"OUTCOME OF PAPILLARY NECROSIS CAUSING ACUTE RENAL FAILURE – A ONE YEAR LONGITUDINAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"

REG NO. BG0112003

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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ENDORSEMENT

This is to certify that the dissertation entitled "**OUTCOME OF PAPILLARY NECROSIS CAUSING ACUTE RENAL FAILURE – A ONE YEAR LONGITUDINAL STUDY IN KLES DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is a bonafide research work done by **CANDIDATE REG NO. BG0112003.**

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LIST OF ABBREVIATIONS USED

ARF	-	Acute renal failure
C. tropicalis	-	Candida tropicalis
C/S	-	Culture / sensitivity
CABG	-	Coronary artery bypass grafting
CKD	-	Chronic kidney disease
CNS	-	Central nervous system
COX	-	Cyclooxygenase
CT	-	Computed tomography
Cumm	-	Cubic millimeter
CVS	-	Cardiovascular system
DJ	-	Double-J
DOA	-	Date of admission
DOD	-	Date of discharge
e GFR	-	Estimated glomerular filteration rate
E. coli	-	Escherichia coli
e.g.	-	For example
FBS	-	Fasting blood sugar
gm	-	Gram
H/O	-	History of
HIV	-	Human immunodeficiency virus
i.e.	-	That is,
IVU	-	Intravenous urography
KUB	-	Kidney ureter bladder
MDRD	-	Modification of diet in renal disease

mg/Dl	-	Milligram per deciliter
n	-	Total number
NSAID	-	Nonsteroidal anti-inflammatory drugs
RBC	-	Red blood cell
RBS	-	Random blood sugar
RPG	-	Retrograde pyelography
RPN	-	Renal papillary necrosis
RS	-	Respiratory system
SIRS	-	Systemic inflammatory response syndrome
USG	-	Ultrasound
UTI	-	Urinary tract infection
WBC	-	White blood cell
WHO	-	World Health Organization

ABSTRACT

Background and objectives

Renal papillary necrosis is potentially disastrous andmay lead to renal failure. This study was planned to investigate the etiology, clinical spectrum, clinical and short term functional outcome of patients with renal papillary necrosis causing acute renal failure.

Methodology

This one year longitudinal study was done at the Department of Medicine, Nephrology and Urology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Of the 2000 patients who presenting with acute renal failure from January 2013 to December 2013, 40 patients of acute renal failure due to renal papillary necrosis were studied.

Results

Of the 40 patients 27 had renal papillary necrosis (RPN) with ARF without CKD and 13 patients had RPN with ARF on CKD. The male to female ratio was1.5:1 and > 70% of the patients were aged > 50 years. Common clinical feature was fever followed by abdominal pain and the commonest co-morbid condition was diabetes mellitus noted in 82.5% of the patients. Diabetes mellitus with pyelonephritis was the commonest etiological factor. On urine microscopy, the presence of WBCs and RBCs was noted in all the patients. Maximum patients with RPN with ARF without CKD had proteinuria 66.67% and E. coli and candida were the common organisms isolated. Imaging showed 87.5% patients with hydronephrosis and hydroureter. The overall functional outcome at 6 months

showed that 7.69% were in CKD stage 3, 46.15% in CKD stage 4 and 46.15% were in CKD stage 5. In patients who underwent intervention, renal function improved in 30% patients without change of CKD stage and deteriorated in 70% among the patients having RPN with ARF without CKD. In patients who were managed conservatively, renal function improved in 66.67% patients and deteriorated in 33.33%.

Conclusion and interpretation

Renal papillary necrosis (RPN) causing acute renal failure (ARF) or acute renal failure on chronic kidney disease (CKD) is more common in males. Most common etiology is Diabetes Mellitus with Pyelonephritis. Diabetics with good glycaemic control also develop RPN with ARF. There is significant increase in e GFR in immediate post treatment period in patients with RPN with ARF without CKD in comparison to ARF with CKD. Outcome of RPN with ARF with or without CKD depends on severity of ARF, etiology, proteinuria and associated sepsis / septicemic shock at presentation. In patients with RPN with ARF with CKD, there is deterioration of renal function in spite of surgical intervention.

Keywords

Acute renal failure; Chronic kidney disease; Renal papillary necrosis;

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INTRODUCTION

Renal papillary necrosis (RPN), first described by Friedrich in 1877 is characterized by coagulative necrosis, demarcation and sequestration of the renal medullary pyramids and papillae, which slough into the pelvi-calyceal system and may be passed in urine. It is brought on by several associated conditions and toxins that exhibit synergism toward the development of ischemia.[1] The clinical course of renal papillary necrosis varies depending on the degree of vascular impairment, the presence of associated causal factors, the overall health of the patient, the presence of bilateral involvement, and specifically, the number of affected papillae.

Renal papillary necrosis can lead to secondary infection of desquamated necrotic foci, deposition of calculi, and/or separation and eventual sloughing of papillae, with impending acute urinary tract obstruction. Multiple sloughed papillae can obstruct their respective calyces or can congregate and embolize to more distal sites (e.g. pelviureteric junction, ureter, ureterovesical junction). Previously undiagnosed congenital anomalies (e.g. partial pelviureteric junction obstruction) can provide a narrowed area where the sloughed papilla can nest and obstruct.

Renal papillary necrosis is potentially disastrous and, in the presence of bilateral involvement or an obstructed solitary kidney, may lead to renal failure. The infectious sequelae of renal papillary necrosis are more serious if the patient has multiple medical problems, particularly diabetes mellitus.

Clinical course of RPN ranges from a chronic, protracted, and relapsing form to an acute, rapidly progressive malignant form. The acute form needs immediate

intervention, as the effects are devastating, resulting in death from septicemia and renal failure. Early recognition and treatment of acute ureteral obstruction caused by sloughed necrotic tissue can minimize the decline in renal function.[2]

Till date there is no Indian study related to the clinical and functional outcome of RPN in patients presenting with acute renal failure.

This study is an effort to investigate the etiology and clinical spectrum of renal papillary necrosis causing acute renal failure and to study the clinical and short term functional outcome after treatment in comparison to the renal function status at the time of presentation.

OBJECTIVES

- To study etiology and clinical spectrum and of renal papillary necrosis causing acute renal failure.

- To study the clinical and short term functional outcome after treatment in comparison to the renal function status at the time of presentation.

REVIEW OF LITERATURE

Historical aspects

In 1877, Dr. Nikolaus Friedreich first described renal papillary necrosis in a patient with urinary obstruction resulting from hypertrophy of the prostate and secondary hydronephrosis.[1] Later, Gunther and Edmondson et al described renal papillary necrosis as a lesion associated with diabetes.[2,3] These authors also observed renal papillary necrosis in cases of urinary tract obstruction even in the absence of diabetes mellitus. In 1952, Mandel's report corroborated the latter findings, suggesting that urinary tract infection played a role in the pathogenesis of RPN.[4] His report showed the presence of urinary infection in 95% of cases of RPN, in autopsy studies. Many studies have reported that 17-90% of patients with renal papillary necrosis have diabetes and 25-73% of patients have urinary tract obstructions. In 1945, Spuhler and Zollinger documented the first description of analgesic nephropathy.[5]

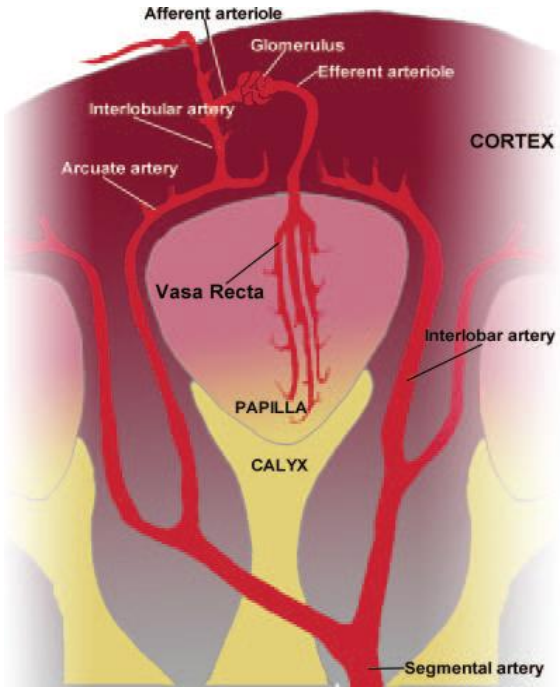
Ludwig von Beethoven's 1827 autopsy report predates all of these descriptions.[6] Beethoven was a long-term abuser of alcohol and analgesics as he was prone to headaches, back pain, and attacks of rheumatism or gout. His alcohol abuse was compounded by a viral hepatitis infection that led to liver cirrhosis and chronic pancreatitis.[7] Davies postulated that Beethoven developed diabetes mellitus secondary to chronic pancreatitis.[8] Beethoven had no reported history of urinary obstruction, nor was it mentioned in his autopsy report.

Wagner's autopsy, as translated by von Seyfried into German, reported "calcareous concretions" filling every calyx of both kidneys. He described the concretions as symmetrical and soft like a pea cut across the middle.[9] According to Davies and Schwarz, this finding is so typical of renal papillary necrosis that the diagnosis is as near to certain as possible without a histological examination.[6,8] Researchers postulate that Beethoven's renal papillary necrosis was most likely a consequence of analgesic abuse and decompensated liver cirrhosis, which ultimately caused his death. Davies contests that Beethoven also had diabetes and that this illness was the primary risk factor for him developing renal papillary necrosis.[8] Indeed, all 3 conditions may have been synergistic factors. In any case, Wagner's protocol from his autopsy of Beethoven represents the first description of papillary necrosis recorded in the literature.[9]

Relevant Anatomy

Briefly reviewing basic renal anatomy and histology allows a clear understanding of the pathophysiology of the underlying ischemia of renal papillary necrosis and how this ischemia is distributed.

The renal papilla is the rounded apex of each medullary pyramid and represents the confluence of the collecting ducts from each nephron within that pyramid. An individual minor calyx cups each papilla; these calyces represent the most proximal aspect of the renal collecting system and are lined with transitional cells.



The main renal artery is divided into four or more segmental arteries that are further subdivided into lobar and interlobar arteries. At the base of each renal pyramid, the interlobar arteries branch into arcuate arteries, which parallel the renal contour along the corticomedullary junction. The arcuate arteries give rise to multiple radial arterial branches called interlobular arteries, which in turn have multiple side branches from the afferent arterioles to the glomeruli.

The renal papillary blood supply is derived from 2 sources: the vasa rectae, which disperse blood from the efferent arteriole, and the interlobar branches of the renal artery, which run within the adventitia of the minor calyces. The vasa rectae arise from the efferent arteriole within the renal cortex and form wide and plentiful vascular bundles at the base of the medullary pyramid. The bundles taper as they continue distally toward the apex and papilla. This process results in the papillary tip

receiving only a marginal supply of blood, which appears to be a predisposing factor for the central role of ischemia in the development of renal papillary necrosis.

The already tenuous vasculature is further impaired by several pathophysiologic states, including the above-described boggy inflammatory interstitium of pyelonephritis, the microangiopathy diabetes mellitus, increased pyelovenous pressure of urinary obstruction, chronic hyperbilirubinemia of liver cirrhosis, oxidative damage of analgesic nephropathy, and the intraluminal stasis of sickle cell disease.

Epidemiology

Renal papillary necrosis generally affects individuals who are in the middle decades of life or older. The typical patient is aged 53 years, with nearly half of cases occurring in individuals older than 60 years and more than 90% of cases occurring in individuals older than 40 years.[10] Renal papillary necrosis is uncommon in individuals younger than 40 years and in the paediatric population, except in patients with sickle cell hemoglobinopathies, hypoxia, dehydration, and septicemia.

