

## Epidemiology and Classification of Chronic Kidney Disease and Management of Diabetic Nephropathy

a report by

**Althea Mahon**

President, European Dialysis & Transplant Nurses Association/European Renal Care

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The number of patients with chronic kidney disease (CKD) and the subsequent need for renal replacement therapy (RRT) has reached epidemic proportion and is anticipated to rise further. Worldwide, it is estimated that over 1.1 million patients with end-stage renal disease (ESRD) currently require maintenance dialysis, and this number is increasing at a rate of 7% per year.<sup>1</sup> If the trend continues, the number will exceed 2 million by 2010.<sup>2</sup> This figure excludes developing countries, where there is less availability of and access to dialysis services, and is therefore an underestimate of the true demand. The most common cause of chronic renal failure is diabetic nephropathy. This article examines the epidemiology and classification of CKD and the management of diabetic nephropathy.

### The Burden of ESRD and CKD

In the UK, the incidence of ESRD has doubled over the last ten years and has now reached 101 patients per million of population (pmp).<sup>3</sup> This is below the European and US averages of approximately 135pmp and 336pmp, respectively.<sup>4</sup> Studies that have supplied data on the prevalence of CKD provide the opportunity to plan nephrology service requirements and develop stronger working relationships with the primary care teams in the community.

Studies such as the National Health And Nutrition Examination Survey (NHANES), which provided data on an adult unselected population, estimated that 4.7% of US adults had CKD stage 3 or higher (defined as an estimated glomerular filtration rate (eGFR) of <60ml/min/1.73m<sup>2</sup>). They also estimated that up to 11% of the general population (19.2 million) has some degree of CKD.<sup>5</sup> Similarly, a study of 112,215 patients registered with general practices in Greater Manchester, Kent and Surrey, UK, showed a prevalence of 4.9%.<sup>4,6</sup> They also estimated that 5.9 million people may have stage 1 CKD with normal kidney function. In the Australian Diabetes, Obesity and Lifestyle (AusDiab) study of 10,949 patients, a prevalence of 11.2% of CKD stages 3–5 was found, but this does not provide an estimate for the general population.<sup>7</sup>

### Rise in CKD Detection

The rise in diagnosis of CKD is multifactorial but associated with the ageing population. As technology and medical interventions are improving, people live longer, which also impacts on chronic disease populations. The incidence of diabetes has reached epidemic proportions throughout the world, with an expected doubling in the number of patients with type 2 diabetes in the next 25 years.<sup>8</sup> This, in turn, will lead to an increased incidence of diabetic



Althea Mahon is President of the European Dialysis & Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA), a multidisciplinary association with the mission to provide educational initiatives to assist in the development of all renal healthcare professionals. She is a consultant nurse at Barts and The London NHS Trust, where she is responsible for the chronic kidney disease screening programme. Ms Mahon is also a visiting honorary senior lecturer for City University. She has been working in renal care for the past 15 years in all areas of nephrology nursing and represents renal nursing nationally in many policy groups.

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Table 1: Categories Recommended for the KDOQI Staging of CKD<sup>21</sup>

CKD Stage	GFR	Description
1	>90ml/min/1.73 m <sup>2</sup> *	Kidney damage with normal GFR
2	60–89ml/min/1.73 m <sup>2</sup> *	Kidney damage with mildly reduced GFR
3	30–59ml/min/1.73 m <sup>2</sup>	Moderately reduced GFR
4	15–29ml/min/1.73 m <sup>2</sup>	Severely reduced GFR
5	<15ml/min/1.73 m <sup>2</sup>	Kidney failure

\*To classify stage 1 or 2 CKD, there must also be other evidence of chronic kidney damage defined by (if present for at least three months) structural or functional abnormalities of the kidney, e.g. proteinuria and haematuria.

nephropathy, with approximately 30% progressing to stage 5 CKD. CKD prevalence increases with age, and men with CKD have a more rapid decline in renal function and progression of their renal disease than women.<sup>9,10</sup> Some ethnic populations have a higher prevalence of CKD.<sup>11,12</sup> For example, people from South Asia are at higher risk of CKD linked to diabetes, as there is a higher incidence of diabetes in this community.<sup>13</sup> Afro-Caribbeans and Africans are at greater risk of CKD due to their higher prevalence of hypertension.<sup>14</sup> The rise may also be due to the development of guidelines and simple blood-test-based formulae (e.g. eGFR) that allow for easier and earlier diagnosis of CKD and, thus, increased reporting.

