The epidemic of chronic kidney disease

Chronic kidney disease (CKD) is increasingly being acknowledged as a worldwide public health problem which leads to progressive renal failure, cardiovascular disease and premature death.[1,2] The Third National Health and Nutrition Examination Surveys (NHANES III) in the USA found that an estimated 20 million Americans have CKD.[3] It is among the leading causes of death in the industrialised world, and the 9th most important cause of death in the USA. Even those patients who do not progress to end-stage renal disease (ESRD) requiring dialysis or transplantation have an increased risk of death from heart and cerebrovascular disease from any cause.[4] The presence of CKD, whether it is manifested by proteinuria or reduced glomerular filtration rate (GFR), is now acknowledged as an independent risk factor for cardiovascular disease events (CVD) in the most recent report from the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure (JNC VII) and in a position statement of the American Heart Association.[5,6] Patients with CKD are considered to be in the highest-risk group by JNC VII and the US National Kidney Foundation, with JNC VII including CKD as a 'compelling' indication for optimal blood pressure control, justifying lower target blood pressure and treatment with specific antihypertensive agents.

Worldwide there are well over 1 million people on maintenance dialysis today, and this number is projected to reach 2 million by 2010. In the USA, over 370 000 are on treatment for ESRD, and this number is projected to exceed 600 000 by 2010.[7] Over 6% of the US Medicare budget is spent on ESRD.[8] Based on the US average of $66 000 per patient per annum, it is estimated that 1 trillion dollars would be needed to care for ESRD patients worldwide from 2001 to 2010.[7] In South Africa, no current information is available on the numbers or the outcomes of patients with CKD or ESRD. However, the SA Dialysis and Transplant Registry is being re-launched by the South African Renal Society and their initial reports should be released in the first half of 2006.

Diabetic nephropathy is one of the leading causes of CKD and ESRD, and the global epidemic of obesity and type 2 diabetes will therefore result in millions of new cases of CKD. What is of particular concern is that most of these cases will be from the developing world, where there are usually scant resources available to deal with the problem.[9] It is therefore imperative that the focus be turned to the prevention of CKD, and the slowing of the progression of the early stages of CKD to ESRD with its serious and costly complications.

There is convincing evidence that the adverse complications of CKD can be prevented or delayed by effective treatment of the earlier stages of CKD, using strategies which include (among others) good blood pressure control and blockade of the renin angiotensin system.[10,11] However, there is much variability in the translation of research findings to improvements in clinical practice. The successful implementation of rigorously developed evidence-based clinical practice guidelines offers a way of reducing this variability of care and improving patient outcomes.

Poor outcomes and variations in clinical practice

Differences in renal patient survival in different countries came to the fore in 1989 at the Dallas symposium on morbidity and mortality of dialysis patients, with the USA recording the highest all-cause annual mortality (22 - 24%).[12] For a patient with CKD in the USA, the outcome is worse than for an equivalent patient with a diagnosis of colon or prostate cancer.[13] It is thought that differences in practice patterns may be responsible for these differences in outcomes. The Third National Health and Nutrition Examination Surveys (NHANES III) in the USA revealed that only 27% of patients with CKD had a blood pressure < 140/90 mmHg, and a majority of patients had severe anaemia (mean haematocrit 27.7%), with only one quarter being prescribed erythropoietin despite insurance cover being available for most of them. Despite the clear benefits of renal transplantation, most eligible patients had not been placed on a transplant waiting list 6 months after beginning dialysis. Lastly, more than 50% of patients on the US ESRD programme are malnourished.[13]

While we lack good data for South Africa, there is no reason to believe that we do not have similar problems, with failure to reach therapeutic targets and lack of awareness of clinical practice guidelines or guidelines not being effectively implemented.[14]

Evidence-based clinical practice guidelines

The first clinical practice guidelines in nephrology were developed in 1993 and dealt with the measurement of the dose of haemodialysis.[15] In 1995 the US National Kidney Foundation (NKF) launched its Dialysis Outcomes Quality Initiative (DOQI), focusing on the

adequacy of haemodialysis and peritoneal dialysis, vascular access and anaemia management.[16] These guidelines changed clinical practice patterns and impacted favourably on the quality of care.[17] In 1999 a new initiative was launched by the NKF – the Kidney Disease Outcomes Initiative (K/DOQI) broadened the scope of the earlier project to include all patients with kidney disease, from the earliest stages of kidney damage to end-stage kidney failure requiring dialysis and transplantation. The European Renal Association-European Dialysis and Transplantation Association have produced the European Best Practice Guidelines (EBPG), and clinical practice guidelines have also been developed by the Canadian Society of Nephrology, the United Kingdom Renal Association, and the Australian and New Zealand Society of Nephrology.[1]

Kidney disease: Improving global outcomes

While there may be regional differences in risk factors and in available resources, the complications and problems of patients with kidney disease are universal and so is the science and evidence-based approach to these problems. It has therefore become clear that a uniform and global approach to developing and implementing clinical practice guidelines is required. To this end a new global organisation, Kidney Disease: Improving Global Outcomes (KDIGO), has been formed in an attempt to 'improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines'.[1] The KDIGO Board of Directors includes world leaders in nephrology, with representation from North and South America, Europe, Africa and the Far East. Different work groups will focus on (*i*) a uniform system of evidence rating; (*ii*) the adoption of a common evaluation, classification and nomenclature for CKD worldwide; (*iii*) the establishment of a database of currently available guidelines; (*iv*) the implementation of guidelines; (*v*) development efforts in regions without guidelines; (*vi*) fostering co-ordination between K/DOQI and EBPG; and (*vii*) bone and mineral metabolism.

