol-9 inhibits the growth of lactobacilli. Lactobacilli produce hydrogen peroxide, which protects the vaginal ecosystem against pathogens. Frequent sexual intercourse causes local mechanical trauma to the urethra in both partners. Atrophic vaginal mucosa in post-menopausal

women predisposes to the colonization of urinary tract pathogens and UTIs because of the higher pH (5.5 vs 3.8) and the absence of lactobacilli. Bacterial prostatitis (acute or chronic) produces bacteriuria, whereas nonbacterial prostatitis and pelvic perineal pain syndrome (prostadynia) do not.

Unusual organisms include *Mycoplasma*, *Pseudomonas*, and urea-splitting organisms. *Pseudomonas aeruginosa* has several mechanisms that promote adherence, including alginate, other membrane proteins, pili, and surface-associated exo-enzymes. Urea-splitting organisms produce urease, which hydrolyzes urea, yielding ammonia, bicarbonate, and carbonate; this leads to a more alkaline urine and allows crystal formation (staghorn calculus) from the supersaturation of carbonate, apatite and struvite. Staghorn calculi continue to grow in size, leading to infection, obstruction, or both. Complications of obstruction with superimposed infection include hydronephrosis, pyonephrosis, urosepsis, and xanthogranulomatous pyelonephritis. Additionally, the pathogens can sequester in the struvite stones, protected from the host's immune system. *Proteus* species are the most common urea-splitting organisms. *E.coli, Klebsiella*, *Pseudomonas*, and *Staphylococcus* can also produce urease, however, and are sometimes involved in staghorn calculus formation. Pregnancy produces hormonal and mechanical changes that predispose the woman to upper urinary traction infections. Hydroureter of pregnancy, secondary to both hormonal and mechanical factors, manifests as dilatation of the renal pelvis and ureters (greater on the left than on the right), with the ureters containing up to 200 mL

of urine. Progesterone decreases ureteral peristalsis and increases bladder capacity. The enlarging uterus displaces the bladder, contributing to urinary stasis.

Complicated UTI can result from one or more diverse factors. In patients with AIDS, urinary tract infections are quite common. The infections are frequently hematogenous with unusual organisms such as *Pneumocystis carinii,* cytomegalovirus, and *Mycobacterium avium–intracellulare.* The infections may also be apparent in other abdominal structures, Such as the liver, spleen, and adrenal glands. Diabetes mellitus produces autonomic bladder neuropathy, glucosuria, leukocyte dysfunction, microangiopathy, and nephrosclerosis; additionally, it leads to recurrent bladder instrumentation secondary to the neuropathy.

Complicated UTIs in patients who have diabetes mellitus include the following:

- Renal and perirenal abscess
- Emphysematous pyelonephritis
- Emphysematous cystitis
- Fungal infections
- Xanthogranulomatous pyelonephritis
- Papillary necrosis.

Renal Abscess :

Renal cortical and corticomedullary abscesses and peri-renal abscesses occur in 1 to 10 per 10,000 hospital admissions. Patients usually present with fever, chills, back or abdominal pain, and costovertebral angle tenderness, but they may have no urinary symptoms or findings if the abscess does not communicate with the collecting system, as often occurs with a cortical abscess.

Renal abscess formation is more common with hematogenous infection than with ascending infection. Bacteremia may be primary (cortical abscess) or secondary (corticomedullary or perirenal). 25 to 39% of abscesses are intra-nephric, 19 to 25% are both intra-nephric and peri-nephric and 42-51% are perinephric alone[8].

The clinical presentation may be insidious and nonspecific, especially with peri-renal abscess, and the diagnosis may not be made until admission to a hospital or at autopsy[37]. Empiric antibiotic therapy should be broad and cover *S. aureus* and other uropathogens causing complicated UTI and modified once urine culture results are known.

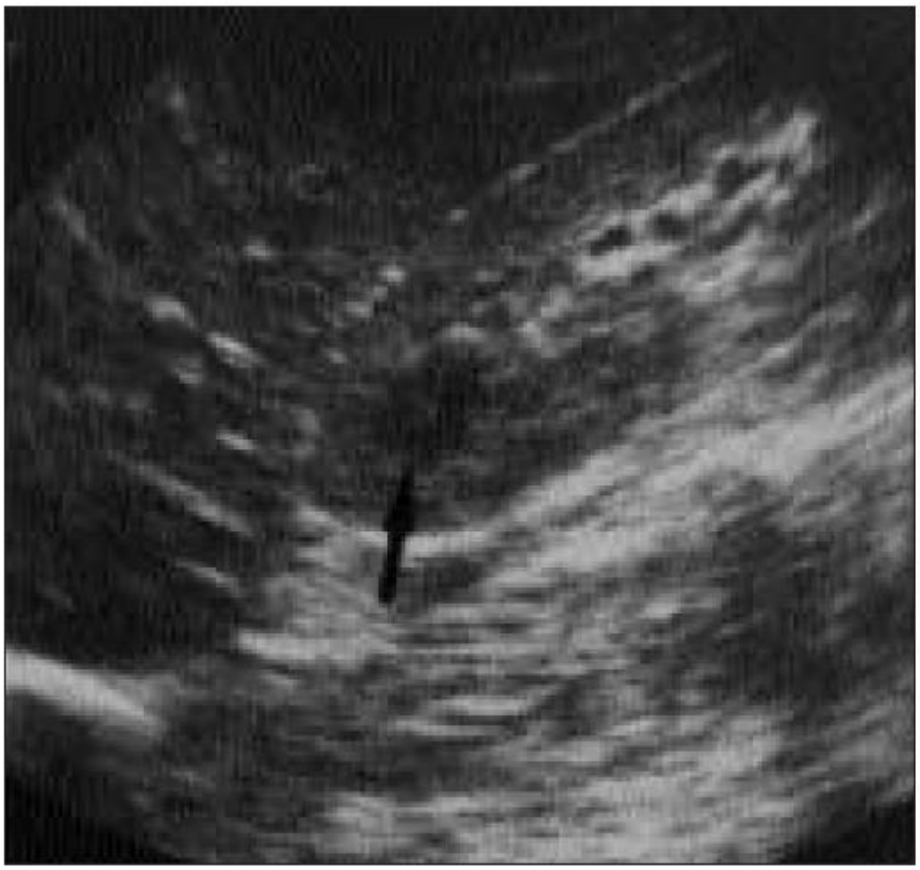


Fig.1.3. USG showing cavity of a small renal abscess.

A *renal cortical abscess* (renal carbuncle) is usually caused by *S. aureus*, which reaches the kidney by hematogenous spread. Treatment with antibiotics is usually effective, and drainage is not required unless the patient is slow to respond. A *renal corticomedullary abscess,* in contrast, usually results from ascending UTI in association with an underlying urinary tract abnormality, such as obstructive uropathy or VUR, and is usually caused by common uropathogenic species such as *E. coli* and other gram-negative bacilli. Such abscesses may extend deep into the renal parenchyma, perforate the renal capsule, and form a perirenal abscess.

EMPHYSEMATOUS PYELONEPHRITIS:

Emphysematous pyelonephritis (EPN) is a severe infection of the renal parenchyma that causes gas accumulation in the tissues (9). Gas is localized in and around the kidneys in pyelonephritis (10).EPN most often occurs in persons with diabetes mellitus, especially women. Its presentation is similar to that of acute pyelonephritis, but EPN often has a fulminating course, and can be fatal if not recognized and treated promptly.

Historicallly, EPN has been described by terms such as renal emphysema and pneumonephritis; Schultz and Klorfein recommended the term emphysematous pyelonephritis in 1962.

The infection often has a fulminating course and can be fatal if left untreated. However, urinary tract infections are common in persons with diabetes, and not all of these infections lead to EPN. The factors that predispose to EPN in persons with diabetes may include uncontrolled diabetes, high levels of glycosylated hemoglobin, and impaired host immune mechanisms.

Fermentation of glucose with carbon dioxide production by the pathogens has been proposed as the cause of gas in the tissues. Schainuck et al proposed that fermentation products from tissue necrosis produced carbon dioxide. Three analyses of the gas content in EPN demonstrated that the major

components include nitrogen (60%), hydrogen (15%), carbon dioxide (5%), and oxygen (8%). Huang et al concluded that mixed acid fermentation is the mechanism of gas production, based on the presence of hydrogen.

Although carbon dioxide is released by the bacteria, the final tissue equilibrium achieved by tissues and gas bubbles determines the final carbon dioxide content. Diabetic microangiopathy may also contribute to the slow transport of catabolic products and may lead to accumulation of gas.

Patients typically present with fever (79%), abdominal or flank pain (71%), nausea and vomiting (17%), dyspnea (10%), acute renal impairment (35%), altered sensorium (19%), shock (29%), and thrombocytopenia (46%).

Crepitus over the flank area may occur in advanced cases of EPN. Pneumaturia is uncommon unless emphysematous cystitis is present. Subcutaneous emphysema and pneumomediastinum have also been reported in a case of EPN. Comorbidities include alcoholism, malnourishment, renal calculi, and diabetic ketoacidosis. A high index of suspicion is important when attempting to diagnose emphysematous pyelonephritis (EPN) promptly. Recommended laboratory studies and expected results include:

- Urinalysis - Pyuria, infected urine
- Complete blood cell count with differential - Leukocytosis with a left shift, thrombocytopenia
- Renal function tests - Elevated creatinine level
- Blood cultures - Positive

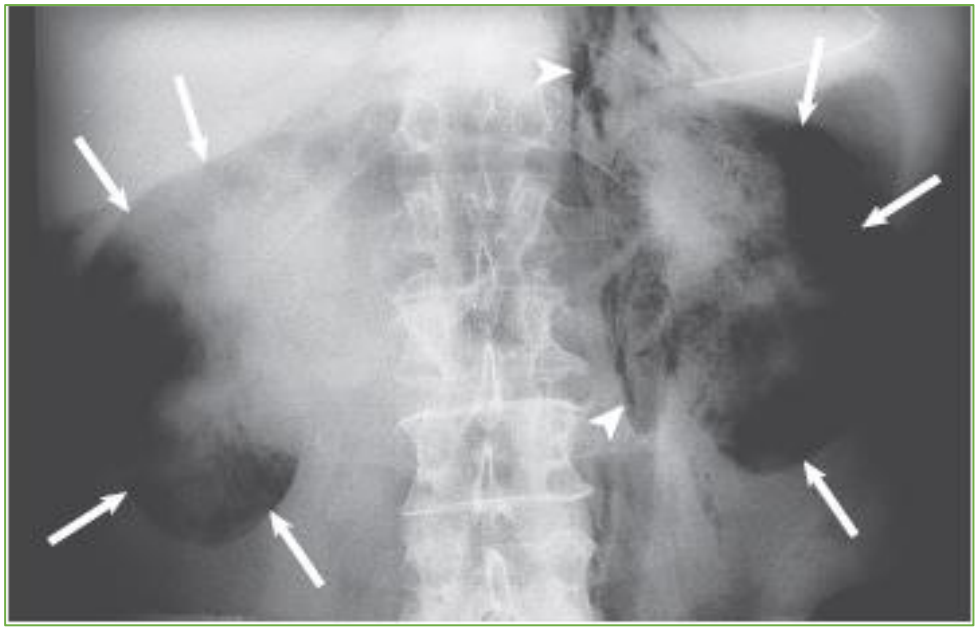


Fig1.4. Plain radiograph showing diffuse gas formation throughout both the kidneys (arrows) and gas dissecting in left retroperitoneal space (arrowhead).

PAPILLARY NECROSIS

More than half of patients who develop papillary necrosis have diabetes, almost always in conjunction with a UTI, but the condition also complicates sickle cell disease, analgesic abuse, and obstruction.

Renal papillae are vulnerable to ischemia because of the sluggish blood flow in the vasa recta, and relatively modest ischemic insults may cause papillary necrosis. The clinical features are those typical of pyelonephritis. In addition, passage of sloughed papillae into the ureter may cause renal colic, renal impairment or failure, or obstruction with severe urosepsis.

Papillary necrosis in the setting of pyelonephritis is associated with pyuria and a positive urine culture. Causative uropathogens are those typical of complicated UTI.

XANTHOGRANULOMATOUS PYELONEPHRITIS:

Xanthogranulomatous pyelonephritis (XGP), first described by Schlagenhaufer in 1916, is a rare, serious, chronic inflammatory disorder of the kidneys characterized by destruction and replacement of renal parenchyma by granulomatous tissue containing histiocytes and foamy cells[11,12].

XGP is most commonly associated with *Proteus* or *E.coli*. *Pseudomonas* species have also been implicated. The kidney is usually non-functional. Most cases of XGP involve a diffuse process; however, up to 20% are focal. Stones (frequently of staghorn proportions) develop in 80% of patients with XGP but are not required to make the diagnosis.

XGP is often observed in patients with diabetes, immunocompromised or both. Abnormal lipid metabolism has also been hypothesized as an etiologic factor in individuals with XGP. XGP displays neoplasm-like properties capable of local tissue invasion and destruction and has been referred to as a pseudo-tumour. Adjacent organs, including the spleen, pancreas, or duodenum, may be involved.

Malek and Elder have proposed the following stages of XGP involvement :

- Kidney
- Perinephric fat
- Adjacent retroperitoneal structures

The gross appearance of XGP is that of a mass of yellow tissue with regional necrosis and hemorrhage, superficially resembling renal cell carcinoma.

The pathognomonic microscopic feature is the lipid-laden foamy macrophage accompanied by both chronic- and acute-phase inflammatory cells. Focal abscesses may be observed.

The primary mechanisms involved in XGP include nephrolithiasis, collecting system obstruction, and infection. No single factor can explain the process; rather, an inadequate host response to the acute inflammatory response occurs in the obstructed, necrotic kidney. Patients with xanthogranulomatous pyelonephritis (XGP) often appear chronically ill. Symptoms include anorexia, fever, chills, weight loss, and flank pain. The pain of XGP is not colicky in nature; it is usually dull and persistent.

XGP is notorious for fistulization. Pyelo-cutaneous and uretero-cutaneous fistulae have been well described. Other organs are occasionally involved in this process, including surrounding viscera (with resulting pyeloenteric fistulae).

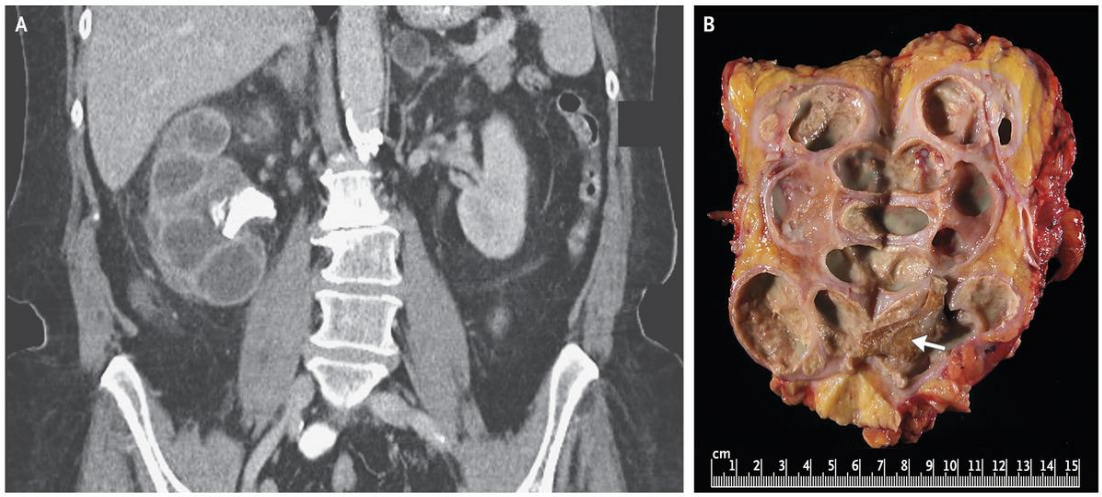


Fig.1.5. Xanthogranulomatous pyelonephritis

Catheter-Associated Infections:

The Center for Disease Control and prevention (CDC) and the National Healthcare Safety Network (NHSN) define CAUTI as a UTI episode for which an indwelling catheter has been placed for >2 days on the date of diagnosis and an indwelling catheter was in place on the date of event or the day before[13].Approximately 15% to 25% of patients in general hospitals have a urethral catheter inserted at some time during their stay, and approximately 5% to 10% of long-term care facility residents are managed with urethral catheterization, in some cases for years.

