Editorial Review

The impact of CKD identification in large countries: the burden of illness

Vivekanand Jha1, Angela Yee-Moon Wang2 and HaiYan Wang3

1Department of Nephrology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 2Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, China and 3Renal Division, Department of Medicine, Peking University First Hospital, Beijing, China

Correspondence and offprint requests to: Vivekanand Jha; E-mail: vjha@pginephro.org

Abstract

Chronic kidney disease (CKD) is becoming a major public health issue worldwide and an important contributor to the overall non-communicable disease burden. It is associated with major serious consequences including increased risk of mortality, end-stage renal disease, accelerated cardiovascular disease (CVD), mineral and bone disease, adverse metabolic and nutritional consequences, infections, reduced cognitive function and increased risk of acute kidney injury. Mortality from CVD is estimated to be at least 8- to 10-fold higher in CKD subjects compared to non-CKD subjects. Estimates from different parts of the world, especially large countries, reveal an increasing incidence and prevalence of CKD. This is partly attributed to the global increasing prevalence of diabetes, hypertension, obesity and CVD. The global economic impact of CKD is tremendous. This calls for the need of a global effort to raise awareness of CKD, to incorporate prevention of CKD progression program in the public health agenda and to implement programs for early screening and detection of CKD, especially in high-risk population so to allow early institution of treatment to prevent further CKD progression. Hopefully, by doing so, we may reduce CKD burden globally over time and, most importantly, improve the health outcomes of patients with CKD.

Keywords: burden of disease; cardiovascular disease; chronic kidney disease; diabetes; health care costs

Over the last quarter-century, chronic non-communicable diseases (NCDs) have emerged as important causes of morbidity and mortality throughout the world. In 2005, NCDs were estimated to cause >60% (35 million) of all deaths [1], with over 80% in the low- and middle-income countries.

Chronic kidney disease (CKD) is an important contributor to the NCD burden. The major consequences of CKD include loss of kidney function leading to end-stage renal disease (ESRD), accelerated cardiovascular disease (CVD) and death. Other important complications include anemia, bone disease, infections, reduced cognitive function and increased risk of acute kidney injury (AKI).

Reliable, inexpensive and periodic assessment of disease burden is required to understand of disease trends, role of specific causes, detect new conditions and develop evidence-based health policy, allocate health care resources and evaluate efficacy of existing programs. Disease burden can be estimated by measuring the deaths or disability adjusted life years (DALYs) attributable to the disease, estimating disease incidence and prevalence rates and burden of risk factors and by measuring its economic impact.

Eight of the 10 largest countries in the world (China, India, Pakistan, Bangladesh, Russia, Brazil, Indonesia and Nigeria) have been classified as ‘developing countries’ by the World Bank. These countries are home to a large, quickly growing and predominantly poor population; China and India alone account for over one-third of world population. Measuring disease burden in large underdeveloped countries presents unique challenges. Large country populations are heterogeneous in terms of ethnic composition, socioeconomic development, rural–urban divide and access to health care. Parts of these countries exhibit characteristics found in developed countries, with an affluent urban population experiencing a steady increase in services, whereas the remainder is plagued with problems associated with poor economies. Burden of disease is also impacted by the administrative systems. Many large countries have a federal structure, in which local administrative units make major decisions about health care delivery, introducing another level of diversity. Region-wide data collection is important, as regional administrative unit subpopulations might exceed the populations of many countries.

Death and DALYs due to CKD

Accurate recording of cause of death (COD) is the most robust indicator of the effect of a disease on populations.

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Incidence and prevalence

End-stage renal disease

A major consequence of CKD is ESRD. The global dialysis population was 1.1 million in 2002 and, with a 7% annual growth, is projected to exceed 2 million [6]. ESRD registries have allowed calculation of incidence rates in several countries. Lack of organized ESRD treatment programs has precluded establishment of ESRD registries in some large developing countries. Reported data are rough estimates based on individual experience. Hospital-based data cannot provide incidence estimates because of incomplete coverage, the inability of many patients to reach a hospital and the lack of a proper referral system [7]. Figure 1 gives the ESRD incidence rates (per million population, p.m.p.) in selected large countries.

