Evaluation of Pre-Tertiary Hospital Care of Patients with Chronic Kidney Disease Stage 5

A dissertation submitted to the Tamil Nadu Dr. M.G.R.Medical University in partial fulfillment of the University regulations for the award of

D.M. Degree (Nephrology)

DEPARTMENT OF NEPHROLOGY

CHRISTIAN MEDICAL COLLEGE, VELLORE

Certificate

This is to certify that "Evaluation of Pre-Tertiary Hospital Care of Patients with Chronic Kidney Disease Stage 5" which is submitted as thesis requirement of the DM Branch III examination of the Dr. MGR Medical University is the bonafide work of the candidate:

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Acknowledgement

Doing this study has been an interesting experience. I am indebted to a lot of people who made this study possible by rendering their timely and expert guidance.

I would like to thank the Lord Jesus Christ who provided the right circumstances and enabled me by His wisdom and grace to complete this work.

I extend my sincere gratitude to my guide, Dr. George T. John, who helped with the idea of the study, advice, valuable suggestions, direction and much needed encouragement. It was indeed a great privilege to have him as my guide.

I thank my teacher and former Head of our Department Dr. Chakko Korula Jacob for all the guidance and mentorship received.

I also thank Dr. Tamilarasi for all her encouragement.

I thank Nithya Neelakantan, my able Biostatistician guide who painstakingly guided the statistical analysis.

Thanks are also due to my colleagues of the Department of Nephrology for their help in sending the patients to me for interviewing.

Finally, I thank my family and my friends for all the support and encouragement they provided.

Contents

Chronic Kidney Disease as a Public Health Problem

Chronic kidney disease (CKD) is a worldwide public health problem with a rising incidence and prevalence of kidney failure, with poor outcomes and high cost[1]. There is an even higher prevalence of earlier stages of CKD, which often goes unnoticed.

Even in affluent western countries, despite the magnitude of the resources committed to the treatment of Chronic Kidney Disease stage 5 (CKD 5) and the substantial improvements in the quality of dialysis therapy; these patients continue to experience significant mortality and morbidity, and a reduced quality of life. Survival probabilities for dialysis patients at 1, 2, 5 and 10 years are approximately 80, 67, 40, and 18 percent, respectively[2].

Moreover, 50 percent of dialysis patients have three or more comorbid conditions, the mean number of hospital days per year is approximately 14 per patient, and self-reported quality of life is far lower in dialysis patients than in the general population.[3, 4]

In the past two decades, there has been increasing evidence that the adverse outcomes of CKD, such as kidney failure, cardiovascular disease, and premature death, can be prevented or delayed. Earlier stages of CKD can be detected only through periodic health check-ups and laboratory testing. Treatment of earlier stages of CKD is effective in slowing the progression toward stage 5. Initiation of treatment for cardiovascular risk factors at earlier stages of CKD should be effective in reducing cardiovascular disease events both before and after the onset of kidney failure[1]. Unfortunately, CKD is “under-diagnosed” and “under-treated” resulting in lost opportunities for prevention.

There is therefore a need for uniform application of the current recommendations designed to retard the progression of CKD; to optimize the medical management of

comorbid medical conditions, such as cardiovascular disease, diabetes mellitus and lipid disorders; and to decrease the complications secondary to progression of CKD, including hypertension, anemia, secondary hyperparathyroidism, and malnutrition[1].

Once the disease has progressed to CKD 5, patients have decreased quality of life, high morbidity, and an annual mortality of about 22%.

The high morbidity and mortality seen in dialysis patients may decrease significantly if patients were healthier at the time of initiating renal replacement therapy (RRT).

Data from India is lacking on how patients with CKD 5 are treated in the community. Data obtained about the pre-tertiary hospital care of patients with CKD 5 would form the background to see the pitfalls in treatment and would allow us to address the problem better and provide better treatment to the patients who come to us for help.

Consensus Definition

In 2000, the National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) Work Group set about to develop clinical practice guidelines to define chronic kidney disease (CKD) and to classify stages in its progression. The work group consisted of experts in nephrology, pediatric nephrology, epidemiology, laboratory medicine, nutrition, social work, gerontology and family medicine. An Evidence Review Team, consisting of nephrologists and methodologists, was responsible for assembling the evidence.

Defining CKD and classifying the stages of severity would provide a common language for communication among providers, patients and their families, investigators, and policy-makers and a framework for developing a public health approach to affect care and improve outcomes of CKD. This would also permit more reliable estimates of the prevalence of earlier stages of disease and of the population at increased risk for development of CKD. From this would come recommendations for laboratory testing to detect earlier stages and progression. It was also possible to find associations of stages with clinical manifestations of disease.

The staging of CKD is useful because it endorses a model in which primary physicians and specialists share responsibility for the care of patients with CKD. This classification also offers a common language for patients and the practitioners involved in the treatment of the disease.

Based on these stages of CKD, one could now evaluate treatments to slow progression or prevent other adverse outcomes.

The Work Group defined CKD to include conditions that affect the kidney, with

the potential to cause either progressive loss of kidney function or complications resulting from decreased kidney function.

CKD was thus defined as the ***presence of kidney damage*** or ***decreased level of kidney function for three months or more, irrespective of diagnosis***. (Table 1)

Table 1 - Definition of Chronic Kidney Disease[1]

Calculation of Glomerular Filtration Rate (GFR)

An essential requirement for the classification and monitoring of CKD is the measurement or estimation of glomerular filtration rate (GFR). Serum creatinine is not an ideal marker of GFR, because it is both filtered at the glomerulus and secreted by the proximal tubule. Creatinine clearance (CrCl) is known to overestimate GFR by as much as 40% in normal individuals and by even more in patients with CKD[2].

Estimates of GFR based on 24-hour CrCl require timed urine collections, which are difficult to obtain and often involve errors in collection. Classic methods for measurements of GFR, including the gold-standard inulin clearance, are cumbersome, require an intravenous infusion and timed urine collections, and are not clinically feasible. In adults, the normal GFR based on inulin clearance and adjusted to a standard body surface area of 1.73 m^2 is 127 ml per minute per 1.73 m^2 for men and 118 ml per minute per 1.73 m^2 for women, with a standard deviation of approximately 20 ml per minute per 1.73 m^2. After age 30, the average decrease in GFR is 1 ml per minute per 1.73 m^2 per year[1].

Equations based on serum creatinine but factored for gender, age, and ethnicity are the best alternative for estimation of GFR. The most commonly used formula is the

Cockcroft-Gault equation[3]. This equation was developed to predict CrCl, but has been used to estimate GFR.

CrCl = [(140-age) x Weight (Kg)]/[S. Cr x 72] [x 0.85 in women]

The Cockcroft–Gault formula is reasonably accurate in mild renal impairment with a GFR of around 50 ml/min but can overestimate GFR by up to 100 per cent when GFR is less than 10 ml/min.

The Modification of Diet in Renal Disease (MDRD) Study equation was derived on the basis of data from more than 500 patients [using the clearance of Iothalamate] with a wide variety of kidney diseases and GFRs up to 90 ml per minute per 1.73 m^2. The abbreviated MDRD equation[4,5] is recommended for routine use and requires only serum creatinine, age, gender and race.

$GFR = 186.3 \times (S.\ Cr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black})$

This formula is more accurate especially at low clearance and in preferred to the Cockcroft-Gault method. A caveat is that this method has only been validated in Black and White Americans and not in other racial groups.

Why "Kidney"?

The word "kidney" is of Middle English origin and is immediately understood by patients, their families, providers, health care professionals, and the lay public of native English speakers. On the other hand, "renal" and "nephrology," derived from Latin and Greek roots, respectively, commonly require interpretation and explanation.

Classification of CKD

Table 2 shows the classification of stages of CKD, including the population at increased risk of developing CKD, and suggested actions to prevent the development of

CKD and to improve outcomes in each stage.

Table 2 - Classification of Chronic Kidney Disease

The shaded area identifies patients who have CKD. The unshaded area designates individuals who are at increased risk for developing CKD.

Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

* Includes actions from preceding stages.

Adverse outcomes of CKD are based on the level of kidney function and risk of loss of function in the future. It has almost been a uniform observation that CKD tends to worsen over time. Therefore, the risk of adverse outcomes increases over time with disease severity. Many disciplines in medicine, including related specialties of hypertension, cardiovascular disease, diabetes, and transplantation, have adopted classification systems based on severity to guide clinical interventions, research, and professional and public education. Such a model is essential for any public health approach to disease.

The extent of the problem and Epidemiology of CKD

Chronic kidney disease is a worldwide public health problem with rising incidence and prevalence of kidney failure, with poor outcomes and high cost. Data from the United States suggests that the incidence and prevalence of CKD 5 have doubled in the past 10 years and are expected to continue to rise steadily in the future.

The third National Health and Nutrition Examination Survey (NHANES III: 1988–1994) estimated that 3% of the population of the United States of America (USA) (5.6 million individuals) had an elevated serum creatinine (1.4–1.6 mg/dl)[6]. About 12%

of the population has a GFR of less than 60 ml/min.

Figure 1 (given below) shows the incidence and prevalence of CKD 5 in the United States based on the USRDS 2000 Annual Data Report[7]. Incident patients refers to new cases during the year. Point prevalent patients refers to patients alive on December 31st of the year. Projections for future years are based on extrapolation of regression equations.

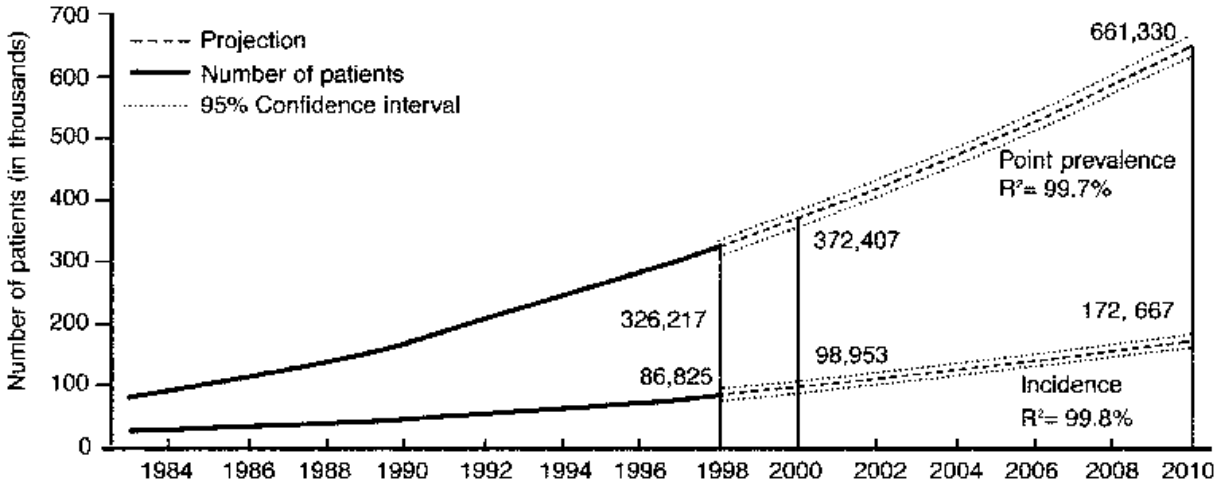

Figure 1 - Incidence and prevalence of CKD 5 in United States
Data from the USRDS 2000 Annual Data Report

In the United Kingdom (UK), the prevalence of renal impairment (serum creatinine of >1.36mg/dl) was 6.1% in known hypertensives, 12.6% in known diabetics and 16.9% in patients with both these conditions in the age group 50–75 years[8]. It is estimated that the dialysis population will double in the next 15 years consisting predominantly of elderly patients with diabetes mellitus and hypertension. All these

patients were detected by routine screening in a primary health care setting.

In developed countries like USA and UK, most patients are sent in a stable state to the renal outpatient clinic. At the first visit a thorough medical history and physical examination are obtained and the patient's previous case records are carefully scrutinized. Additional investigations are carried out to fill in the gaps. Thus, a diagnosis can be established and decisions about management may be made. Some patients present as an 'acute uraemic emergency' with a short history and no diagnosis; they are first resuscitated and then investigated to detect or exclude an acute renal condition which will require specific treatment. Thereafter, establishing a diagnosis can proceed at leisure in those countries.

Epidemiology of Chronic Kidney Disease in India

Similar date regarding epidemiology of CKD is unavailable in our country. There are only two population based studies from India to date. The first study was from Apollo Hospital, Chennai by Dr. M. K. Mani.[9] Prevalence of CKD in the surveyed community was 0.16% and other renal diseases (short of CRF) in 0.7% of patients. However, all the patients were not evaluated with blood tests for urea and creatinine, and only those who had some abnormality in the urine test or blood pressure and/or a positive response to a questionnaire were subjected to a blood test for urea and creatinine.