The incidence of bacteriuria associated with indwelling catheters is 3% to 10% per day of catheterization, and the duration of catheterization is the most important risk factor for the development of catheter-associated bacteriuria.

Catheter-associated bacteriuria is the most common source of gram negative bacteremia in hospitalized patients[32]. Complications of long-term

catheterization (≥30 days) include almost universal bacteriuria, often with multiple antibiotic-resistant flora, and (in addition to cystitis, pyelonephritis, and bacteremia, as seen with short-term catheterization) frequent febrile episodes, catheter obstruction, stone formation associated with urease-producing uropathogens, and local genitourinary infections.

INVESTIGATIONS IN ACUTE PYELONEPHRITIS:

URINALYSIS

URINE CULTURE

BLOOD CULTURE

COMPLETE BLOOD COUNT

ESR /CRP

RENAL ULTRASONOGRAPHY

CONTRAST-ENHANCED COMPUTED TOMOGRAPHY (CECT)

1. URINALYSIS:

Urinalysis is one of the key tests to evaluate kidney and urinary tract disease.

Acceptable methods of collection are the following:

a. Midstream urine voided into a sterile container after careful washing (water or saline) of external genitalia (any soap must be rinsed away)
b. Urine obtained by single catheterization or suprapubic needle aspiration of the bladder
c. Sterile needle aspiration of urine from the tube of a closed catheter drainage system (do not disconnect tubing to get specimen).

Bacteria and leukocytes are the hallmarks of urinary tract infection, in association with superficial transitional epithelial cells and isomorphic erythrocytes. Struvite crystals can also be present when the infection is caused by urease-producing bacteria, such as U. urealyticum. In patients with renal infection, leukocyte casts and casts containing microorganisms may be found. The correlation between the urine sediment findings and the urine culture is usually good. The finding of WBC casts, signifying infection within the tubules, is of primary diagnostic value for both acute and chronic pyelonephritis

LEUKOCYTE ESTERASE

The leukocyte esterase dipstick test evaluates the presence of leukocytes based on the activity of an indoxyl esterase released from lysed neutrophil granulocytes. Leukocyte esterase may be positive when microscopy is negative and when leukocytes are lysed, because of low relative density, alkaline pH, or a delay in sample handling and examination.

Nitrites

The dipstick nitrites test detects bacteria that reduce nitrates to nitrites by nitrate reductase activity. This includes most gram negative uropathogenic bacteria, but not Pseudomonas, Staphylococcus albus, or Enterococcus.

URINE CULTURE:

A urine specimen for culture should be obtained before initiation of antimicrobial therapy in every case of suspected pyelonephritis. Urine specimens must be cultured promptly within 2 hours or be preserved by refrigeration or a suitable chemical additive (e.g., boric acid sodium formate preservative).

The culture will confirm the diagnosis of urinary tract infection and identify the specific infecting organism and susceptibilities so that antimicrobial therapy can be optimized. In more than 95% of women with pyelonephritis, 10^5 CFU/mL of organisms or more are isolated from the urine culture. Most common organisms isolated include gram negative bacilli such as Escherichia coli, Klebsiella species, Pseudomonas aeruginosa, Acinetobacter species and gram positive cocci such as Staphylococci.

Table 1.5: Quantitative counts of bacteria in urine

CONDITION	QUANTITATIVE CRITERIA
Voided	
Women: acute uncomplicated	
Cystitis	$\geq 10^3$ CFU/mL
Pyelonephritis	$\geq 10^4$ CFU/mL*
Asymptomatic	$\geq 10^5$ CFU/mL†
Men	$\geq 10^3$ CFU/mL
External condom collection	$\geq 10^5$ CFU/mL
Catheter	
In-and-out Indwelling‡	$\geq 10^2$ CFU/mL
Asymptomatic	$\geq 10^5$ CFU/mL
Symptomatic	$\geq 10^2$ CFU/mL
Suprapubic or percutaneous aspiration	Any growth

BLOOD CULTURE:

Bacteremia is identified in 10% to 25% of women presenting with acute pyelonephritis if blood cultures are collected routinely. However, the clinical utility of routine blood cultures is limited because bacteremia does not alter therapy, nor is it predictive of outcome[14,15].Thus blood cultures should be obtained selectively, usually only if the diagnosis is uncertain or the clinical presentation is severe. Growth of the same organism from both blood and urine usually confirms a urinary source for the infection. However, bacteria isolated from the urine are occasionally attributable to bacteremia from a source outside the urinary tract. This may be a result of hematogenous seeding with development of renal microabscesses, which is well described for Staphylococcus aureus in particular.

OTHER BLOOD INVESTIGATIONS:

Additional investigations recommended for most patients presenting with acute pyelonephritis are measurements of peripheral leukocyte count and serum creatinine. The leukocyte count is usually elevated and may be useful as a parameter to monitor the response to therapy.

C-reactive protein and procalcitonin levels are elevated in most women with acute pyelonephritis[2,16,17]. An elevated level of C-reactive protein at discharge has been associated with prolonged hospitalization and subsequent recurrence. The serum procalcitonin level at presentation, however, is not predictive of outcome.

IMAGING:

Imaging is rarely used or needed in the uncomplicated case of acute pyelonephritis. It is reserved for patients who are not responding to conventional antibiotic treatment, patients with an unclear diagnosis, patients with coexisting stone disease and possible obstruction, patients with diabetes and poor antibiotic response, and immunocompromised patients.

When the clinical presentation of pyelonephritis is mild or moderate and the clinical response after initiation of antimicrobial therapy is prompt, routine diagnostic imaging is not indicated[18,19]. Women whose clinical presentations are severe, who fail treatment, or who experience early post-treatment recurrent

infection, should undergo prompt imaging to rule out obstruction or abscesses and to determine whether intervention is necessary.

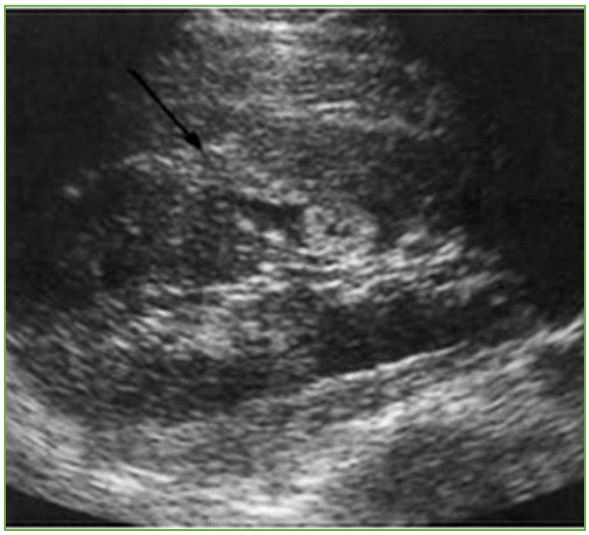
Imaging is used to assist in confirming the diagnosis and determining the extent of the disease. It is also used in assessing complications of acute pyelonephritis, including renal abscess, emphysematous pyelonephritis, and perinephric abscess.

ULTRASONOGRAPHY:

Ultrasonography is often the initial imaging modality because it is safe and widely accessible[20]. The ultrasound examination in women with uncomplicated pyelonephritis usually yields normal results, but enlargement and edema in one or both kidneys is observed in 20% of patients[21].

Ultrasonography is less sensitive or specific for pyelonephritis than is either CT or MRI. Imaging study findings that can raise suspicion of EPN include the presence of intrarenal gas on renal ultrasonography.

Fig.1.6. USG showing focal pyelonephritis



CHRONIC PYELONEPHRITIS

This chronic inflammatory state is usually the result of frequent previous inflammatory/infective episodes. The kidney may be small and often has focal scarring present. Scar tissue has the appearance of a hyperechoic, linear lesion which affects the smooth renal outline and crosses the renal cortex.

RENAL CT:

ACUTE PYELONEPHRITIS:

Abnormalities observed on CT are characterized as unilateral or bilateral, focal or diffuse, focal swelling or no focal swelling, and renal enlargement or no renal enlargement. In addition to renal enlargement and oedema, dilation of the collecting system in the absence of obstruction, wedge-shaped areas of decreased attenuation, and rounded low-attenuation masses with delayed enhancement may be observed.

CHRONIC PYELONEPHRITIS

Imaging findings include renal scarring, atrophy, and cortical thinning; hypertrophy of residual normal tissue (which may mimic a mass lesion); calyceal clubbing secondary to retraction of the papilla from the overlying scar; dilatation of the calyceal system; and overall renal asymmetry.

RENAL ABSCESS:

CT is recommended to establish the diagnosis and location of a renal or peri-renal abscess.

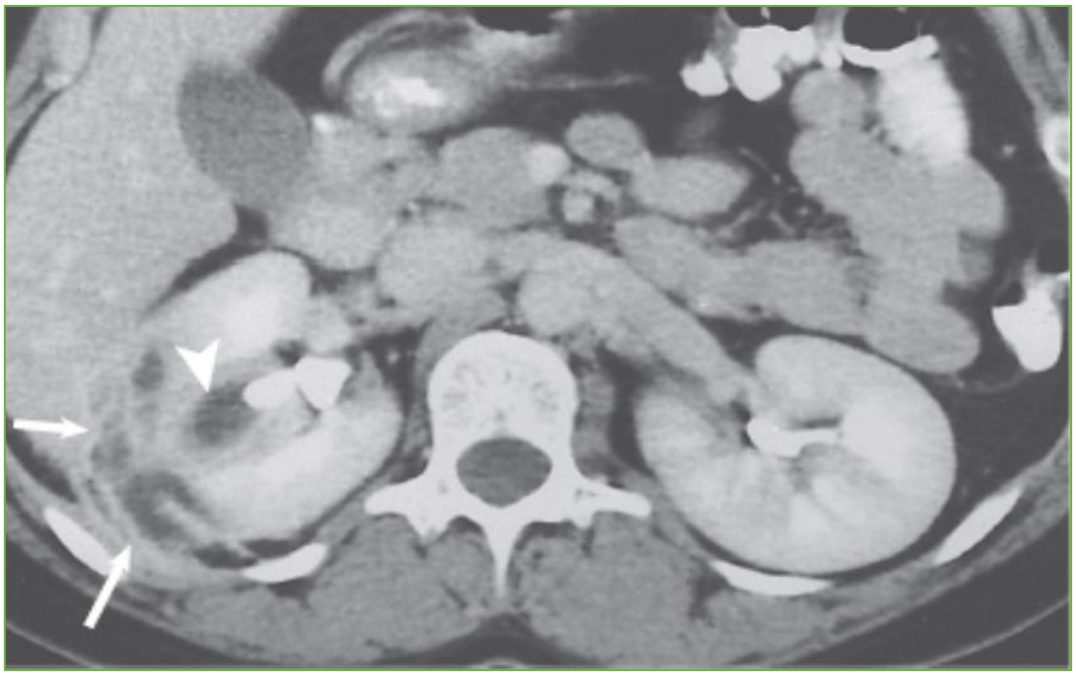


Fig.1.7. CECT shows abscess in the renal medulla (arrowhead) with extension into the perinephric space (arrows)

EMPHYSEMATOUS PYELONEPHRITIS:

Computed tomography (CT) scanning is the definitive imaging test for EPN.[9,20].

In 2000, Huang and Tseng modified the staging proposed by Michaeli et al, as follows :

- Class 1 - Gas confined to the collecting system
- Class 2 - Gas confined to the renal parenchyma alone
- Class 3A - Perinephric extension of gas or abscess
- Class 3B - Extension of gas beyond the Gerota fascia
- Class 4 - Bilateral EPN or EPN in a solitary kidney.

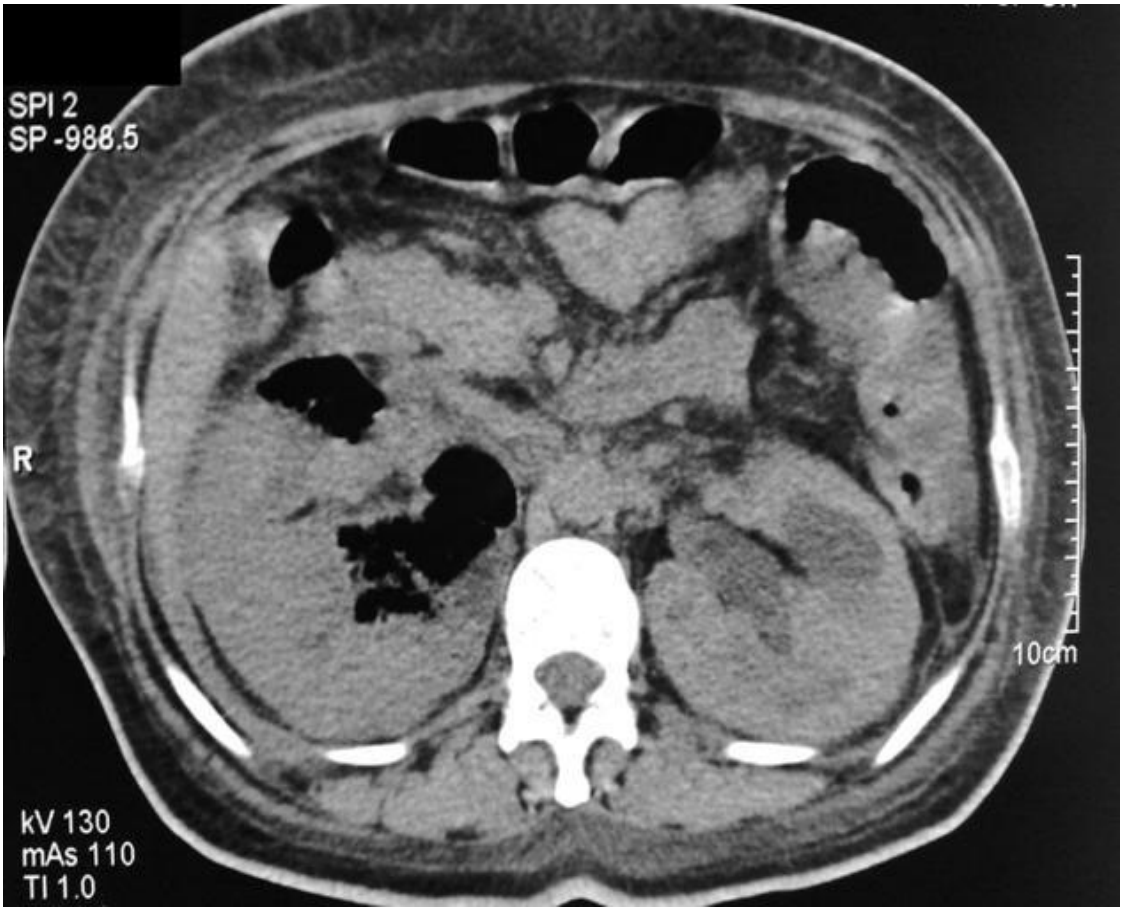


Fig.1.8.CECT showing right emphysematous pyelonephritis

CT FINDINGS IN PAPILLARY NECROSIS:

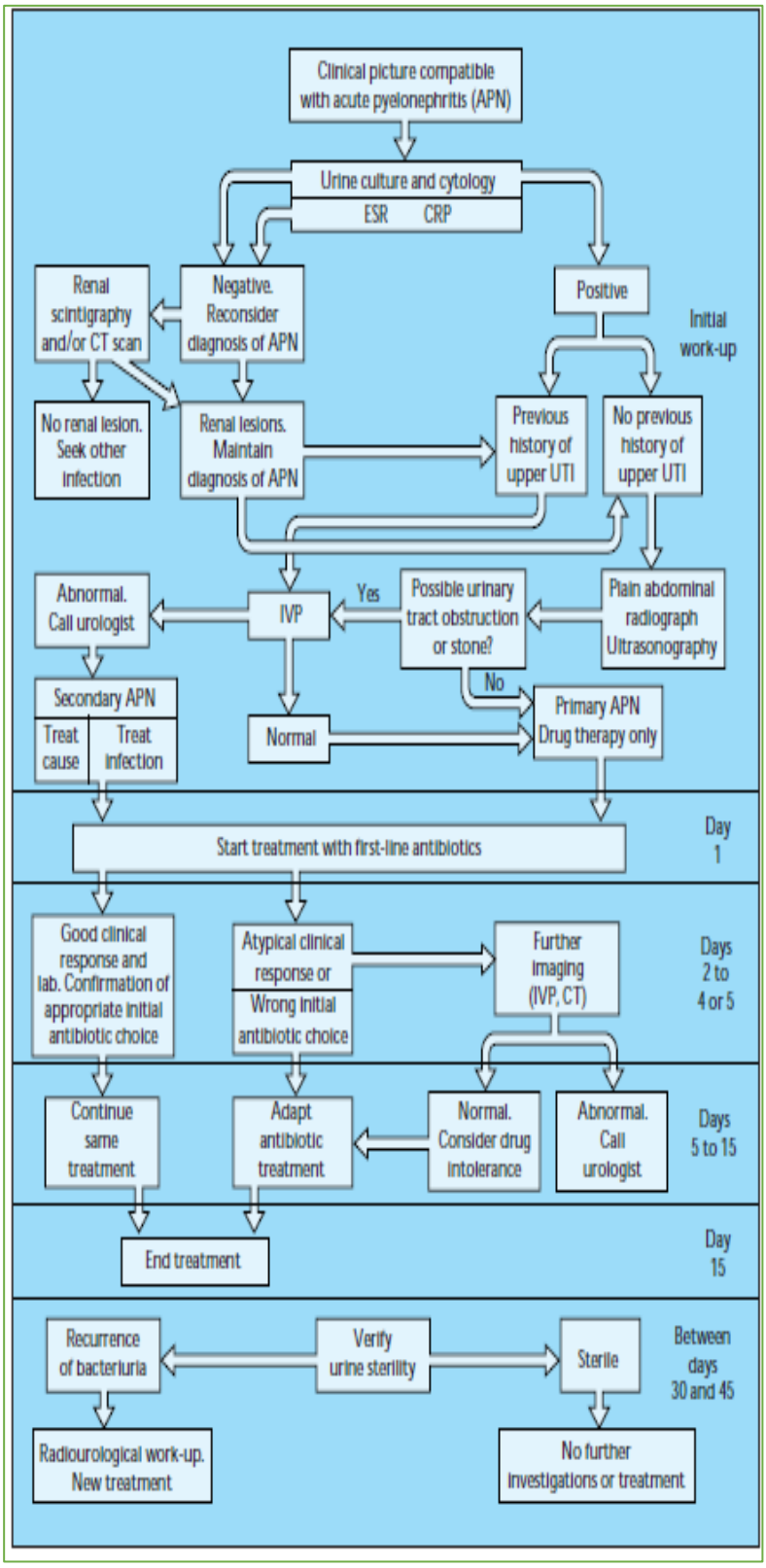
CT is the preferred diagnostic procedure. Radiologic findings include an irregular papillary tip; dilated calyceal fornix; extension of contrast material into the parenchyma; and a separated crescent-shaped papilla surrounded by contrast, called “the ring sign”.

CT IN XANTHOGRANULOMATOUS PYELONEPHRITIS:

CT scanning is the most useful radiographic technique in evaluating xanthogranulomatous pyelonephritis (XGP), although XGP cannot be diagnosed solely on the basis of radiographic findings. It identifies the abnormality in 74% to 90% of the cases. A CT scan demonstrates a heterogenous, non-enhancing mass on a hydronephrotic, non-functioning kidney with a central stone. In higher stage disease, the mass may appear to involve adjacent organs. CT scans may also reveal a large staghorn calculus within the collecting system.

MRI shows abnormalities similar to those observed with CT[21].

Fig.1.9 General algorithm for investigations and management of pyelonephritis



The majority of women with uncomplicated pyelonephritis can receive treatment as outpatients[22]. Indications for hospitalization include pregnancy, hemodynamic instability, uncertain gastrointestinal absorption or compliance with oral therapy, the need to exclude complicating factors such as obstruction or abscess, or the necessity of monitoring or treatment of associated medical illnesses.

Appropriate supportive management for hypotension, nausea and vomiting, and pain control should be initiated promptly. When oral tolerance is uncertain because of nausea and vomiting, a strategy frequently used in emergency room management is to provide a single parenteral dose of ceftriaxone, 1 g, or of gentamicin, 120 mg, followed by oral therapy once gastrointestinal symptoms are controlled. Many parenteral antimicrobial regimens are effective for pyelonephritis. *E. coli* strains generally remain susceptible to aminoglycosides, and these agents are useful for empirical treatment.

Aminoglycosides also have unique efficacy for the treatment of renal infection in that they are bound in high concentrations in the renal cortex[23]. Extended-spectrum cephalosporins, such as cefotaxime or ceftriaxone, and fluoroquinolones, such as ciprofloxacin and levofloxacin, are other options for parenteral therapy[24]. Ceftriaxone is the preferred empirical regimen for pregnant women.

Although it is suggested that gentamicin be avoided in pregnancy because of potential fetal ototoxicity, excess otologic impairment has not been reported in large cohorts of newborn infants stratified by gentamicin exposure in utero[25]. Thus, when cephalosporins cannot be used because of antimicrobial resistance or patient intolerance, gentamicin remains an alternate antimicrobial for treatment of pregnant women.

A satisfactory clinical response is usually observed by 48 to72 hours after initiation of antimicrobial therapy. Oral therapy selected on the basis of urine culture results can then be prescribed to complete the antimicrobial course[34].In most young, non-pregnant women, acute pyelonephritis is effectively managed with outpatient oral therapy[26,27].

Table.1.6.Antibiotic regimes for pyelonephritis

FIRST-LINE THERAPY	OTHER THERAPY
Oral	
Ciprofloxacin, 500 mg bid or 1000 mg extended-release preparation, od × 7 days Levofloxacin, 750 od × 5 days	TMP/SMX, 160/800 mg bid × 7-14 days Amoxicillin, 500 mg PO tid × 14 days* Amoxicillin/clavulanic acid, 500 mg tid or 875 mg PO bid × 14 days* Cephalexin, 500 mg qid × 14 days* Cefuroxime axetil, 500 mg bid × 14 days* Cefixime, 400 mg od × 14 days*
Parenteral†	
Ciprofloxacin, 400 mg q12h × 7 days Levofloxacin, 750 mg od × 5 days Gentamicin or tobramycin, 3-5 mg/kg od, ± ampicillin, 1 g q4-6hr Ceftriaxone, 1-2 g od* Cefotaxime, 1 g q8hr*	Ertapenem, 1 g od Meropenem, 500 mg q6h Piperacillin/tazobactam, 3.375 g q6hr

*Recommended for pregnant women.
†Change to oral therapy to complete course once condition is clinically stable.
TMP/SMX, Trimethoprim/sulfamethoxazole.

TREATMENT OF THE COMPLICATIONS:

RENAL ABSCESS:

Treatment with antimicrobial agents without drainage may be effective if the abscess is small and if the underlying urinary tract abnormality can be corrected. Aspiration of the abscess may be necessary in some patients, and nephrectomy may occasionally be required in patients with diffuse renal involvement or with severe sepsis. Perirenal abscesses usually occur in the setting of obstruction or other complicating factors and result from ruptured intrarenal abscesses, hematogenous spread, or spread from a contiguous infection.

A previously high mortality rate has been lowered with earlier diagnosis and therapy. In contrast to the other types of abscesses, drainage of pus is the cornerstone of therapy, and nephrectomy may be indicated[28,29,30].

EMPHYSEMATOUS PYELONEPHRITIS:

Patients with emphysematous pyelonephritis (EPN) are extremely ill and need resuscitative measures in the intensive care unit, including oxygen, intravenous (IV) fluids, and correction of acid-base imbalances, along with glycaemic control. Systolic blood pressure should be maintained above 100 mm Hg, with fluid or inotropic support if required. Surgical intervention should be performed only after stabilization of the cardiorespiratory status.

Prompt initiation of empiric IV antibiotic therapy is critical. The regimen chosen should be broad spectrum, primarily target gram-negative bacteria, and take into account individual patient characteristics and local patterns of antibiotic resistance.

Conservative treatment using percutaneous drainage/ percutaneous nephrostomy[31] with antibiotics is indicated as follows:

- Patients with compromised renal function
- Early cases associated with gas in the collecting system alone and patient is in otherwise in stable condition
- Class 1 and class 2 EPN

- Class 3 and class 4 EPN - In the presence of fewer than 2 risk factors (eg, thrombocytopenia, elevated serum creatinine levels, altered sensorium, shock).

The use of nephrectomy is indicated as follows:

- Treatment of choice for most patients
- No access to percutaneous drainage or internal stenting (after patient is stabilized)
- Gas in the renal parenchyma or "dry-type" EPN
- Possibly bilateral nephrectomy in patients with bilateral EPN
- Class 3 and class 4 EPN - In the presence of two or more risk factors (eg, thrombocytopenia, elevated serum creatinine, altered sensorium, shock).

PAPILLARY NECROSIS:

Broad-spectrum antibiotics are indicated. Papillae obstructing the ureter may require removal with a cystoscopic ureteral basket or relief of obstruction by insertion of a ureteral stent.

XANTHOGRANULOMATOUS PYELONEPHRITIS:

Xanthogranulomatous pyelonephritis (XGP) is a surgically managed disease that is treated with either nephrectomy or, in rare circumstances, partial nephrectomy .Antibiotics are used in all cases, but medical care rarely suffices for treatment[12]

MATERIALS AND METHODS

Study Design: Prospective observational study

Sample Size : 100 patients.

{ based on formula : $ss = Z^2 \times p \times (1-p) / C^2$

Where z= z value

p= percentage picking a choice

c=confidence interval}

Statistical methods:

Values are expressed as mean +/- standard deviation.

$P < 0.05$ was taken as an upper limit of statistical significance.

Inclusion Criteria:

- Patients with diagnosis of acute pyelonephritis (Both emphysematous and non-emphysematous) with type 2 diabetes mellitus.

- Age >40 years

Exclusion Criteria:

Patients with inflammatory conditions other than pyelonephritis, including:

History of trauma,

Pregnancy,

Malignancies,

Other immunosuppressed conditions.

Data Collection and methods :

- Acute pyelonephritis said to be present when patient complained of fever with chills and rigors, flank pain, nausea and vomiting.
- USG KUB studies suggestive of pyelonephritis if there was a combination of enlarged kidney, presence of collection and perinephric fat stranding.
- Urine sample collection: Methods of collection are the following:

a. Midstream urine voided into a sterile container after careful washing (water or saline) of external genitalia

b. Urine obtained by single catheterization or suprapubic needle aspiration of the bladder

c. Sterile needle aspiration of urine from the tube of a closed catheter drainage system

- Urine culture positive: $> 10^5$colony forming units/ml of bacteria found.
- Glycaemic control-defined as good if HbA1c<7%, moderate if HbA1c 7-7.5% and poor if HbA1c >7.5%.

On the basis of CT scan (when necessary), patients with emphysematous pyelonephritis can be classified into the following classes:

(1) Class 1: Gas in the collecting system only

(2) Class 2: Gas in the renal parenchyma without extension to the extra-renal space

(3) Class 3A; Extension of gas or abscess to the perinephric space;

Class 3B: Extension of gas or abscess to the pararenal space

(4) Class 4: Bilateral EPN or solitary kidney with EPN.

Investigations done include Complete Blood Count, urinalysis including urine culture and sensitivity, HbA1C, serum creatinine, fasting and postprandial blood glucose levels, ultrasound KUB (baseline), CECT-KUB (whenever necessary, in case of suspected renal abscess and non-recovering pyelonephritis).

Management:

Patients were treated with antibiotic as per culture sensitivity reports. Patients with NEPN were treated with parenteral antibiotics for 1 week followed by oral antibiotics for 2 weeks and EPN patients received antibiotics for at least 3 weeks. Patients with fungal UTI were initially treated with fluconazole for Candida species and amphotericin for non-candida species and changed as per culture sensitivity and continued for 2 weeks. Percutaneous drainage (PCD) with pigtail or percutaneous nephrostomy tube was inserted into pelvis or perirenal space to drain out fluid collection/gas in addition to antibiotics. Nephrectomy was carried out in patients refractory to antibiotics, PCN and/or clinical deterioration.

Patients were divided into “good” and “poor” outcome groups to elucidate the risk factors. The patients who were successfully treated with antibiotics alone or with PCN were assigned to “good” outcome group. Those who had nephrectomy or died were classified as “poor” outcome group.

RESULTS

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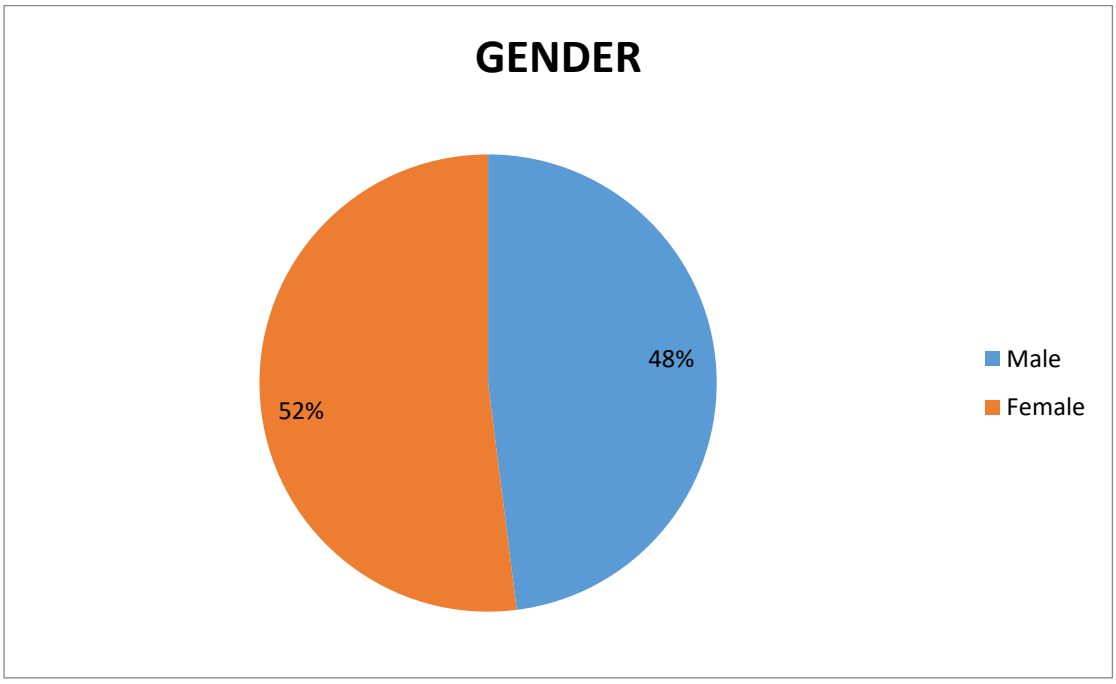
Table 2.1: Distribution of study subjects based on gender

GENDER	FREQUENCY	PERCENT
Male	48	48.0
Female	52	52.0
Total	**100**	**100.0**

Fig.2.1: Representation of study subjects based on gender



In our study, 48 patients were males and 52 patients were females.