The prevalence of patients on dialysis (p.m.p.) in China was 33.2 in 1999, 51.7 in 2008 and 92.3 in 2009 (F.F. Hou, unpublished data). The rate of growth of the dialysis population in China is estimated at 20–30% per year [14]. In one population-based study conducted in the Central Indian city of Bhopal where a hospital provides free medical care to ~570 000 individuals, the crude- and age-adjusted ESRD incidence rates were determined at 151 and 232 p.m.p., respectively [8]. If these figures are validated, it would mean that ~170 000–250 000 new patients need renal replacement therapy (RRT) every year in India. The prevalence of ESRD patients in India is not known but is estimated to be ~55 000 and growing by ~10% every year. Currently, it is estimated that only ~10–15% of all ESRD patients receive RRT in China and India. The prevalent dialysis population has a high turnover rate, as patients who have initiated dialysis recently drop out due to economic reasons and are replaced by newly diagnosed patients [7]. According to the Brazilian Dialysis Census [15], ~92 000 patients were on dialysis in 2010, constituting the third largest dialysis population of any country in the world.

Chronic kidney disease

According to Wave III of the US National Health and Nutrition Evaluation Survey, 11% (19.2 million) of adults surveyed between 1988 and 1994 had CKD [16]. A repeat survey conducted between 1999 and 2004 estimated a higher prevalence of 13% [17]. Other large countries including China, Australia and other countries report similar CKD prevalence as the USA at 11%. This illustrates that the CKD burden is several folds higher than that of ESRD.

Data on CKD burden in developing countries are scanty, unvalidated and heterogeneous, making comparisons difficult. Older studies provided estimates based on creatinine cutoffs or Cockroft–Gault (CG) equation to define CKD, limiting their usefulness for comparative analysis. Recent studies have employed the Kidney Disease Outcomes Quality Initiative classification ([18, 19] Zhang, 2012 #231). New equations or correction factor for the original equation have been derived for Chinese, Japanese and Korean populations [20–22]. Such formulae have not yet been developed for populations in other large countries such as India, Pakistan, Bangladesh, Indonesia or Nigeria. Difference in reference glomerular filtration rate (GFR) method used in different studies and difference of GFR distribution in the population in which equation was developed also influence the expression of estimated GFR equation [23, 24].

A population-based survey from Brazil showed the prevalence of CKD (as defined by serum creatinine >1.3 and 1.1 mg/dL in men and women, respectively) to be 0.5% in adults (18–59 years) and 5.1% for the elderly (>60 years) [25]. In India, Mani [26] reported a prevalence of GFR <80 mL/min at 8.6/1000 population in rural areas that were served by a prevention program, whereas it was ~14/1000 in neighboring villages. Agarwal et al. [27] screened over 4700 individuals in urban communities of Delhi and found a 0.79% point prevalence of individuals with serum creatinine over 1.8 mg/dL on two occasions 3 months apart. In a cross-sectional survey of ~3400 healthy subjects over the age of 18 years, Varma et al. [19] found the prevalence of microalbuminuria and reduced GFR using the Chronic Kidney Disease Epidemiology Collaboration formula to be 10 and 13%, respectively. In another community-based study of ~5250 adults,
Singh et al. [18] found low GFR (<60 mL/min) using the CG equation in 13.3% and proteinuria in 2.5% of subjects.

A community-based screening for CKD in over 2000 subjects over the age of 40 years in Central Beijing reviewed that although 11.3% of subjects had at least one indicator of kidney damage, the awareness rate was only 7.2% among those with markers of injury [28]. A community-based screening of 2554 subjects in Shanghai reported a prevalence rate of CKD of 11.8% with the rate of awareness of 8.2% [29]. In a large cross-sectional national survey of 47 204 participants in China, testing for albuminuria and reduced renal function revealed the overall prevalence of CKD to be 10.6% (95% confidence interval 10.1–11.2%), yielding an estimated number of patients with CKD in China at 117.3 million [30].

Causes of CKD

The causes of ESRD are variable in different parts of the world. Table 1 gives a comparative listing of various causes of CKD in different countries. Diabetes and hypertension are emerging as the major causes in most countries [31]. Glomerulonephritides remain important in China, India and sub-Saharan Africa. Kidney disease associated with HIV infection was responsible for a major part of ESRD burden in Africa. It is estimated that ∼1–3.5 million black Africans will develop ESRD due to HIV associated nephropathy.

CKD is associated with an increased risk of AKI [34]. Compared to patients without CKD, patients with CKD who showed a transient increase in serum creatinine of as little as 0.3 mg/dL had an increased rate of progression to ESRD as well as mortality [35]. AKI may occur with the use of non-steroidal anti-inflammatory drugs, certain antibiotics, some cardiovascular medications or herbal medicine, thus emphasizing the need for early CKD detection and recognition, allowing adjustment or avoidance of medications.

CKD risk factor burden

Diabetes, hypertension, obesity, CVD and smoking are some of the major risk factors associated with CKD. A study from Southeast Asia with a 12-year follow-up in individuals with normal initial renal function found systolic hypertension, hyperuricemia and high body mass index to be independent predictors of the development of decreased kidney function [36]. Other risk factors include dependence on indigenous herbal systems of medicine, maternal malnutrition and low birth weight. Almost all these risk factors are exaggerated among the poor.