The second study was from All India Institute of Medical Sciences by Dr. Sanjay Agarwal[10]. This was a community based study done in urban Delhi where 4972 subjects were screened with blood urea and serum creatinine estimation with a specific aim to find out the prevalence of CKD. The prevalence of CKD, defined as serum creatinine > 1.8mg % persisting for more than 3 months in the absence of any reversible factor, was found to

be 0.79% or 7852 per million population. Extrapolating the estimate of the number of CKD 5 to be 10% of this number, the prevalence is about 785 per million population in India.

Clinical Features and Investigations in Chronic Kidney Disease

When the patient presents with CKD and is referred early in the course of the disease, the need for a diagnosis is self-evident. The difficulty of obtaining a precise diagnosis increases as the patient approaches CKD 5 and the rewards diminish. Consequently, a substantial proportion of patients starting dialysis have no more precise a diagnosis than 'CKD – native kidney disease - unknown'.

Although it is virtually impossible to establish a firm diagnosis in some patients presenting in CKD 5 with small fibrotic kidneys, it is prudent to pursue a vigorous diagnostic approach in all others, since a precise diagnosis is invaluable in identifying the groups of diseases causing CKD which affect patient management.

Etiology of Chronic Kidney Disease

Renal insufficiency can ensue from a primary renal disease or a systemic disease which affects the kidneys.

Renal causes

Glomerulonephritides

These manifest as haematuria, signs of a nephrotic syndrome (tiredness, weight gain, oedema, susceptibility to infection, hyperlipidaemia), and/or hypertension. With more frequent, regular health screening, one of the most common presentations of chronic glomerulonephritis (e.g. IgA nephropathy) is the detection of dipstix proteinuria (and/or haematuria), hypertension and/or elevated serum creatinine in an asymptomatic

patient.

Reflux nephropathy

Usually diagnosed in childhood during investigation of urinary infection or screening in families, it may, however, escape discovery until adult life when it is detected during investigation of urinary infection, especially in pregnancy, hypertension, or renal failure. Though often silent, there may be a history of recurrent episodes of flank pain, dysuria, fever, and rigors. CKD in adult life peaks in the twenties and thirties and is uncommon after the age of 50.

Secondary chronic pyelonephritis

This is the etiology in patients with CKD and a history of stone disease, obstruction, or neuropathic bladder.

Medication related

Both over the counter as well as prescribed and recreational drugs are implicated in this category. Chinese herb nephropathy (caused by Aristolochia fangchi) is an example where fibrosis and tubulointerstitial changes persist for months or years after discontinuation of the toxin though slow recovery may occur on stopping. Prolonged consumption of non-steroidal anti-inflammatory drugs (NSAIDs) and selective COX-2 agents has also been implicated in the etiology of CKD (analgesic nephropathy). These drugs also cause a reduction in GFR in patients with glomerulonephritis, due to inhibition of vasodilatory prostaglandins, acute interstitial nephritis, nephrotic syndrome or papillary necrosis. Angiotensin-converting enzyme (ACE) inhibitors and/or Angiotensin II Receptor Blockers may cause renal insufficiency in patients with bilateral renal artery stenosis or renal artery stenosis in a single kidney due to renal hypoperfusion.

Hereditary nephritis

Autosomal Dominant Polycystic Kidney Disease (APKD) is the most frequent cause of CKD in hereditary nephritis. Renal failure usually occurs in the third to fifth decade; family history is positive in ~ 75% cases. Similarly, a positive family history is usual in the rarer types of renal cystic disease such as tuberous sclerosis and medullary cystic disease. Alport's syndrome is another important hereditary nephritis characterized by progressive nephritis with haematuria and sensori-neural hearing loss.

Infections

Renal tuberculosis is a rare cause of CKD. Classically, the presentation is of dysuria, fever and sterile pyuria and is confirmed by urine culture and renal imaging (calcified renal substance). Interstitial renal tuberculosis causing renal failure with small kidneys on imaging and without the tell-tale renal calcification is diagnosed by renal biopsy or inferred from evidence of tuberculosis in other systems. Another infection associated with CKD 5 that shows a geographic variation is schistosomiasis which is an important cause in Egypt.

Substance abuse

Heroin-associated nephropathy (was an important cause of CKD 5 in New York)

Systemic diseases

Diabetes mellitus

Diabetes mellitus is the most frequent cause of renal involvement in a systemic disease. Renal involvement occurs as frequently in type II as in type I diabetes. The increasing prevalence of CKD in the developed world in particular is predominantly

accounted for by type II diabetic nephropathy[11]. Hence, the need for good control of blood sugars to prevent microalbuminuria and therafter ACE inhibitors and/or ARBs to retard progression.

Hypertension

Long-standing 'benign' hypertension is also an important cause of CKD, particularly in the elderly age group, but is difficult to differentiate from occult renal diseases with secondary hypertension except by renal biopsy.

Systemic Lupus Erythematosus (SLE)

A diagnosis of SLE may be initially suspected clinically and then a renal biopsy is done to assess the severity of renal illness or else it is diagnosed when a renal biopsy is performed in any patient with proteinuria or abnormal urinary sediment. Therefore most patients should have one at the time of their initial assessment for renal insufficiency.

Amyloidosis

Secondary amyloidosis is suspected when CKD complicates long-standing inflammatory diseases (like severe rheumatoid arthritis) or chronic infections (such as destructive lung tuberculosis). It presents as a nephrotic syndrome. Primary amyloidosis occurs due to the proliferation of a single clone of plasma cells in middle and old age presenting with renal insufficiency and proteinuria. In patients with plasma cell dyscrasias, renal failure may also result from myeloma cast nephropathy, light chain deposition disease or hyperviscosity syndrome.

Systemic vasculitis and Anti-glomerular basement membrane disease

Systemic vasculitis and Anti-glomerular basement membrane disease usually present as rapidly progressive renal failure. A history of haemoptysis and dyspnoea, together with rapidly deteriorating renal function and an active urine sediment, suggest antiglomerular basement membrane disease (Goodpasture's syndrome) but can also occur in systemic vasculitis. Other significant symptoms are of persistent sinusitis with dyspnoea, cough, and haemoptysis (Wegener's disease) or only systemic symptoms (microscopic polyangitis).

Thrombotic microangiopathy

This may occur due to haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura or anti phospholipids antibody syndrome.

Occupational renal diseases

Occupational renal diseases causing CKD is an extremely rare entity with the exception of lead toxicity. Theses patients have hyperuricaemia, hypertension and small kidneys. The diagnosis is best made by demonstrating an increase in urinary lead excretion following an infusion of EDTA. More recently, long-term occupational or environmental exposure to relatively low levels of cadmium has been shown to cause CKD[12].

Postrenal causes

Prostatic hypertrophy

This presents with obstruction of the lower urinary tract is common in elderly males and is usually symptomatic. However, 40 per cent of men over the age of 65 have some of the symptoms of hesitancy, slow and forked stream, urgency with or without urge incontinence, frequency, intermittency, nocturia, and terminal dribbling[13]. Pressure-

flow measurements have shown that two-thirds of these patients have some degree of outflow obstruction and are at risk of urinary retention[14]. A useful clinical clue to serious outflow obstruction is palpation of a distended bladder after micturition (confirmed more reliably by ultrasonography before and after micturition).

Other causes of obstruction are retroperitoneal fibrosis, sloughed papillae and renal calculi inducing hydronephrosis and a deterioration of renal function.

Clinical examination

At the patient's first visit, although a full standard physical examination, as taught during undergraduate medical studies is recommended, it is seldom practiced in busy outpatient clinics. The common clinical findings in practice are of anemia and fluid overload. Other occasionally found features are those of overt uremia such as asterixes or pericardial rub. Abdominal examination alerts the clinician to the presence of palpable kidneys (in ADPKD or hydronephrosis) or palpable bladder in bladder oulet obstruction.

Rarer findings are of clues such as the body habitus of Lawrence Moon Biedl syndrome (a rare cause of CKD), a saddle nose (in Wegener's disease), deafness (in Alport's disease) and skin manifestations of Systemic Lupus Erythematosus. Per rectal examination may reveal an enlarged prostate or a pelvic mass causing urinary obstruction. The neurological examination may detect the neuropathies associated with diabetes, vasculitis and and primary amyloidosis. Fundus examination (through a dilated pupil) shows presence of retinal haemorrhages and exudates. There may also be corneal calcification, pingueculae or rarely the 'uraemic red eye' of acute hypercalcaemia usually precipitated by overdose of vitamin D analogues.

Laboratory investigations

After history and clinical examination, the relevant investigations (urine, blood, radiology and histology) are to be done to confirm the diagnosis.

Urine

Urinalysis and microscopy

Dipstick examination of a fresh mid-stream urine sample is useful to assess the urinary pH and screen for leucocyturia, proteinuria, haematuria, and glucosuria. The pH is usually low in CKD, unless the patient is on a very low protein diet. If the urine contains non-albumin proteinuria, then the dipstick test will be negative with the 24-hour quantification showing significant proteinuria.

Microscopy of the urine sediment may reveal erythrocytes (dysmorphic if glomerular in origin), leucocytes and casts. Erythrocyte casts are seen in glomerulonephritis (IgA, postinfectious, and SLE) and in cases of vasculitis. Leukocyte casts identify pyuria as coming from the kidney and are found in stone disease, tuberculosis, analgesic nephropathy and other causes of chronic interstitial nephritis.

Quantitation of proteinuria (24-hours)

Quantitation of proteinuria (24-hours) is used to measure proteinuria. Proteinuria is almost universal in CKD with the proteinuria in the nephrotic range in conditions like diabetic nephropathy. The accuracy of the collection is checked by quantitating total urinary creatinine, which is fairly constant (range 10–14 mmol/day in females and 12–18 mmol/day in males). The degree of proteinuria can be also be “measured” by the spot urine protein/creatinine ratio and a good correlation has been shown between the two

measures,[15] although the accuracy decreases at extremes of creatinine excretion (e.g. muscular men who have high and cachextic patients who and low urinary creatinine concentrations, respectively).

Blood

Hematology

A full hemogram is important to establish the type of anaemia in a patient with CKD. A Coomb's test is done if clinically indicated to exclude autoantibody-induced haemolysis (as can occur in SLE). A peripheral blood smear may show microangiopathic haemolytic anaemia (fragmented and helmet-shaped erythrocytes and burr cells). If this occurs in combination with thrombocytopenia, it is suggestive of the haemolytic uraemic syndrome or thrombotic thrombocytopenic purpura.

Biochemistry

Serum creatinine concentration provides only a rough approximation of GFR as the amount excreted increases with a decline in GFR[16].

The electrolyte profile shows the presence of hyperkalemia and severe metabolic acidosis. Blood sugar estimation and liver function tests provide information about underlying diseases such as diabetes mellitus and liver failure.

Serology

Serological tests can give additional support in the assessment of a diagnosis and underlying disease activity. Serum total haemolytic complement and C3 can be decreased in mesangiocapillary glomerulonephritis, postinfectious glomerulonephritis (including

endocarditis), cryoglobulinaemia and lupus nephritis. Elevated titres of serum anti-nuclear antibody and anti-double-stranded DNA support the diagnosis of lupus. In a patient with rapidly progressive renal failure with an active urine sediment, antiglomerular basement membrane antibodies confirm a diagnosis of Goodpasture's disease while Anti-Neutrophil Cytoplasmic Antibodies support a diagnosis of systemic vasculitis (Anti-proteinase 3 - specific for Wegener's granulomatosis or Anti-myeloperoxidase - associated with microscopic polyangitis).

Virology

Patients with CKD are commonly tested for antibodies against Human Imunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) and Hepatitis B surface antigen (HBsAg). HBsAg is associated with membranous glomerulopathy, IgA nephropathy and mixed cryoglobulinaemia. HCV infection is associated with type 1 membranoproliferative glomerulonephritis and cryoglobulinaemia. About 95 per cent of patients with mixed essential cryoglobulinaemia have evidence of HCV infection (by testing for anti-HCV antibodies and HCV RNA).

Knowing the virology status is also important in vaccinating against Hepatitis B virus to protect against infection from dialysis and blood transfusions.

Radiological investigations

Renal ultrasonography is invaluable in assessment of a patient of CKD. The renal size, renal cortical thickness and echogenicity can be determined. The presence of cysts and hydronephrosis can be demonstrated. If calculi are suspected, plain x-ray of the

urinary tract can be done followed by intravenous urography (if renal function is normal) or non-contrast spiral computerized tomography (CT). CT with intravenous contrast and arteriography (or magnetic resonance imaging with angiography) is required for diagnosis of classical polyarteritis nodosa and renovascular disease. However, angiogaphy remains the 'gold standard' for diagnosing renovascular disease.