In general, renal papillary necrosis is more common in women than in men.[4,10,11] Mandel organized the first comprehensive review to focus attention on renal papillary necrosis.[4] In his series, which examined 160 cases of renal papillary necrosis from the world literature, 96 patients (60%) had diabetes mellitus, 48 patients (30%) had urinary tract obstruction, and 15 patients (9.4%) had both. In the group with diabetes, women outnumbered men, and in the group of patients without diabetes, men outnumbered women, further reflecting the frequency and significance of urinary tract obstructions in elderly men with renal papillary necrosis. An autopsy

report from 1957 by Simon and associates documented the presence of acute or chronic pyelonephritis in 95%.[12]

Analgesic nephropathy, another associated condition and causal factor of renal papillary necrosis, is also more common in women than in men.[13,14,15] Analgesic nephropathy is particularly prevalent in individuals with recurrent headaches or chronic, unremitting muscle and joint pain and in patients with psychoneuroses. Occupational risks are not associated with developing renal papillary necrosis.

Etiology

Generally, any condition associated with ischemia predisposes an individual to papillary necrosis. Important general considerations include shock, massive fluid sequestration (e.g. as in pancreatitis), dehydration, hypovolemia, and hypoxia. Certain conditions have a known association with renal papillary necrosis, and the underlying mechanism of these conditions is ischemia, which ultimately leads to renal papillary necrosis.

<u>Conditions associated with renal papillary necrosis</u>

- Diabetes mellitus
- Pyelonephritis
- Urinary tract obstruction
- Analgesic abuse
- Sickle cell hemoglobinopathies
- Renal transplant rejection

- Cirrhosis of liver
- Dehydration, hypoxia and jaundice of infants
- Miscellaneous – Renal vein thrombosis, cryoglobulinemia, renal candidiasis, contrast media injection, amyloidosis, calyceal arteritis, necrotizing angitis, rapidly progressive glomerulonephritis, hypontensive shock, acute pancreatitis

More than half the patients with renal papillary necrosis have 2 or more of these causative factors.[10]Multiple conditions exhibit synergism and, therefore, worsen both the severity of the disease and the prognosis.

1. *Diabetes mellitus:*

The propensity of diabetic patients to papillary necrosis was first emphasized in 1937.[2,16] From the outset a strong association was made between coexistent urinary tract with RPN, and most of the initial reports considered RPN as a fulminant terminal complication of severe acute pyelonephritis in diabetic patients.[3,17,18,19] Subsequent reports described a more indolent chronic form of RPN in diabetics, generally in those with recurrent episodes of urinary tract infection, but not necessarily with coexistent pyelonephritis.

The pathogenesis in diabetics is generally accepted to be small vessel disease arteriolar and arterial sclerosis. Increased vulnerability to infection, increased infection rate and high concentration of glucose in the vasa recta inducing thrombus formation are also considered contributing factors. Wright, in his paper on an eight year survival of a diabetic with papillary necrosis, lists the autopsy findings: end stage kidneys with hyalinization and fibrosis of glomeruli, dilation of tubules,

glomerulosclerosis, arterionephrosclerosis and chronic pyelonephritis.[20] He observed no active papillary necrosis but instead, incomplete loss of papillae bilaterally. This description gives us some good insight into the pathology of the diabetic kidney with papillary necrosis. The reputation of diabetes as having the worse prognosis among the different conditions associated with papillary necrosis probably stems from the observations that the pathology of such kidneys includes more than just necrosis of pyramid tips, but also other renal injuries such as chronic pyelonephritis, arteriolonephrosclerosis and glomerulosclerosis, sometimes leading to end stage kidneys with loss of vital renal function.[1,6,20]

2. *Nonsteroidal anti-inflammatory drugs (NSAID):*

One of the most common and most preventable etiologic factors is the use of analgesics. Analgesic induced RPN is more common in Australia and England.[15,21]Recently, however, the rising popularity of nonsteroidal anti-inflammatory drugs (NSAIDs), particularly those that inhibit cyclooxygenases (i.e., COX-1, COX-2) has led to a relatively high frequency of adverse events in patients at risk for renal papillary necrosis.

In healthy individuals in whom renal arterial blood flow is not compromised, NSAIDs have little effect unless they are used in excess. This is mostly true because the kidney is not relying on the vasodilatory effects of prostaglandin to supply adequate perfusion. However, in patients who are predisposed to renal hypoperfusion, local prostaglandin synthesis protects the glomeruli and tubules from ischemia. The inhibition of prostaglandin synthesis by NSAIDs that inhibit COX-1 and, as recently reported, COX-2, removes this protective mechanism and

predisposes the kidney to further renal hypoperfusion and, ultimately, ischemia. An extremely important precaution is to strictly monitor patients with prior renal disease or any of the above-mentioned etiologic conditions when prescribing NSAIDs.[22,23]

Other possible mechanism is a direct toxic effect on cells in the medulla. The initial target in analgesic nephropathy may be the medullary interstitial cell, as previously mentioned.[14,24,25] Toxic effects to the interstitial cells could come about from reactive intermediates, acetylation of critical cellular proteins, or inhibition of cellular functions.[26,27] Because medullary interstitial cells synthesize both prostaglandins and proteoglycans, damage to these cells could lead to many effects, including changes in the matrix and effects on the vasculature. Changes in the interstitial matrix would affect the kidneys' ability to concentrate urine, one of the earliest signs of RPN.[25]

3. *Sickle cell trait:*

The hyperosmolar interstitium draws water from cell resulting in an increased concentration of sickle cell haemoglobin, the most important determining factor in sickling. Another factor that may contribute to red blood cell sickling is the low oxygen tension present in renal medulla. As sickling occurs there is an increase in blood viscosity which may further slow the flow in medullary capillaries. RBC sickling in vasa recta causes formation of microthrombi and infarction which eventually leads to papillary necrosis.[28,29]

4. *Fungal:*

Most Indian studies have shown C. tropicalis as the most common of nosocomial candidemias followed by Candida albicans.[30] Systemic candidiasis is an

opportunistic mycosis that can involve almost any organ. Primary infection of the urinary tract by the Candida species results in cystitis and ascending pyelonephritis that may be occasionally complicated by papillary necrosis. Hyperosmolarity of the renal medulla also encourages fungal growth.[31] Apart from the risk factors mentioned above, certain added risk factors for candidal papillary necrosis include urinary catheterization, stenting, lithotripsy and other invasive procedures.[32]

5. *Indinavir:*

Recently, multiple publications have described indinavir-induced renal papillary necrosis. In one study, diagnosis was delayed as the initial symptoms were attributed to suspected urinary tuberculosis. These studies demonstrate the necessity of renal function monitoring during antiretroviral treatment above that of calculus monitoring.[33,34]

6. *Renal transplantation rejection:*

RPN can also occur as a complication of transplant rejection.[35,36] Recognition of the condition is important because RPN can lead to infection, urinary obstruction, and renal failure or indicate rejection.[35]

Pathophysiology

Renal papillary necrosis is classified as

a. focal (i.e. involving only the tip of the papilla) or
b. diffuse (i.e. involving the whole papilla and areas of the medulla), depending primarily on the patient's degree of impaired vasculature.

Renal papillary necrosis may simply affect a single papilla, or the entire kidney may be grossly involved. Once again, renal papillary necrosis is more often a bilateral process; many of the predisposing factors are systemic. Renal papillary necrosis never involves the entire medulla; the disease is always strictly limited to the inner, more distal zone of the medulla and the papilla.

Researchers recognize *two pathologic forms* of renal papillary necrosis

a. Medullary form and
b. Papillary form.

The pathogenic form is dictated by the degree of vascular impairment. The medullary form is characterized by intact fornices, discrete grain-sized necrotic areas, and later defects in the papillae. Clinicians often observe sinus tracts extruding from irregular medullary cavities. In the papillary form, the calyceal fornices and the entire papillary surface are destroyed, demarcated, and sequestered. If these fornices and papillary surfaces are not sloughed, they reepithelialize and acquire a smoother appearance.

Patients with medullary ischemia develop decreased glomerular filtration rates, salt wasting, an impaired ability to concentrate, and polyuria because the vasa rectae supply the medulla and serve the counter current exchange mechanism.

The pathologic findings on a cut section include gray-white to yellow necrosis that resembles infection on the tips or distal two thirds of the pyramids. Microscopically, the tissue shows characteristic coagulative infarct necrosis, with preserved tubule outlines. The leukocytic response is limited to the junctions between preserved and destroyed tissue. After the acute phase, scars that can be

observed on the cortical surface as fibrous depressions replace the inflammatory foci. This pyelonephritic scar is usually associated with inflammation, fibrosis, and a deformation of the underlying calyces and pelvis.

Clinical features

Renal papillary necrosis has a variable clinical course that ranges from a chronic, protracted, and relapsing form to an acute, rapidly progressive form. The acute progressive form is particularly rare, but the effects are devastating, resulting in death from septicemia and renal failure. Patients with the more common chronic form may remain asymptomatic until diagnosed incidentally through the appearance of a ring shadow on a radiographic image, by the passage of sloughed papillae in the urine, or during autopsy. The symptomatic form manifests as episodes of pyelonephritis and hydronephrosis, and it mimics nephrolithiasis.

The most common presenting symptoms in symptomatic patients include fever and chills, flank and/or abdominal pain, and hematuria. Acute renal failure with oliguria or anuria is rare; when these symptoms develop, the disease may be fulminant, requiring dialysis and potentially resulting in death.[6,10]

If renal function deteriorates suddenly in a patient with confirmed diabetes or in a patient with a known history of chronic obstruction and/or pyelonephritis, consider the diagnosis of papillary necrosis, even if the patient is asymptomatic.

Acute ureteral obstruction from sloughed papillae manifests as flank pain and colic due to hydronephrosis or pyonephrosis; hematuria is invariably present. Pyonephrosis or secondary acute or relapsing pyelonephritis compounds the presentation with fever, chills, prostration, and sepsis.

Differential diagnosis

The differential diagnoses of flank pain or hematuria includes a plethora of conditions with infectious, neoplastic, congenital, metabolic, and hematogenous sources. Intraluminal and extraluminal lesions may result in ureteral obstruction.[37]

If acute ureteral obstruction manifests as hematuria, colic, and flank pain, consider that nephrogenic calculi may have embolized to the ureter. Approximately 15% of all calculi, particularly uric acid stones, are not radiopaque (i.e. visible on radiographs); therefore, the examining clinician needs to perform further imaging studies for an accurate identification.

CT scanning is an excellent imaging modality for identifying all calculi (including uric acid stones), except for the rare indinavir (Crixivan) crystal concretions that form in the ureters of patients with HIV infection who are taking this protease inhibitor. If calculi are not seen on a CT scan, consider the possibility of an obstructing urothelial tumor; cytology and endoscopic procedures help to determine this diagnosis.

Blood coagulum downstream from a bleeding source in the kidney (e.g. renal cell carcinoma, angioma, angiomyolipoma, arteriovenous malformation, trauma to a pyelonephritic or multicystic kidney) can also manifest with a similar clinical picture. If a patient has acute ureteral obstruction with fever and leukocytosis, the preferred treatment is drainage of the system.

Pyonephrosis may or may not be present; therefore, the initial short-term management of an obstructed system should be conservative, with resuscitation, drainage, and intravenous antibiotics. Further diagnostic studies can be performed

later, once the physician is certain that the system is sterile. This strategy prevents further clinical deterioration.