**Diabetes**

Diabetes is the biggest contributor to worldwide CKD and ESRD burden, accounting for 30–50% of all cases. Data calculated on the basis of studies from 91 countries projected the current world prevalence of diabetes among adults (aged 20–79 years) to be 6.4%, affecting 285 million adults, and is predicted to go up to 7.7% by 2030 at which time there will be 439 million adult diabetics [37]. The increase will be 69% in developing countries and a 20% in developed countries. India and China already have the largest number of diabetics in the world. The prevalence of diabetes in urban areas of China increased from 4.6% in 1996 to 6.4% in 2004 [14]. The number of diabetics is estimated to rise from ∼50 million currently to ∼87 million by 2030 in India and from 43 million to 63 million in China [37]. These projections, based on more recent studies, are more than those calculated by the WHO in 2004. Since diabetic nephropathy is already the most frequent cause of CKD, a significant increase in the CKD burden can be foreseen.

**Hypertension**

Hypertension is both a common cause as well as a major consequence of CKD. More than a quarter of the world’s adult population was estimated to have hypertension in 2000, two-thirds of which in developing countries. This number is projected to increase by ∼60% to 1.56 billion in 2025 [38]. It is therefore anticipated that the prevalence of CKD will also increase. Hypertension has been associated with an increased risk of development and progression of kidney disease [39, 40] as well as to the global increase in CVD. Furthermore, hypertension

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aData from [9, 15, 31, 32, 33] and Chen, APCN 2010.
control is poorer in the presence of CKD. This is evident from the Kidney Early Evaluation Program showing a prevalence of hypertension of 86%; despite treatment in 70% of subjects with high risk for CKD, only 13% achieved good blood pressure control [41]. A cross-sectional study conducted in three urban cities in northeast China from 2009 to 2010 including a total of over 25 000 adult subjects showed an overall prevalence of hypertension of 28.7%, only 28.2% received treatment and 3.7% had adequately controlled blood pressure [42]. Another nationwide survey conducted in over 1000 CKD subjects from China between 1999–2000 and 2004–2005 showed improved awareness and treatment over the two time periods, but adequate control of blood pressure remained low at 7.9 and 5.5%, respectively [43].

Cardiovascular disease

CVD is the most common NCD, accounting for about one third of all deaths globally. CVD and CKD share common risk factors such as hypertension, diabetes, smoking, obesity, hyperlipidemia and aging as well as some non-traditional risk factors, such as vitamin D deficiency, hyperphosphatemia, anemia and albuminuria/proteinuria. In addition, CVD is a well-recognized risk factor for CKD [44, 45]. The presence of CVD increases the risk of developing CKD and accelerates progression to ESRD [45, 46]. On the other hand, patients with CKD are at an accelerated risk of developing CVD and dying of it [47]. There is a strong independent graded relationship between decline in GFR with an increased risk of death, cardiovascular events and hospitalizations [48]. The inverse relationship between kidney function and increased mortality and cardiovascular risk appeared to continue even among patients approaching ESRD requiring dialysis [49, 50]. Furthermore, the presence of kidney dysfunction has been associated with an increased risk of mortality and adverse outcomes among subjects with heart failure or myocardial infarction [51, 52].

In an analysis conducted by pooling four community-based studies including over 26 000 individuals with over 10 years follow-up, CKD and CVD were strong additional independent predictors of mortality and adverse cardiovascular outcomes [33]. Even Stage 1 or 2 CKD is associated with an increased risk of adverse cardiovascular and renal outcomes [54]. In the Cardiovascular Health Study which included 6000 USA subjects over the age of 55 years, patients with CKD alone showed an equivalent risk for cardiovascular events and mortality to those with diabetes or previous myocardial infarction [55]. These data suggest CKD should be considered a risk factor equivalent to that of diabetes or heart disease.

Nutrition and indigenous medicines

Despite the improvement in maternal and infant mortality rates, a high prevalence of maternal malnutrition and low birth weight deliveries is still seen in these countries. The role of intrauterine factors on the development of CKD in adulthood has been postulated but not been explored properly. In an Indian cohort, low birth weight and early malnutrition were shown to be associated with later development of metabolic syndrome, diabetes and diabetic nephropathy [56]. The finding of a high prevalence of proteinuria and blood pressure in South Asian children and CKD of unknown etiology may also be explained by this mechanism [57, 58].