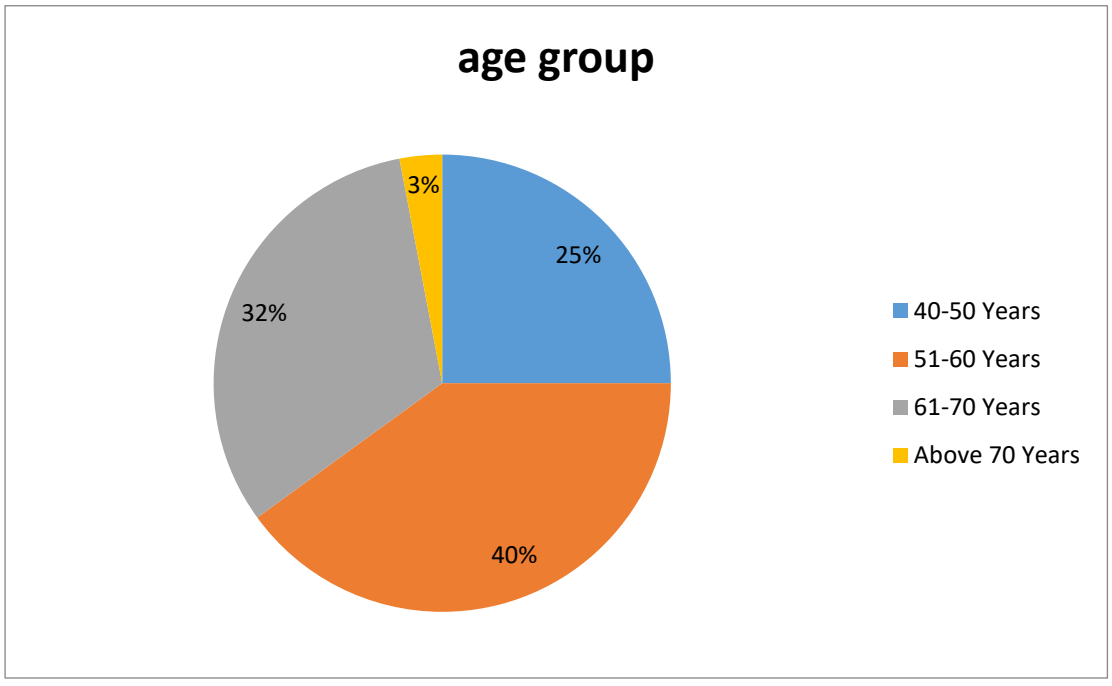
Table 2.2:

Distribution of study subjects based on age group –

[41-50yrs, 51- 60yrs, 61-70 yrs, >70 yrs]

AGE_GROUP	FREQUENCY	PERCENT
40-50 Years	25	25.0
51-60 Years	40	40.0
61-70 Years	32	32.0
Above 70 Years	3	3.0
Total	**100**	**100.0**

Fig.2.2: Representation of study subjects based on age group



Around 40% patients were in the age group of 51-60 years, 32% were between 61-70 years, 25% patients were between 41-50 years and remaining 3% were above 70 years.

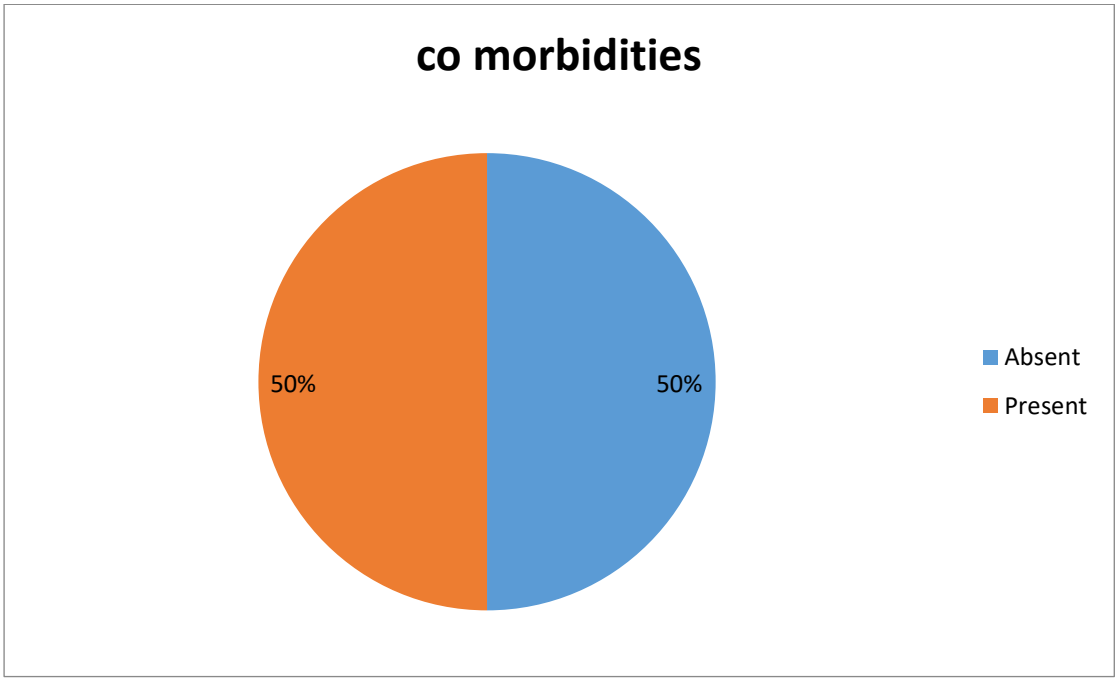
Table 2.3:

Distribution of study subjects based on co-morbidities - [present/absent]

CO-MORBIDITIES	FREQUENCY	PERCENT
Absent	50	50.0
Present	50	50.0
Total	**100**	**100.0**

Fig.2.3:

Representation of study subjects based on presence/absence of comorbidities



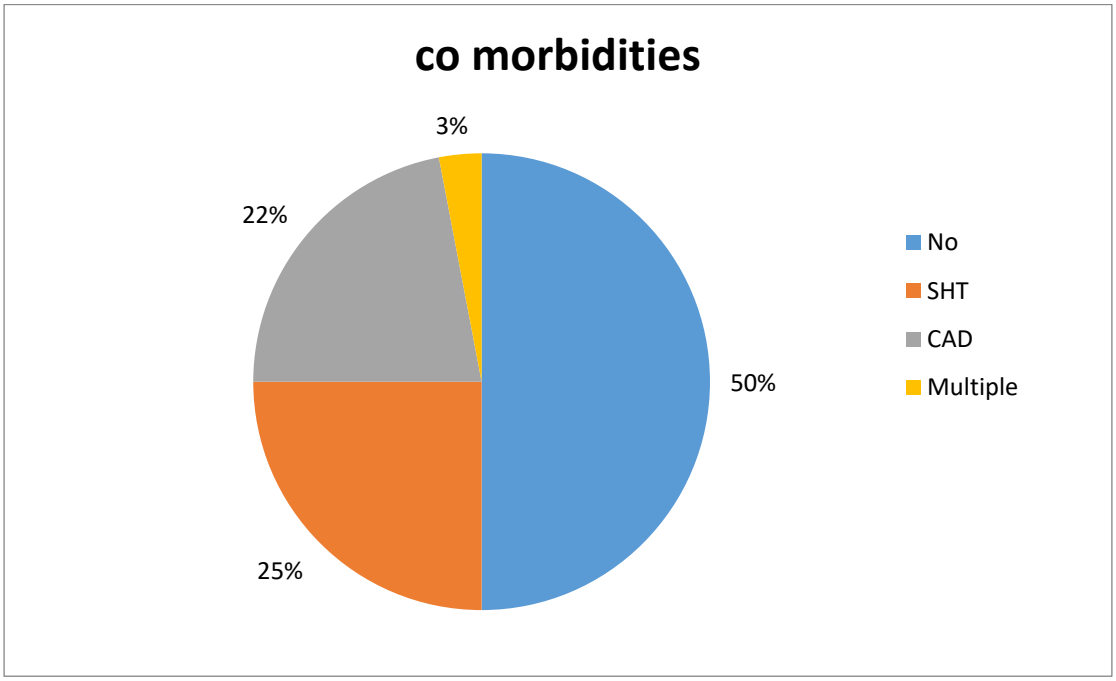
50% of the patients had no additional comorbidities other than diabetes mellitus.

Table 2.4: Distribution of study subjects based on type of co-morbidity

(History of SHT/CAD/CKD/>1 comorbidity)

CO-MORBIDITIES	FREQUENCY	PERCENT
No	50	50.0
SHT	25	25.0
CAD	22	22.0
Multiple comorbidities (+SHT/CAD/CKD combined)	3	3.0
Total	**100**	**100.0**

Fig.2.4: Representation based on type of comorbidity



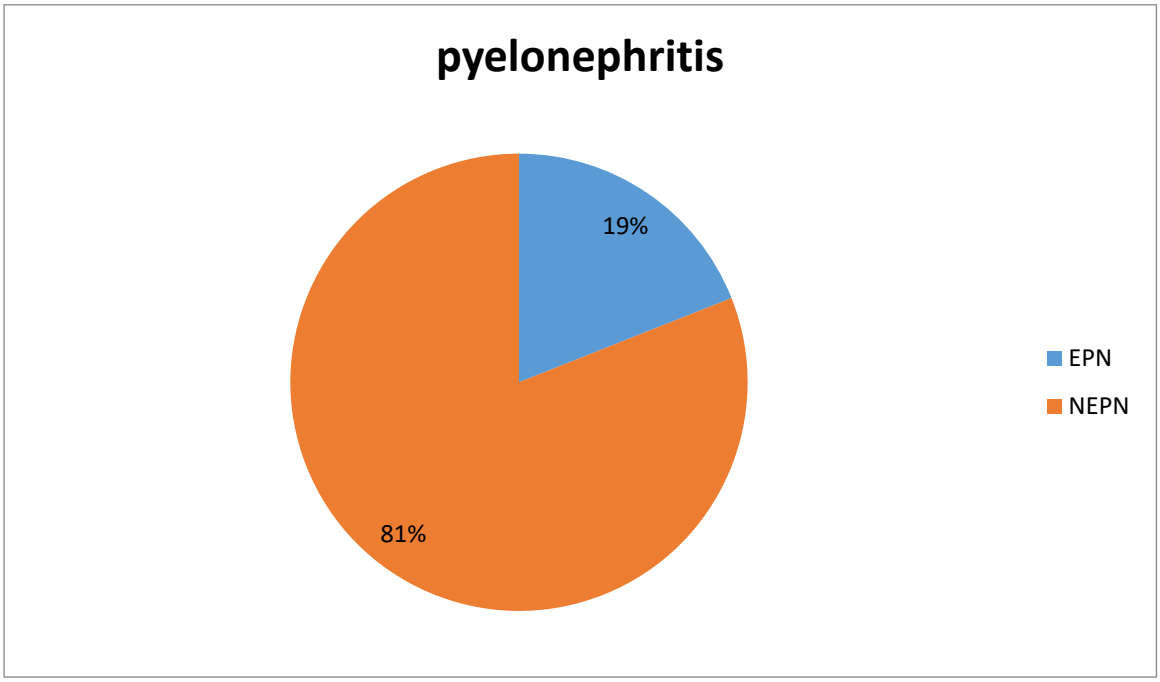
25% patients had systemic hypertension, 22% had history of coronary artery disease, 3% had multiple comorbidities in addition to diabetes mellitus

Table2.5:

Distribution of study subjects based on type of pyelonephritis[NEPN/EPN]

PYELONEPHRITIS	FREQUENCY	PERCENT
EPN	19	19.0
NEPN	81	81.0
Total	**100**	**100.0**

Fig.2.5: Representation based on type of pyelonephritis



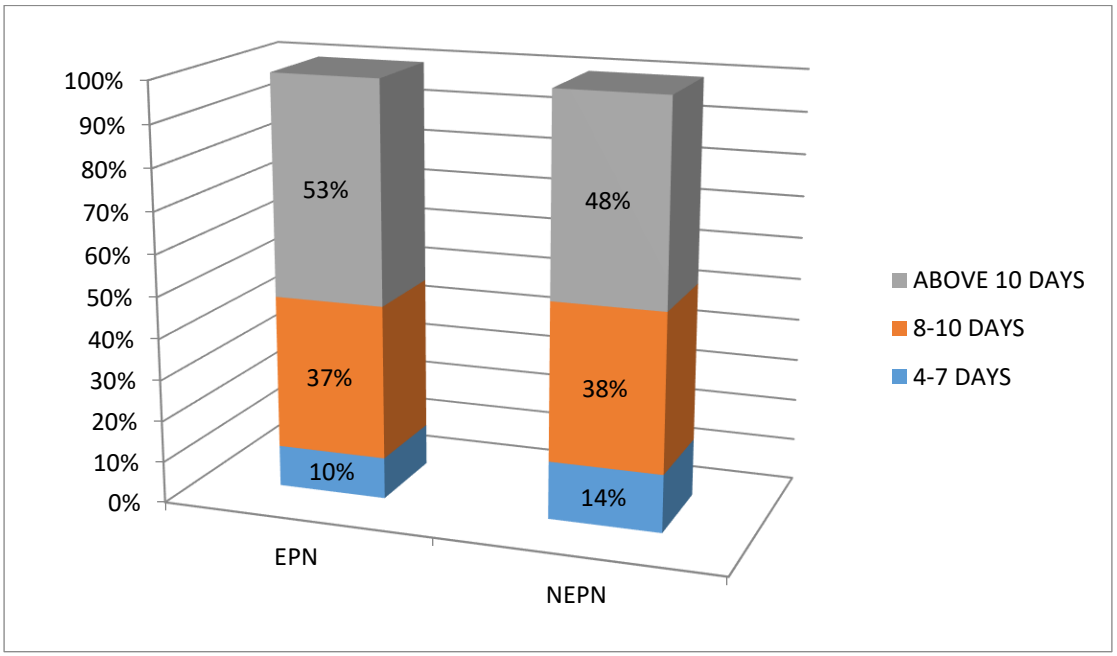
Out of the 100 patients admitted with acute pyelonephritis with type 2 diabetes mellitus, 81% patients had NEPN and 19% had EPN.

Table 2.6: Distribution of study subjects based on duration of fever

					Total
			EPN	NEPN	
FEVER_DAYS_	4-7 DAYS	Count	2	11	13
		%	10.5%	13.6%	13.0%
	8-10 DAYS	Count	7	31	38
		%	36.8%	38.3%	38.0%
	ABOVE 10 DAYS	Count	10	39	49
		%	52.6%	48.1%	49.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=0.182 P= 0.913

Fig.2.6: Representation of study subjects based on duration of fever



At the time of admission, 49% patients had duration of fever >10 days, 38% had fever for 8-10 days and only 13% had fever for <7 days.