Role of biopsy

In places where routine health checks are commonplace or if the patient has presents early in the course of the illness, a renal biopsy is mandatory (in most) to establish a diagnosis, to assess the extent of damage and to plan therapy. In others, it may have been deemed unnecessary because the diagnosis was established on clinical grounds, for example, in diabetes. If the kidneys are small, the hazards of the procedure are increased and have to be weighed against the small chance of finding a reversible cause.

Establishing chronicity in CKD

In a patient with no prior medical illness presenting with renal impairment, it is necessary to establish chronicity based on clinical and laboratory evidence.

The factors that suggest chronicity are:

- Duration of symptoms for several months
- Nocturia
- Absence of severe symptoms despite very high urea and creatinine
- Anaemia of chronic disease

- Bone disease
- Sexual dysfunction
- Skin disorders, nail changes and pruritus
- Neurological complications
- Small kidneys on renal imaging

Treatment of CKD

Attenuation of progression

Once a diagnosis of CKD is made, there are certain medical measures that can be undertaken to attenuate the progression.

Blood pressure control

The importance of the control of blood pressure in patients with renal disease cannot be overemphasised. Hypertension is common in patients with CKD and the rate of decline in renal function increases with increasing blood pressure[17,18] and also reduction in blood pressure attenuates the deterioration of renal function (first convincing demonstration was in diabetic nephropathy).[19,20]

Two important factors contribute to the rise in blood pressure of patients with CKD. First, most renal diseases are associated with sodium retention, which results in an increase in extracellular fluid volume and an increase in peripheral vascular resistance. Second, activation of the renin–angiotensin–aldosterone system results in increased circulating angiotensin II, which in addition to being a potent vasoconstrictor, also enhances sodium retention by the kidney. Hence, the two initial steps in the treatment of hypertension in CKD should consist of a reduction in sodium intake, with or without the

use of diuretics, and treatment with agents that block the effects of angiotensin II, that is, ACE inhibitors or ARBs. Other antihypertensives that are commonly prescribed are calcium channel blockers, beta adrenergic antagonists, α-adrenoceptor blockers and diuretics.

The target blood pressure in patients with CKD is 120/70 mmHg especially with proteinuria of over 1 g/day[21,22]. Regular follow-up is essential as it has been demonstrated that patient compliance, efficacy of antihypertensive treatment, and retardation of renal failure are clearly related to the number of outpatient visits[23].

Dietary recommendations

Sodium restriction

In patients with CKD, the ability to excrete sodium usually is limited. Thus, a sodium-restricted diet of 6 g/day is a useful initial step in the treatment of hypertension. Determining a 24 h urinary sodium excretion can check compliance with the sodium restricted diet.

Sodium depletion may occur in patients with CKD due to tubulointerstitial disease such as pyelonephritis, interstitial nephritis or hydronephrosis. In these, sodium has to be monitored closely and often restriction is not advisable.

Protein restriction

The initial observations in the rat model with reduced renal mass had shown that protein restriction attenuated the development and progression of renal failure. Thereafter, some retrospective studies and several (but not all) randomized prospective studies confirmed that a low protein diet might have the same effect in humans. In the initial analysis of the Modification of Diet in Renal Disease (MDRD) Study,[4] (which was

the largest trial to date on the effect of protein restriction on CKD in man) the effects of dietary protein restriction and blood-pressure control on the progression of CKD, the investigators reported a small beneficial effect of the low-protein diets on the course of renal function after an average follow-up period of 2.2 years. When the initial 4 months of low-protein diet were excluded from the analysis, the decline in GFR of protein-restricted patients was attenuated[24]. This secondary analysis of the MDRD trial patients also revealed a high protein intake was associated with a more rapid decline in GFR. It was calculated that each 0.2 g/kg body weight reduction in protein intake resulted in a 29 per cent reduction in the rate of decline in GFR.

The effect of protein restriction on the progression of CKD has been analysed in two meta-analyses.[25, 26]

Altogether, it can be concluded from these studies that protein restriction causes a modest reduction in the progression of CKD in man. It was concluded that dietary protein restriction significantly reduced the risk for renal insufficiency or death with a relative risk of 0.67 (95% confidence interval 0.50–0.89) in patients with non-diabetic renal failure and 0.56 (95% confidence interval 0.40–0.77) in patients with diabetic nephropathy. Currently, mild protein restriction to 0.6 to 0.8 grams per kg is recommended. Calorie intake is kept at 30 kcal/kg body weight/day or more.

Dietary protein restriction also helps to alleviate the symptoms of uraemia in those not being considered for dialysis in addition to attempting to slow the progression of renal insufficiency without negatively jeopardizing nitrogen balance. Dietary compliance is monitored most readily by measuring the serum urea : creatinine ratio (which should be reduced by treatment) and the 24-h urinary urea excretion. For

example, a 40 g protein diet should produce about 150 mmol of urea.

Fluid balance

In CKD, the regulatory capacity of the kidney is progressively reduced. Both excretion and conservation of electrolytes and water are impaired; when sudden loads of potassium, acid, or fluid has to be handled the limitations of renal functional reserve become apparent and signs of decompensation may occur. Consequently, water and electrolyte intakes must be adapted to renal excretory capacity.

In the subset of patients who are fluid overloaded, both sodium and water have to be restricted. On the other hand, in patients with conditions that predominantly affect the renal medulla (for example, interstitial nephritis and pyelonephritis), defective urinary concentrating ability is particularly common and dehydration occurs easily in patients with inadequate fluid intake, due to persistent diuresis despite fluid deprivation. Several mechanisms are responsible for the inability to excrete concentrated urine, including the increased solute load in remnant nephrons resulting in an osmotic diuresis, alteration of medullary interstitial solute concentrations as a result of the damaged countercurrent exchange system and impaired medullary blood flow. In addition, impaired sensitivity to antidiuretic hormone causes decreased outward water transport in the distal nephron segments. As a result of decreased concentrating capacity, urine osmolality is roughly that of plasma, approximately 300 mOsm/kg H2O, in patients with CKD. If the obligatory osmolar production in an adult is around 600 mOsm/kg H_2O, daily urine output will be roughly 2 l per day. Fluid intake should therefore be approximately 2–3 l/day in order to ensure adequate urine flow rates and to prevent dehydration. In some patients who are 'salt losers', fluid requirements may be even greater.

Potassium

Patients with CKD are usually able to maintain serum potassium within normal limits until oliguria occurs or GFR is less than 5 ml/min. Preservation of normokalaemia results from an adaptive increase in potassium excretion by remnant nephrons and increased bowel loss. However, hyperkalaemia may be an early feature of renal failure in patients with hyperchloraemic metabolic acidosis and hyporeninaemic hypoaldosteronism, which occur particularly in patients with chronic tubulointerstitial nephritis and diabetic nephropathy. Hyperkalaemia also complicates an acute potassium load (e.g. blood transfusion, or medication, which interferes with potassium secretion, for example, potassium sparing diuretics, ACE inhibitors, β-blockers, and NSAIDs) Foods containing high levels of potassium like nuts, chocolate, fruits, wine and fruit juice and salt substitutes (containing potassium) are particularly dangerous. Therefore a judicious restriction of potassium rich diet and monitoring of serum potassium while on ACE inhibitors and ARBs is warranted.

Other medications

Phosphate binders and calcitriol

Skeletal abnormalities occur early in renal failure, well before symptoms develop.[27] A variety of biochemical and radiological investigations are available to assist in the diagnosis and monitoring of renal osteodystrophy of which serum parathyroid hormone (PTH) remains the single most useful biochemical test in predicting bone histology in an individual patient.[28]

In early CKD, it would appear that adynamic bone disease is the principal type of bone lesion with high turnover bone disease developing with more advanced renal

failure. As renal insufficiency progresses, higher levels of PTH are necessary for normal bone remodeling. The cause of this 'skeletal resistance' to PTH in uraemia is probably multifactorial. Inhibition of osteoclastic bone resorption appears to be the central mechanism. Therefore a plasma PTH of two to three times the normal value is usually required to maintain normal bone turnover.

When the patient is seen in the early phases of CKD, the objective is to maintain normal bone turnover by maintaining serum calcium, phosphate, PTH and calcitriol and blood pH in the normal range.

The mainstay in preventing secondary hyperparathyroidism is strict phosphorus control. Some dietary phosphate restriction is usually required once GFR is less than 50 ml/min. Care must be taken in maintaining a sufficient protein intake, however, and adequate nutrition must be maintained. Dietary restriction alone is usually inadequate in controlling serum phosphate once GFR is less than 25 ml/min. Phosphate binders are then added to reduce phosphorus absorption from the intestine. Calcium carbonate (500-2000mg thrice daily) is effective and probably the most widely used phosphate binder. It must be taken with food to give optimal phosphorus binding and to reduce the risk of hypercalcaemia. If hyperphosphataemia persists despite administration of calcium carbonate, excess dietary intake (e.g. dairy products) should be excluded and alternative phosphorus binding agents substituted. Another commonly used calcium containing binders is calcium acetate. It is a more effective binder than calcium carbonate and is less likely to be associated with hypercalcaemia. The downside of using calcium containing phosphate binders is the risk of a positive calcium balance which in dialysis patients is associated with vascular calcification and a raised calcium x phosphate product is

associated with a higher relative risk of death. In the face of hypercalcemia, other phosphate binders like sevelemar hydrochloride and lanthanum carbonate may need to replace calcium based products. Others still being evaluated include polynuclear iron preparations.

In some patients, aluminium-containing phosphate binders have to be resorted to. If needed, they should be used only for a limited period of time since aluminium is absorbed to a variable extent and can lead to aluminium overload, manifesting as anaemia and aluminium-mediated bone disease.

In patients with lower stages of CKD, administration of 1,25-$(OH)_2$ D3 (calcitriol) 0.25 μg/day causes a rise in serum calcium, a fall in serum phosphorus and alkaline phosphatase, and retards the development of histological bone abnormalities.[29]

Careful monitoring of serum calcium is required, since hypercalcaemia may accelerate the decline in renal function. Though new vitamin D metabolites are available such as 22-oxacalcitriol, paracalcitriol (19 nor-1,25 dihydroxy-vitamin D2), and doxercalciferol (1-hydroxy-vitamin D2), their benefits over conventional calcitriol and alfacalcidol remain to be established[30]. Bone biopsy is generally reserved for patients with unusual biochemical and radiological evidence of bone disease.

Treatment of anemia

Anaemia is a predictable consequence of CKD and is directly related to its severity. It frequently occurs early with one study reporting a prevalence of 45% in patients with a serum creatinine ≤ 2 mg/dl[31] Monitoring anaemia is important to determine if it becomes disproportionate to the stage of CKD. A haemoglobin of less than 6 g/dl is rarely due to CKD alone. Red cell indices should be scrutinized to detect the

onset of iron, folate or vitamin B12 deficiency. Functional iron deficiency is common and should be confirmed by measurement of percentage of hypochromic red cells, serum iron, transferrin and ferritin. As oral iron is often poorly tolerated, intravenous iron is now frequently administered to predialysis patients. Occult gastrointestinal bleeding is common in patients with advanced stages of CKD and is most commonly due to superficial upper gastrointestinal lesions[32].

Recombinant human erythropoietin (rhEPO) is effective in treating anaemia in adults and children with CKD both prior to and while on dialysis. Benefits of correcting anaemia include increased quality of life, reduced morbidity and improved survival. This may be related to reduction in left ventricular mass and normalization of cardiac output with partial correction of anaemia. There is also evidence to suggest that rhEPO therapy may retard the progression of CKD and delay the onset of dialysis by as much as 6 months[33, 34].

Treatment of hyperlipidemia

Hyperlipidaemia is often present in patients with CKD[35]. Nonetheless, there are only a limited number of studies, usually with a small number of patients, in which the effects of treatment of hyperlipidaemia has been investigated. A meta-analysis by Freid et al showed clearly that treatment of hyperlipidaemia ameliorates the progression of CKD[36, 37].

Other recommendations

Obesity is clearly associated with hypertension, and reduction of body weight should be recommended to obese patients. Increasing physical exercise and reducing calorie intake may achieve this. In patients with advanced CKD, caution must be

exercised in severe calorie restriction because of the risk of catabolism.

Alcohol abuse can also contribute to hypertension and may also interfere with adherence to antihypertensive or other therapy. It is advisable to limit alcohol intake to less than 21 units in men and 14 units in women.