Extraureteric causes of ureteral obstruction include retroperitoneal lymphadenopathy from metastatic tumours or lymphoma, retroperitoneal fibrosis, uterine myoma, bladder masses, and high-stage pelvic tumours (e.g. cervical cancer).

Anything that causes severe bladder outlet obstruction leads to bilateral hydronephrosis or hydronephrosis of a solitary kidney. Congenital anomalies can also directly obstruct or provide stasis that may lead to pyelonephritis and papillary necrosis. Duplicate collecting systems, vesicoureteral reflux, and ureteroceles are important offenders to consider.

In the clinical scenario of fever, chills, prostration, and sepsis without hydronephrosis, the differential diagnoses include pyelonephritis, perinephric abscess, renal hemorrhage, tubulointerstitial nephritis, and glomerulonephritis.

In asymptomatic patients who present with acute renal failure characterized by azotemia, the physician must consider bilateral obstruction or the presence of a solitary obstructed kidney. Renal ultrasonography is a wise first test in this scenario, along with tests for urine and plasma urea, creatinine, sodium, and osmolality. After excluding postrenal causes, consider prerenal and renal sources.

Investigations

- The general diagnostic studies include a urinalysis (i.e. routine, microscopic), a complete blood cell count, a complete metabolic panel, and prothrombin

time and activated partial thromboplastin time determinations. If patients have concomitant fever, obtain urine and blood cultures under sterile conditions. If patients are prostrate and obtunded, measure arterial blood gases and perform standard electrocardiography and chest radiography. If acute obstruction is suspected, perform renal ultrasonography or another radiographic evaluation.

- Patients, who present with hematuria, even if diagnostic interventions indicate papillary necrosis, require a full urologic workup for their hematuria because they may have a concomitant bladder tumour or similar lesion.

- Perform a routine and microscopic urinalysis from properly collected specimens (i.e., sterile catheterization, clean-catch midstream).

- Perform a urine culture obtained via sterile catheterization or clean-catch midstream.

- Obtain a urine cytology study on a voided specimen.

- Perform an imaging study, preferably with intravenous contrast, to evaluate the upper urinary tract. Use CT scanning or intravenous urography (IVU), depending on preference. Perform the imaging study prior to cystoscopy because if the study is limited or incomplete, a urologist may need to perform bilateral retrograde pyelography (RPG) in addition to routine cystoscopy. The test of choice to evaluate the upper tracts of patients with contraindications to intravenous contrast is a bilateral RPG.

- The most common urinalysis findings include proteinuria, pyuria, bacteriuria, and low urine-specific gravity. More than 50% of patients develop leukocytosis and azotemia.

- An acutely elevated serum creatinine may be the result of either a bilateral or unilateral process. This process can be obstructive or may be the manifestation of some toxic, metabolic, or inflammatory insult.

- If the clinical picture is suggestive, investigate for any of the conditions associated with renal papillary necrosis, including pyelonephritis, obstructed urinary tract, hemoglobinopathies, tuberculosis, liver cirrhosis, analgesic abuse, renal transplant rejection, and diabetes mellitus.

- Clinical findings may also prompt performing haemoglobin electrophoresis, a subdermal tuberculin test, liver function tests, serum ammonium measurements, serum and urine salicylate and acetaminophen levels, a hemoglobin A1C measurement, and cyclosporin or tacrolimus levels.

Imaging Studies

Plain radiography

Standard radiography of the abdomen that visualizes the span of the kidneys, ureters, and bladder is very good for visualizing radiopaque calculi and may offer hints as to whether the patient has two kidneys. However, this imaging modality neither yields information on the integrity of the urinary tract nor helps to diagnose hydronephrosis or to elucidate kidney function.

Thus, plain radiography is not paramount because it is generally not diagnostic for renal papillary necrosis. Much better radiographic tools are available for this purpose.[38]

CT scanning

If the clinical scenario suggests acute obstruction, CT scanning is the imaging modality of choice, mostly because it is extremely accurate for diagnosing calculi one of the prime differential diagnoses of a sloughed papilla.

A CT scan also shows the entire anatomy of the collecting system and easily reveals hydronephrosis, inflammatory changes, and purulent collections, all without the administration of intravenous contrast. With the administration of contrast and delayed films, if necessary, clinicians can easily visualize filling defects. Contrast images also provide a good, albeit unquantified, estimate of cortical function.

CT scans can also be used to accurately diagnose renal papillary necrosis. Historically, subsequent verification via IVU was required. However, Lang et al have shown that they can identify papillary and medullary necrosis at an early and reversible stage using multiphasic helical CT scan.[39,40] When adequately treated with antibiotics reperfusion improved in approximately 60% of patients within 3 months.

When intravenous contrast is contraindicated, CT scanning without contrast may be ideal for diagnosing acute obstruction, estimating renal function, and, most importantly, excluding nephrolithiasis or ureterolithiasis. Ultrasonography has similar capabilities but, without high-grade obstruction, is not as sensitive for diagnosing calculi. Although less expensive and less invasive (i.e., no radiation

exposure), ultrasonography is operator-dependent and less sensitive for diagnosing calculi. A bilateral RPG is preferred in patients with contraindications to intravenous contrast and in those in whom the urinary tract must indispensably be opacified.

CT findings include;

(1) Small kidneys,

(2) Ring shadows in the medullae,

(3) Contrast-filled clefts in the renal parenchyma, and

(4) Renal pelvic filling defects.

Lang et al describe the ischemic changes of early medullary and papillary necrosis as "a circumscribed, yet often poorly marginated area of diminished enhancement in the tip of the medullary period." They claim these changes can be seen on scans taken in the early corticomedullary phase but are best seen on scans taken in the nephrographic phase.[39,40]

Intravenous urography with nephrotomography

This modality provides an excellent display of the anatomy; even very minor morphological changes in the urinary tract are precisely documented.

IVU is typically the imaging method of choice for diagnosing renal papillary necrosis, although it has its limitations. Clear IVU imaging largely depends on a paucity of stool or bowel gas, which is usually not the case, meaning that images can be obscured. Additionally, approximately 15% of calculi are not radiopaque; thus, IVU is not the best initial test in patients who present with colic, in whom stones are

more common and who require a different workup and treatment plan. In addition, in severe cases, renal function may be so poor that diagnostic changes cannot be demonstrated. Lastly, IVU is contraindicated in patients with azotemia and in patients with coexisting diseases, particularly allergy, asthma, dehydration, diabetes mellitus, thyrotoxicosis, and plasmocytoma. With the advances in CT imaging and the limitations of IVU, many clinicians and radiologists consider CT scan the imaging modality of choice for renal papillary necrosis.[38]

If, for any reason, IVU is not the best choice, contrast-enhanced CT scan, with its far superior contrast resolution, may demonstrate necrotic detached papillae within medullary cavities, thus establishing the diagnosis.

IVU findings include[38]

(1) Dhrinkage and irregularity of papillae, with consequent widening of calyceal fornices, creating what are described as hooks and spurs;

(2) Desquamated papilla in situ, demarcated by contrast material as a ring shadow, often in a triangular shape (commonly referred to as the ***ring sign***);

(3) A calyx without a papilla;

(4) A partially calcified filling defect in the renal pelvis (i.e., sequestered papilla); and

(5) Contrast-containing rice-grain–sized cavities in the papilla, which are pathognomonic for the medullary form of renal papillary necrosis.

Renal ultrasonography

This imaging modality is safe, quick, inexpensive, noninvasive, and diagnostic for hydronephrosis, certain anomalies, and stones large enough to provide a shadow. It is also operator-dependent, which should be taken into consideration.

Ulreich could not duplicate his IVU-confirmed diagnosis of renal papillary necrosis when reviewing the sonograms of the same patients.[41]

Vijayaraghavan et al describe sonographic features of necrotic sloughed papillae representing filling defects in the ureter.[42] In one third of their patients, necrosed papillae were visualized in cavities in the medullary region communicating with the calyces.

Ultrasonography findings may suggest the diagnosis late in the course of the disease but is not sensitive enough to be confirmatory in the earlier, more reversible phases of renal papillary necrosis.

Retrograde pyelography

This test is more invasive because it requires endoscopic access. Images may reveal a clubbed calyx or a filling defect in the ureter.

Precautions such as intravenous antibiotic prophylaxis must be taken because this procedure involves retrograde introduction of contrast, which can increase intrapelvic pressure and may lead to pyelovenous backflow of infectious material, thus predisposing the patient to sepsis. Gentle slow introduction of contrast decreases the likelihood of this complication, but intravenous antibiotic are warranted nonetheless.

Although CT scanning, IVU, and ultrasonography findings can suggest the diagnosis of renal papillary necrosis, urologic intervention confirms the diagnosis and excludes other obstructing agents (i.e. tumours, stones, blood clots).

Histologic Findings

The characteristic pathologic finding is coagulative infarct necrosis.

Medical Therapy

Because ischemia is such a prominent underlying factor in the development of renal papillary necrosis, promptly resuscitate patients and treat their hypoxia, if present. In addition, patients with acute disease may require broad-spectrum intravenous antibiotics, hydration, glycaemic control, and urinary alkalinization. Cessation of analgesic abuse stabilizes and may improve renal function.

In patients without acute ureteral obstruction, treat the infectious and metabolic complications of renal papillary necrosis by replacing insensible losses, maintaining hydration, alkalinizing the urine, and administering antibiotics directed toward the pathogen (as revealed by culture or Gram stain and by observing for the development of obstruction or sepsis). Patients with hematuria significant enough to cause an acute drop in their hematocrit level may require blood transfusions. Patients with sickle cell disease may require exchange transfusions, and patients with diabetes who have acute infectious complications and refractory hyperglycemia may require insulin therapy. Basically, ameliorate the ischemia with hydration and alkalinization, treat the underlying cause of the renal papillary necrosis (e.g. maintain normal glycaemic state), and institute targeted antibiotic therapy.

Surgical Therapy

Patients with renal papillary necrosis may require diagnostic and therapeutic urologic intervention. The urologist is responsible for evaluating any obstruction, hematuria, overwhelming infection, and associated malignancies and for preventing recurrences of these sequelae.

Acute obstruction with concomitant urinary tract infection is a urologic emergency that requires immediate percutaneous nephrostomy to relieve the obstruction, ureteral stent placement, or endoscopic retrieval of the obstructing sloughed papillae. Endoscopic retrieval is not recommended unless the offending papillae are crowning or extruding from the ureteral orifice; even then, the procedure is challenging. Retrograde pyelography and ureteroscopy are useful diagnostic tools, but consider these only when the patient is afebrile and after intravenous administration of antibiotics. Otherwise, a ureteral stent would suffice, delaying retrograde instrumentation until the patient is afebrile.[42,43]

The recommended treatment is to drain the dilated collecting system either endoscopically or percutaneously.[42,43] In patients with severe disease who are febrile and have smoldering sepsis, percutaneous nephrostomy is preferred because it does not require general anesthesia and carries a smaller risk of pyelovenous reflux and worsening sepsis. Cystoscopy and ureteral stent placement allow cystoscopic surveillance of the bladder, which is necessary if hematuria is the presenting symptom. However, in a patient with hydronephrosis, high fever, leukocytosis, and overt sepsis, the preferred treatment is to percutaneously drain the kidney. Perform

diagnostic cystoscopy and RPGs (if necessary) later, when the patient's situation is not so dire.

In selected patients, ureteroscopic investigation of a ureteral filling defect may be warranted. A basket catheter can be introduced through the ureteroscope to extract the offending sloughed papilla. This is performed only in afebrile patients, after broad-spectrum intravenous antibiotics have been administered.