#### Risk Factors for CKD

Risk factors for CKD include diabetes, cardiovascular disease, smoking, obesity, sedentary lifestyle and low socioeconomic status. UK studies have shown a higher incidence of CKD in deprived areas, which is consistent with US and Swedish studies.<sup>15–19</sup> Obesity

has become a global issue in developed countries, adding to the population of people with chronic disease. Those with diabetes and hypertension are at greatest risk and have a higher rate of renal problems than the normal population.<sup>20</sup> In the UK, diabetic nephropathy accounts for 18% of new patients commencing renal replacement therapy and makes up 11% of the prevalent patient population. This is not solely a UK phenomenon; in 2002, Australia reported that the country accepted 94pmp for RRT, of which 26% were diabetics. In Pakistan, the incidence of diabetics entering the programme is 42%, in Japan 37% and in the US 14.8%. This is a worldwide problem that needs to be addressed.<sup>1</sup>

#### Classification of CKD

There are clear guidelines and an internationally agreed staging system for CKD, which facilitates diagnosis and management. The National Kidney Foundation/Kidney Disease Outcome Quality Initiative (NKF/KDOQI) classification system is based on eGFR.<sup>21</sup> Until recently, the serum creatinine test was used as the standard test of renal excretory function. This is not, however, reliable as a screening test, as the relationship between GFR and serum creatinine is not linear. By the time the creatinine becomes elevated, there may already be a 50% reduction in kidney function. The most effective way to assess renal function and gauge the need for further investigation or referral is by using eGFR, a formula-based calculation of GFR. There are two recommended formulae to measure eGFR in patients with moderate to

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advanced CKD: modification of diet in renal disease (MDRD) and Cockcroft-Gault; but neither of these is particularly accurate in patients with mild or normal kidney function. Based on current evidence, MDRD is the recommended equation, as it gives an estimate of GFR that is normalised to a body surface area of 1.73m<sup>2</sup> and does not require the patient's weight. For Afro-Caribbean patients, the eGFR is then multiplied by 1.21. The eGFR is not an appropriate measure for patients with acute renal failure, as it relies on a stable serum creatinine for its predictive accuracy.<sup>22</sup>

An eGFR of 60–90ml/min/1.73m<sup>2</sup> on its own, without another physiological or structural renal abnormality, is not indicative of CKD. Only a minority of people with stage 1 or 2 CKD will go on

to develop more advanced renal disease, with symptoms usually only appearing at stage 4.<sup>9</sup> In order to diagnose CKD stage 1 or 2, a urinalysis is essential.<sup>23,24</sup>

### CKD Interventions

CKD is progressive, but the progression can be slowed down with good management. Several studies have shown that good glycaemic control can decrease the risk of macrovascular disease in both type 1 and 2 diabetes.<sup>25–27</sup> There is also evidence that tight control in CKD patients can slow the progression from microalbuminuria to macroalbuminuria. Interventions to minimise progression of CKD include lifestyle changes and reduction in blood pressure, irrespective of the diagnosis of hypertension or diabetes. The use of angiotensin-converting enzyme (ACE) inhibitors or

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angiotensin receptor blockers (ARBs) is effective at reducing progression when there is concurrent proteinuria. Target blood pressure is below 130/75 millimetres of mercury (mmHg), and this is supported by the National Institute of Clinical Excellence (NICE), which found that reducing the blood pressure to less than 130/75mmHg correlated to a reduction in the progression of renal disease in type 2 diabetics with albuminuria.<sup>28</sup> Early treatment preserves kidney function and is cost-effective.<sup>23</sup> Other interventions to minimise progression of CKD in diabetics include

outcomes of kidney disease patients worldwide through promoting co-ordination, collaboration and integration of initiatives to develop and implement clinical practice guidelines.” The KDIGO and the ISN are now working together on the development of a CKD strategy.<sup>29,30</sup>

### Summary

The majority of the CKD population have one or more co-morbid condition with a known higher

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lifestyle changes, e.g. smoking cessation, low-cholesterol diet and an increase in exercise.

The main hurdle to overcome is to ensure the implementation of guidelines and develop a global preventive approach. Locally agreed referral guidelines from primary care and agreed guidelines between diabetic and nephrology teams will improve the detection and management of CKD. The International Society of Nephrology (ISN) has, for some time, had a focus on prevention, and the Commission on Global Advancement of Nephrology (COMGAN) believes in improving global outcomes of kidney disease. The new initiative by the Kidney Disease: Improving Global Outcomes (KDIGO) group aims to develop a global approach to managing the CKD epidemic. The group’s mission statement is: “Improve the care and

prevalence in ethnic minorities and lower socio-economic groups. Without effective prevention and early detection programmes, the incidence rate of CKD will continue to rise. Early detection and referral of CKD patients to nephrology teams is pivotal to slowing the progression to ESRD and reducing the demand for dialysis. It has also been demonstrated that patients referred early have better outcomes.<sup>29,31</sup> Diabetic nephropathy progression can be slowed by effectively tightening glycaemic control, lowering blood pressure to a minimum of 130/75mmHg with ACE inhibitors or ARBs, lowering cholesterol and educating patients on how to lead a healthy lifestyle. The World Health Organization (WHO) has set a goal to reduce chronic disease mortality by 2% a year for the next decade and, therefore, more emphasis needs to be placed on prevention of CKD and the need for RRT in this patient population.<sup>32</sup> ■

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