In patients with CKD, it has been shown that cigarette smoking enhances the rate of progression of disease.[38, 39] Thus, patients with CKD should be strongly advised to quit smoking.

Follow-up assessment and treatment

The aims of follow-up are the following:

1. Monitor the progression to CKD 5 and slow or arrest it where possible;
2. Detect and treat the complications of CKD and the primary disease;
3. Detect those symptoms of uraemia that call for dialysis and transplantation;
4. Plan and implement an orderly preparation for RRT.
5. Timely vascular access or CAPD catheter placement to allow a smooth transition to dialysis

The ability to predict confidently the rate of progression of CKD is invaluable in making these plans. This is largely, though not exclusively, dependent on early referral to a nephrologist[40]. The factors most likely to speed progression that can be modified include control of blood pressure, diet, avoidance of unnecessary drugs, and, in some instances, control of the underlying disease. Partial correction of anaemia with rhEPO may also slow progression. Care can be shared with the general practitioner in monitoring some of these parameters such as blood pressure.

Monitoring decline in GFR

Serum creatinine concentration

Serum creatinine is the most widely used serial measurement of GFR but has important limitations. When GFR declines, serum creatinine initially changes only slightly.[41] (See Fig 2 below). Minor changes in serum creatinine may, therefore, reflect major changes in GFR. When the GFR declines to less than 40 ml/min/1.73m^2, the loss of nephrons over-rides the effects of enhanced tubular secretion and decreased generation of creatinine, and large increases in serum creatinine correspond to small changes in GFR.

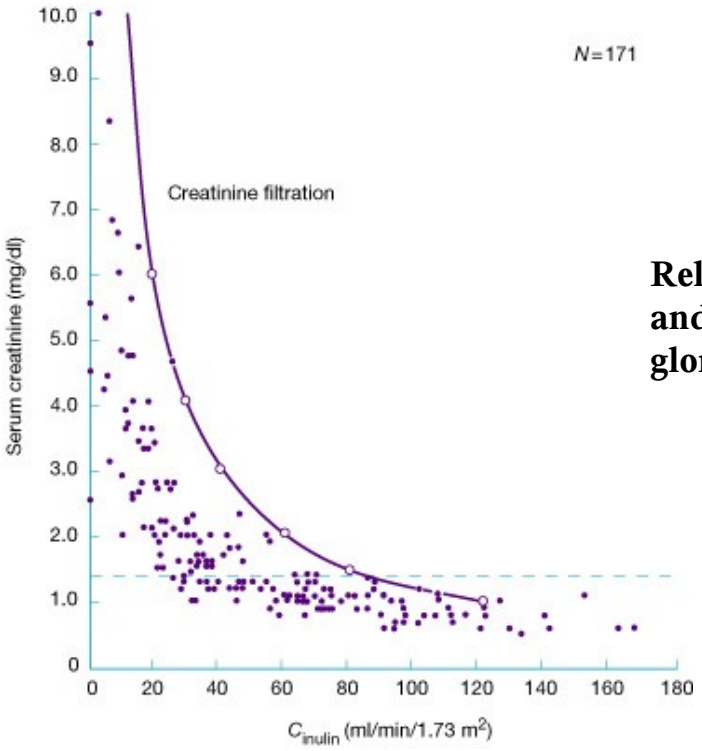

Figure 2

Relation between serum creatinine and GFR in 171 patients with glomerular disease.

Thus, serum creatinine concentration is a poor indicator of renal function in patients with CKD and cannot be used to assess GFR accurately. In addition, serum

creatinine concentration is affected by other factors such as changes in muscle mass and nutritional status, physical activity and gut metabolism of creatinine[42].

Any reduction in serum creatinine in late CKD may well reflect a loss in muscle mass rather than improvement in renal function. Another more suitable endogenous marker for GFR is the protein cystatin C which is produced by all nucleated cells and which is almost exclusively eliminated from the circulation by glomerular filtration[43]. It is sowly being tried in in clinical practice. Its use has yet to become routine.

Most clinicians use the Cockcroft–Gault formula but the MDRD formula being more accurate especially at low clearance is now preferred.

Reciprocal of serum creatinine

In every CKD patient on follow up, the reciprocal of the serum creatinine against time should be plotted. Linear regression of this produces a straight line in most patients making it possible to predict the time when dialysis will be required. (See Fig 3).

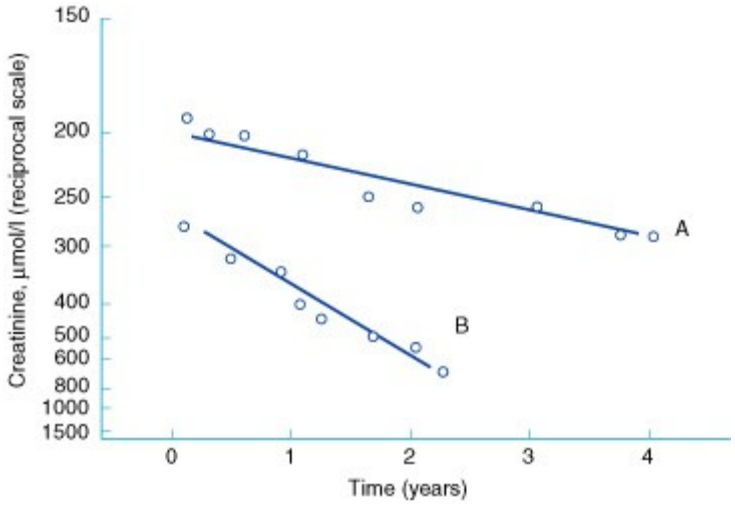

Figure 3 - The reciprocal plots of two patients with CKD on follow up illustrating a linear progression in decline in renal function

Several limitations of the reciprocal creatinine plot must be kept in mind. The accuracy of this prediction increases with the number of observations of serum creatinine. Also, a proportion of patients do not have a linear decline in renal function. Nine per cent of adults[44] and 13 per cent of children[45] deviated significantly from a straight line. Even among those that do follow a straight line, 20 per cent deviate from it at least once during their follow-up[46].

However, despite these limitations, the plot is useful in drawing attention to episodes of acute-on-chronic kidney disease, monitoring response to treatment, and predicting when stage 5 will be reached.

Preparing for RRT

Once the renal function is seen to be deteriorating, it is time to plan for RRT. A checklist is useful at this stage in the management of the patient. The check-list given below (Table 3) is one such list to ensure that all appropriate measures have been taken.

From previous follow-up visits		
Full blood count Calcium, magnesium, phosphate Liver function tests Alkaline phosphatase Blood sugars	Other appropriate tests, e.g. complement, VDRL, HBsAg, CRP,serum electrophoresis, HbA1C, 24-h urinary protein	Midstream urine Radiography Renal ultrasound ECG
Test	***Reason for test***	
In preparation for dialysis and transplant		
Ferritin, iron, transferrin	Iron status to look for concomitant iron deficiency	
Folate and vitamin B 12	To rule out another cause of anaemia	
PTH, vitamin D	To assess degree of renal osteodystrophy and as baseline	
Aluminium level	As a baseline for dialysis and to assess toxicity	
Glucose tolerance test	If fasting blood sugar is abnormal, to assess diabetic status	
HIV status	If positive, will affect decisions regarding management. Special precautions with blood letting	
Hepatitis C status	If positive, special precautions with blood letting	
Blood group, tissue typing and cytotoxic antibodies	Relevant for future transplant	
Fasting lipids	Patients are at risk of hyperlipidaemia	
CMV serology	Relevant to future transplant and donor CMV serology	
Skeletal survey	To assess renal osteodystrophy	
Micturating cystourethrogram	A routine in some centres to assess the bladder and exclude reflux before transplant	
Dental assessment	To look for occult dental sepsis pretransplant and for dental treatment predialysis	
Ophthalmology assessment	In diabetics	
Urological assessment	In certain conditions, e.g. reflux or stone disease	
Family planning	In females of child-bearing age regarding contraception and in males for consideration of sperm banking	
Assessment by gastroenterologist	It is routine in some centres to examine pretransplant patients by endoscopy	
Assessment by cardiologist	For ischaemic heart disease	
Assessment by social	To assess need for social support and counselling	

worker	
Assessment by dialysis administrator	To assess need for home adaptation for home haemodialysis
Family interview	For education and to assess possible family donors
Assessment by dialysis nursing staff	To assess suitability for CAPD/haemodialysis and counselling

Table 3 Pre-renal replacement therapy assessment checklist

Social and psychological assessment

Assessment of the patient's circumstances including distance from the nephrology clinic, cost and difficulty of travel determines the success of therapy. The occupational history is of great importance in judging the patient's suitability for the various types of RRT and the possible need for a change in occupation. It is important to discuss and educate the patient with respect to all aspects of therapy including compliance to diet and medication, prognosis and the various aspects of RRT. Once the patient has moderate renal impairment, it is imperative to psychologically prepare him/her for RRT, especially if renal transplantation is planned.

The patient entering a dialysis and transplant programme has to face many changes in life style due to such factors as dependence and change of body image. The patient must receive consistent and realistic advice about future treatment options. The renal unit should function as a multi-disciplinary team of which the social worker is a vital member, providing the social assessment on which many decisions hinge and counseling the patient during an extremely stressful period. The social worker assesses the patient's grasp of what is happening and establishes good communication. This will depend on their intelligence, level of education, and linguistic skills. Also the patient’s family and social relationships and the strength of these support systems need to be

assessed. Their housing is important in deciding whether peritoneal dialysis or home haemodialysis is a treatment option. Rehousing on medical grounds is a major issue even in affluent countries and usually not a feasible idea in our country. The patient's employment record and financial situation are needed to be explored so that the RRT is a financially viable option. Interviewing the family is also part of the social assessment, giving a better understanding of the patient and his or her social inter-relationships and provides an opportunity to discuss the possibility of a live related transplant.

Hepatitis screening

All patients should be screened for hepatitis B and C. Patients who are negative for HBsAg are to be offered vaccination if they do not have naturally acquired immunity. As CKD reduces the effectiveness of vaccination, it is best to arrange this early. It is preferred to use a double dose schedule of the Hepatitis B vaccine. The preferred injection site is the deltoid in adults and the anterolateral thigh in children because the buttock site is associated with a smaller chance of response. Approximately 75 per cent of subjects who are HCV antibody positive also have viral particles in their blood and are therefore infectious. In them, hepatitis C mRNA should be sought. Some strains (genotype 1) are less responsive to treatment with interferon alpha.

HIV testing

It is advisable to test for HIV infection prior to dialysis with appropriate counselling when indicated. HIVAN is the third leading cause of CKD5 in Blacks in the age group 20–64 years after diabetes and hypertension in the United States[47].

The most likely mode of transmission to hospital staff is through inoculation of infected blood by needle prick and there is so far no evidence of epidemic spread in

dialysis units. The majority of HIV infections are picked up by routine testing and if the patient is known to be HIV positive, continuous ambulatory peritoneal dialysis (CAPD) or home haemodialysis would be the treatment of choice in most cases. Blood taking should be kept to a minimum and special care should be taken in handling, transporting, and analysing samples. Healthcare workers need to be aware of the need for assessment for postexposure HIV prophylaxis in the event of a needle stick injury.

Vascular access

The planning of vascular access is of great importance for a smooth start to haemodialysis. If a fistula is required for haemodialysis, it should be created at least 3 months before the estimated date of starting dialysis in males and up to 6 months in a female with small veins. This allows time for maturation of the fistula, prepares the patient psychologically for the inevitable and avoids the need for temporary access such as a jugular or femoral vein catheter with all the attendant risks of such procedures viz trauma, septicaemia, venous stenosis, and thrombosis. Because of the high risk of stenosis in the subclavian vein, which seriously jeopardizes future fistula attempts and venous hypertension in the fistula, the use of subclavian catheters should be avoided[48].

Suitability for continuous ambulatory peritoneal dialysis

During the predialysis assessment period, suitability for CAPD must be assessed. There are few absolute contraindications to CAPD though some, such as a major diaphragmatic defects will only become apparent after CAPD has been started. A colostomy, ileostomy, or nephrostomy is a firm contraindication and previous major abdominal operations form relative contraindications. For young children, for those with severe physical handicaps such as blindness, crippling arthritis, paralysis, or severe

incoordination and for the mentally handicapped a family member such as the spouse or parent will be trained, and thus the suitability of the helper will need to be assessed. However, blind patients and some with severe arthritis have been trained to perform CAPD successfully themselves.

Obesity and hyperlipidaemia get worse more frequently in CAPD patients than in haemodialysis patients, so they are a relative contraindication to CAPD. Abdominal wall hernias are aggravated by CAPD and should be repaired before CAPD is started. CAPD will also result in an exaggerated lumbar lordosis, and if pre-existing lumbar disc disease is present, this will almost always deteriorate on CAPD.