If the infection severity increases and the patient does not improve despite supportive measures and proper antibiotic coverage, a nephrectomy may be life-saving.

Outcome and Prognosis

The prognosis of renal papillary necrosis depends on the etiology of the ischemic insult, the number of associated pathologic factors, the dispersal of the necrosis, the involvement of one or both kidneys, and the overall health of the patient. Elderly debilitated patients with multiple medical problems have a poor prognosis, as do patients with overwhelming sepsis and multiple comorbidities. The prognosis is generally worse in patients with diabetes, specifically those who are not compliant and who are prone to severe episodes of hyperglycaemia because of the systemic nature of their disease.[44,45]

METHODOLOGY

This study was conducted in the Department of Medicine, Nephrology and Urology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2013 to December 2013.

Study design and duration: A one year longitudinal study.

Study period: The present study was conducted from January 2013 to December 2013.

Source of Data: Patients presenting with acute renal failure due to renal papillary necrosis at Department of Medicine, Nephrology and Urology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were studied.

Sample size: A total of 40 patients with renal papillary necrosis presenting with acute renal failure were included in the study.

Sampling procedure: All the patients fulfilling the selection criteria during the study period were included.

Selection criteria

Inclusion Criteria

- All patients presenting with renal papillary necrosis with acute renal failure.

Exclusion Criteria

- Patients with acute renal failure secondary to causes other than renal papillary necrosis.

Ethical clearance: The study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed consent: The selected patients were briefed about the purpose of study in detail and a written informed consent was obtained (Annexure–I).

Data collection: Demographic data, clinical presentation, history of other comorbid conditions and treatment history were obtained. Further these patients underwent clinical examination followed by systemic examination. These findings were noted on a predesigned and pretested proforma (Annexure-II).

Investigations

Patients underwent following investigations.

- Complete blood count
- Urine routine
- Urine culture and sensitivity
- Random blood sugar
- Serum creatinine
- e GFR
- Ultrasound
- CT KUB

All patients underwent appropriate treatment i.e. either conservative or urological intervention based on their clinical presentation and investigations. After treatment the short term clinical and functional outcome of the patients was assessed immediately after treatment, and at 3 months (1st follow up) and 6 months (2nd follow up)

Outcome variables

Based on clinical presentation, examination and investigations, patients were evaluated for;

- Symptom profile
- Etiology
- Stage of chronic kidney disease / e GFR
- Management
- Complications
- Outcome

Statistical methods

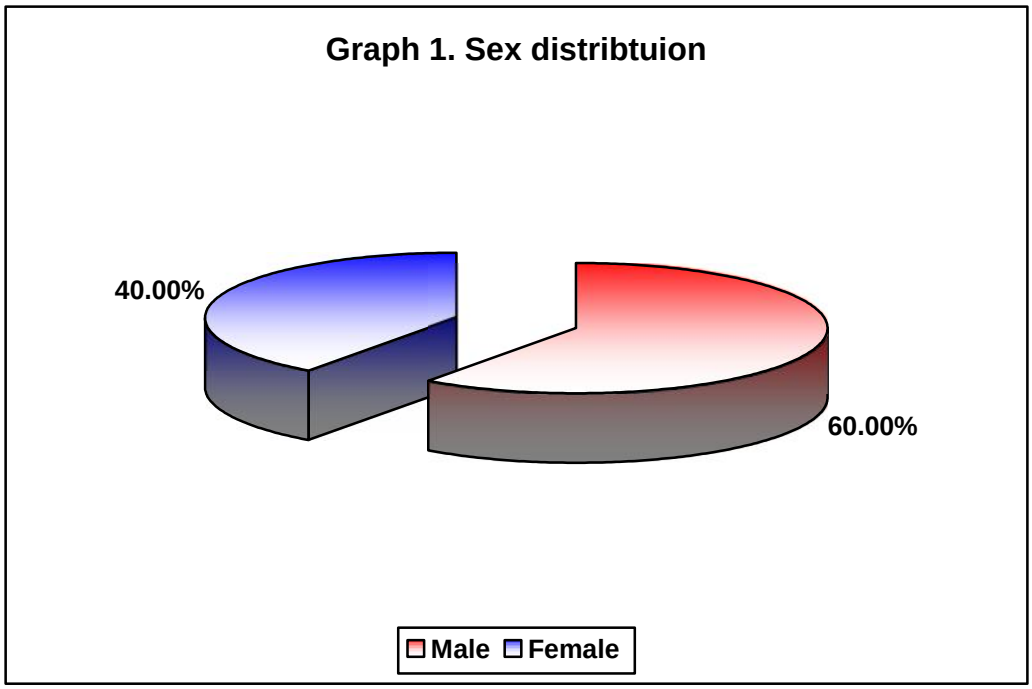
The data obtained was coded and entered into the Microsoft Excel Spreadsheet (Annexure III). The categorical data was expressed in terms of rates, ratios and percentages and continuous data was expressed as mean ± standard deviation.

RESULTS

A one year longitudinal study was conducted in the Department of Medicine, Nephrology and Urology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Out of 2000 patients presenting with acute renal failure from January 2013 to December 2013, 40 patients of acute renal failure due to renal papillary necrosis were included in the study.

Table 1. Sex distribution

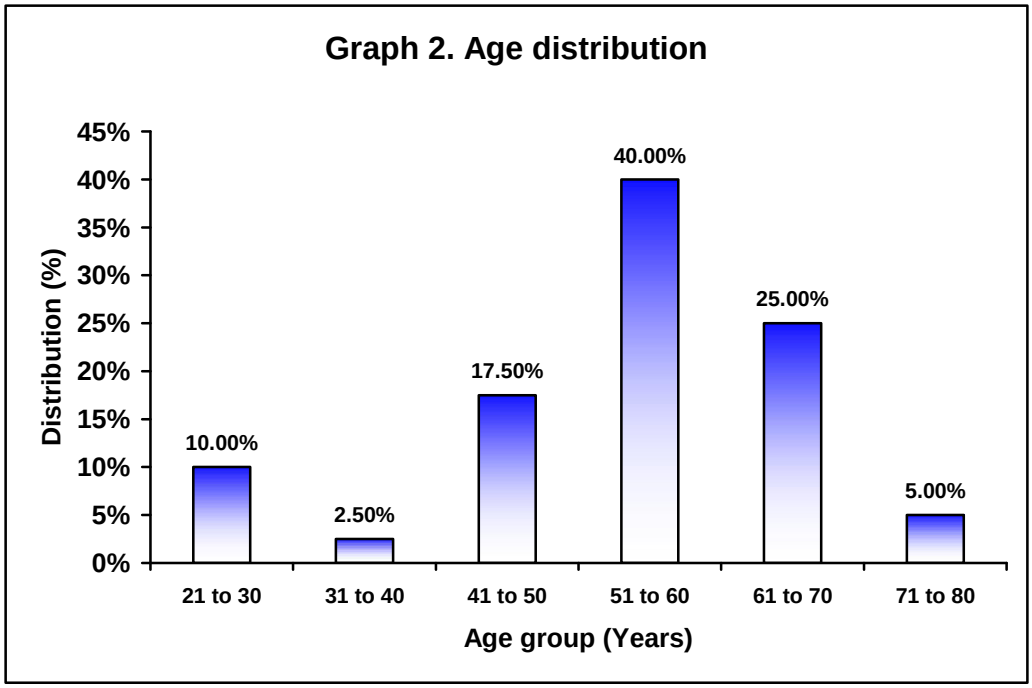
Sex	Distribution (n=40)	
	Number	**Percentage**
Male	24	60.00
Female	16	40.00
Total	**40**	**100.00**



In the present study 60% of the patients were males and 40% were females. The male to female ratio was 1.5:1.

Table 2. Age distribution

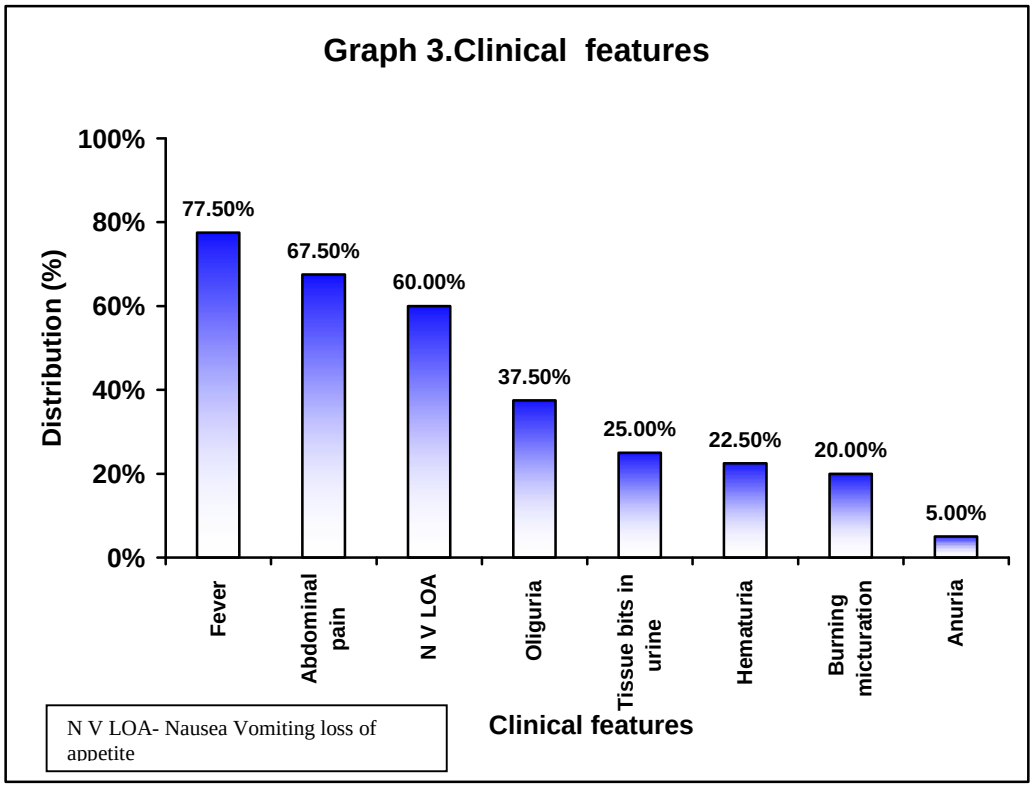
Age group (Years)	Distribution (n=40)	
	Number	**Percentage**
21 to 30	4	10.00
31 to 40	1	2.50
41 to 50	7	17.50
51 to 60	16	40.00
61 to 70	10	25.00
71 to 80	2	5.00
Total	**40**	**100.00**



In this study most of the patients were aged between 51 to 60 years (40%).

Table 3. Clinical features

CLINICAL FEATURES	Distribution (n=40)	
	Number	**Percentage**
Fever	31	77.50
Abdominal pain	27	67.50
Nausea, Vomiting, loss of appetite	24	60.00
Oliguria	15	37.50
Tissue bits in urine	10	25.00
Hematuria	9	22.50
Burning micturition	8	20.00
Anuria	2	5.00



In this study the commonest presentation was fever (77.5%), followed by abdominal pain (67.5%), and followed by nausea, vomiting and loss of appetite in 60%.