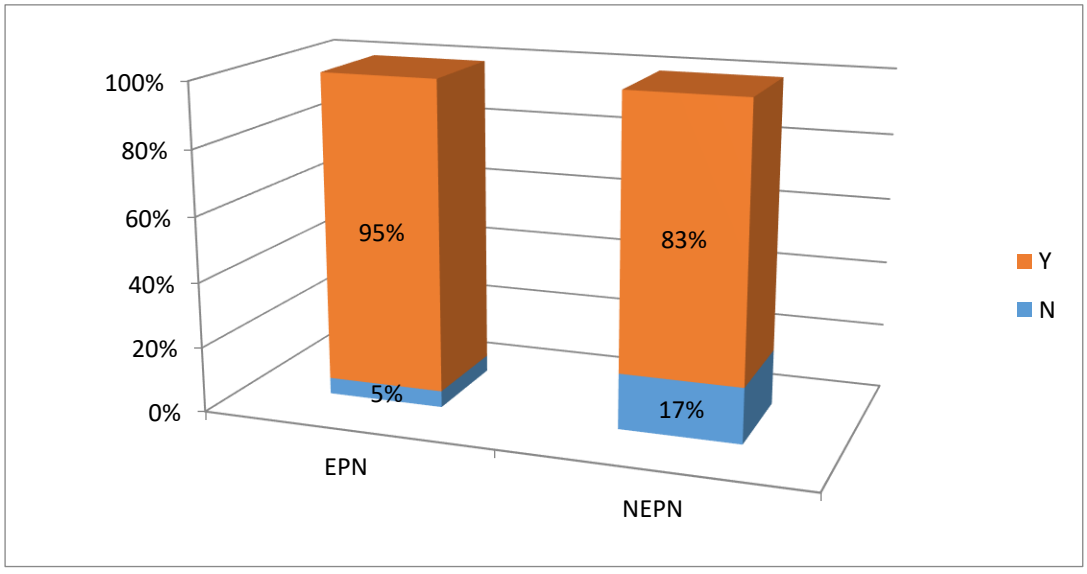
Table 2.7:

Distribution of study subjects based on loin pain(present/absent)

				Total
		EPN	NEPN	
LOIN_PAIN	N Count	1	14	15
	N %	5.3%	17.3%	15.0%
	Y Count	18	67	85
	Y %	94.7%	82.7%	85.0%
Total	Count	19	81	100
	%	100.0%	100.0%	100.0%

Pearson Chi-Square=1.744 P= 0.187

Fig.2.7: Representation based on loin pain(present/absent)



Loin pain was present in 95% of patients with EPN and 83% of patients with NEPN.

Table 2.8: Distribution of study subjects based on other symptoms

					Total
			EPN	NEPN	
Other_Symptoms	Burning micturition	Count	2	23	25
		%	10.5%	28.4%	25.0%
	Decreased urine output	Count	1	8	9
		%	5.3%	9.9%	9.0%
	None(N)	Count	14	39	53
		%	73.7%	48.1%	53.0%
	Vomiting	Count	2	11	13
		%	10.5%	13.6%	13.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=4.333 P= 0.228

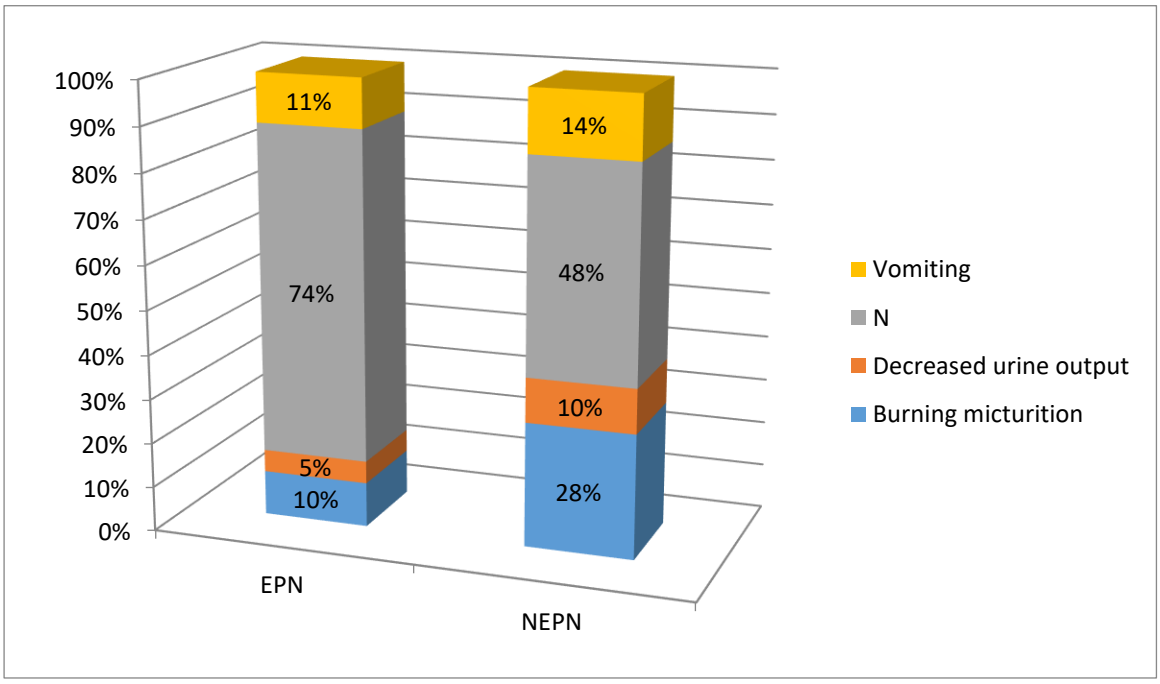


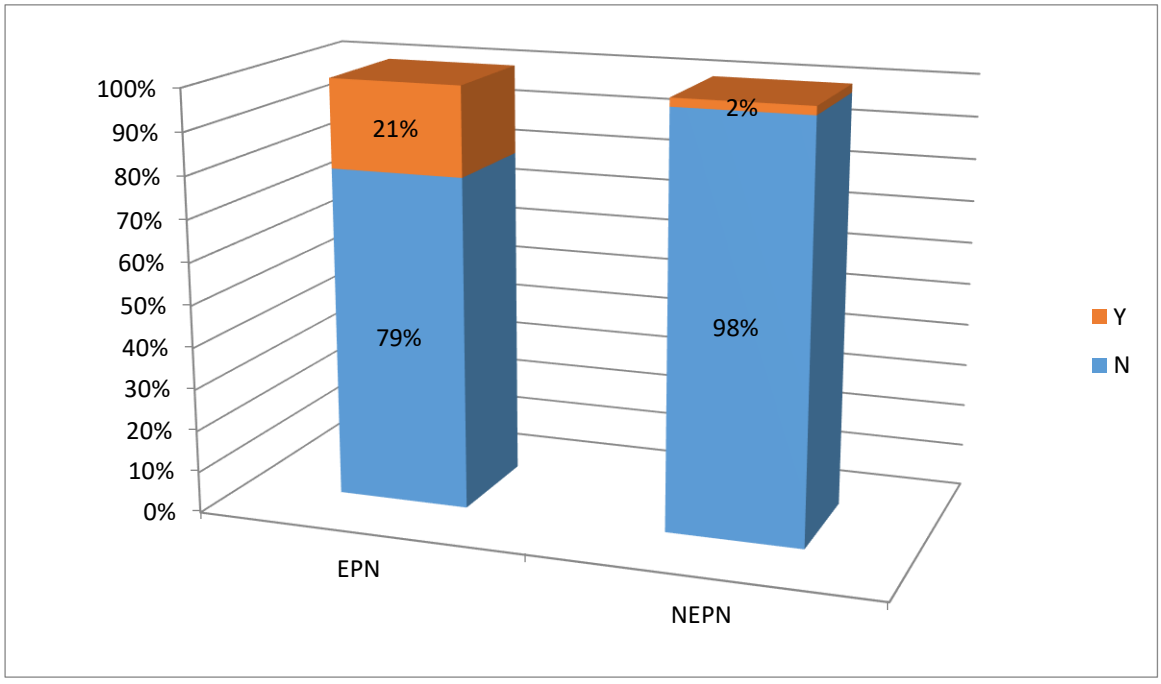
Table 2.9:

Distribution of study subjects based on altered sensorium(present/absent)

				Total
		EPN	NEPN	
Altered Sensorium	N Count	15	79	94
	N %	78.9%	97.5%	94.0%
	Y Count	4	2	6
	Y %	21.1%	2.5%	6.0%
Total	Count	19	81	100
	%	100.0%	100.0%	100.0%

Pearson Chi-Square=9.424* P= 0.002

Fig.2.9: Representation based on presence of altered sensorium



Altered sensorium was seen in 21% of EPN and 2% of NEPN patients.

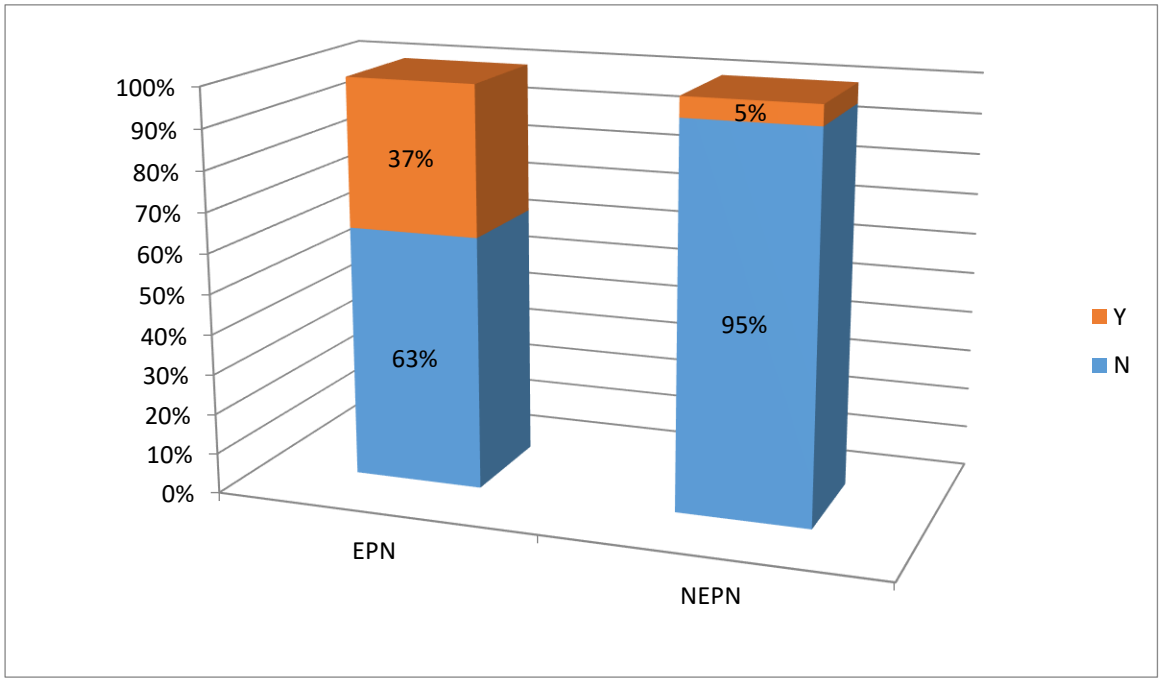
Table 2.10:Distribution of study subjects based on shock

(present/absent)

				Total
		EPN	NEPN	
Shock	N Count	12	77	89
	N %	63.2%	95.1%	89.0%
	Y Count	7	4	11
	Y %	36.8%	4.9%	11.0%
Total	Count	19	81	100
	%	100.0%	100.0%	100.0%

Pearson Chi-Square=16.001** P< 0.001

Fig.2.10: Representation based on presence of shock

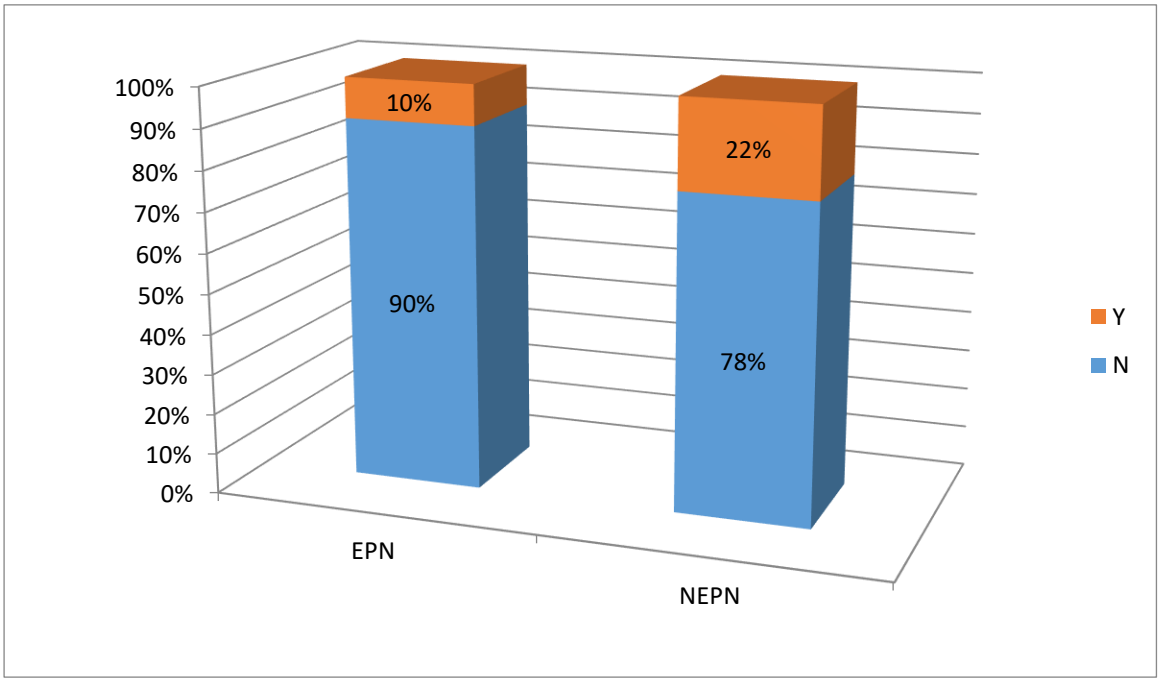


Shock was present on admission in 37% of EPN and 5% of NEPN patients.

Table 2.11:Distribution of study subjects based on HUN (present/absent)

					Total
			EPN	NEPN	
HUN side	N	Count	17	63	80
		%	89.5%	77.8%	80.0%
	Y	Count	2	18	20
		%	10.5%	22.2%	4.0%
Total		Count	19	81	100
		%	100.00 %	100.00%	100.00 %
Pearson Chi-Square=1.316 P=0.251					

Fig.2.11: Representation based on presence of HUN



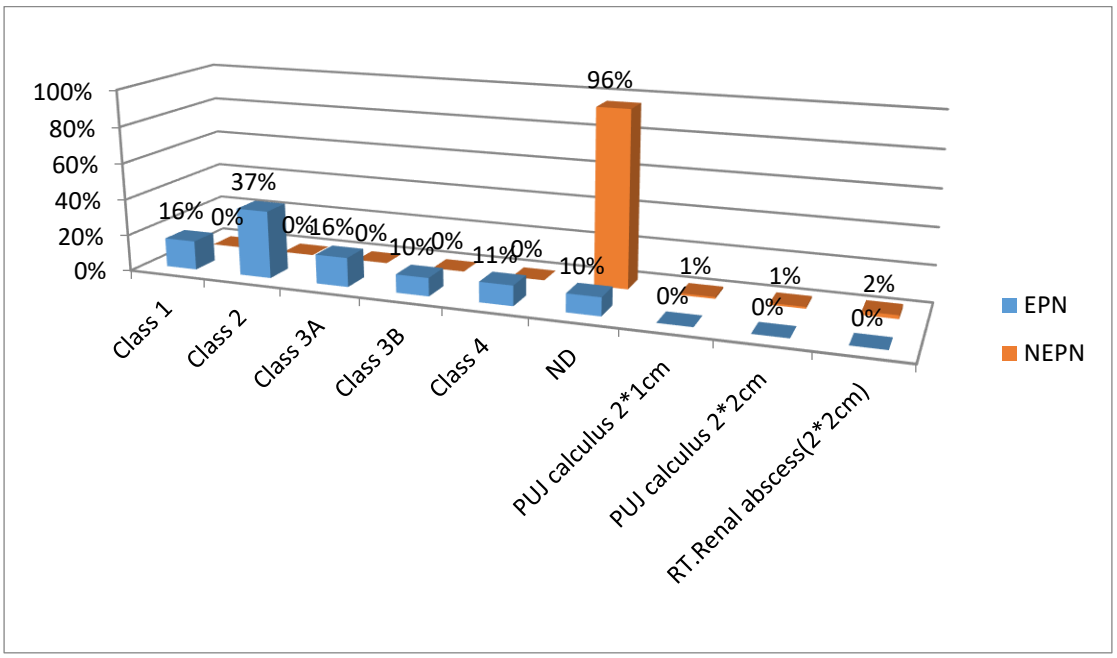
HUN was present in 10% of EPN and 22% of NEPN patients

Table 2.12: Summary of findings in CECT-KUB

			EPN	NEPN	Total
CECT KUB	Class 1	Count	3	0	3
		%	15.8%	.0%	3.0%
	Class 2	Count	7	0	7
		%	36.8%	.0%	7.0%
	Class 3A	Count	3	0	3
		%	15.8%	.0%	3.0%
	Class 3B	Count	2	0	2
		%	10.5%	.0%	2.0%
	Class 4	Count	2	0	2
		%	10.5%	.0%	2.0%
	ND	Count	2	78	80
		%	10.5%	96.3%	80.0%
	PUJ calculus 2*1cm	Count	0	1	1
		%	.0%	1.2%	1.0%
	PUJ calculus 2*2cm	Count	0	1	1
		%	.0%	1.2%	1.0%
	RT.Renal abscess(2*2cm)	Count	0	1	1
		%	.0%	1.2%	1.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=87.329** P<0.0001

Fig.2.12: Representation of the findings in CECT-KUB



According to CECT-KUB, patients with EPN categorized. 15.8% belonged to class 1, 36.8% belonged to class 2, 15.8% belonged to class 3A, 10.5% belonged to class 3B, 2% belonged to class 4. PUJ calculi seen in 2% patients and renal abscess in 1%.