Suitability for pre-emptive transplantation

Pre-emptive renal transplantation, if contemplated, should obviously be planned early in the assessment of the patient. When possible, it obviates all the attendant risks and cost of dialysis. It is appropriate in patients with a predictable cause, such as diabetes, so that stage 5 can be accurately dated. It is also easier to plan when a family donor is available. Interestingly, pre-emptive transplantation compared to transplantation from long-term dialysis is associated with better graft survival. In a study by Mange et al[49], there was a 52 per cent reduction in the risk of allograft loss in the first year in patients who underwent renal transplantion without prior dialysis.

Palliative care

Some patients approaching CKD 5 do not wish to have RRT and in others it may be inappropriate if multiple other comorbid conditions coexist. In such cases, providing good palliative care at the end of life is essential. Many symptoms can be alleviated with the use of drugs such as rhEPO and diuretics, analgesics, and later, sedatives. Frequently

nephrologists lack appropriate training in palliative care and a multidisciplinary approach should be adopted drawing on facilities such as the local hospice, district nurses, and general practitioners according to local circumstances.

Monitoring uraemic symptoms and when to start RRT

Monitoring the patient to assess when dialysis will be required is one of the main aims of follow-up and one of the most difficult. The timing of the start of dialysis is controversial, not least because of financial and practical implications and consequently the practice varies widely. Recently there has been a general trend in the developed world to initiate dialysis at an earlier stage of renal failure which would be in line with the DOQI recommendations that dialysis should be commenced once the GFR declines to less than 10.5 ml/min/1.73 m^2 or the creatinine clearance is in the range of 9–14 ml/min. This guideline is based on opinion only. The decision of when to start dialysis should involve a combination of clinical acumen in assessing symptomatology, discussed below, and identifying early signs of malnutrition in association with measurements of declining GFR discussed above. Evidence currently would also suggest that delaying dialysis till the GFR is less than 6 ml/min irrespective of symptoms is unsafe.

The complaints of patients on starting dialysis (Malangone et al,)[50] were:

- anorexia–nausea–vomiting 76%
- fatigue-weakness 72%
- pruritus 40%
- dyspnoea-orthopnoea 26%
- insomnia 14%

- bleeding tendency 14%
- apathy—mental changes 12%
- asterixis-muscle twitching-cramps 11%
- dysguesia 8%

The authors found that none of these symptoms had a significant relationship to biochemical measurements reflecting GFR (creatinine clearance, serum creatinine, and urea) except bleeding tendency.

The onset of pericarditis or symptomatic peripheral neuropathy, with no alternative explanation, is an indication that dialysis is already late and should be started at once. Nausea and vomiting are signs that dialysis is needed very soon. Restless limbs (a symptom which patients have difficulty in describing and often refer to as pain, itching, or discomfort until questioned closely) are usually a sign that dialysis is needed soon; a more generalized restlessness syndrome is an uncommon but dramatic indication that it is overdue. Severe pruritus and excoriated rash is an indication for early dialysis if not explained by drug allergy or coincidental skin disease. Other warnings that uraemia is becoming troublesome are myoclonic jerks (particularly on falling asleep), sleep disturbance, severe lethargy, mental clouding, loss of concentration and sexual dysfunction in younger adults, unexplained by drug therapy. In a significant minority of our patients, the trigger to starting dialysis is difficulty in controlling fluid balance and blood pressure rather than the symptoms or biochemical evidence of severe uraemia. A check for ankle oedema, crepitations at the lung bases, a raised jugular venous pressure and the presence of cardiomegaly, a third heart sound and functional cardiac murmurs is therefore a routine part of the follow-up assessment.

The National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) guidelines recommends that dialysis is initiated when the nPNA (normalized protein catabolic rate (nPNA) falls to below 0.8 g/kg per day. This is a measure of the level of protein intake.

The problem of late referral to nephrology services

Timely referral of patients with CKD to specialist nephrological care is needed to ensure the introduction of such measures early enough in the disease process to provide benefit. However, worldwide 30–40% of patients are referred to a nephrologist at a very late stage of renal disease.[51, 52, 53, 54]

In a study called "Late referral for dialysis: improving the management of chronic renal disease", Roderick et al found that one in six of all those starting RRT who were avoidably late-referred, and might have benefited from earlier intervention under care of a nephrologists[54].

Late referral is likely to result in the patients having a lower serum calcium and albumin and they were less likely to have a permanent vascular access in place at the start of dialysis. They were also more likely to have a hematocrit less than 28% and were less likely to have received Erythropoeitin[55].Late referral has also been shown to influence early mortality[56].

In the United Kingdom, the Renal Association has recommended that all patients with serum creatinine > 150μmol/l (1.7mg/dl) be referred to a nephrologist[57]. While this might be an extreme, an early referral once the diagnosis of CKD is established is advantageous. The patients can then be followed up on a regular basis by his personal physician with reviews with the nephrologist on a periodic basis and thus care can be

complementary.

Aim:

To evaluate patients with Chronic Kidney Disease Stage 5 [CKD 5] regarding:

1. Their pre-tertiary hospital care and
2. To assess their knowledge of the disease and its treatment

Objectives:

1. To assess the pre-tertiary hospital care of consecutive patients with CKD 5 who presented themselves to the nephrology services of Christian Medical College, Vellore.
2. To describe the demographic profile, education, occupation, socio-economic status, previous treating personnel, referral pattern, native kidney disease (if known), previously done investigations, vaccination against Hepatitis B virus, treatment received, prior patient education and decision towards renal replacement therapy.
3. To determine if the care given prior to coming to a tertiary hospital was appropriate and whether early referral to a nephrologist improved the adequacy of treatment.

Study Design:

The study was a cohort study on pre-tertiary hospital care of consecutive patients with Chronic Kidney Disease stage 5 (CKD 5) who presented to the nephrology services of Christian Medical College, Vellore.

Setting:

The study was conducted among the out-patients of the Department of Nephrology, Units I and II of the Christian Medical College (CMC), Vellore, South India which is a 1800 bedded tertiary care teaching hospital. Nephrology services have been offered here for over 3 decades.

Subjects

Inclusion Criteria:

a. Subjects were newly diagnosed cases of CKD 5 based on history, calculated glomerular filtration rate less than 15ml/min (by the Modification of Diet in Renal Disease formula)
b. They had compatible ultrasonographic evidence of CKD 5.

Exclusion Criteria:

a. The study excluded subjects who had been diagnosed to have CKD at CMC prior to the study period.
b. The study excluded the cases of renal insuffiency where the diagnosis of chronicity

was in doubt and required verification by further investigations.

Evaluation:

Consecutive pts with CKD 5 presenting to Nephrology services (over an eight month period) were prospective enrolled upon making a diagnosis of CKD 5. Both the patient and his relatives were interviewed by the investigator with regard to the pre-tertiary hospital management. The data thus collected was then entered into an electronically compatible proforma.

Statistical Analysis:

Summary statistics and tests of significance [*Chi squared* tests for categorical variables and Student *t* tests for continuous variables] were calculated using the software package SPSS version 9 on an IBM compatible PC.

In this study on pre-tertiary hospital care of patients with CKD 5, there were a total of **561** patients who were included in this study. During this period, 10843 patients were seen as outpatients by the department of nephrology while 518 patients underwent hemodialysis and 82 underwent renal transplantation.

Demographic Data

Age

Age Group	**No.**	**%**
< 16	8	1.43
16 - 24	77	13.73
25 - 34	112	19.96
35 - 44	113	20.14
> 44	251	44.74

Table – 4 - Age group profile

The mean age at presentation was 41.1 (± 14.5) years and the range was from 5 years to 79 years. It can be seen from Table 4 that the majority of patients were aged 35 years or above with 44.74% in more than 44 years age bracket. Figure 4 graphically illustrates the data below.

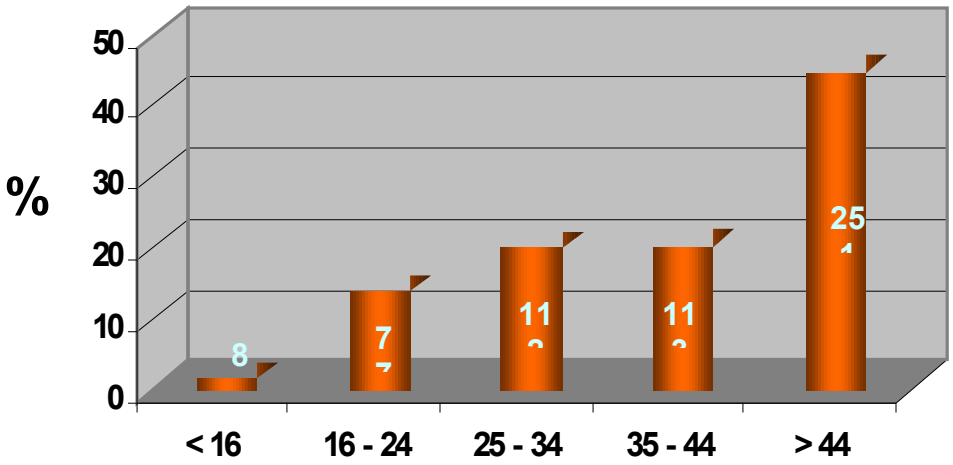

Figure 4 - Age Groups

Gender and Marital Status

The population under study was predominantly male forming 76.4% of cases [429 of 561 cases]. (Figure 5). Most of the men and the women in the study were married.

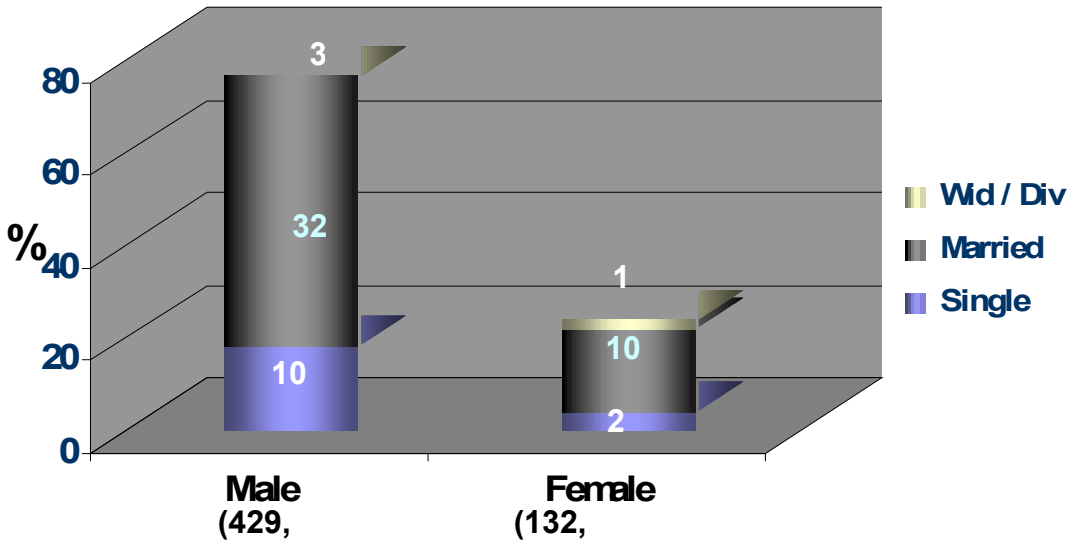

Figure 5 – Gender and marital status of patients

Occupation

The occupation profile of the patients shows that occupations among these patients was varies from that of a manual labourer to a housewife. There were people from all walks of life. The occupation profile is shown in Table 5. A large number - 126 patients (22.5%) of the patients have been designated under others – which included clerks, salesmen, mechanics, telephone operators, welders, barbers, tailors, weavers, bus conductors, lawyers and accountants.

Occupation	No.	%
Housewife	95	16.9
Labourer	76	13.5
Student	69	12.3
Professional	66	11.8
Skilled Worker	65	11.5
Unemployed	64	11.4
Others	126	22.5

Table 5 – Occupation profile

Educational status

Five hundred and one patients (89.3%) had received secondary level education or higher. (Table 6).

Level of Education	Number	%
College	189	33.7
Higher Secondary	83	14.8
Secondary [6th – 10th]	229	40.8
Primary [1st – 5th]	45	8.0
Illiterate	15	2.7

Table 6 – Educational status

Socio-economic status

For the purpose of the study, the patients were categorized based on their annual total family income.

They were arbitrarily divided into three groups:

LOW income group – Annual family income < Rs. 22500

MIDDLE Rs. 22500 – 70000

HIGH > Rs. 70000

From Table 7, we see that the nearly half the patients (264, 47.1%) were in the middle income category with roughly a quarter each in the remaining two groups.