Table 4. Clinical profile of patients with multiple presentations

Clinical features	Distribution (n=40)	
	Number	**Percentage**
Abdominal pain +oliguria +fever + NVLOA	8	20.00
Abdominal pain +fever + NVLOA	6	15.00
Abdominal pain + oliguria	5	12.50
Fever + hematuria + tissue bits	5	12.50
Fever + Burning micturition + NVLOA	5	12.50
Abdominal pain + hematuria	4	10.00
Fever + burning micturition + tissue bits + NVLOA	3	7.50
Abdominal pain + oliguria + tissue bits + fever	2	5.00
Abdominal pain + anuria + fever + NVLOA	2	5.00
TOTAL	**40**	**100%**

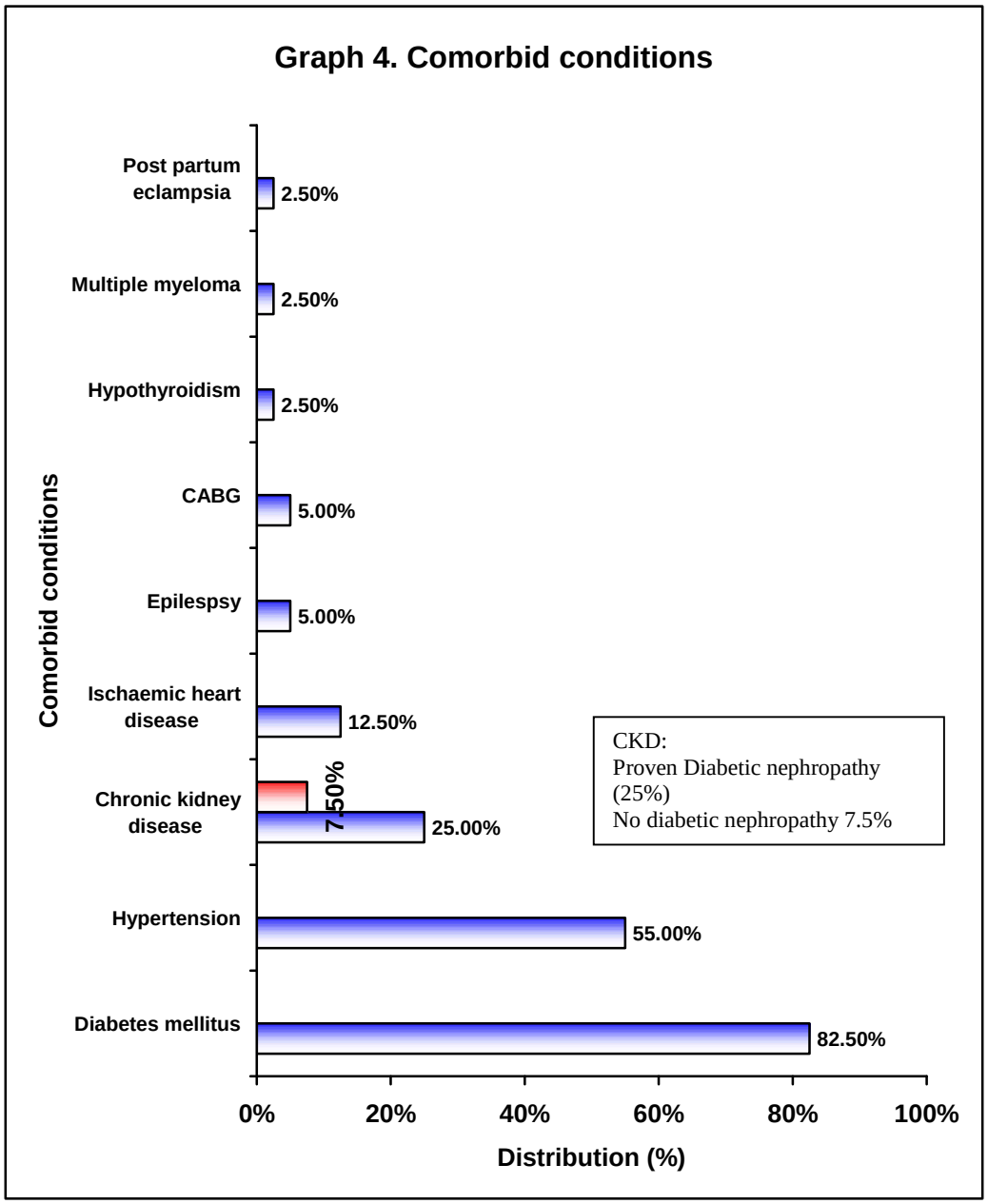
NVLOA: Nausea, Vomiting and Loss of appetite

Table 5. Patients presenting with SIRS / Sepsis / Septicemic shock

SIRS	SEPSIS	SEPTIC SHOCK	NONE
14 (35%)	10 (25%)	6 (15%)	10(25%)

Table 6. Comorbid conditions

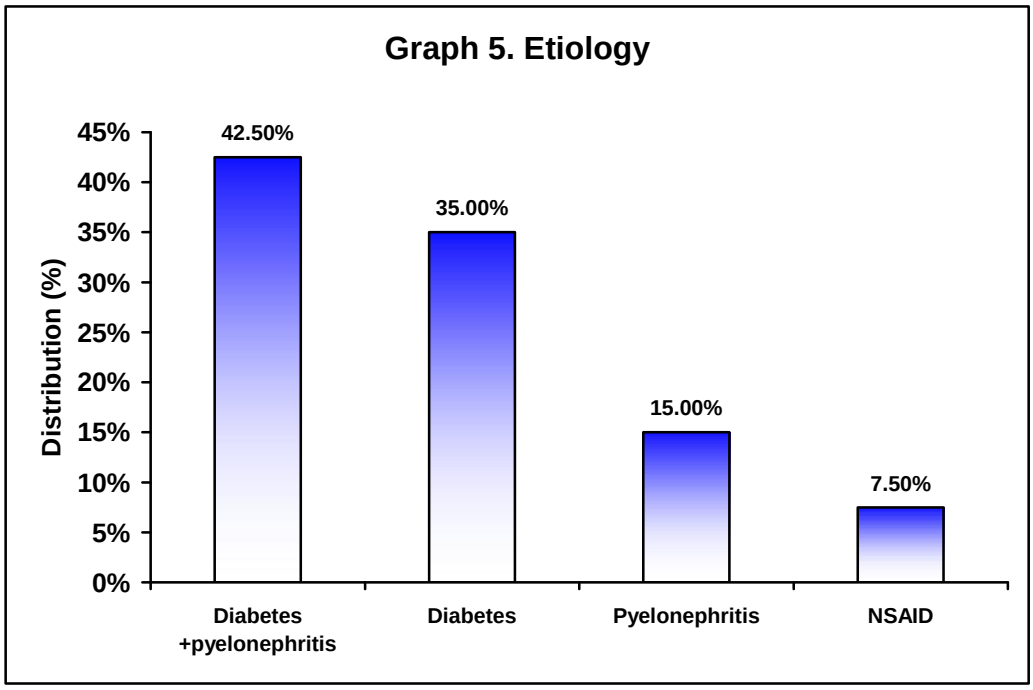
Comorbid conditions	Distribution (n=40)	
	Number	**Percentage**
Diabetes mellitus	33	82.50
Hypertension	22	55.00
Chronic kidney disease	13	32.50
a. Proven diabetic nephropathy	10	25.00%
b. No Diabetic nephropathy	3	7.50
Ischemic heart disease	5	12.50
CABG	2	5.00
Epilepsy	2	5.00
Hypothyroidism	1	2.50
Multiple myeloma	1	2.50
Post partum eclampsia	1	2.50



In the present study majority of the patients had history of diabetes mellitus (82.5%) and hypertension was present in 55%. History of chronic kidney disease was noted among 32.5%. The other comorbid conditions are as shown in table 4.

Table 7. Etiology

ETIOLOGY	Distribution (n=40)	
	Number	**Percentage**
Diabetes Mellitus + pyelonephritis	17	42.5%
Diabetes mellitus	14	35%
Pyelonephritis	6	15%
NSAID	3	7.5%
Total	**40**	**100.00**



In this study diabetes with pyelonephritis was most common etiology noted among 42.5%, followed by Diabetes mellitus alone in 35% of patients.

Table 8. Haematological profile and blood sugar levels

Variables	Findings	Distribution (n=40)	
		Number	**Percentage**
Haemoglobin (gm %)	≥ 12	10	25.00
	10.0 to 11.9	15	37.50
	8.0 to 9.9	13	32.50
	4 to 7.9	2	5.00
	< 4	0	0.00
	Total	**40**	**100.00**
White blood cell count (Cu mm)	< 4000	2	5.00
	4000 to 11000	13	32.50
	> 11000	25	62.50
	Total	**40**	**100.00**
Random blood sugar (mg/dL)	< 140	19	47.50
	140 to 200	9	22.50
	200 to 300	5	12.50
	300 to 400	4	10.00
	> 400	3	7.50
	Total	**40**	**100.00**

In the present study haematological profile revealed most (37.5%) of the patients with lower haemoglobin levels (10.0 to 11.9 gm %) and raised white blood cell count (62.5%). The random blood sugar levels were less than 140mg/dl in 47.5%of patients.

Table 9. Urine routine

Variables	Findings	Distribution (n=40)	
		Number	**Percentage**
Protein	Traces	2	5.00
	+	15	37.50
	++	6	15.00
	+++	4	10.00
	Absent	13	32.50
	Total	**40**	**100.00**
WBC	< 5	10	25.00
	5 to 10	7	17.50
	11 to 20	5	12.50
	Plenty	18	45.00
	Total	**40**	**100.00**
RBC	< 5	5	12.50
	5 to 10	25	62.50
	11 to 20	1	2.50
	Plenty	9	22.50
	Total	**40**	**100.00**
Glucose	+	31	77.50
	++	5	12.50
	Absent	4	10.00
	Total	**40**	**100.00**

The urine routine examination findings are as shown in table 8.

Table 10. Urine culture

Variables	Findings	Distribution (n=40)	
		Number	**Percentage**
Urine culture	Positive	14	35.00
	Negative	26	65.00
	Total	**40**	**100.00**
Isolates (Organisms)	E. coli	7	50.00
	Candida	4	28.57
	Citrobacter	1	7.14
	Enterobacter C.	1	7.14
	Klebsiella pneumoniae	1	7.14
	Total	**14**	**100.00**

In the present study urine culture was positive in 14 (35%) patients. Of these E. coli was the commonest organism isolated in 7 patients (50%).

Table 11. Imaging findings

Findings	Distribution (n=40)	
	Number	**Percentage**
Hydronephrosis with Hydroureter	35	87.50
Pyelonephritis	22	55.00
Small kidney (non affected side)	3	7.50
Renal calculi (affected side)	5	12.50

In the present study imaging findings revealed hydronephrosis with hydroureter in 87.5% of the patients.

Table 12. Treatment

Treatment	Distribution (n=40)		
	ARF without CKD	**ARF with CKD**	**Total**
Intervention	21	10	31 (77.50%)
Conservative	6	3	9(22.50%)

In the present study 77.50% of the patients required intervention while 22.5% of the patients underwent conservative treatment.