Table 2.13: Distribution of study subjects based on class of EPN

			EPN
CLASS	Class 1	Count	3
		%	15.8%
	Class 2	Count	7
		%	36.8%
	Class 3A	Count	3
		%	15.8%
	Class 3B	Count	2
		%	10.5%
	Class 4	Count	2
		%	10.5%
	ND	Count	2
		%	10.5%
	TOTAL		19

Fig.2.13: Representation of class of EPN

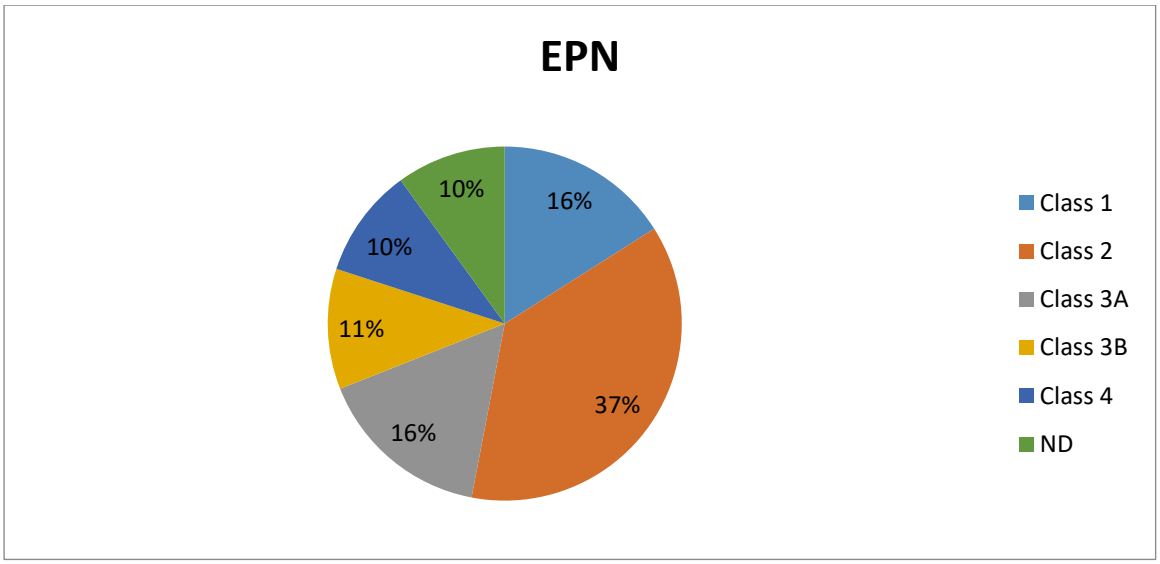


Table 2.14:Distribution of study subjects based on HBA1C

					Total
			EPN	NEPN	
hba1c group	6.5-7.0	Count	0	50	50
		%	0.0%	61.7%	50.0%
	7.01-7.50	Count	2	26	28
		%	10.5%	32.1%	28.0%
	Above 7.50	Count	17	5	22
		%	89.5%	6.2%	22.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=62.828** P<0.0001

Fig.2.14: Representation based on HBA1C

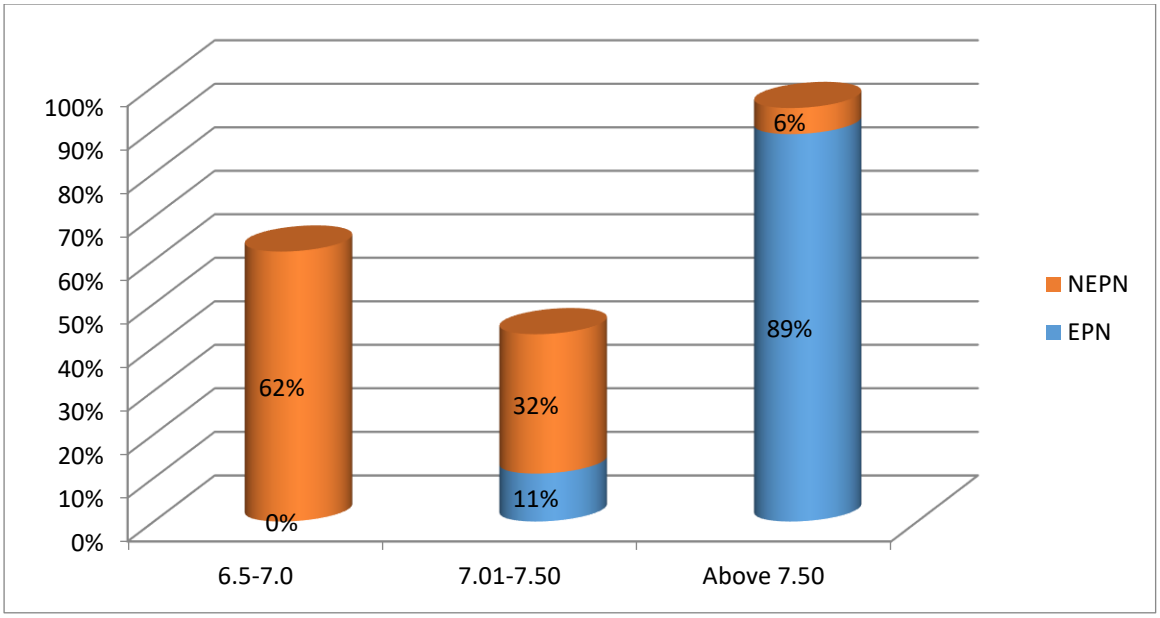
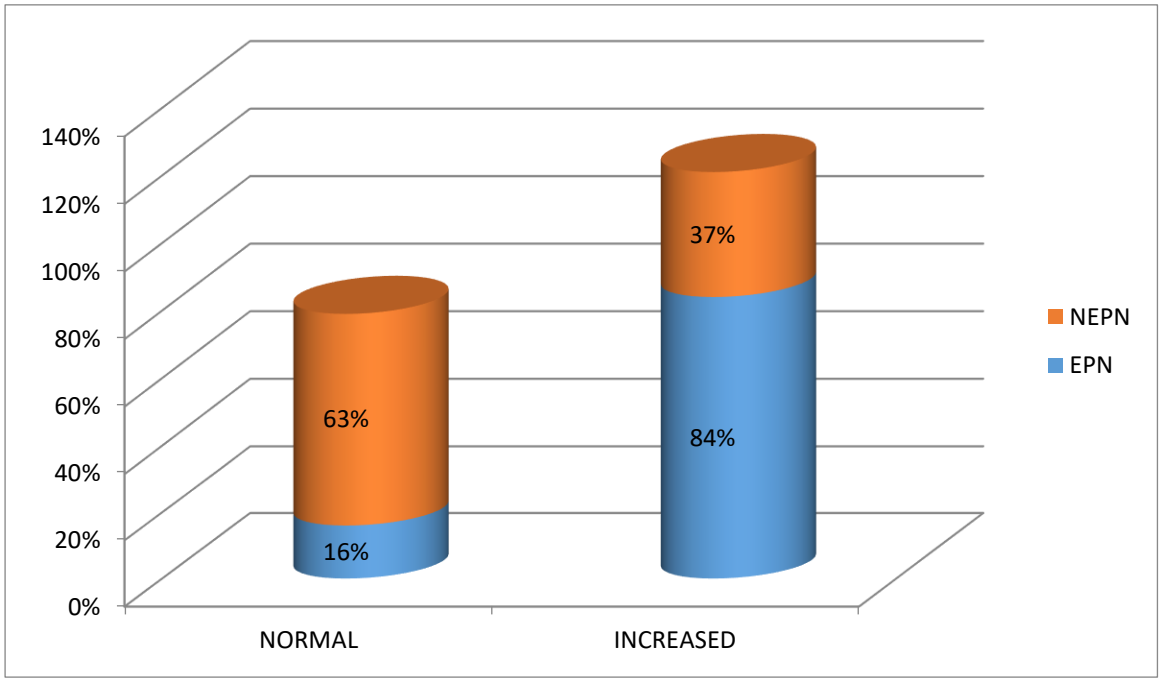


Table 2.15:Distribution of study subjects based on serum creatinine.(normal, Increased)

				Total
		EPN	NEPN	
SR_CR	NORMAL Count	3	51	54
	NORMAL %	15.8%	63.0%	54.0%
	INCREASED Count	16	30	46
	INCREASED %	84.2%	37.0%	46.0%
Total	Count	19	81	100
	%	100.0%	100.0%	100.0%

Pearson Chi-Square=13.787** P<0.0001

Fig.2.15: Representation based on serum creatinine levels



Serum creatinine was increased in 84% of EPN and 37% of NEPN patients.

Table 2.16:

Distribution of study subjects based on urine culture organisms in NEPN

		NEPN	
		Count	Column N %
Urine_C/S	Acinetobacter	6	7.4%
	Candida albicans	2	2.5%
	Candida non-albicans	1	1.2%
	E.coli	46	56.8%
	Klebsiella	1	1.2%
	No growth	14	17.3%
	Polymicrobial	10	12.3%
	Pseudomonas	1	1.2%

Fig.2.16: Representation based on organisms in NEPN

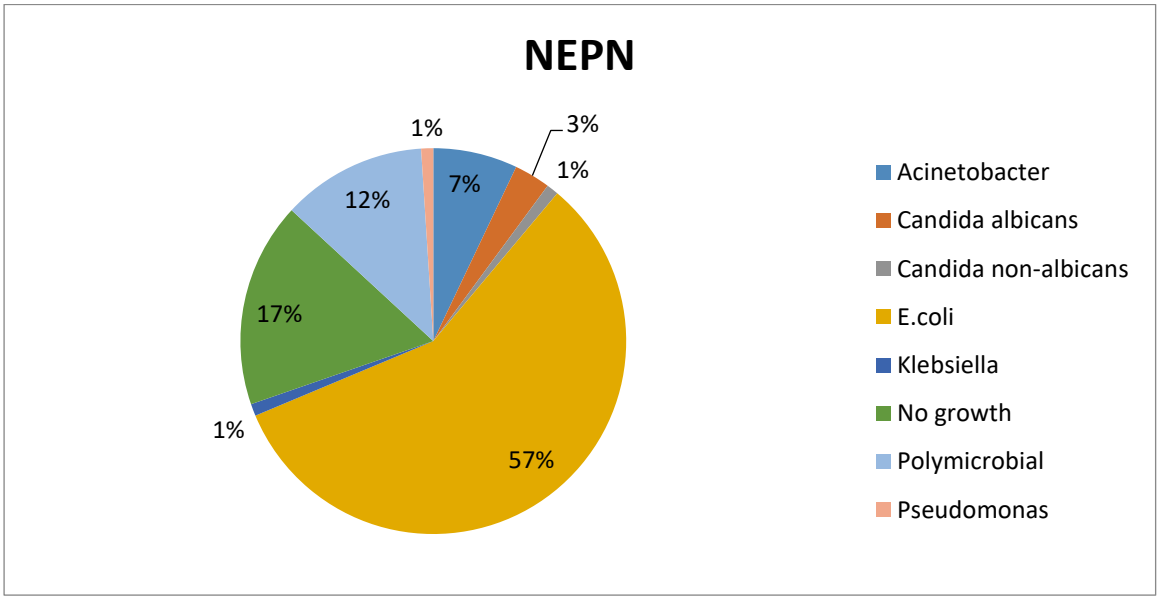
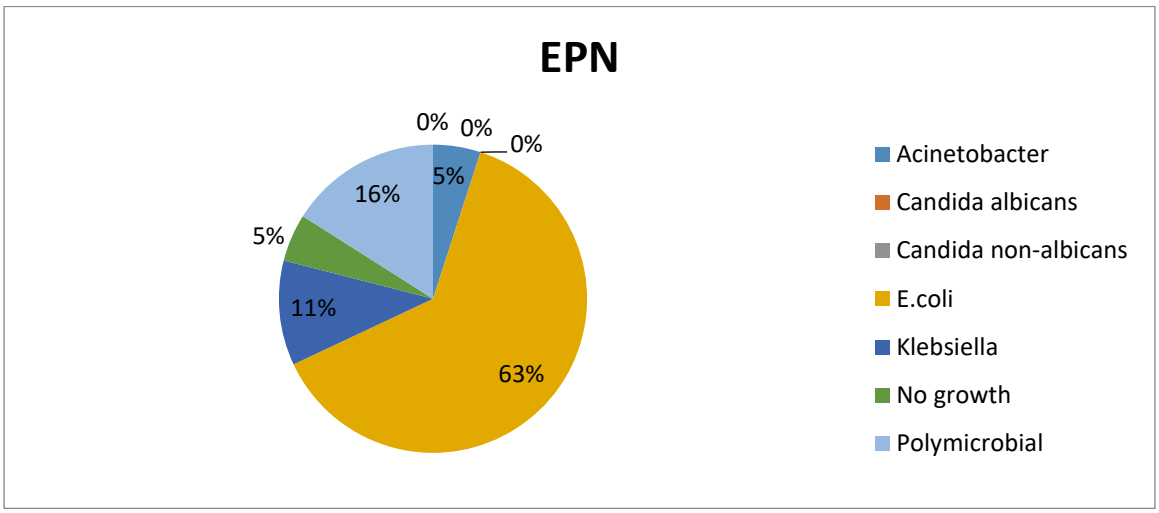


Table 2.17:

Distribution of study subjects based on urine culture organisms in EPN

		EPN	
		Count	Column N %
Urine_C/S	Acinetobacter	1	5.3%
	Candida albicans	0	.0%
	Candida non-albicans	0	.0%
	E.coli	12	63.2%
	Klebsiella	2	10.5%
	No growth	1	5.3%
	Polymicrobial	3	15.8%
	Pseudomonas	0	.0%

