Epidemiology and causes of chronic kidney disease

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Abstract

Chronic kidney disease (CKD) is a common condition that has significant implications for patients' health and healthcare budgets. CKD is diagnosed if evidence of kidney damage has been present for more than 3 months; it is divided into stages depending on the estimated glomerular filtration rate (eGFR) and urine albumin:creatinine ratio (UACR). CKD is often asymptomatic; populations must be screened to determine its prevalence, so the reported prevalence depends on the population studied and screening methods used. Risk factors for CKD can be divided into initiating and perpetuating factors, and include genetic factors, ethnicity, socio-economic factors and age. There are several causes of CKD, the most common being diabetes mellitus. In order to reduce the burden of CKD, it is essential to recognize which patients are at most risk so that they can be screened and treated early. It is hoped that, with early recognition and treatment, the number of patients with CKD progressing to end-stage kidney disease (ESKD) and the need for renal replacement therapy will be reduced.

Keywords Causes; chronic kidney disease; chronic kidney failure; definition; prevalence; renal replacement therapy; risk factors

What's new?

- There is a new CKD classification that uses estimated GFR and urinary albumin to creatinine ratio
- This means patients can be risk stratified and allows focused treatment
- Acute kidney injury is increasingly being recognized as a risk factor for future CKD

Introduction

Chronic kidney disease (CKD) is a common condition, associated with a significantly increased risk of hospital admission, morbidity and death due to cardiovascular disease.[1] CKD can also progress to end-stage kidney disease (ESKD), which results in patients requiring dialysis and/or renal transplantation, together termed renal replacement therapy (RRT). This has a considerable effect on quality of life and survival: chronic dialysis is associated with an annual mortality rate of approximately 20%. The treatment of CKD also represents a considerable economic burden; in 2009–2010 the cost of CKD to the NHS in England was estimated at £1.44–1.45 billion, which accounted for 1.3% of the total NHS budget.[1] In the USA, Medicare spending for 616,000 patients with ESKD in 2011 reached $49.3 billion, representing 7.2% of total Medicare spending.[2]

To reduce the burden of ESKD for individuals and healthcare systems, and facilitate interventions to reduce risk, it is essential to understand the causes of CKD and associated risk factors. Once CKD develops, treatment aims to minimize the effect of associated risk factors on the rate of CKD progression.

This article will discuss the definition and epidemiology of CKD as well as highlight risk factors for its development and progression.

Definition and staging of CKD

The publication in 2012 of the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for evaluation and management of CKD modified the classification of CKD first proposed in 2002. Diagnosis still requires evidence of kidney damage that has been present for at least 3 months, but staging is then based on the estimated glomerular filtration rate (eGFR) and the urinary albumin: creatinine ratio (UACR) combined (see Table 2 in Management of chronic kidney disease, pages 454–461 of this issue). This allows a patient's risk of developing CKD-associated morbidity to be stratified into low, moderate and high. For example, a patient with stage G4A3 CKD would at greater risk than someone with stage G1A1 CKD. Therefore treatment and frequency of follow-up can be tailored accordingly. The KDIGO classification has recently also been adopted by the National Institute for Health and Care Excellence. GFR is estimated from a measurement of serum creatinine, using a mathematical formula that also takes into account age, gender and ethnicity. The formula now recommended is the CKD-EPI equation as it has less bias, improved precision and greater accuracy compared with the previously used MDRD equation.[3]

Epidemiology

As CKD is often asymptomatic, studies to determine its prevalence must rely on community-based screening. As Table 1 shows, there is considerable variation in prevalence depending on the methods used and the populations studied. Data are limited for many developing countries and research to obtain data in these countries is being promoted by the International Society of Nephrology. CKD prevalence may be increasing in some countries. Analysis of a sample of the US population between 1999 and 2004 quoted a population prevalence for CKD stages 1–5 of 13.1%, a value substantially higher than the 10% reported in the previous cohort (1988–1994). However, this may not represent a true increase, given differences in creatinine measurement and calibration over time.[4]

Risk factors

It is important to identify factors that are associated with an increased risk of developing CKD, so that screening programmes

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CKD prevalence in a range of populations