Table 13. Serum creatinine

Interval	Serum creatinine (mg/dL)	ARF		ACUTE ON CKD	
		No	**%**	**No**	**%**
Admission	<1.5	0	0.00	0	0.00
	1.5-2.0	8	29.63	1	7.69
	2.1-4.0	8	29.63	5	38.46
	4.1-6.0	5	18.51	3	23.08
	6.1-8.0	4	14.82	3	23.08
	8.1-10.0	2	7.41	1	7.69
	Total	**27**	**100.00**	**13**	**37.50**
Post treatment (Before discharge)	<1.5	9	33.33	0	0.00
	1.5-2.0	6	22.23	1	7.69
	2.1-4.0	9	33.33	6	46.15
	4.1-6.0	2	7.41	3	23.08
	6.1-8.0	1	3.70	2	15.39
	8.1-10.0	0	0.00	1	7.69
	Total	**27**	**100**	**13**	**100**
First follow up (3months)	<1.5	12	44.45	0	6.67
	1.5-2.0	5	18.51	3	23.08
	2.1-4.0	6	22.23	5	38.46
	4.1-6.0	1	3.70	2	15.39
	6.1-8.0	2	7.41	1	7.69
	8.1-10.0	1	3.70	2	15.39
	Total	**27**	**100**	**13**	**100**
Second follow up (6 months)	<1.5	12	44.45	0	0.00
	1.5-2.0	6	22.23	1	7.69
	2.1-4.0	6	22.23	6	46.15
	4.1-6.0	2	7.41	2	15.39
	6.1-8.0	0	0.00	2	15.39
	8.1-10.0	1	3.70	2	15.39
	Total	**27**	**100**	**13**	**100**

Table 14. eGFR (MDRD Equation)

Interval	eGFR	ARF GROUP			ARF ON CKD GROUP		
		No	%	CKD STAGE	No	%	CKD STAGE
Admission	≥90	0	0.00	-	0	0.00	1
	60-89	0	0.00	-	0	0.00	2
	30-59	10	37.03	-	6	46.15	3
	15-29	8	29.63	-	6	46.15	4
	<15	9	33.33	-	1	7.69	5
	Total	**27**	**100**	**-**	**13**	**100**	
Post treatment (before discharge)	≥90	1	3.70	-	0	0.00	1
	60-89	2	7.40	-	0	0.00	2
	30-59	13	48.14	-	2	15.38	3
	15-29	8	29.63	-	5	38.46	4
	<15	3	11.11	-	6	46.15	5
	Total	**27**	**100**	**-**	**13**	**100**	
First follow up (3months)	≥90	2	7.40	1	0	0.00	1
	60-89	5	18.51	2	0	0.00	2
	30-59	11	40.74	3	1	7.69	3
	15-29	6	22.22	4	7	53.84	4
	<15	3	11.11	5	5	38.46	5
	Total	**27**	**100**		**13**	**100**	
Second follow up (6months)	≥90	2	7.40	1	0	0.00	1
	60-89	6	22.22	2	0	0.00	2
	30-59	11	40.74	3	1	7.69	3
	15-29	5	18.51	4	6	46.15	4
	<15	3	11.11	5	6	46.15	5
	Total	**27**	**100**		**13**	**100**	

Table 15. Overall functional Outcome of RPN with ARF without CKD at 6months

OUTCOME		Distribution (n=27)	
		Number	**Percentage**
Complete recovery of renal function		7	26.92
ARF to CKD	Stage 3	11	40.74
	Stage 4	5	18.52
	Stage 5	4	14.82
Total		**27**	**100.00**

COMPLETE RECOVERY 26.92%

ARF TO CKD 74.07%

Table 16. Overall functional Outcome of RPN with ARF with CKD at 6 months.

CKD STAGE	**OUTCOME**		
	Improved renal function	No improvement / deterioration	**TOTAL (13)**
Stage 3	1	0	1 (7.69%)
Stage 4	4	2	6(46.15%)
Stage 5	0	6	6(46.15%)
TOTAL	5	8	13(100%)

IMPROVED RENAL FUNCTION 38.46%

NO IMPROVEMENT / DETERIORATION 61.54%

Table 17. Treatment based functional outcome ARF without CKD at 6 months

Treatment	Renal function outcome				Total
	Complete recovery	Stage 3 CKD	Stage 4 CKD	Stage 5 CKD	
Intervention	**4**	**10**	**4**	**3**	**21**
Conservative	**3**	**2**	**1**	**0**	**6**

Intervention group: Complete recovery: 19.04%

ARF to CKD: 80.95%

Conservative group: Complete recovery: 50%

ARF TO CKD: 50%

Table 18. Treatment based functional outcome ARF with CKD at 6 months

CKD STAGE (6months)	OUTCOME			
	INTERVENTION			
	Improved renal function		No improvement / deterioration	
Stage 3	0		0	
Stage 4	3	IV-IV-IV	2	IV-IV-IV
		IV-IV-IV		IV-IV-IV
		IV-IV-IV		
Stage 5	0		5	V-IV-V
				V-V-V
				V-V-V
				V-V-V
				IV-V-V
TOTAL	3		7	

Improved renal function: 30%

Deterioration: 70%

Table 19. Treatment based functional outcome ARF with CKD at 6 months

CKD STAGE (6months)	OUTCOME			
	CONSERVATIVE			
	Improved renal function		No improvement / deterioration	
Stage 3	1	V-IV-III	0	
Stage 4	1	IV-IV-IV	0	
Stage 5	0		1	V-V-V
TOTAL	2		1	

Improved outcome: 66.66%

Deterioration of renal function: 33.33%

TABLE 20. Correlation of outcome of RPN+ARF without CKD and SIRS, SEPSIS, SEPTIC SHOCK

CKD STAGE AT 6 MONTHS	CLINCAL PRESENTATION					
	SIRS		SEPSIS		SEPTIC SHOCK	
	I	NI	I	NI	I	NI
STAGE 3	4	0	2	0	3	0
STAGE 4	1	1	1	0	1	0
STAGE 5	0	0	0	3	0	1
TOTAL	**5 (83.33%)**	**1 (16.67%)**	**3 (50%)**	**3 (50%)**	**4 (75%)**	**1 25%**

I – IMPROVED RENAL FUNCTION

NI –NOT IMPROVED

TABLE 21. Correlation of outcome of RPN+ARF without CKD with proteinuria at presentation

Functional outcome at 6 months	With proteinuria	Without proteinuria (n=27)	Total
Complete recovery	7(25.92%)	1(3.72%)	8(29.62%)
Progression to CKD	11(40.74%)	8(29.92%)	19(70.37%)
Total	18	9	27

In patients with RPN with ARF on CKD, 40.74% patients progressed to CKD in patients with proteinuria and 29.92% patients progressed to CKD in patients without proteinuria.

DISCUSSION

Renal papillary necrosis has a variable clinical course that ranges from a chronic, protracted, and relapsing form to an acute, rapidly progressive form. The acute progressive form is particularly rare, but the effects are devastating, resulting in death from septicaemia and renal failure[46]. In this one year longitudinal study patients with renal papillary necrosis with acute renal failure (ARF) and acute renal failure on chronic kidney disease (CKD) were included. The demographic data, clinical features, co-morbid conditions, etiology, treatment received and short term functional outcome were studied.

Out of 2000 patients with acute renal failure from January 2013 to December 2013, a total of 40 patients with renal papillary necrosis who presented with acute renal failure and acute renal failure on chronic kidney disease were included in this study. As the outcome in acute renal failure patients without CKD and with CKD is different, it was studied in the two groups i.e. Group I-Renal papillary necrosis with ARF without CKD and Group II- Renal papillary necrosis with ARF on CKD.

In this study 60% of the patients were males and 40% were females. The male to female ratio was 1.5:1. This is in contrast with other studies which have showed female predominance.[4,10,11,47,48]

In this study the youngest patient is 21 years and oldest is 74 years. Renal papillary necrosis was predominantly seen in > 50 years of age (70%).

The clinical features were fever (77.50%), abdominal pain (67.50%), nausea, vomiting, loss of appetite (60%), oliguria (37.5%), tissue bits in urine (25%), gross

hematuria (22.5%), burning micturition (20%), and anuria (5%). All the patients had multiple clinical features with the most common being fever, abdominal pain, nausea, vomiting, loss of appetite, oliguria in 20% patients. At presentation 35% were having systemic inflammatory response syndrome (SIRS), 25% were in sepsis and 15% were in septicaemic shock.

In this study the common co-morbid conditions were diabetes mellitus (82.5%), hypertension (55%) and chronic kidney disease (32.5%).

In this study 42.5% patients had more than one etiology (diabetes mellitus and pyelonephritis), 35% had diabetes, 15% had pyelonephritis and 7.5% had NSAIDS as the etiological factor for renal papillary necrosis.

Haematological studies at presentation revealed 75% patients were anaemic out of which 37.5% had mild, 32.5% had moderate and 5% had severe anaemia (as per WHO classification). Most of the patients presented with leucocytosis (62.5%) and 5% patients presented with leukopenia.

In this study 47.5% patients had well controlled, 22.50% had mildly elevated and 30% had uncontrolled blood sugar levels.

In this study urine analysis at presentation showed proteinuria in 62.5% patients, pyuria in 100% and gluocosuria in 90% patients. Urine microscopy of all the patients showed RBCs. Urine culture was positive 35% patients. The most common organism isolated was E. coli (50%) followed by Candida (28.57%), Citrobacter (2.5%), Enterobacter (2.5%) and Klebsiella pnemoniae (2.5%).

In this study imaging showed hydronephrosis with hydroureter in 87.5% patients and findings suggestive of pyelonephritis present in 55% patients.

In this study 77.5% patients underwent intervention in the form of DJ (Double-J) stenting or URS (uretero-renoscopy) with removal of necrotic tissue obstructing the ureter. 22.5% patients were managed conservatively.

Serum creatinine levels and e GFR were assessed during the immediate post treatment period, at first follow up (3 months) and at second follow up (6 months).

In this study in Group I, immediate post treatment period, serum creatinine levels decreased in 92.59% patients as compared to admission, out of which 33% patients had normalized serum creatinine levels (considered to be <1.5mg/dl). During the 1st follow up, another 11.45% patients' serum creatinine normalized. During the 2nd follow up none of the remaining patients had normalized serum creatinine levels.

In the group II in the immediate post treatment period, 53.84% patients had decreased, 30.76% had the same and 15.38% patients had increased sr. creatinine levels as compared to admission. At the 1st follow up 46.15%, 7.69% and 46.15% patients had decreased, same and increased sr. creatinine levels respectively as compared to the immediate post treatment sr. creatinine levels. At the 2nd follow up 30.76%, 23.07% and 46.15% patients had decreased; same and increased levels respectively as compared to first follow up.

In this study the e GFR was calculated by using the MDRD equation based ST. Georges University of London, excel chart e GFR calculator. In Group I, e GFR was found to be increased in 92.59% patients and it remained the same in 7.41%

patients in the immediate post treatment period as compared to e GFR at admission. At the 1st follow up the e GFR was further increased in 66.67% patients, remained same in 22.22% patients and decreased in 11.11% patients as compared to the e GFR in the immediate post treatment period. At the 2nd follow up the e GFR further increased in 33.33% patients, remained the same in 40.74% patients and decreased in 25.93% patients in comparison to the e GFR at first follow up.

In the group II in the immediate post treatment period, 53.84% patients had increased, 30.76% had the same and 15.38% patients had decreased e GFR as compared to admission. At the 1st follow up 46.15%, 7.69% and46.15% patients had increased, same and decreased e GFR respectively as compared to the immediate post treatment values. At the 2nd follow up 30.76%, 23.07% and 46.15% patients had increased, same and decreased e GFR respectively as compared to first follow up.

On assessing the overall functional outcome of these patients at 6 months, the study showed that in group I, 26.92% recovered completely and 74.07% patients progressed to CKD.

The overall functional outcome of patients in group II at 6 months showed that 7.69% were in CKD stage 3, 46.15% in CKD stage 4 and 46.15% were in CKD stage 5.

Treatment based functional outcome in Group I showed that in the patients who underwent intervention, renal function recovered completely in 19.04% and 80.95% patients progressed to CKD. In patients who were managed conservatively 50% had complete recovery of renal function 50% patients progressed to CKD.