Annual Family Income	**Number**	**%**
Low [< Rs. 22500]	152	27.1
Middle [Rs. 22500 – 70000]	264	47.1
High [> Rs. 70000]	145	25.8

Table 7 – Socio-economic status

Places of origin

The largest number of patients (207, 36.9%) was from the state of West Bengal. Sixty-one patients (10.9%) were from the neighbouring country of Bangladesh and 57 (10.2%) were from our own state of Tamil Nadu. There were patients from all over the country and also from the other neighbouring countries of Bhutan and Nepal. Figure 4 below shows the data graphically. Overall, it was seen that 76.1% were from the eastern

and north-eastern regions, 16.9% from southern India and 6% from the northern and western regions.

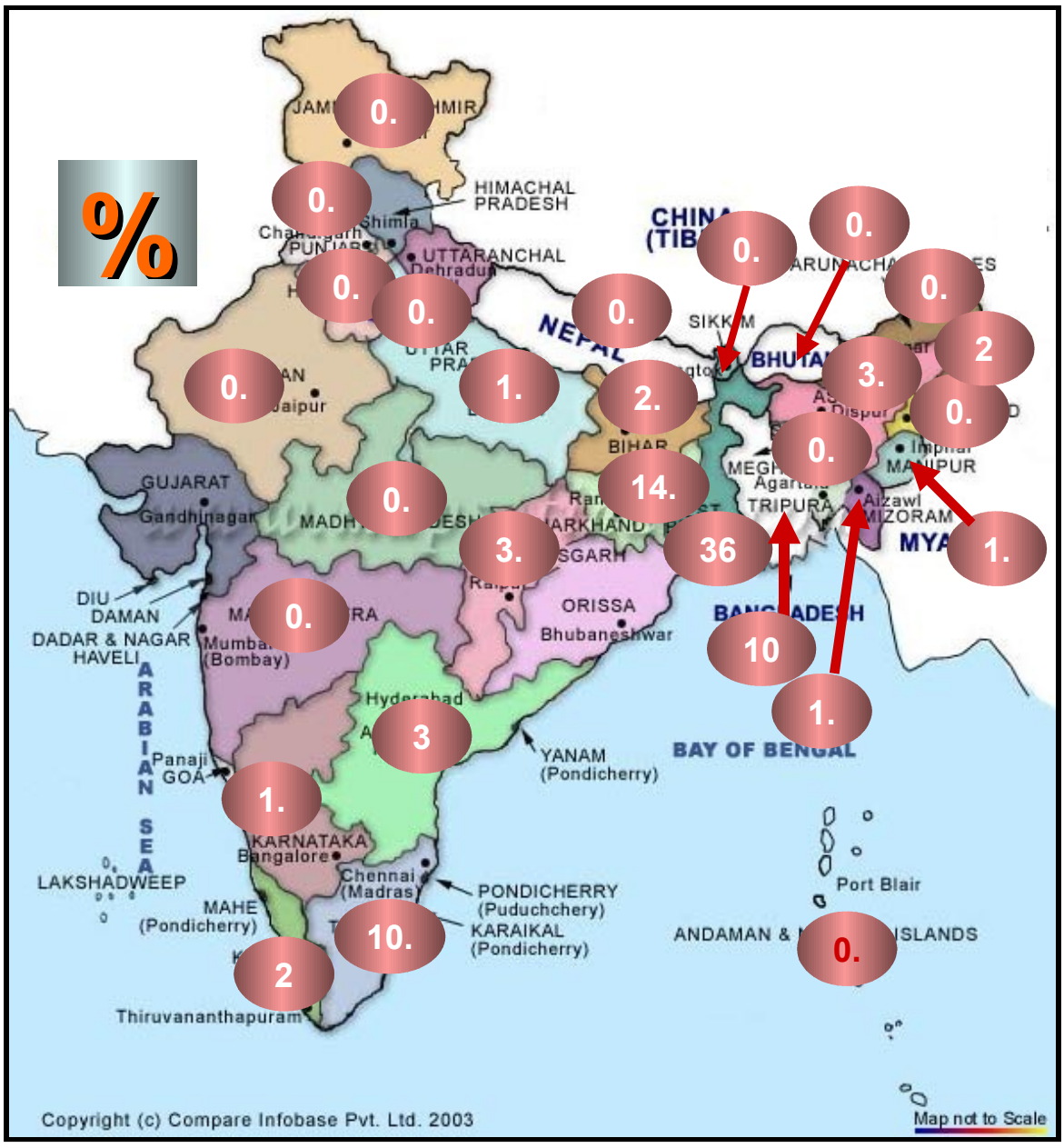

Figure 6 - Places of origin

Duration of illness

The mean known duration of renal illness was 12.4 ± 23.1 months (range 0 to 184 months) and the mean known duration of CKD 5 was 3.2 ± 3.5 months (range 0 to 24 months).

Initial presentation of renal illness

Three hundred and five patients (54.4%) were diagnosed to have CKD 5 on their first visit to a doctor. Of these, 22 (7.2%) were diagnosed at Christian Medical College, Vellore. Of the 283 (92.8%) who had CKD 5 as their initial presentation of renal illness, 194 (68.6%) had been to a nephrologists prior to visiting Vellore. (Figure 7)

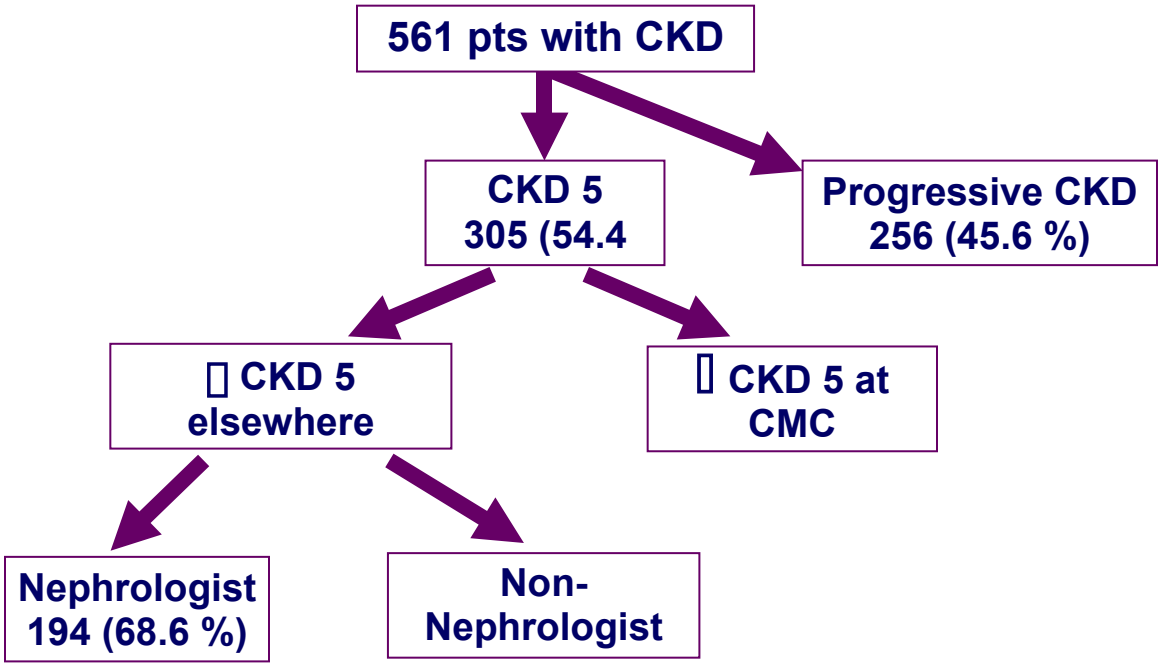

Figure 7 – Initial presentation of CKD

Native Kidney Disease diagnosed previously

As can be seen from Table 8, the native kidney disease was unknown in 59.2% of

patients. Diabetic nephropathy was the most common diagnosis that was made (123 patients, 21.2%) and glomerular disease was previously diagnosed in 47 patients (8.4%) (Figure 8).

Native Kidney Disease	Number	%
Unknown	332	59.2
Diabetic Nephropathy	123	21.8
Glomerular disease	47	8.4
Obstructive Uropathy	18	3.2
Hypertensive nephropathy	15	2.7
CIN	15	2.7
ADPKD	9	1.6
Others	2	0.4

Table 8 - Native Kidney Disease diagnosed previously

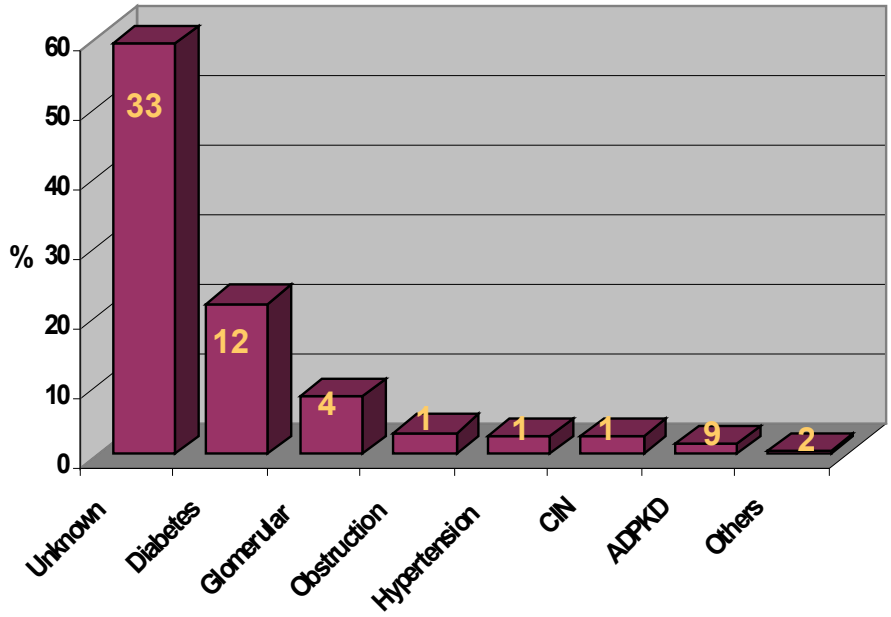

Figure 8 – Native Kidney Disease diagnosed previously

Previous treating personnel

About two-thirds of the patients (369, 65.8%) had been under the care of a nephrologist prior to visiting our centre and 26.7% were seen earlier by a general medicine physician. (Table 9). This is graphically illustrated in figure 9 given below.

Treating Person	Number	%
Nephrologist	***369***	***65.8***
General medicine physician	150	26.7
No Treatment	76	23
Primary doctor	10	1.8
Others	69	9

Table 9 – Previously treating personnel

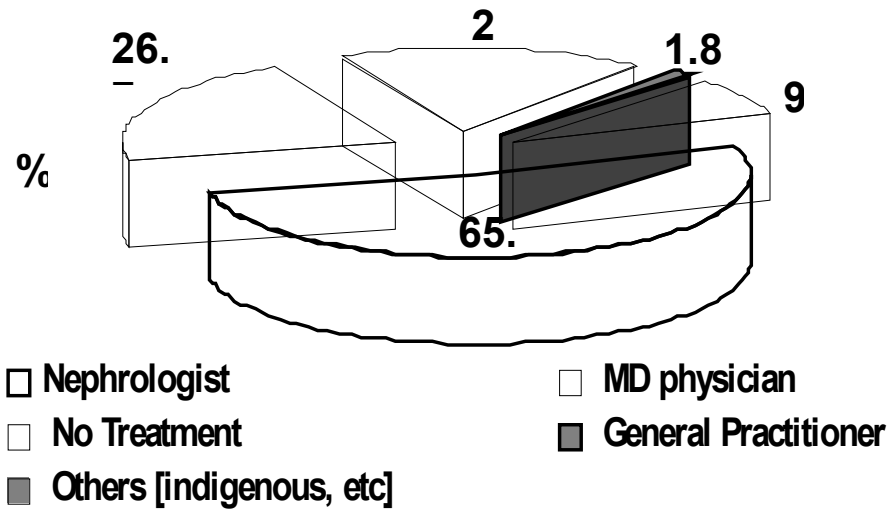

Figure 9 – Previous treating personnel

Referral pattern

The majority were self-referred (373, 66 .5%) while about 12 per cent were referred by the treating nephrologist (70, 12.5%) and the physician (64, 11.4%). (Table 10 and figure 10). The rest were by other patients (14, 2.5%), their primary physician (10, 1.8%) or others.