Fig.2.17: Representation based on organisms in EPN

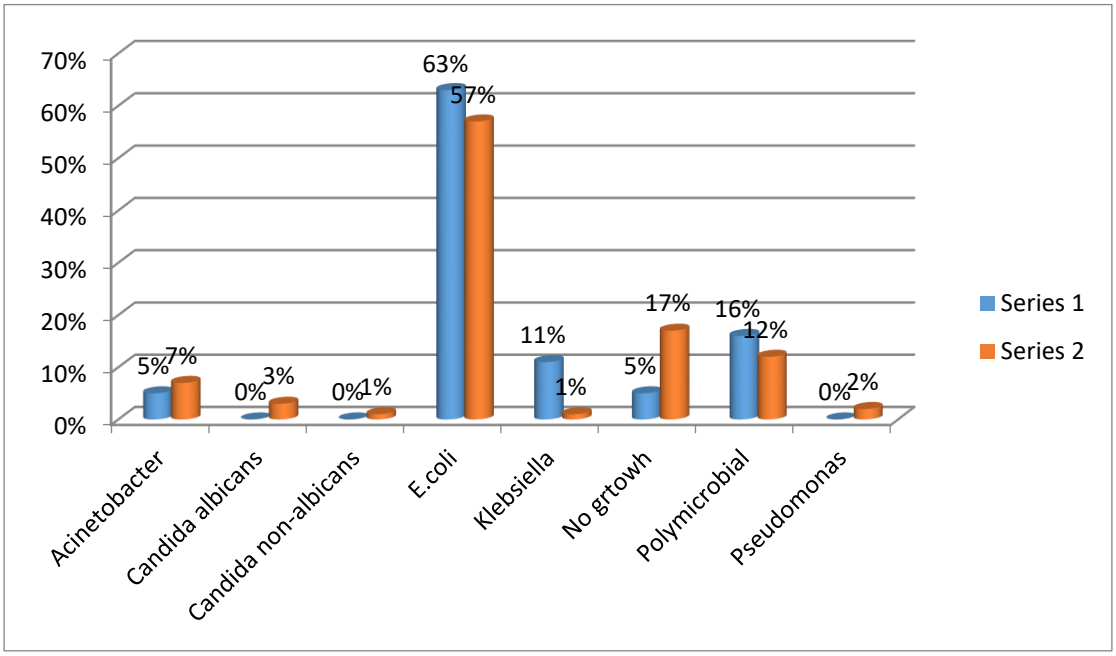


Pearson Chi-Square=7.199 P= 0.499

Table 2.18: Comparison of urine culture in EPN and NEPN					Total
			EPN	NEPN	
Urine_C/S	Acinetobacter	Count	1	6	7
		%	5.3%	7.4%	7.0%
	Candida albicans	Count	0	2	2
		%	0.0%	2.5%	2.0%
	Candida non-albicans	Count	0	1	1
		%	0.0%	1.2%	1.0%
	E.coli	Count	12	46	58
		%	63.2%	56.8%	58.0%
	Klebsiella	Count	2	1	3
		%	10.5%	1.2%	3.0%
	No growh	Count	1	14	15
		%	5.3%	17.3%	15.0%
	Polymicrobial	Count	3	10	13
		%	15.8%	12.3%	13.0%
	Pseudomonas	Count	0	1	1
		%	0.0%	1.2%	1.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Fig.2.18: Representation of comparison of urine culture in

EPN (series 1) and NEPN (series 2)



In patients with EPN, 63.2% of the cultures were positive for E.coli, 15.8% positive for multiple organisms (polymicrobial), 10.5% cultures were positive for Klebsiella, 5.3% cultures had no growth and 5.3% of the cultures were positive for Acinetobacter species.

In patients with NEPN, 56.8% cultures positive for Escherichia coli, no growth in culture seen in 17.3% cases, 12.3% cultures positive for multiple organisms (polymicrobial), 7.4% cultures positive for Acinetobacter, 2.5% of the cultures positive for Candida albicans, 1.2% cultures positive for Candida non-albicans, 1.2% of the cultures positive for Klebsiella and 1.2% cultures were positive for Pseudomonas.

Table 2.19: Distribution of study subjects based on Treatment other than i.v. antibiotics in NEPN and EPN.

			EPN	NEPN	TOTAL
Treatment Other Than IV Antibiotics	DJ stent(RT)	Count	0	1	1
		%	.0%	1.2%	1.0%
	Anti-fungals	Count	0	3	3
		%	.0%	3.7%	3.0%
	DJ stent(B/L)	Count	0	4	4
		%	.0%	4.9%	4.0%
	DJ stent(LT)	Count	0	4	4
		%	.0%	4.9%	4.0%
	DJ stent(RT)	Count	0	6	6
		%	.0%	7.4%	6.0%
	HD	Count	0	4	4
		%	.0%	4.9%	4.0%
	N	Count	9	57	66
		%	47.4%	70.4%	66.0%
	Nephrectomy(RT)	Count	1	0	1
		%	5.3%	.0%	1.0%
	PCN(LT)	Count	4	0	4
		%	21.1%	.0%	4.0%
	PCN(RT)	Count	5	0	5
		%	26.3%	.0%	5.0%
	URSL(LT)+DJ stent	Count	0	1	1
		%	.0%	1.2%	1.0%
	URSL(RT)+DJ stent	Count	0	1	1
		%	.0%	1.2%	1.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson chi square =49.495**p<0.001

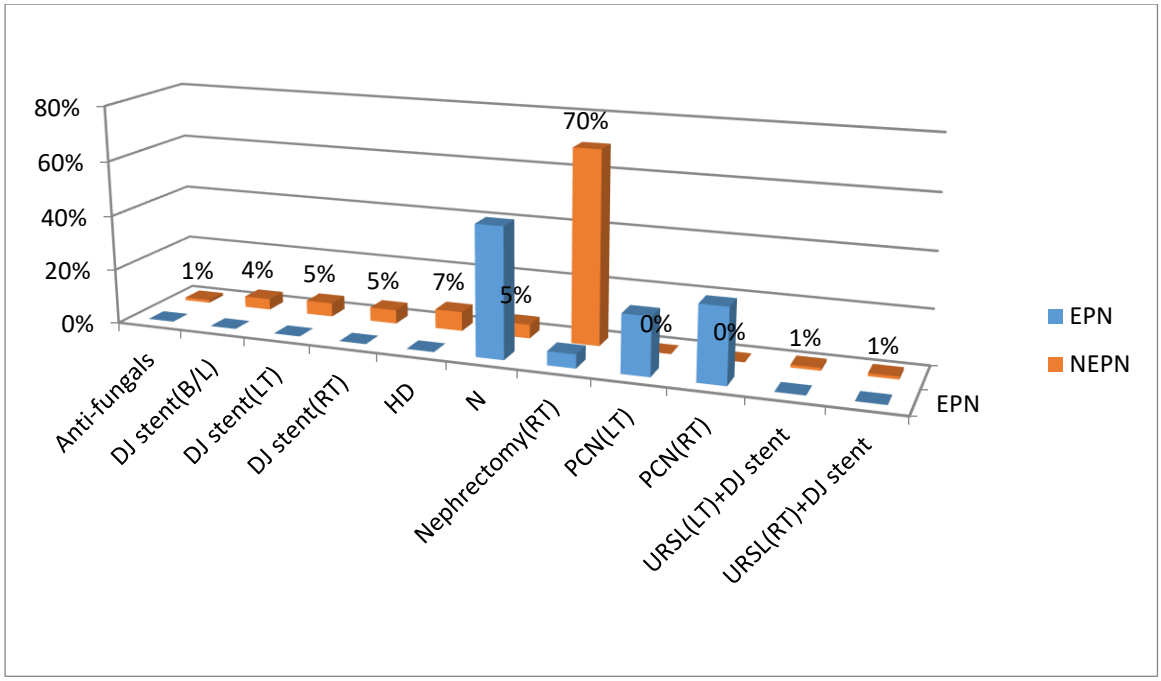


Fig.2.19: Representation of treatment given other than I.V.antibiotics

In patients with NEPN, only antibiotics were used for treatment in 70% patients, in addition to antibiotics 37% patients were treated with anti-fungals, for 17.2% patients DJ stenting was done, HD was done for 4.9% patients and URSL+DJ stenting done for 2.4% patients.

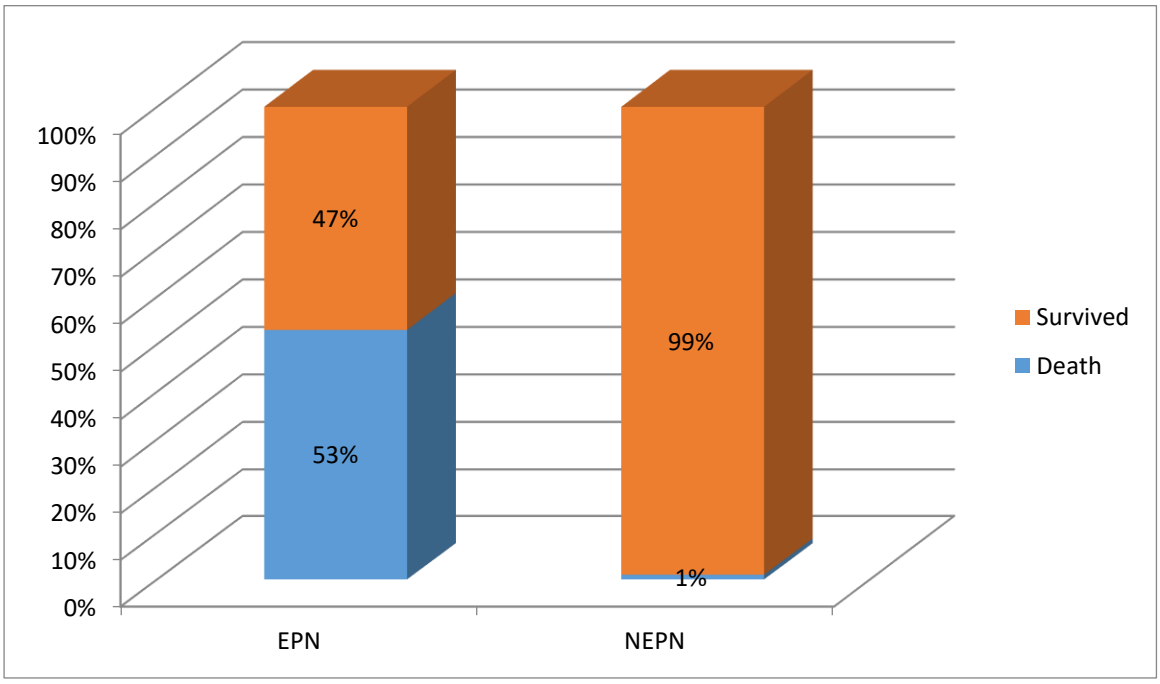
In patients with EPN, PCN was done for 47.7% patients, nephrectomy done in 5.3% patients and antibiotics along with supportive medical management alone given for 47.4% patients

Table 2.20: Treatment outcomes in NEPN and EPN

			EPN	NEPN	TOTAL
Outcome1	Death	Count	10	1	11
		%	52.6%	1.2%	11.0%
	Survived	Count	9	80	89
		%	47.4%	98.8%	89.0%
Total		Count	19	81	100
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=41.527**p<0.001

Fig.2.20: Treatment outcomes in NEPN and EPN



99% of NEPN group survived while only 47% of EPN group survived.

Table 2.21: Outcome of EPN and NEPN based on treatment (good= successfully treated with antibiotics/PCN....Poor=patients who expired / had nephrectomy]

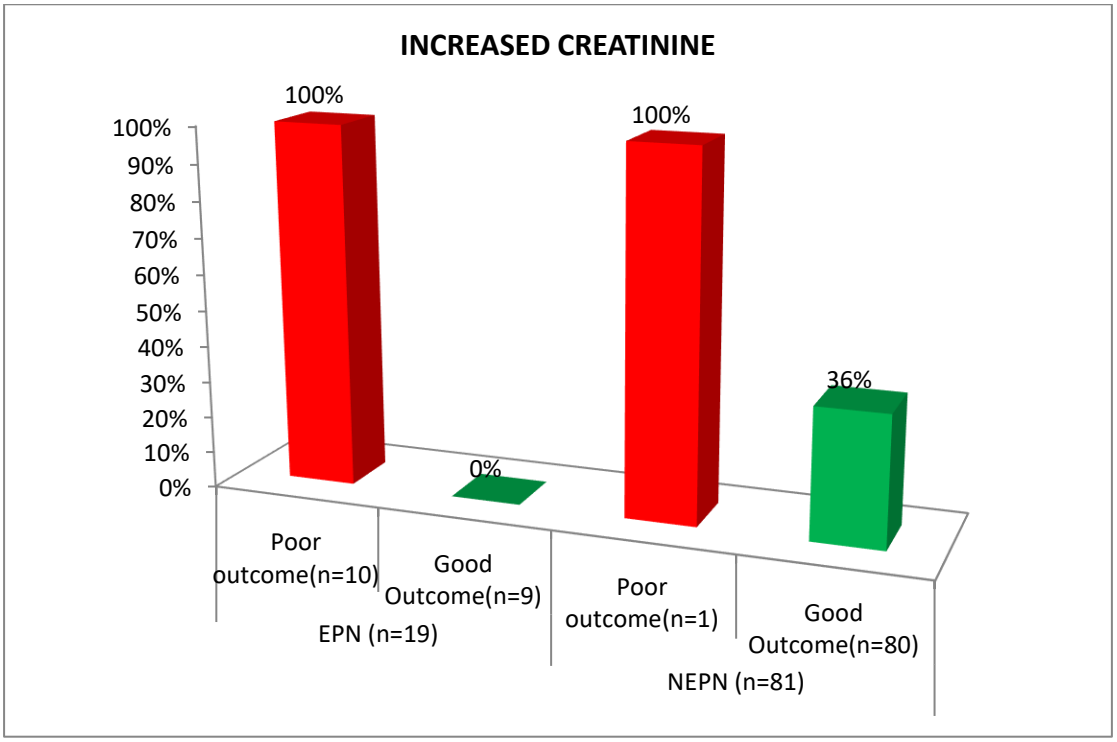
			EPN		NEPN	
			Count	Column N %	Count	Column N %
Treatment	Anti-fungals	Death	0	.0%	0	.0%
		Survived	0	.0%	3	100.0%
	DJ stent	Death	0	.0%	0	.0%
		Survived	0	.0%	15	100.0%
	HD	Death	0	.0%	0	.0%
		Survived	0	.0%	4	100.0%
	N	Death	7	77.8%	1	1.8%
		Survived	2	22.2%	56	98.2%
	Nephrectomy	Death	0	.0%	0	.0%
		Survived	1	100.0%	0	.0%
	PCN	Death	2	22.2%	0	.0%
		Survived	7	77.8%	0	.0%
	URSL+DJ stent	Death	0	.0%	0	.0%
		Survived	0	.0%	2	100.0%

Table 2.22:

Comparison of prognostic indicators of good and poor outcomes in EPN and NEPN. (Variables -HBA1C>7.5, ALTERED SENSORIUM, SHOCK, RENAL DYSFUNCTION (increased creatinine), need for HD).

		usg							
		EPN (n=19)				NEPN (n=81)			
		Poor outcome(n=10)		Good Outcome(n=9)		Poor outcome(n=1)		Good Outcome(n=80)	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
hba1c_group	Above 7.50	9	90%	8	89%	1	100%	4	5%
SHOCK	Y	7	70%	0	0%	1	100%	3	4%
ALTERED_SENSORIUM	Y	3	30%	0	0%	1	100%	1	1%
INCREASED CREATININE	Y	10	100%	0	0%	1	100%	29	36%

Fig.2.22.Outcomes based on raised serum creatinine levels

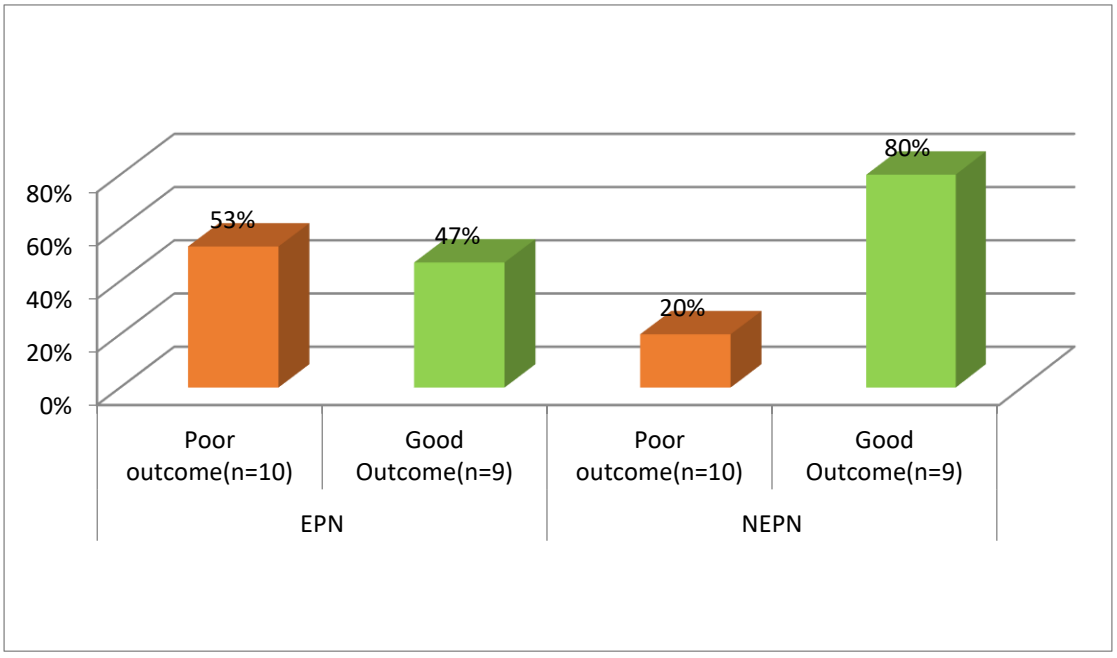


.Patients presenting with raised serum creatinine levels had poor outcomes, with p value<0.0001, which was statistically significant.