In group II, in the patients who underwent intervention renal function improved in 30% without change of CKD stage and deteriorated in 70%. In patients who were managed conservatively 66.67% patients had improved renal function, 33.33% patients had deterioration of renal function.

In Group I, 40.74% patients progressed to CKD in patients with proteinuria and 29.92% patients progressed to CKD in patients without proteinuria.

CONCLUSION

1) Renal papillary necrosis (RPN) causing acute renal failure (ARF) or acute renal failure on chronic kidney disease (CKD) is more common in males.
2) Most common etiology is Diabetes Mellitus with Pyelonephritis.
3) Common clinical features are fever, abdominal pain, nausea, vomiting, loss of appetite, oliguria and tissue bits in urine.
4) Diabetics with good glycaemic control also develop RPN with ARF.
5) There is significant increase in e GFR in immediate post treatment period in patients with RPN with ARF without CKD in comparison to ARF with CKD.
6) Outcome of RPN with ARF with or without CKD depends on severity of ARF, etiology, proteinuria and associated sepsis / septicemic shock at presentation.
7) In patients with RPN with ARF with CKD, there is deterioration of renal function in spite of surgical intervention.

SUMMARY

- A total of 40 patients were included in this study of which 27 patients had renal papillary necrosis (RPN) with ARF without CKD and 13 patients had RPN with ARF on CKD.
- Male to female ratio was 1.5:1 indicating male predominance in this study.
- More than 70% patients belonged to the age group of more than 50 years.
- Common clinical features were fever, abdominal pain, nausea, vomiting and loss of appetite, oliguria and tissue bits in urine.
- Most common co-morbid condition was diabetes mellitus (82.5%).
- Most common etiological factor was diabetes mellitus with pyelonephritis.
- Haematological studies revealed that 75% patients were anaemic and 62.5% had leucocytosis at the time of presentation.
- Blood sugar levels were well controlled in 47.5% patients and 30% patients had uncontrolled blood sugar levels at the time of presentation.
- Urine microscopy revealed the presence of WBCs and RBCs in all patients.66.67%patients with RPN with ARF without CKD had proteinuria.
- E. coli and candida were the common organisms isolated on urine culture.
- Imaging showed that 87.5% patients had hydronephrosis with hydroureter and 55% patients had pyelonephritis.
- Intervention was done in 77.5% patients
- In patients with RPN with ARF without CKD,
    - e GFR increased in 92.59% patients and it remained the same in 7.41% patients in the immediate post treatment period.

- At second follow up 26.92% patients recovered completely and 74.07% patients progressed to CKD.
- In patients who underwent intervention, the renal function recovered completely in 19.04% and 80.95% patients progressed to CKD.
- In patients who were managed conservatively, 50% patients had complete recovery of renal function and 50% patients progressed to CKD.

- In the patients with RPN with ARF with CKD,
  - e GFR increased significantly in only 15.38% at 6 months as compared to admission.
  - The overall functional outcome at 6 months showed that 7.69% were in CKD stage 3, 46.15% in CKD stage 4 and 46.15% were in CKD stage 5.
  - In patients who underwent intervention, renal function improved in 30% patients without change of CKD stage and deteriorated in 70%.
  - In patients who were managed conservatively, renal function improved in 66.67% patients and deteriorated in 33.33%

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ANNEXURE I – CONSENT FORM

A one year longitudinal study of the outcome of papillary necrosis causing acute renal failure in patients presenting to KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Objective and purpose of the study

This research is intended to study the outcome of papillary necrosis causing acute renal failure. The principal investigator of the study is Dr. **** ****** under the guidance of Dr. **** ****** and Dr. **** ******. Respected Sir/Madam, we invite you to participate in our study as, you are eligible for the same. During the study you will be asked some questions in detail regarding your chief complaints, associated co-morbid conditions and the treatment you underwent for the same. Your co-operation will be of great help in understanding the detailed etiology, and outcome of acute renal failure due to papillary necrosis .It will help in reducing the significant morbidity associated with acute papillary necrosis.

Procedure

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood and urine samples for the necessary investigations.

Risk and Benefits

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

The result of you taking part in this research would help health care providers towards a better understanding of this disease, and thus we will be able to provide improved patient care

Alternatives

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part now, you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

Privacy and confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution/sponsor's policy

Does not apply to this research

Financial incentives for participation

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish results

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

Queries

If you have any questions about your rights as a participant during study or in future you may contact:

Dr. **** ******, Principal Investigator

Post graduate in Department of Medicine, Phone - **** *****

Dr. ***** ******, Guide

HOD, Department of Nephrology.

Dr. **** ******

Chairman, J.N.M.C Ethical Committee for Human Research.

Consent statement

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me in language understood by me, this entire consent form, and have had all my questions answered.

Name of the Participant: _____ Signature / Thumb print _____

Name of the Witness _____ Signature _____

Name of the Investigator _____ Signature _____

Date: Place:

ANNEXURE II – PROFORMA

Name:	Age/Sex:
DOA:	DOD:
Address:	In-patient no.:

Clinical presentation:

Abdominal pain:	Yes/No
Hematuria:	Yes/No
Tissue bits in urine:	Yes/No
Oliguria/Anuria:	Yes/No
Fever:	Yes/No
Burning micturition:	Yes/No

Nausea, vomiting, loss of appetite

Co-morbidities:

Diabetes mellitus	Yes/No
Hypertension	Yes/No
Chronic kidney disease	Yes/No

Significant past history:

Recurrent UTI	Yes/No
Analgesic abuse	Yes/No
Tuberculosis	Yes/No
H/O Urological intervention in past	Yes/No

PHYSICAL EXAMINATION

1. VITALS

Pulse: Blood pressure:

Temp: Respiratory rate:

2) GENERAL PHYSICAL EXAMINATION:

3) SYSTEMIC EXAMINATION

a. Per abdomen:
b. CVS :
c. RS:
d. CNS:

INVESTIGATIONS:

Hb

WBC

Serum creatinine

FBS/RBS

Urine R/M

Urine C/S

eGFR

USG KUB

NON CONTRAST CT KUB:

IVU (OPTIONAL):

CT IVU (OPTIONAL)

INTERVENTION DONE:

POST-OPERATIVE RECOVERY:

COMPLICATIONS:

FOLLOW UP:

Serum Creatinine

e GFR

OUTCOME OF DISEASE:

ANNEXURE III –KEY TO MASTER CHART

-	-	Absent
+	-	Present
CABG	-	Coronary artery bypass grafting
CKD	-	Chronic kidney disease
E. Coli	-	Escherachia coli
eGR	-	Estimated glomerular filtration rate
Enterobacter C-		Enterobacter cloacae
F	-	Female
gm	-	Gram
gm/dL	-	Gram per decilitre
IHD	-	Ischaemic heart disease
Kleb. Pneu	-	Klebsiella pneumoniae
M	-	Male
mg/dL	-	Milligram per decilitre
NSAID	-	Non steroidal anti-inflammatory drugs
PL	-	Plenty
SIRS	-	Systemic inflammatory response syndrome
Sr.	-	Serum
TR	-	Traces

ANNEXURE III - MASTER CHART

Serial number	In patient number	Age (Years)	Sex	Date of admission	Date of discharge	Etiology			Comorbidities									Clinical features							Investigations						
																											Urine			
						Diabetes	Pyelonephritis	NSAID	Diabetes mellitus	Hypertension	Chronic kidney disease	IHD	Hypothyroidism	Epilepsy	CABG	Multiple myeloma	Post partum eclampsia	Abdominal Pain	Hematuria	Oliguria	Fever	Burning micturation	Tissue bits in urine	Nausea vomiting loss of appetite	Haemoglobin (gm%)	White blood cell count (/cumm)	RBS/FBS (mg/dL)	Protein	WBC	RBC	Glucose	Culture
1	491109	57	F	10/2/2012	10/10/2012	+	-	-	+	+	+	-	-	-	-	-	-	+	-	+	+	-	-	+	9.3	10900	334	++	2 TO 3	6TO7	-	-
2	455214	50	F	10/15/2012	10/20/2012	+	+	-	+	-	-	-	-	-	-	-	-	+	-	-	+	-	-	+	9.2	11400	146	-	4 TO 5	8TO10	-	-
3	390601	59	M	10/30/2012	11/6/2012	+	-	-	+	+	-	+	-	+	-	-	-	-	-	-	+	+	-	+	7.8	30900	78	+++	PL	4TO5	-	+
4	390931	60	M	11/2/2012	11/9/2012	+	+	-	+	+	-	+	-	-	+	-	-	+	-	+	-	-	-	-	10.8	21500	210	+	PL	6TO7	-	+
5	471012	50	M	11/12/2012	11/14/2012	+	+	-	+	-	+	-	-	-	-	-	-	-	-	-	+	+	+	+	9.2	8200	127	-	PL	9TO10	-	-
6	334355	60	F	12/14/2012	12/19/2012	+	+	-	+	+	+	-	-	-	-	-	-	-	-	-	+	+	-	+	11.5	9000	154	++	PL	7TO8	-	-
7	509191	52	M	1/4/2013	1/28/2013	+	+	-	+	-	-	-	-	-	-	-	-	+	-	+	+	-	-	+	11.7	6000	66	+	10TO15	8TO10	-	-
`8	509374	50	F	1/5/2013	1/11/2013	+	+	-	+	+	+	-	-	-	-	-	-	+	+	-	-	-	-	-	9.3	16200	322	+++	PL	PL	-	-
9	573473	47	M	1/8/2013	1/10/2013	+	-	-	+	-	-	-	-	-	-	-	-	-	+	-	+	-	+	-	11.4	8000	128	+	2TO3	PL	-	-
10	467609	53	F	1/10/2013	1/13/2013	+	-	-	+	-	-	-	+	-	-	-	-	-	+	-	+	-	+	-	10.8	15300	137	++	PL	PL	++	-
11	517939	57	M	1/10/2013	1/14/2013	+	-	-	+	+	+	-	-	-	-	-	-	+	+	-	-	-	-	-	9.1	12600	183	-	4 TO 5	PL	+	-
12	510934	48	F	1/15/2013	1/19/2013	+	+	-	+	-	-	-	-	-	-	-	-	+	+	-	-	-	-	+	11.6	12300	300	-	8TO10	PL	-	+
13	400895	60	M	1/15/2013	1/25/2013	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	13.4	17800	110	+	15TO20	4TO5	-	+
14	350599	52	M	1/19/2013	1/21/2013	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	-	+	16.5	19600	112	-	3TO5	1TO2	-	-
15	575530	55	M	1/21/2013	1/24/2013	+	+	-	+	+	-	-	-	-	-	-	-	+	-	-	+	-	-	+	16.8	19300	90	+	4TO5	6TO7	-	-
16	576050	65	F	1/23/2013	2/3/2013	+	-	-	+	+	-	-	-	-	-	+	-	+	-	-	+	-	-	+	10.5	33700	367	+	15TO20	8TO10	+	-
17	456173	53	F	1/25/2013	1/30/2013	+	+	-	+	-	-	-	-	-	-	-	-	+	-	-	+	-	-	+	9.7	5900	450	-	8TO10	5TO6	-	-
18	582347	60	F	2/27/2013	3/4/2013	+	+	-	+	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-	10.8	20300	181	-	3 TO 4	6TO7	-	+
19	583176	64	M	3/4/2013	3/14/2013	+	+	-	+	+	-	-	-	-	-	-	-	+	-	+	+	-	-	+	9	25500	243	+	PL	8TO10	++	+
20	472132	55	M	3/9/2013	3/12/2013	+	+	-	+	+	-	-	-	+	-	-	-	+	-	+	+	-	-	+	13.1	27900	150	-	6TO8	1TO2	-	+
21	356431	70	M	3/6/2013	3/25/2013	+	+	-	+	+	-	-	-	-	-	-	-	+	-	-	+	-	-	+	11.1	9800	-	+++	PL	9TO10	++	+
22	522416	56	M	3/25/2013	3/27/2013	+	+	-	+	+	-	-	-	-	-	-	-	+	-	+	+	-	-	+	12	9800	564	++	4TO5	5TO6	++	-