Referring person	**Number**	**%**
Self-referred	***373***	***66.5***
Nephrologist	70	12.5
MD physician	64	11.4
Another patient	14	2.5
Primary doctor	17	3.0
Others	23	4.1

Table 10 – Referral pattern

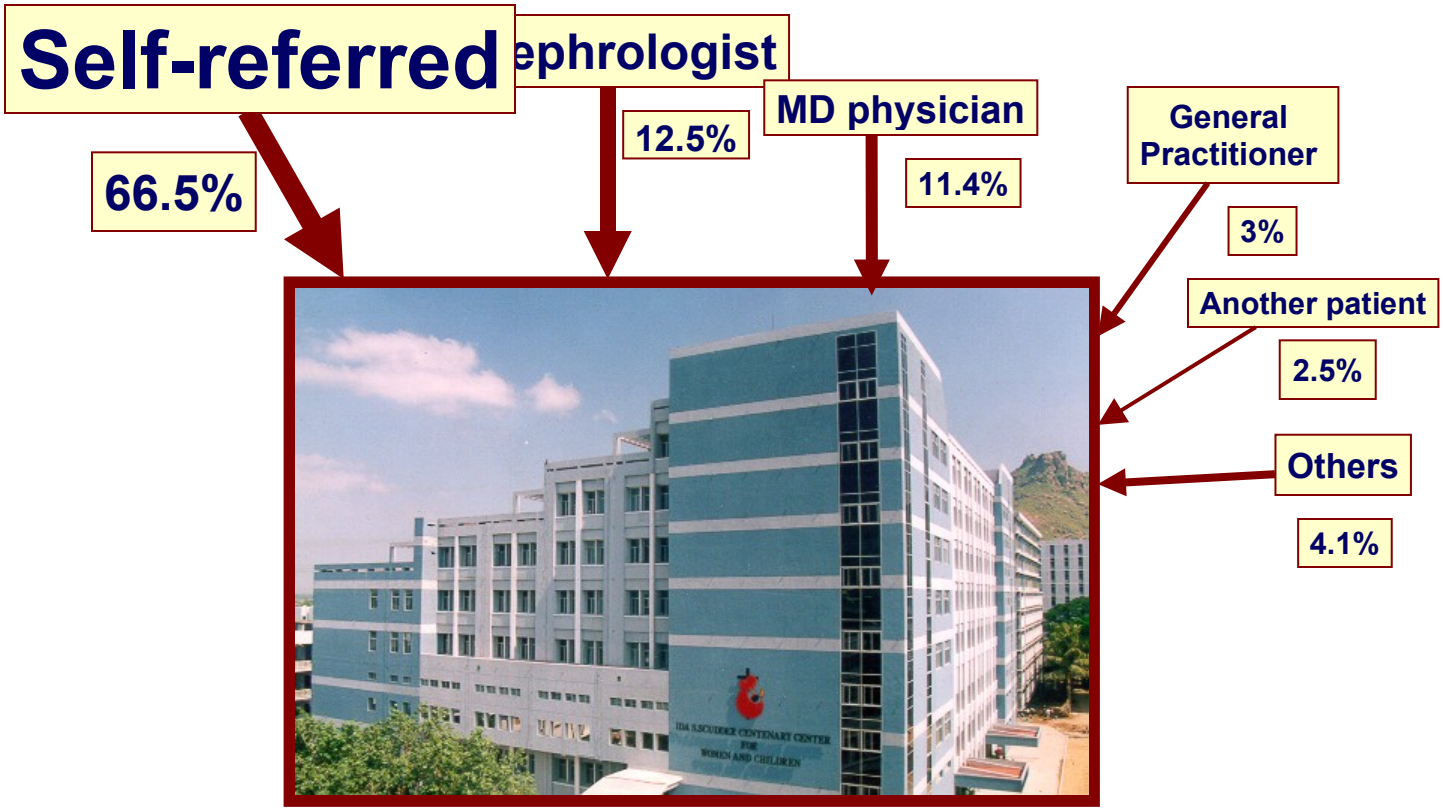

Figure 10 – Referral pattern

Documented investigations done previously

Upon checking the investigations that had been done previously, (Table 11) it was found that a basic hemogram and biochemistry had been done in most of the patients (529, 94.3%). An ultrasound of the abdomen was done in the majority (482, 86%). However less than half had quantification of their proteinuria. Testing for the common blood borne pathogenic viruses (Hepatitis B virus surface antigen, Anti-Hepatits C virus

antibody and Human Immunodeficiency Virus) was done in only 199 (35.5%), 124 (22.1%) and 155 patients (27.6%) respectively. Vaccination against Hepatitis B virus was done in less than a quarter of the patients (133, 23.7%).

Investigations done	**Number**	**%**
Hb/PCV, Urine RE, Urea, Creat, K	529	94.3
Ultrasound Abdomen	482	86.0
24 hour protein	269	48.0
HBsAg	199	35.5
Anti HCV	124	22.1
HIV	155	27.6

Table 11 – Documented investigations done previously

Patients with hypertension

From the study it was seen that 531 patients (94.6%) had hypertension. Of these, 453 (85.3%) had been prescribed anti-hypertensive medication. Despite this, only 172 (38%) had a blood pressure less than 130/90 mm of Hg. Overall 329 patients (62%) had uncontrolled hypertension at presentation. This is illustrated in figure 11 given below.

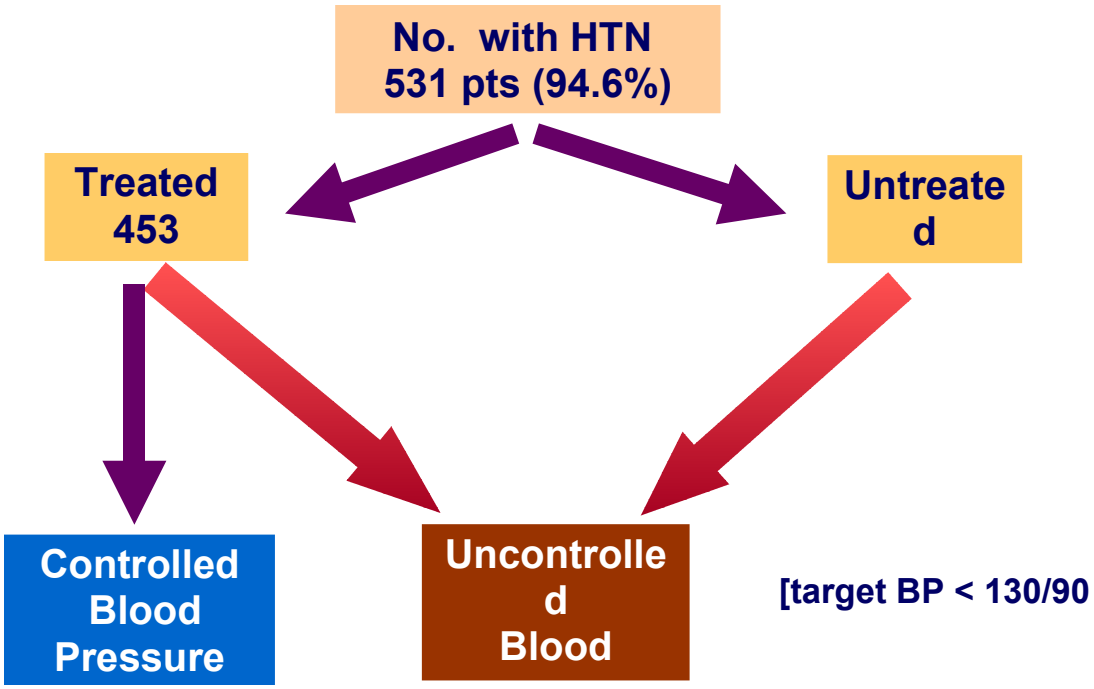

Figure 11 – Patients with Hypertension

Prior treatment given

As given in table 12 below, dietary recommendations had been given to 344 patients (67.3%). Three hundred and fifty-seven patients (63.6%) were prescribed phosphate binders and 242 (43.6%) were on calcitriol therapy.

Only 87 patients (15.5%) had undergone prior arterio-venous fistula construction. One hundred and one patients (18%) were on rhEPO therapy and 228 patients (40.6%) had received blood transfusion/s.

Treatment given	Number	%
Dietary advice	344	61.3
Phosphate Binders	357	63.6
Vitamin D Therapy	242	43.1
Oral iron	314	56.0
Blood Transfusion	228	40.6
Erythropoietin	101	18.0
AV fistula constructed	87	15.5

Table 12 – Prior treatment given

Prior patient education

Upon interviewing the patient and his relatives, it was found that 228 patients (40.6%) had adequate knowledge regarding CKD 5. About a fifth were informed regarding the need for constructing an arterio-venous fistula for a permanent hemodialysis vascular access (128, 22.8%) and Erythropoeitin use (19.1%). Knowledge regarding RRT was poor with 248 patients (43.9%) being aware about hemodialysis. Prior information regarding possibility of renal transplantation was known only to 20.9%. Education regarding peritoneal dialysis was done in only 6.8%. (Table 13)

Educated regarding	Number	%
Original Disease	228	40.6
AV fistula	128	22.8
Erythropoeitin	107	19.1
Hemodialysis	248	43.9
Transplantation	117	20.9
Peritoneal Dialysis	38	6.8

Table 13 – Prior patient education

Preference of renal replacement therapy modality

Three hundred and twenty six patients (59%) said that they would prefer definitive therapy in the form of RRT. Of the modalities, renal transplantation was clearly the most preferred (181, 32.3%). One hundred and thirty-two patients (23.5%) expressed their preference for maintenance hemodialysis while a small number (13, 2.3%) preferred

Continuous Ambulatory Peritoneal Dialysis (CAPD). The rest either opted for conservative therapy (182, 32.4%) or were undecided (53, 9.4%). (Table 14 and figure 12)

Decision	Number	%
Conservative Treatment	182	32.4
Transplantation	181	32.3
Maintenance Hemodialysis	132	23.5
CAPD	13	2.3
Undecided	53	9.4

Table 14 – Decision regarding renal replacement therapy

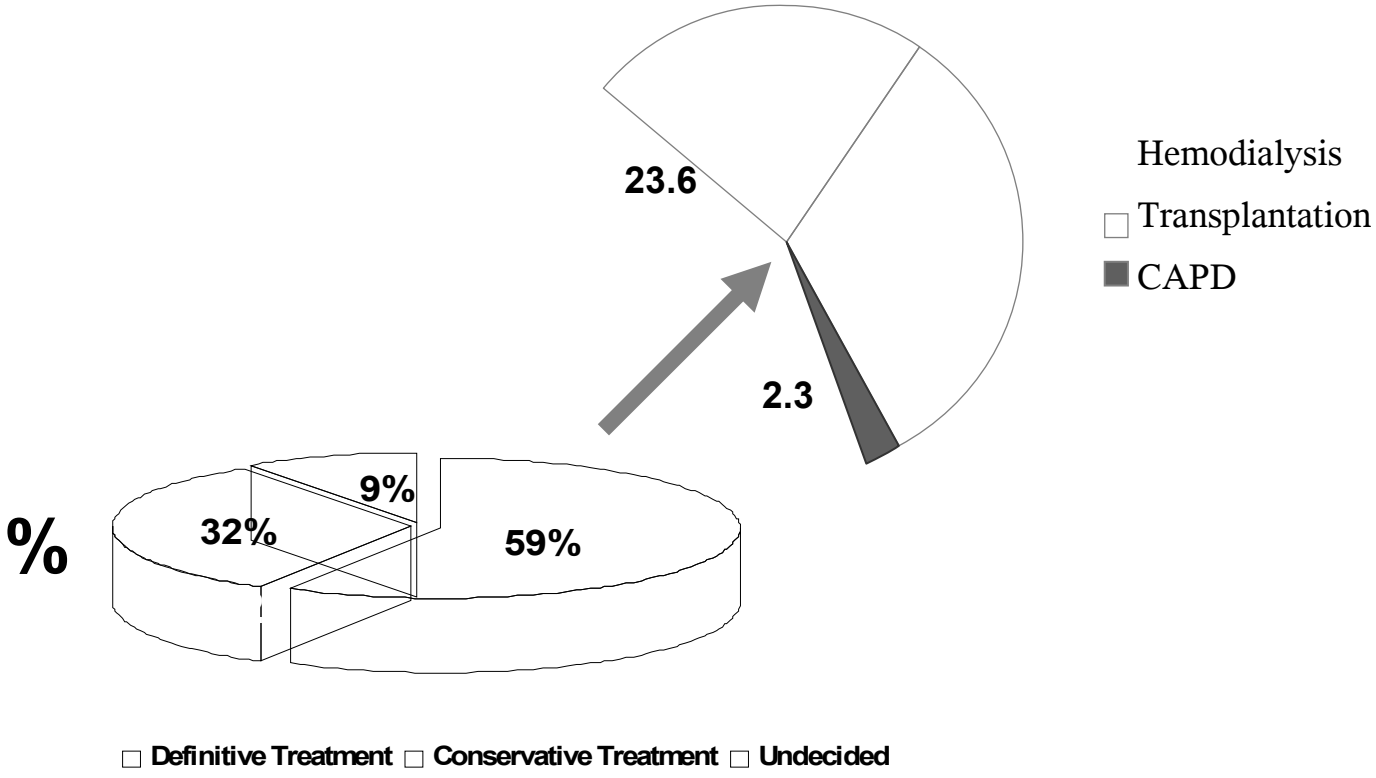

Figure 12 – Renal replacement therapy

Care under a nephrologist

Upon evaluating the care given by various treating personnel, it was found that

the care under a nephrologist was more likely to result in appropriate investigations (99.2% vs 90.1%), treatment (97.8% vs 81.3%) and patient education (73.4% vs 39.1%). ($p<0.001$). They were also more likely to opt for renal replacement therapy ($p<0.001$). Blood pressure control did not differ whether treated by a nephrologist or other physician.

