The Global Epidemiology of Diabetes and Kidney Disease

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The prevalence of diabetes is increasing worldwide, with the greatest increases occurring in low- and middle-income countries. In most developed countries, type 2 diabetes is presently the leading cause of end-stage renal disease and also contributes substantially to cardiovascular disease. In countries with weaker economies type 2 diabetes is rapidly replacing communicable diseases as a leading cause of kidney disease and is increasingly competing for scarce health care resources. Here, we present a narrative review of the prevalence and incidence of diabetes-related kidney disease worldwide. Mortality among those with diabetes and kidney disease will also be explored. Given the high morbidity and mortality associated with chronic kidney disease, we will also examine the level of awareness of this disease among people who have it.

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INTRODUCTION

Diabetes mellitus is a major public health challenge, both in developed and developing nations.[1] In 2015, an estimated 8.8% or 415 million people were living with diabetes worldwide, nearly double the 4.6% (151 million) estimated in 2000, and this number is expected to increase to 10.4% (642 million) by 2040.[2] The most commonly diagnosed forms of diabetes are type 2 and type 1. Other types of diabetes, including gestational diabetes, monogenic diabetes, and secondary forms of diabetes, are much less common.

Type 2 diabetes accounts for 87% to 91% of the global burden of diabetes and is the most frequent cause of kidney complications.[3] The onset of type 2 diabetes, unlike that of type 1 diabetes, often goes undetected and therefore both prevalence and incidence rates are generally underreported. The age-adjusted prevalence of type 2 diabetes is highest in North America, the Caribbean, Western Pacific, Middle East, and North Africa and lowest in sub-Saharan Africa.[2,4] Most people with type 2 diabetes live in urban areas and in low- and middle-income countries, which are also projected to experience the highest increase in national prevalence of type 2 diabetes over the coming decades.[2] The highest rates of type 2 diabetes are reported in certain ethnic groups across the globe, including the indigenous people of Nauru, American Indians in the United States, First Nations people in Canada, and indigenous people in Australia and New Zealand.[4-6]

Type 1 diabetes accounts for 7% to 12% of the global burden of diabetes,[2,3,7] its incidence varying substantially by geography,[8] from around 60 cases per 100,000 people/y in Finland[9] and 40 cases per 100,000 people/y in Sardinia[10] to about 0.1 cases per 100,000 people/y in China, India, and Venezuela.[10] Half a million children aged <14 years lived with type 1 diabetes worldwide in 2015, with the highest number residing in Europe, North America, and South-East Asia.[2] In the United States, 1.25 million children and adults have type 1 diabetes[11] and this number continues to increase.[12]

Although the latest estimate from the International Diabetes Federation shows that prevalence of diabetes is increasing,[2] reports have emerged indicating that prevalence may be stabilizing in some populations. A recent study on adults in the United States,[13] using the National Health Interview Survey (NHIS), showed a doubling in the prevalence and incidence of diagnosed diabetes during 1990 to 2008 followed by a plateauing between 2008 and 2012. The age-adjusted prevalence of diabetes was 3.5% in 1990, 7.9% in 2008, and 8.3% in 2012. The age-adjusted incidence per 1000 persons was 3.2 in 1990, 8.8 in 2008, and 7.1 in 2012. The study also reported that both prevalence and incidence of diabetes continue to increase in non-Hispanic black and Hispanic subpopulations and those with less than high school education. Similarly, a study using a large US claims database reported that the overall prevalence of type 2 diabetes in adults remained stable from 2007 (1.24 million cases/15.07 million enrolled; 8.2%) to 2012 (2.04 million cases/24.52 million enrolled; 8.3%), whereas the percentage of newly diagnosed cases fell dramatically from 2007 (152,252 cases; 1.1%) to 2012 (147,011 cases; 0.65%).[14] In Laxa, central Sweden, the prevalence of diabetes has not increased since 1988, and the incidence rate was relatively stable for both type 1 and type 2 diabetes since the 1970s.[15] In Scotland, the incidence

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of type 2 diabetes remained stable between 2004 and 2013.[16] By contrast, in Taiwan the total population with diabetes increased by more than 70% between 2000 and 2009, representing a 35% increase in age-standardized prevalence rate, whereas the age-standardized incidence rate was nearly constant from 2000 to 2009.[17,18] Nonetheless, incidence rates of type 2 diabetes are increasing rapidly in persons aged <35 years, which may be of particular relevance with regard to personal and societal cost of long-term complications, and in those older than 75 years, in part because of greater longevity in developed countries.