ANNEXURE III - MASTER CHART

Serial number	In patient number	Investigations													CKD Stage at 6 momths	Treat-ment		Compli-cations		
		Urine	Sr. creatinine (mg/dL)				eGFR				Imaging									
		Organism	At presentation	Post treatment	First follow up	Second follow up	At presentation	Post treatment	First follow up	Second follow up	Hydronephrosis with hydrouret	Pyelonephritis	Small kidney	Renal calculi		Conservative	Intervention	SIRS	Sepsis	Septic Shock
1	491109	-	6.3	2.5	1.96	6.39	7.3	21.1	27.9	7.1	+	-	-	-	5	-	-	-	-	-
2	455214	-	1.8	1.3	0.9	0.8	31.7	46.1	70.4	80.7	+	+	-	-	-	-	-	-	-	-
3	390601	E. coli	3.7	2.9	2.2	2.3	18	23.8	32.7	31.1	+	-	-	-	3	-	-	-	+	-
4	390931	E. coli	6.3	3.9	3.2	3.3	9.7	16.8	21.2	20.4	-	+	-	-	4	-	-	-	+	-
5	471012	-	3.4	3.3	3.2	3.5	20.5	21.2	22	19.8	+	+	-	-	4	-	-	-	-	-
6	334355	-	3.3	2.2	2.8	2.8	15.2	24.2	18.3	18.3	+	+	+	-	4	-	-	-	-	-
7	509191	-	8.27	4.7	4.2	4	7.3	14	15.9	16.8	-	+	-	-	4	-	-	+	-	-
`8	509374	-	3.5	4.5	5.9	5	14.7	11	8	9.7	+	+	-	-	5	-	-	-	-	-
9	573473	-	1.7	1.3	1.2	1.1	46.1	62.9	69	76.3	+	-	-	+	-	+	-	-	-	-
10	467609	-	1.6	0.5	0.5	0.5	35.8	137.2	137.2	137.2	+	-	-	-	-	+	-	-	-	-
11	517939	-	9.03	6.28	4.92	7.2	6.5	9.8	13	8.4	+	-	-	-	5	-	-	-	-	-
12	510934	E. coli	1.78	1.46	1.1	1.07	32.3	40.6	56.3	58.2	+	+	-	-	3	-	-	-	+	-
13	400895	Enterobacter C	2.2	1.3	1.5	0.7	32.6	59.8	50.7	122.3	+	+	-	-	-	+	+	-	-	-
14	350599	-	3	2.6	2.7	2.8	23.5	27.7	26.5	25.4	+	-	-	+	4	-	-	+	-	-
15	575530	-	2.28	1.61	1.5	1.56	31.9	47.6	51.6	49.4	+	+	-	-	3	-	-	+	-	-
16	576050	-	7.4	2.29	2.64	3.26	5.9	22.7	19.3	15.1	+	-	-	-	4	-	-	-	-	+
17	456173	-	1.8	1.4	1.1	1.2	31.3	41.8	55.2	49.9	-	+	-	-	3	-	-	+	-	-
18	582347	E. coli	6.19	6.1	6.4	4.7	7.3	7.5	7.1	10.1	-	+	+	-	5	-	-	-	+	-
19	583176	Candida	4.5	2.5	1.82	1.8	14.1	27.8	40.1	40.6	+	+	-	-	3	-	-	-	-	+
20	472132	E. coli	2.5	1.7	1.3	1.5	28.6	44.7	60.9	51.6	+	+	-	-	3	-	-	-	-	-
21	356431	Candida	4.1	3.2	8.4	8.9	15.4	20.5	6.7	6.3	+	+	-	-	5	-	-	-	-	+
22	522416	-	1.99	1.5	1.6	1.56	37.1	51.5	47.8	49.2	+	+	-	-	3	-	-	-	-	-

ANNEXURE III - MASTER CHART

Serial number	In patient number	Age (Years)	Sex	Date of admission	Date of discharge	Etiology			Comorbidities									Clinical features							Investigations						
																											Urine				
						Diabetes	Pyelonephritis	NSAID	Diabetes mellitus	Hypertension	Chronic kidney disease	IHD	Hypothyroidism	Epilepsy	CABG	Multiple myeloma	Post partum eclampsia	Abdominal Pain	Hematuria	Oliguria	Fever	Burning micturation	Tissue bits in urine	Nausea vomiting loss of appetite	Haemoglobin (gm%)	White blood cell count (/cumm)	RBS/FBS (mg/dL)	Protein	WBC	RBC	Glucose	Culture
23	359407	64	M	3/29/2013	4/6/2013	-	-	+	-	+	+	-	-	-	-	-	-	-	+	-	+	-	+	-	9.8	16200	122	+	PL	PL	-	+
24	411207	72	M	3/29/2013	4/2/2013	+	-	-	+	+	-	+	-	-	+	-	-	+	-	+	+	-	+	-	10.9	3700	56	+	4TO5	5TO6	-	-
25	476319	65	F	5/8/2013	5/22/2013	+	+	-	+	-	+	-	-	-	-	-	-	-	-	-	+	+	+	+	10.4	13500	86	+++	PL	8TO10	-	+
26	473446	63	M	5/17/2013	5/20/2013	+	-	-	+	+	+	-	-	-	-	-	-	+	-	+	-	-	-	-	13.1	7800	137	++	PL	6TO8	+	+
27	319109	65	M	5/25/2013	6/1/2013	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	+	-	-	+	10.5	11400	120	++	PL	8TO10	-	-
28	475874	21	M	5/29/2013	6/4/2013	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	+	-	12.9	7000	91	+	4TO5	PL	-	-
29	533571	23	F	5/31/2013	6/4/2013	-	+	-	-	-	-	-	-	-	-	-	+	+	-	+	+	-	-	+	7.7	13000	80	+	5TO6	3TO4	-	-
30	476418	62	F	6/4/2013	6/6/2013	+	-	-	+	+	+	+	-	-	-	-	-	+	-	+	+	-	-	+	9.7	12000	200	+	15TO20	8TO10	-	-
31	482917	74	M	7/13/2013	7/17/2013	-	+	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-	-	+	10	3800	830	+	PL	10TO12	-	-
32	610416	53	M	7/21/2013	25/7 13	+	-	+	+	+	-	-	-	-	-	-	-	+	+	-	-	-	-	-	14.2	14600	157	+	4TO6	PL	-	-
33	544115	48	M	7/26/2013	7/31/2013	+	-	-	+	+	+	-	-	-	-	-	-	+	-	+	-	-	+	-	15.8	8900	131	-	4 TO 5	6TO8	-	+
34	612486	55	M	8/1/2013	8/5/2013	+	+	-	+	-	+	-	-	-	-	-	-	-	-	-	+	+	-	-	8.8	17500	192	+	PL	6TO8	-	-
35	546232	40	M	8/7/2013	8/9/2013	+	+	-	+	+	+	+	-	-	-	-	-	-	-	-	+	+	+	+	11.4	9800	114	-	PL	5TO6	-	+
36	482305	49	F	9/10/2013	9/12/2013	+	-	-	+	+	+	-	-	-	-	-	-	+	-	+	+	-	-	-	9.6	14900	221	TR	PL	8TO10	-	-
37	553376	63	F	9/18/2013	9/20/2013	+	-	-	+	+	-	-	-	-	-	-	-	+	-	-	+	-	-	+	11.4	6900	97	TR	PL	8TO10	+	-
38	562272	30	F	11/5/2013	11/7/2013	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-	-	12.4	16900	266	-	10TO15	PL	+	-
39	559316	67	M	9/25/2013	10/5/2013	+	-	-	+	+	-	-	-	-	-	-	-	+	-	+	+	-	-	+	9.9	18200	160	-	PL	6TO8	-	+
40	562272	30	F	11/7/2013	11/12/2013	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	+	-	-	+	9	11500	88	-	6TO8	9TO10	-	-

ANNEXURE III - MASTER CHART

Serial number	In patient number	Investigations													CKD Stage at 6 momths	Treat-ment		Compli-cations		
		Urine	Sr. creatinine (mg/dL)				eGFR				Imaging									
		Organism	At presentation	Post treatment	First follow up	Second follow up	At presentation	Post treatment	First follow up	Second follow up	Hydronephrosis with hydroureter	Pyelonephritis	Small kidney	Renal calculi		Conservative	Intervention	SIRS	Sepsis	Septic Shock
23	359407	E. coli	5.9	4.6	2.6	2.25	10.3	13.7	26.5	31.4	+	-	-	-	3	+	-	-	-	+
24	411207	-	3.2	2.7	2.5	2.72	20.4	24.8	27.1	24.6	+	-	-	-	4	+	-	+	-	-
25	476319	E. coli	6.3	6.4	10	9.9	7.1	6.9	4.1	4.2	-	+	-	-	5	+	-	-	+	-
26	473446	Candida	4.2	4	2.9	3.84	15.3	16.2	23.5	17	+	-	-	-	4	-	-	-	-	-
27	319109	-	6.9	3.6	2.4	1.9	8.6	18.2	29	38	+	+	-	-	3	-	-	+	-	-
28	475874	-	4.7	2.7	0.9	1.1	16.8	31.9	113.2	89.8	+	-	-	-	-	+	-	+	-	-
29	533571	-	4.6	1.9	1.4	1.3	12.6	34.8	49.5	54	+	+	-	-	3	-	-	-	-	+
30	476418	-	2	1.8	2	2.2	26.8	30.3	26.8	24	+	-	-	+	4	-	-	-	-	-
31	482917	-	11	1.4	1.3	1.2	4.9	52.7	57.4	62.9	+	+	-	-	-	-	-	-	-	-
32	610416	-	3.59	1.55	1.34	1.29	19	50.1	59.3	61.9	+	-	-	-	-	-	-	-	-	-
33	544115	Candida	7.3	8.9	8.2	8.24	8.5	6.8	7.5	7.4	+	-	-	+	5	-	-	-	-	-
34	612486	-	5.01	4.65	2.54	2.56	12.8	14	28.1	27.9	+	+	-	-	4	-	-	-	-	-
35	546232	Kleb. Pneu	2.57	2.54	7.1	5.5	29.6	30	9.2	12.3	+	-	+	+	5	-	-	-	-	-
36	482305	-	2.7	2.8	1.8	2	19.9	19.1	31.8	28.1	+	-	-	-	4	+	-	-	-	-
37	553376	-	1.7	0.74	0.8	0.82	32.3	84.2	77	74.8	+	-	-	-	-	-	-	-	-	-
38	562272	-	2.7	2.06	1.86	1.8	22	30.1	33.8	35.1	+	+	-	-	3	+	-	-	-	+
39	559316	Citrobacter	6	5.4	6.1	6	10	11.3	9.8	10	+	-	-	-	5	-	-	-	+	-
40	562272	-	1.8	1.3	1.08	1.2	35.1	51.1	63.3	56.1	+	+	-	-	3	-	-	+	-	-