Also not investigated is the role of herbal medicines on CKD burden. A significant proportion of the population in these countries, especially in Asia and Africa, depend on indigenous systems of medicine. Studies from Taiwan and Beijing have documented an association between use of aristolochic acid-containing herbs and development of CKD [59, 60]. In the national survey in Taiwan, regular users of Chinese herbal medicines showed a 20% increased risk of developing CKD [61].

Economic burden of CKD

The economic consequences of CKD can be in the form of direct loss of gross domestic product as a result of ill health, losses due to household financing of care, changes in consumption patterns and welfare costs as well as the financial cost incurred in managing patients with CKD and ESRD. Analysis from developed nations showed that 2–3% of the health care expenditure is used to provide treatment for ESRD patients even though they accounted for only 0.02–0.03% of the total population [62]. The expenditure on ESRD was estimated to be 6.4% of the entire US Medicare budget in 2006, 4.1% of the total health care budget in Japan and 3.24% of the national for health expenditure in South Korea. The Australian Institute of Health and Welfare estimated that the total recurrent health expenditure on CKD in 2000–01 was $647 million, 1.3% of total recurrent health expenditure [63].

The economic cost associated with milder forms of CKD was even higher. For instance, according to data from the US Renal Data System, Medicare expenditures on CKD patients exceeded $60 billion in 2007 versus $25 billion for ESRD and represented 27% of the total Medicare budget. The expenditures further increased with the presence of diabetes and heart failure [64]. Treatment of AKI is also expensive, estimated at ~$10 billion per year in the USA, and roughly represented 40% of the costs of treating patients with ESRD [65].

The economic burden of CKD has not been evaluated as well in the developing countries but is expected to be even higher. Experience suggests that care for NCDs is expensive, far out of proportion to the income. A session of hemodialysis costs US$100 in Nigeria [32], twice the minimum monthly wage paid to federal government workers. In India, the cost varies from US$20 to 60, depending on the type of facility. CKD care, particularly among those presenting for the first time with advanced disease, is likely to lead to “catastrophic” or “impoverishing” health expenditure [66]. Patients must travel, often with families, to urban hospitals that can provide specialized care including dialysis. A majority of ESRD patients present to hospital with multiple complications, need admission and emergency dialysis [7]. The cost of treatment in emergency setting further adds to the costs.
Future outlook

The burden of CKD in large countries is expected to rise because of the increase in risk factor burden as well as demand for treatment as a result of improved economy. The population is aging constantly as a result of improvement in life expectancy and reduced fertility rates. This will lead to an increase in the elderly population who has the highest CKD prevalence. Unless there is commensurate improvement in social welfare and public health, this has the potential to affect the development of these countries.

The high CKD burden and projected increase coupled with the high cost and lack of resources for treating patients with advanced stages of CKD make prevention the most rational approach. This can be achieved by early identification of those at risk of developing CKD, screening and detecting early disease in the high-risk population using cheap and simple tests and using appropriate renoprotective measures to reduce progression. A number of studies have shown that it is possible to slow down or even halt the progression of kidney disease. Raising public awareness, lifestyle modification and risk factor control will also help CKD burden. In view of the close linkage and overlapping management strategies, programs to combat CKD, diabetes, hypertension, obesity and CVD need to be closely integrated. Policy makers, health care workers and primary care physicians need to be engaged in the process. Studies are required to examine the cost-effectiveness of such approaches in different countries.

Promotional activities by the organizations such as the International Society of Nephrology (ISN) including events such as the World Kidney Day have increased awareness about CKD. The prevention projects funded by the ISN Global Outreach program have allowed determination of CKD burden in many areas and are now evaluating risk factors [67]. Setting up efficient data collection systems is necessary to continuously evaluate, monitor and measure the success of these programs. Experience has shown the need for independence, transparency and easy and routine access to data since disease control program officials have been known to over- or underreport disease and success metrics to suit their own interest. Many of these goals can be achieved through the use of information technology tools.

Conclusions

Measurement of kidney disease burden is important for understanding disease trends and development of evidence-based health policy. There is no reliable data on the contribution of CKD on overall population mortality. Despite limitations, the prevalence studies suggest a staggering CKD load and present a major public health problem for the health care planners. Diabetes and hypertension are the leading causes of CKD throughout the world. CKD increases risk of development of CVD and AKI. CKD care is expensive and imposes large micro- and macro-economic burden on individuals and countries. The projected increase in the prevalence of diabetes, hypertension and CVD is likely to increase the CKD burden further. High-quality studies using uniform definitions and methodology are required to accurately assess disease burden and help health care policy planners to devise appropriate preventive strategies.

Conflict of interest statement. None declared.

References


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