Country	Study	Number of subjects	Age of subjects	Definition of CKD	Prevalence of CKD
Australia	AUSDIAB[12]	11,247	≥25	CKD 1–5	16%
D.R. of Congo	Sumaili et al.[13]	503	≥20	CKD 1–5	12.4%
Norway	HUNT 2[14]	65,604	≥20	CKD 3–5	4.7%
South China	Chen et al.[15]	6311	>20	CKD 1–5	12.1%
UK	HSE 2010[16]	6000	≥16	CKD 1–5	13%
USA	NHANES IV[5]	13,233	≥20	CKD 1–4	13.1%

Table 1

can be targeted at high-risk groups. Risk factors relating to CKD can be divided into two main groups: initiating factors that increase the risk of developing CKD; and perpetuating factors that increase the risk of CKD progression to ESKD (Table 2).[5]

Genetic factors

Hereditary renal diseases that result from single gene defects (e.g. polycystic kidney disease, Alport's disease and Fabry's disease) make up only a small proportion of cases. More significant are genetic factors that increase the risk of developing multi-factorial CKD in a person with a family history of CKD. For example, the increased risk of developing diabetes mellitus, a strong initiating risk factor for CKD, associated with a positive family history is well recognized. Furthermore, if one first-degree relative has ESKD, the risk of ESKD has been shown to increase 1.3 times (95% CI 0.7–2.6), and if two are affected, 10.4 times (95% CI 2.7–40.2).[6]

CKD initiating and perpetuating factors[6]

Initiating factors	Perpetuating factors
Increasing age	African–American race
Gender	Proteinuria
Ethnicity	Hypertension
Family history of CKD	High dietary protein intake
Socio-economic status	Obesity
Metabolic syndrome	Anaemia
High normal urinary albumin excretion	Dyslipidaemia
Dyslipidaemia	Nephrotoxins
Nephrotoxins (NSAIDs, antibiotics, radiological contrast, light chains)	Smoking
Primary renal disease	Cardiovascular disease
Urological disorders (obstruction, recurrent urinary infections)	Acute kidney injury
Cardiovascular disease	
Diabetes mellitus	
Acute kidney injury	

CKD, chronic kidney disease; NSAIDs, non-steroidal anti-inflammatory drugs.

Table 2

Ethnicity

Ethnicity is difficult to qualify as a risk factor in isolation, due to its association with a number of confounding factors related to socio-economic status. However, in epidemiological studies, ethnicity remains a significant risk factor even after socio-economic factors are taken into account. The US Renal Data System (USRDS) reports that the annual incidence of ESKD in African Americans and Native Americans is 3.4 and 1.6 times greater, respectively, than in white Americans.[2] However, CKD population prevalences (13.8% in white Americans and 11.7% in African Americans[4]) suggest that, among African Americans, CKD is less prevalent but more likely to progress to ESKD. Similarly, black patients with diabetes have been found to be 2.4–2.7 times, and other ethnic minorities 1.6–1.7 times more likely to progress to ESKD than non-Hispanic whites.[7] Recently, the high prevalence of CKD among African Americans has been attributed to the high prevalence of specific alleles for the *APOL1* gene.[8] Interestingly, these alleles also confer resistance to the tsetse fly-borne parasite, *Trypanosoma brucei*, which causes 'sleeping sickness' in parts of Africa, and this may explain the high prevalence of the risk alleles the African American population.[8]

Socio-economic factors

Socio-economic factors affecting CKD incidence, prevalence and progression include income, education and environmental factors, which are all potentially modifiable. In the UK, there is an approximate 40% increase in CKD incidence among the highest quintile of social deprivation compared with the lowest quintile.[9] Similarly in the USA, white people have an 86% increase in the odds of having CKD if they are in the lowest income quintile compared with the highest.[10]

Age

The prevalence and incidence of CKD increases with increasing age, implying that nephron loss may be a 'normal' part of ageing. In some studies, the rate of GFR decline is reported to be greater with increasing age but, paradoxically, the risk of progression to ESKD is decreased due to the competing risk of death. Thus, most elderly patients with CKD will die before they progress to ESKD.[5]

Gender

Though there is some variation, the most consistent finding across studies is that the incidence of CKD and ESKD is greater in men than women. Men also demonstrate greater progression