A standardised and universally accepted scheme for the detection and classification of CKD will do much to raise awareness of this important problem, and is essential for the international development and implementation of clinical practice guidelines. As one of their first projects, KDIGO recently completed a worldwide survey, then sponsored a controversies conference, which led to the publication of a position paper on the definition and classification of chronic kidney disease.[18] In essence, the K/DOQI definition and classification were accepted, with clarifications. CKD is defined as kidney damage or a glomerular filtration rate (GFR) of < 60 ml/min/1.73 m^2 for 3 months or more, irrespective of the cause. Kidney damage may be indicated by the presence of albuminuria (albumin: creatinine ratio > 30 mg/g) on random urine specimens, while GFR should be estimated from serum creatinine using prediction equations such as the Cockcroft Gault formula or the Modification of Diet in Renal Disease (MDRD) equation. The diagnosis of CKD does not require 24-hour urine collections for creatinine clearance or protein quantification.

Role of nutrition

Restriction of dietary protein slows the progression of CKD in animals, but this has been difficult to demonstrate in humans, and remains the subject of controversy. A meta-analysis of 13 randomised and 11 non-randomised trials found only a modest benefit from protein restriction, and similar results were obtained from the MDRD study, the largest study to examine this issue to date.[19,20] In contrast, the adverse outcomes resulting from malnutrition are clear, and this should be the all-important consideration in the South African situation.

Protein-energy malnutrition and inflammation are common in patients with chronic kidney disease and worsen with progression toward end-stage renal disease. These are major predictors of poor clinical outcome, as reflected by the strong association between hypoalbuminaemia and cardiovascular disease. Among dialysis patients, traditional indicators of overnutrition (high cholesterol or body mass index (BMI)), which are deleterious in the general population, are associated with better outcomes, while a low BMI and low cholesterol or creatinine are risk factors for a poor outcome. These paradoxical relationships between nutritional markers and outcome are referred to as 'reverse epidemiology'.

In the Dialysis Outcomes and Practice Patterns Study (DOPPS), which now includes the investigation of patient profiles, therapies, practices and outcomes in 12 countries, nutrition-related parameters associated with increased mortality included low BMI, low subjective global assessment (SGA) score, and hypoalbuminaemia. Mortality risk was increased 1.38 times with serum albumin levels below 35 g/l. In the US patient cohort there was a 2.12-fold increase of the relative risk of death for the lowest quartile (serum albumin < 33 g/l) compared with the highest quartile (> 40 g/l). A very simple modified SGA was used in DOPPS, and correlated well with other nutritional indices in different populations of patients and when applied by health professionals from different countries and cultures.[19-21]

It has been suggested that inflammation is the cause of both malnutrition and CVD. The terms malnutrition-inflammation complex syndrome (MICS) and

malnutrition-inflammation-atherosclerosis (MIA) syndrome have been coined to indicate this interaction and the important contribution of both of these conditions to poor clinical outcome.[22-24] Causes of inflammation in dialysis patients include, among others, exposure to dialysis membranes or peritoneal dialysis fluid, poor water quality, peritonitis, and other infections. More attention is now being focused on nutritional or anti-inflammatory interventions, but so far no randomised clinical trials have specifically examined the effect of such interventions on malnutrition and improved outcomes. It still remains unclear whether the association with worse outcomes is related to malnutrition at the time of initiation of dialysis or whether it is secondary to changes in nutritional status of ESRD patients over time.[25] Clearly, a definite need exists for outcomes research in CKD related to nutrition, and secondly, for the effective implementation of evidence-based guidelines where these have already been established.

There can be no doubt that the active participation of a dietician is essential for any programme managing patients with CKD. The K/DOQI guidelines, which have been widely accepted, recommend that patients on maintenance dialysis have monthly serum albumin and creatinine measurements, and 6-monthly dietary assessments by a qualified dietician.[26] This includes a subjective global assessment, and a dietary interview which also reviews a 3-day dietary record. The DOPPS survey found wide variability in the availability of a renal dietician, from 20% in Spain to 85% in the UK. The percentage of patients who had been counselled in the previous 6 months varied from 7% (in Italy) to 75% (in the UK).[21]

The survey by Herselman *et al*.[27] in this issue of the *Journal* found that while most South African dieticians are following accepted guidelines, there is still significant uncertainty about, and deviation from, best practices.[27] As this study was done in 2001, it would be important to repeat it, especially with the growth in the number of private dialysis centres. It is likely that as more patients are being managed outside of the main academic hospitals, they would be counselled by a general dietician and not a specialist renal dietician. Providing easy access to relevant nutritional guidelines for dieticians and other interested parties is therefore particularly important and in this light the paper by Herselman and Esau on dietary exchange lists tailored to the South African patient is a welcome addition.[28] This information is available on the website of the Nutrition Information Centre of the University of Stellenbosch (**http://www.sun.ac/nicus**). Future studies should examine not only whether South African dieticians are implementing best practices, but also look at the referral of patients with CKD and whether nephrologists, physicians and providers of dialysis services are making optimal use of the expertise of our dieticians in their ongoing quest to improve the outcomes of their patients.

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