People with diabetes are at increased risk of developing a number of disabling and life-threatening complications, including cardiovascular disease (CVD), kidney disease, blindness, and lower-limb amputations.[2] In this review, we will summarize the current evidence on the epidemiology of one of the most common complications associated with diabetes–CKD. Furthermore, we will explore trends in the incidence and prevalence of CKD in diabetes, mortality among those with CKD, and the level of awareness about kidney disease among patients with CKD.

Search Strategy

We searched PubMed and Medline for published articles with the following search terms "diabetes" AND "kidney disease" or "renal disease" or "ESRD" or ESKD" or "diabetic nephropathies" AND "epidemiology" or "prevalence" or "incidence" or "mortality" or "awareness." The search was limited to articles that are published in the last 10 years, in English. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant.

CLINICAL SUMMARY

- The prevalence of diabetes is increasing in most parts of the world.
- The prevalence and incidence of end-stage renal disease remain high, driven largely by the high prevalence of diabetes and better survival among those with diabetes.
- Chronic kidney disease is associated with most of the excess all-cause and cardiovascular mortality in patients with diabetes.
- The level of chronic kidney disease awareness around the world is very low.

EPIDEMIOLOGY OF CKD IN DIABETES

Risk Factors for CKD in Diabetes

CKD in patients with diabetes, like in other diseases, is clinically defined by the presence of persistent albuminuria (albumin-to-creatinine ratio [ACR] ≥30 mg/g for at least 3 months) and/or persistent low estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m^2) regardless of etiology.[19]

Certain risk factors for diabetic kidney disease are important targets in the prevention or delay of CKD and for personalizing treatment strategies. Genetic factors, male sex, age, and duration of diabetes, are among the nonmodifiable risk factors associated both with onset and progression of kidney disease. The modifiable risk factors include poor glycemic control, hypertension, lipid abnormalities, smoking, obesity, insulin resistance, low intensity of physical activity, high salt intake, birth weight, exposure to diabetes in utero, and periodontal disease (Box 1).[20-23] Many of the listed risk factors prevail in disadvantaged and displaced populations across the globe, predisposing to more frequent and earlier onset of diabetes and CKD.[24,25]

Prevalence of CKD in Diabetes

People with diabetes have nearly 2-fold higher odds of CKD than those without diabetes. The odds ratios for CKD vary between 1.3 and 4.6, depending on the region of the world, and this risk is compounded by the presence of hypertension.[26] Among those with diabetes, CKD prevalence varies widely between countries (Table 1),[27-43] with estimates ranging from 27.1% in Shanghai, China to 83.6% in Tanzania.[36,41] In the US National Health and Nutrition Examination Survey (NHANES) 2009 to 2014, CKD prevalence was 26.2% among adults with diabetes, taken into account albuminuria persistence. In those aged ≥65 years low eGFR was significantly more prevalent than among younger age groups, whereas persistent albuminuria prevalence was comparable.[44] A similar type of survey in Shanghai, China, reports a CKD prevalence of 33.5% among patients with diagnosed diabetes in 2008.[34] Information about diabetes duration was not collected in this study, however, the age-, sex-, body mass index–, and hypertension-adjusted prevalence of CKD was similar among participants with previously diagnosed and undiagnosed diabetes, 24.5% and 23.3%, respectively (median age 59 and 57 years, respectively), suggesting a relatively short duration of diagnosed disease; CKD prevalence was significantly lower without diabetes: 12.1% in participants with prediabetes and 9.8% in those with normal glycemia ($P < .001$ for trend).[34] In contrast, in Singapore, CKD prevalence was 53% in 2011 to 2013 among a multiethnic group of primary care patients with type 2 diabetes[40]; 21% had eGFR–Modification of Diet in Renal Disease <60 mL/min/1.73 m^2, 48% had ACR ≥30 mg/g, and 28% had diabetic retinopathy, a marker of diabetes-related CKD. Patients at high risk of CKD were older, of Malay ethnicity, with longer duration of diabetes, higher body mass index, A1c, blood pressure, and lipid levels. Different from the Chinese survey, this was an ethnically diverse, urban, clinic referred population. Unlike the US survey mentioned previously,[44] the Asian studies used single spot urine ACR measurements to define CKD, which may in part explain the higher CKD prevalence in these Asian populations.

In Europe, where health care is universally subsidized by governments, CKD prevalence is 2 to 5 times higher in those with type 2 diabetes than in those without diabetes and age- and sex-adjusted values vary between 15.4% in the Netherlands and 41.5% in Germany.[45] Factors accounting for the variation may include differences in diabetes