

A Greater than Expected Prevalence of Chronic Kidney Disease (CKD) in Pakistan

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Chronic kidney disease (CKD) is a worldwide public health issue associated with premature mortality, decreased quality of life, and increased health-care expenditures. Untreated CKD can result in end-stage renal disease and necessitate dialysis or kidney transplantation. In the developed countries there is a rising incidence and prevalence of kidney failure with poor outcomes and high cost. Patients with end-stage renal disease (ESRD) consume a disproportionate share of health care resources. The total cost of the ESRD program in the US was approximately \$39.46 billion¹ in 2008. Medicare costs per person per year were nearly \$66,000 overall, ranging from \$26,668 for transplant patients to \$77,506 for those receiving haemodialysis therapy but despite the magnitude of the resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant mortality and morbidity, and a reduced quality of life¹.

The prevalence of CKD has been evaluated based on serum creatinine concentration and/or proteinuria in different populations is 16.8 percent in the USA², 10.2 percent in Norway³, 7 percent in Taiwan^{4,5}, 5 percent in Iceland and a higher than expected in Pakistan from the population-based health survey of 1023 people by Kazmi et al⁶. The number of people surveyed in each province was corresponding to the population in the region. Overall, 36% of patients had GFR 90 ml/min/1.73m², 50% had 60-89 ml/min/1.73 m², 13% had 30 to 59 ml/min/1.73 m² and 1% had 15-29 ml/min/1.73 m². The combined prevalence of stage 3 and 4 was 14

%, with highest 19% in Punjab, followed by 12% in NWFP and Baluchistan and 7% in Sindh⁶. Using total population of Pakistan based on Economic Survey 2005-06, nearly 21 million people in Pakistan have either stage 3 or 4 CKD⁶.

Most chronic nephropathies are characterized by a progressive course that leads, at a variable rate, to loss of kidney function and the need for renal replacement therapy. The progression of chronic kidney diseases (CKD) typically moves through phases from initial diminution of renal reserve to mild, moderate and severe reductions in glomerular filtration rate (GFR), to ESRD. There is growing evidence that some of the adverse outcomes of CKD can be prevented or delayed by preventive measures, early detection and treatment.

It has been argued that screening the general population may decrease the incidence of ESRD. However, screening the general population is unlikely to be cost-effective. Screening for CKD among selected patients who are at risk for development of CKD is justified because therapeutic interventions may slow or prevent the progression toward ESRD. Such patients include those with a history of diabetes, cardiovascular disease, hypertension, hyperlipidemia, obesity, metabolic syndrome, smoking, HIV or hepatitis C virus infection, and malignancy. A family history of CKD, age > 60 years and treatment with potentially nephrotoxic drugs should also be considered for screening. Testing for CKD can be done with a urinalysis, a first morning or a random "spot" urine sample for albumin or protein and creatinine assessment, and a serum creatinine level. Depending upon the presence of particular risk factors, additional testing such as renal ultrasonography may be required, such as in patients with a family history of polycystic kidney disease.

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Once the diagnosis is established and the cause and/or potentially reversible factors are identified and treated, CKD should be staged according to the classification proposed by the NKF-K/DOQI.

Patients with kidney disease may have a variety of different clinical presentations. Some have symptoms that are directly referable to the kidney (gross haematuria or flank pain) or to extrarenal symptoms include anorexia, nausea, vomiting, pericarditis, peripheral neuropathy, and central nervous system abnormalities (ranging from loss of concentration and lethargy to seizures, coma, and death). No direct correlation exists between the absolute serum levels of blood urea nitrogen (BUN) or creatinine, and the development of these symptoms. Some patients have relatively low levels (e.g. a BUN of 60 mg/dL [21.4 mmol/L] in an older patient) but are markedly symptomatic, while others have marked elevations (e.g. a BUN of 140 mg/dL [50 mmol/L]) but remain asymptomatic. To continue life, uremic patients require the institution of renal replacement therapy with haemodialysis, peritoneal dialysis, or renal transplantation. Many patients, however, are asymptomatic and are noted on routine examination to have an elevated serum creatinine concentration or an abnormal urinalysis.

Once kidney disease is discovered, the presence or degree of kidney dysfunction and rapidity of progression are assessed, and the underlying disorder is diagnosed. Early identification of patients with CKD would allow treatment that could slow the progression to ESRD, improve clinical outcome, and constrain the growth of cost in the ESRD program. Although the history and physical examination can be helpful, the most useful information is initially obtained from estimation of the glomerular filtration rate (GFR) and examination of the urinary sediment.

Estimation of the glomerular filtration rate (GFR) is used clinically to assess the degree of kidney impairment and to follow the course of the disease. However, the GFR provides no information on the cause of the kidney disease. This is achieved by the urinalysis, measurement of urinary

protein excretion, and, if necessary, radiologic studies and/or kidney biopsy.

Markers of kidney damage include proteinuria, haematuria, and other abnormalities of the urinary sediment, and radiologic evidence of damage. The most common cause of CKD in adults is diabetes and hypertension, and therefore the most common marker for kidney damage is increased excretion of protein, and specifically of albumin. Measurement of protein excretion is useful in a variety of clinical settings, particularly to establish the diagnosis and to follow the course of glomerular disease.

A variety of chronic kidney diseases may progress to end-stage renal disease (ESRD), including chronic glomerulonephritis, diabetic nephropathy, and polycystic kidney disease. The rate of progression of CKD varies according to the underlying nephropathy and secondary factors that are sometimes unrelated to the activity of the initial disease. These include systemic and intraglomerular hypertension, glomerular hypertrophy, severity of proteinuria, the intrarenal precipitation of calcium phosphate, dyslipidemia, and altered prostanoid metabolism⁷⁻¹¹.

The general management of the patient with chronic kidney disease involves the treatment of reversible causes of renal dysfunction such as hypovolaemia due to vomiting, diarrhoea, diuretic use and bleeding, hypotension caused by myocardial dysfunction or pericardial disease, infection such as sepsis, and the administration of drugs which lower the GFR namely nonsteroidal anti-inflammatory drugs NSAIDs and ACE inhibitors.

Therapy to slow the rate of progression in patients with chronic kidney disease (CKD), independent of treatment of the underlying disease, is centred on attaining the blood pressure goal and, in patients with proteinuric disease, attaining the proteinuria goal. In patients with proteinuric CKD (500 to 1000 mg/day or more), the blood pressure should be lowered to less than 130/80 mmHg while patients with nonproteinuric CKD (less than 500 to 1000 mg/day), the blood pressure should be low-

ered to less than 140/90 mmHg in all patients, and to less than 130 to 135 mmHg systolic if it can be achieved without producing significant side effects. In addition to blood pressure control, reduction in urinary protein excretion to less than 1000mg/day slows the rate of progression of proteinuric CKD.

Strong evidence favours the use of an angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) as first-line therapy to lower blood pressure in patients with proteinuric CKD because these drugs slow the rate of progression of CKD compared with other antihypertensive. In contrast to their renoprotective effects in proteinuric CKD, angiotensin inhibitors do not appear to be more beneficial than other antihypertensive agents in patients with nonproteinuric CKD. Loop diuretics are first-line therapy in patients with edema and, in patients without edema, an angiotensin inhibitor followed by a dihydropyridine calcium channel blocker are preferred for initial therapy. Protein restriction to 0.8 to 1.0 g/kg per day of high biologic value protein, statin therapy, smoking cessation also may offer some renal protection.

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