Table 2.23: Outcomes in patients with HBA1C >7.5

EPN (n=19)				NEPN (n=81)			
Poor outcome (n=10)		Good Outcome (n=9)		Poor outcome (n=1)		Good Outcome (n=80)	
HBA1c Above 7.50 (n=17)				HBA1c Above 7.50 (n=5)			
N	%	N	%	N	%	N	%
9	53%	8	47%	1	20%	4	80%

Fig.2.24: Representation of outcomes in patients with HBA1C >7.5

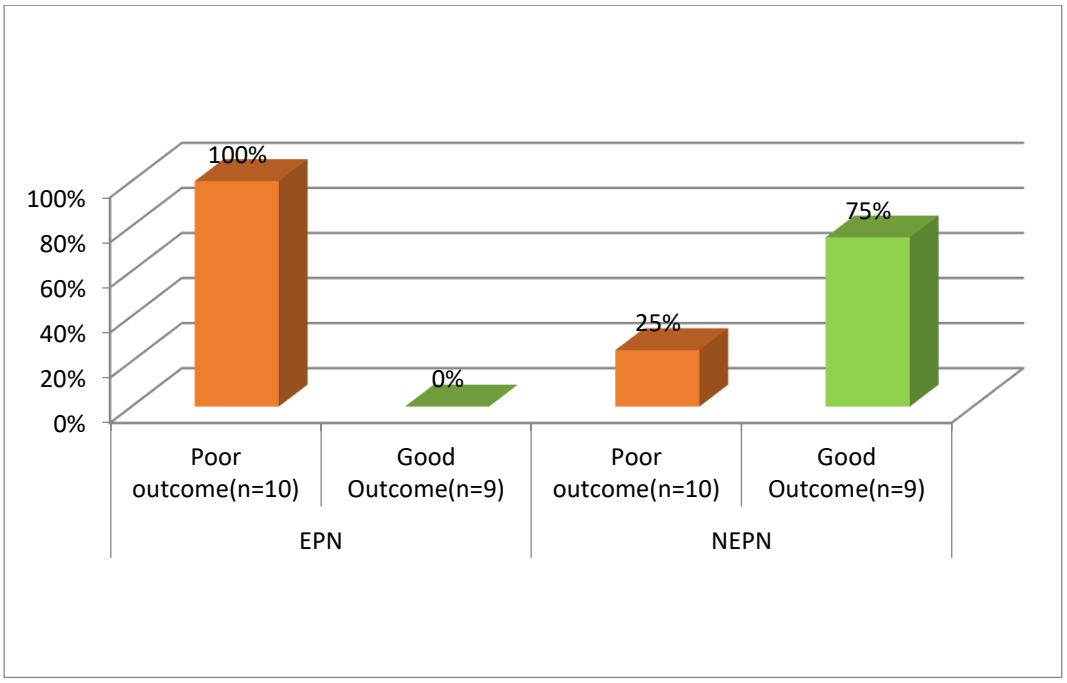


.HBA1c >7.5 was associated with poor outcome and it was statistically significant. P value<0.001.

Table.2.25: Outcomes in patients with shock

EPN (n=19)				NEPN (n=81)			
Poor outcome (n=10)		Good Outcome (n=9)		Poor outcome (n=1)		Good Outcome (n=80)	
SHOCK (n=7)				SHOCK (n=4)			
N	%	N	%	N	%	N	%
7	100%	0	0%	1	25%	3	75%

Fig.2.25: Representation of outcomes in patients with shock

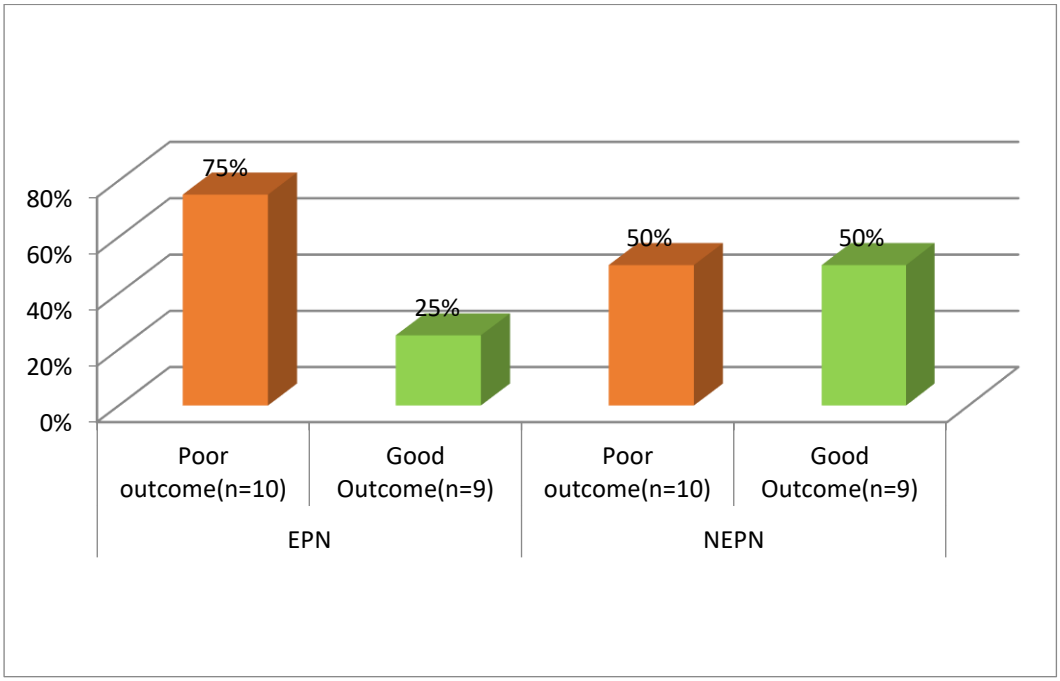


Patients presenting with shock on admission had poor outcome, with p value<0.001, which was statistically significant.

Table 2.26: Outcomes in patients with altered sensorium

EPN (n=19)				NEPN (n=81)			
Poor outcome(n=10)		Good Outcome(n=9)		Poor outcome(n=1)		Good Outcome(n=80)	
Altered sensorium (n=4)				Altered sensorium (n=2)			
N	%	N	%	N	%	N	%
3	75%	1	25%	1	50%	1	50%

Fig.2.26: Representation of outcomes in patients with altered sensorium



Patients presenting with altered sensorium on admission had poor outcome with p value = 0.002, which was statistically significant.

DISCUSSION

During the study period, out of the 100 patients admitted with acute pyelonephritis with type 2 diabetes mellitus, 81% patients had NEPN and 19% had EPN.

Renal abscess was seen in only 1% of the patients.

48 patients were males and 52 were females.

Around 40% patients were in the age group of 51-60 years, 32% were between 61-70 years, 25% patients were between 41-50 years and remaining 3% were above 70 years.

50% of the patients had no additional comorbidities other than diabetes mellitus.

25% patients had systemic hypertension, 22% had coronary artery disease, 3% had multiple comorbidities in addition to diabetes mellitus.

At the time of admission, 49% patients had duration of fever >10 days, 38% had fever for 8-10 days and only 13% had fever for <7 days.

85% of patients had loin pain on admission. Of that, 82.7% of patients with NEPN and 94.7 patients of EPN had loin pain.

Other symptoms including burning micturition was present in 25% of patients, decreased urine output was seen in 9% of patients and history of vomiting was present in 13% of patients.

Altered sensorium at the time of admission was present in 6% of patients. Of that, 21.1% patients with EPN had altered sensorium on admission, while only 2.5% patients with NEPN had altered sensorium. Patients presenting

with altered sensorium on admission had poor outcome with p value = 0.002, which was statistically significant.

Patients presenting with shock at the time of admission was 11%. Of that, 38.6% patients with EPN presented with shock while only 4.9% patients with NEPN presented with shock on admission. Patients presenting with shock on admission had poor outcome, with p value<0.001, which was statistically significant.

About 54% of the patients had normal serum creatinine levels and 46% had raised serum creatinine levels at the time of admission. Of that, 52.6% patients with EPN had raised serum creatinine levels while only 37% patients with NEPN had raised serum creatinine levels. Patients presenting with raised serum creatinine levels had poor outcomes, with p value<0.0001, which was statistically significant.

About 50% patients had HBA1C in the range of 6.5-7.0, 28% had HBA1C of 7.01-7.5, and 22% had HBA1C >7.5.In the EPN group, 17 out of 19 patients had HBA1C >7.5 while it was seen in only 5 out of 81 patients in NEPN group. HBA1c >7.5 was associated with poor outcome and it was statistically significant. P value<0.001.

On Ultrasound KUB, hydroureteronephrosis present in 22.2% patients with NEPN and 10.5% patients with EPN. PUJ calculus was found in 2 patients.

According to CECT-KUB, patients with EPN categorized. 15.8% belonged to class 1, 36.8% belonged to class 2, 15.8% belonged to class 3A, 10.5% belonged to class 3B, 2% belonged to class 4.

CECT-KUB could not be done in 2% of patients with EPN due to early mortality at the time of admission.

In patients with NEPN, 56.8% cultures positive for Escherichia coli, no growth in culture seen in 17.3% cases, 12.3% cultures positive for multiple organisms (polymicrobial), 7.4% cultures positive for Acinetobacter, 2.5% of the cultures positive for Candida albicans, 1.2% cultures positive for Candida non-albicans, 1.2% of the cultures positive for Klebsiella and 1.2% cultures were positive for Pseudomonas.

In patients with EPN, 63.2% of the cultures were positive for E.coli, 15.8% positive for multiple organisms (polymicrobial), 10.5% cultures were positive for Klebsiella, 5.3% cultures had no growth and 5.3% of the cultures were positive for Acinetobacter species.

In patients with NEPN, only antibiotics were used for treatment in 70% patients, in addition to antibiotics 37% patients were treated with anti-fungals, for 17.2% patients DJ stenting was done, HD was done for 4.9% patients and URSL+DJ stenting done for 2.4% patients.

In patients with EPN, PCN was done for 47.7% patients, nephrectomy done in 5.3% patients and antibiotics along with supportive medical management alone given for 47.4% patients.

99% of NEPN group survived while only 47% OF EPN group survived.

CONCLUSION

- A high index of suspicion and early imaging studies are required to diagnose EPN in diabetics presenting with features of pyelonephritis, especially if blood sugars are poorly controlled.

- Majority of the patients were in the age group of 51-70 years.

- Majority of cases with both NEPN and EPN were found to be due to gram negative bacteria.

- EPN patients with Class I, II and IIIA can be managed successfully with either antibiotics or with additional PCN. Class IIIB and IV may need nephrectomy.

- Patients presenting with altered sensorium and shock at presentation portend poor prognosis.

- Pyelonephritis in diabetics may be associated with renal failure and a high mortality rate.

LIMITATIONS OF STUDY

- Single centre study.
- Being a tertiary care referral centre, the results might not be true representation of the population.
- Longer follow up could not be obtained.
- The recurrence rate of the disease could not be assessed.

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A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS

Name :

Age/Sex :

OP/IP No :

Occupation :

Address :

Contact No. :

SYMPTOMS

- Fever
- Chills and rigors
- Loin pain
- Dysuria
- Nausea and vomiting

PATIENT CHARACTERISTICS

- Age
- sex
- pregnancy status

EXAMINATION

- Temperature
- Loin tenderness

INVESTIGATIONS

CBC

SERUM CREATININE

FBS

PPBS

URINE COMPLETE EXAMINATION WITH C/S

HbA1c

USG-KUB (Baseline)

CECT-KUB (When necessary)

INFORMATION SHEET

We are conducting a study on **"A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME OF ACUTE PYELONEPHRITIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS "** among patients attending Rajiv Gandhi Government General Hospital, Chennai.

The purpose of this study is to analyse the clinical features, microbiological profile , prognostic factors and treatment outcome of pyelonephritis in diabetic patients.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator

Signature of Participant

Date :
Place :

PATIENT CONSENT FORM

Study Detail	:	**A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS**
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.	
I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.	
I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.	
I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.	
I hereby consent to participate in this study.	
I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.	

Signature/thumb impression: Signature of Investigator

DR.S.KARTHIKAA

Patient's Name and Address:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.S.Karthikaa
II Year Post Graduate in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003.

Dear Dr.S.Karthikaa,

The Institutional Ethics Committee has considered your request and approved your study titled "**A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS**" - **NO.26082017**

The following members of Ethics Committee were present in the meeting hold on **01.08.2017** conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD., :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH.,Dean, MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3: Member Secretary
4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch : Member
5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
6. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3: Member
8. Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 : Member
9. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
10. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
11. Tmt.J.Rajalakshmi, JAO,MMC, Ch-3 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PLAGIARISM REPORT

URKUND

Urkund Analysis Result

Analysed Document:	new SK thesis.docx (D42535078)
Submitted:	10/14/2018 7:34:00 PM
Submitted By:	karsan.karsan3@gmail.com
Significance:	7 %

Sources included in the report:

Study of clinical and biochemical factors determining prognosis of patients with acute pyelonephritis.pdf (D31020110)
Final thesis.docx (D30790588)
https://emedicine.medscape.com/article/2029011-treatment
http://pgimer.academia.edu/SravanKumar
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4244716/

Instances where selected sources appear:

21

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"A STUDY ON CLINICAL, MICROBIAL PROFILE, PROGNOSTIC FACTORS AND TREATMENT OUTCOME IN PATIENTS OF ACUTE PYELONEPHRITIS WITH TYPE 2 DIABETES MELLITUS"** of the candidate **Dr**.**S.KARTHIKAA** with registration Number **201611010** for the award of **M.D.** in the branch of **GENERAL MEDICINE**. I personally verified the urkund.com website for plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **7 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.