Variable	**Nephrologist [n = 369] n (%)**	**Others [n = 192] n (%)**	***P***
Investigations done			
Hb/PCV + Urine RE Urea + Creat + K (n=561)	***361 (97.8)***	***168 (87.5)***	***< 0.001***
HBsAg (n=561)	***179 (49)***	***20 (10)***	***< 0.001***
Renal Ultrasound (n=561)	***349 (95)***	***133 (69)***	***< 0.001***
BP control	130 (40.4)	46 (35.1)	0.298
Treatment given			
Phosphate Binders (n=561)	***279 (76)***	***78 (41)***	***< 0.001***
Vitamin D (n=561)	***206 (56)***	***36 (19)***	***< 0.001***
HBV vaccination (n=561)	***118 (32)***	***15 (7.8)***	***< 0.001***
Dietary advice (n=561)	***262 (71)***	***82 (43)***	***< 0.001***
Anti-hypertensive therapy (n=453)	***322 (71)***	***131 (29)***	***< 0.001***
BP control (n=453)	130 (40.4)	46 (35.1)	0.298
Blood group testing (n=561)	***244 (66)***	***66 (34.6)***	***< 0.001***
AV fistula formation	***237 (64)***	***77 (40)***	***< 0.001***
Oral Iron	***237 (64)***	***77 (40)***	***< 0.001***
rhEPO	***86 (24)***	***15 (7.9)***	***< 0.001***
Prior Patient Education			
Original disease	***149 (40.6)***	***54 (28)***	***0.004***
Erythropoietin	***95 (25.8)***	***12 (6.2)***	***< 0.001***
AV fistula	***114 (31)***	***14 (7)***	***< 0.001***
Hemodialysis	***212 (57.4)***	***34 (17.7)***	***< 0.001***
CAPD	32 (8.7)	6 (3.1)	0.013
Renal Transplantation	***100 (27)***	***17 (9)***	***< 0.001***
Treatment preferred			
Decision regarding RRT	***251 (73)***	***75 (46)***	***< 0.001***

Table 15 – Care under a Nephrologist versus other treating personnel

Variable	**Nephrologist [n = 369] n (%)**	**Others [n = 192] n (%)**	***P***
Investigations	***366 (99.2)***	***173 (90.1)***	***< 0.001***
Treatment	***361 (97.8)***	***156 (81.3)***	***< 0.001***
Prior Patient Education	***271 (73.4)***	***75 (39.1)***	***< 0.001***
BP control	130 (40.4)	46 (35.1)	0.298
RRT preferred	***251 (73)***	***75 (46)***	***< 0.001***

Table 16 – Care under a Nephrologist versus other treating personnel [Overall]

However, upon evaluating for all the necessary facets of care, it was seen that although care under a nephrologist was better, *all* the appropriate investigations had been done in only 95 patients (25.7%) and only 17 patients (4.6%) had been educated adequately [Table 17].

Variable	**Nephrologist [n = 369] n (%)**	**Others [n = 192] n (%)**	***p***
Investigations	***95 (25.7)***	***9 (4.7)***	***< 0.001***
Treatment	***361 (97.8)***	***1(0.5)***	***< 0.001***
Prior Patient Education	***17 (4.6)***	***1 (0.5)***	***< 0.001***

Table 17 – Care under a Nephrologist versus other treating personnel [Comprehensive]

The increasing incidence and prevalence of Chronic Kidney Disease (CKD) has made it an important worldwide public health problem. From this perspective, prevention of CKD and its progression is undoubtedly an important goal worldwide.

Optimal treatment of CKD patients includes prevention of metabolic disorders, prevention of malnutrition, preservation of quality of life and adequate preparation for renal replacement therapy (RRT). This translates into tight blood pressure control, calcium and iron supplements, phosphate binders, vitamin D supplementation, timely use of erythropoietin, dietary counseling, vaccination against hepatitis B virus and timely creation of an arterio-venous fistula.[58] We looked at these factors in our study.

From the study, it is seen that a basic hemogram, biochemistry and ultrasound had been done in most of the patients. However, less than half had quantification of their proteinuria. In the perspective of factors affecting progression of CKD, severity of proteinuria is an important prognosticating factor. Another important investigation that was sadly deficient was testing for the common blood borne pathogenic viruses. The importance of this investigation cannot be emphasized. Both hepatitis B virus (HBV) and hepatitis C virus (HCV) have important pathogenic role in the etiology of renal illness. Further, these have an important bearing upon the patient during his renal replacement therapy (both dialysis and transplantation).

In the area of patient education and treatment, the nephrologist scores over the primary or family physician. In this study, it is seen that care under a nephrologist was more likely to result in appropriate investigations (99.2% vs 90.1%), treatment (97.8% vs 81.3%) and patient education (73.4% vs 39.1%). ($p<0.001$).

However, all the necessary investigations had been done in only 25.7% and only 4.6% had been educated adequately even under a nephrologist.

Worldwide, 30 – 40% of patients are referred to a nephrologist's care at a very late stage of renal disease.[54]

Late-referred patients were significantly less likely to have received standard therapies like rhEPO (and consequently a lower hematocrit) and vitamin D supplementation,[55] vaccination against Hepatitis B[54] and a permanent dialysis access in place at start of RRT.[60]

This results in a poor clinical state at the initiation of RRT[59], worse prognosis and early death.[56] A perceived lack of training and guidelines for referral of patients with CKD and poor communication influences timely referral.[61]

This calls for improved co-operation between the treating physicians and a consensus decision on timely referral. The introduction of a new concept of a "medical social worker[62] is perhaps a right step in this direction.

Despite 65.8% of the patients being had been under the care of a nephrologist and 26.7% being under the care of a general medicine physician, 329 patients (62%) had uncontrolled hypertension at presentation. Longer pre-dialysis nephrological care is associated with improved long-term survival and better blood pressure control.[63] In this study, however, there was no difference in the difference in blood pressure control showing a lacuna in management.

Paucity of symptoms in the initial stages of CKD results in patients not being investigated for renal function[64] and 54.4% presented with CKD 5 as the initial presentation of renal disease. This underscores the value of periodic medical evaluation

for the otherwise healthy individuals of our community especially those at risk for developing CKD. For the self same reason of late presentation, the native kidney disease was unknown in 59.2% of cases. Diabetic nephropathy was the commonest known etiology (21.8%).

Finally vaccination against HBV is an important measure to attempt prevention in a patient with CKD. In this study, less than a quarter of the patients had been vaccinated against HBV infection. Vaccination of all patients with CKD needs to be carried out meticulously and with double dose of the vaccine. The low vaccination rate is a concern in the dialysis population leading to inadequate protection in this population.[24]

This study highlights the need for a country-wide effort to curtail progression to CKD 5. This effort begins with educating the medical practitioners throughout the country about the disease, its prevention, and steps to slow progression; also about optimal medical management including timely referral to a nephrologist.

In this study on "evaluation of pre-tertiary hospital care of patients with Chronic Kidney Disease Stage 5", the following observations were made:

1. The mean known duration of renal illness was 12.4 ± 23.1 months (range 0 to 184 months).
2. The mean known duration of CKD 5 was 3.2 ± 3.5 months (range 0 to 24 months).
3. CKD 5 was the initial presentation of renal illness in 54.4% of cases.
4. 65.8% had been under care of a nephrologist while 26.7% had been under care of a general medicine physician.

5. Two-thirds of the patients had been self-referred for a second opinion on the diagnosis of their illness.
6. Although a basic hemogram and biochemistry had been done in most (94.3%) and an ultrasonogram in 86%, testing for the blood borne viruses (HIV, HCV and HBsAg) was done in only 27 to 35% of patients. Vaccination against hepatitis B was poor (23.7%).
7. Adequate blood pressure control was achieved in only 38% of the patients.
8. Care under a nephrologist was more likely to result in appropriate investigations (99.2% vs 90.1%), treatment (97.8% vs 81.3%) and patient education (73.4% vs 39.1%). ($p<0.001$). They were also more likely to opt for renal replacement therapy ($p<0.001$).
9. Blood pressure control did not differ whether treated by a nephrologist or other physician.
10. Upon evaluating for comprehensive care, although care under a nephrologist was better, *all* the appropriate investigations had been done in only 95 patients (25.7%) and only 17 patients (4.6%) had been educated adequately.

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Evaluation of Pre-Tertiary Hospital Care of Patients with CKD Stage 5

Serial No:

Name: Age: Sex: M/F

Marital Status: Single / Married / Widow (or) Divorce

Education: 1. Illiterate 2. Primary (1-5) 3. Secondary (6-10) 4. HSC 5. College

Occupation: 1. Labourer 2. Skilled worker 3. Professional 4. House wife 5. Student

6. Other 7. Unemployed

State of Residence [Code No.]:

Socio Economic Status [income]: Low [≤22500] Middle [22501 – 70000] High [≥70001]

Treated By: 0. None 1. MD Physician 2. Nephrologist 3. Primary doctor
4. Another 5. Others.

Referral : 0. None 1. MD Physician 2. Nephrologist 3. Primary doctor
4. Another patient 5. Others.

Renal Disease: RD and CKD-5

Duration of proven Renal Disease (months) :

Diabetic : Yes / No

Native Kidney Disease :

HB / PCV + Urine RE done : Yes / No

Urea + Creat + K done : Yes / No

Proteinuria (> 500mg) : Yes / No

Biopsy Done (if indicated) : Yes / No / Not applicable

Biopsy diagnosis:

HBV tested: : Yes / No
At RD diagnosis / At CKD-5 diagnosis

HCV tested : Yes / No

At RD diagnosis / At CKD-5 diagnosis

HIV tested : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Ultrasound : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Anti-Hypertensives
(to target 130/90 mm Hg) : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Is the BP control adequate : Yes / No

Phosphate binders : Yes / No
At RD diagnosis / At CKD-5 diagnosis

HBV vaccination : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Dietary advice : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Immunosuppression : Yes / No
At RD diagnosis / At CKD-5 diagnosis

Therapy of CKD-5

Duration of CKD-5 (months):

1. AVF formation: Yes / No 2. Iron (Oral): Yes / No 3. NA Iron (IV) : Yes / No /NA

4. EPO : Yes / No / NA 5. Vitamin D : Yes / No / NA

6. Blood Transfusion: Yes / No / NA 7. Blood Grouping : Yes / No / NA

Practical understanding (including costs):

1.Original disease : Yes / No 2.Hemodialysis : Yes / No 3.CAPD: Yes / No

4. Transplant : Yes / No 5. EPO : Yes / No 6. AVF : Yes / No

Final Decision:

1. Undecided 2. HD 3. CAPD 4. HD & TX 5. Medical treatment only

State of residence (option codes):

1. Andaman & Nicobar	2. Andra Pradesh	3. Arunachal pradesh	4. Assam
5. Bihar	6. Chandigarh	7. Chattisgarh	8. Dadar & Nagar

9. Daman & Diu	10. Delhi	11. Goa	12. Gujarat
13. Hariyana	14. Hemacal	15. J & K	16. Jharkand
17. Karnataka	18. Kerala	19. Lakshwadweep	20. MP
21. Maharastra	22. Manipur	23. Meghalaya	24. Mizroam
25. Nagaland	26. Orissa	27. Pondichery	28. Punjab
29. Rajastan	30. Sikkim	31. TN	32. Tripura
33. Uttar Pradesh	34. Uttranchal	35. WB	36. Bangladesh