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The epidemiology of chronic kidney disease

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The epidemiology of chronic kidney disease. The world's disease profile is changing, and chronic diseases now account for the majority of global morbidity and mortality, rather than infectious diseases. The causes of chronic kidney diseases reflect this change and diabetes, together with hypertension, is now the major cause of end-stage renal failure worldwide, not only within the developed world, but also increasingly within the emerging world.

Diabetes is of epidemic proportions, and its prevalence will double in the next 25 years, particularly in the developing countries. This will place an enormous financial burden on countries, including the cost of the management of end-stage renal failure. Thus, it is medically and economically imperative for awareness, detection, and prevention programs to be introduced across the world, particularly in the developing countries. This will require concerted action from global institutions, governments, health service providers, and medical practitioners.

The pattern of disease morbidity and mortality throughout the world is changing both in the developed and the emerging world. During the 20th century, infectious diseases were the major cause of death and disability. However in this century, noncommunicable, noninfectious diseases have become the major cause of mortality and morbidity around the world [1, 2]. This change is reflected in the type of diseases causing chronic kidney failure and in their presentation and progression. Today, the major cause of end-stage renal failure is diabetes as a result of the global pandemic of type 2 diabetes. The rate of progression is extraordinary, and it is predicted that there will be a doubling of the number of patients with type 2 diabetes around the world in the next 25 years [3]. This will lead to a corresponding increase in the number of patients with chronic kidney disease and the number requiring end-stage renal failure management, particularly dialysis.

This paper examines five epidemiologic aspects of chronic kidney disease. First, the prevalence of early kidney damage; second, the prevalence and incidence of end-stage kidney failure; third, the changing patterns of chronic kidney disease; fourth, the diabetes and cardiovascular pandemic; and finally, what can be done to reduce the impending disease burden with all its medical and financial ramifications.

COMMUNITY PREVALENCE OF EARLY KIDNEY DISEASE

The prevalence of early kidney disease in the general community has been studied little [4, 5]. However, a recent AUSDIAB study from 1999 to 2000 evaluated the prevalence of diabetes, metabolic risk factors, and indicators of renal disease in the broad Australian community, and the results have provided an increased understanding of the burden of kidney disease within the community, and this appears to be applicable worldwide [6]. The AUSDIAB study was a cross-sectional prevalence study and included determining the prevalence of diabetes mellitus and abnormal glucose metabolism, hypertension, kidney disease, cardiovascular disease, and lifestyle and health behavior. Adults (11,247) more than 25 years old were screened between April 1999 and December 2000. Albuminuria was determined by urine albumin:creatinine ratio with normal $\leq$3.4 mg/mmol, microalbuminuria = 3.4 to 34 mg/mmol, and macroalbuminuria $\geq$34 mg/mmol. Proteinuria was determined by urine to protein:creatinine ratio (mg/mg) with abnormal proteinuria $\geq$0.2 mg/mg, which approximates 250 mg/24-hour excretion. Renal impairment was measured by the Cockcroft-Gault GFR formula using serum creatinine plus body surface area and gender adjustments. Hematuria was determined initially by a dipstick, and was followed-up by urine microscopy if a dipstick was positive for blood. Hypertension was established by history, treatment, and three sitting blood pressure measurements. Diabetes, impaired fasting glucose, and impaired glucose intolerance were diagnosed by a fasting glucose level and a 2-hour oral glucose tolerance test [6].

The AUSDIAB results showed that 7.2% of adult Australians in the community have diabetes. A portion (3.6%) knew they had diabetes, and 3.6% were undiagnosed. A percentage of adults (16.1%) had impaired glucose metabolism, 60% were overweight or obese, 61% had high cholesterol, and 29% had elevated blood pressure, with only 14% on treatment.

The AUSDIAB study showed the prevalence of renal abnormalities in the Australia community was hematuria

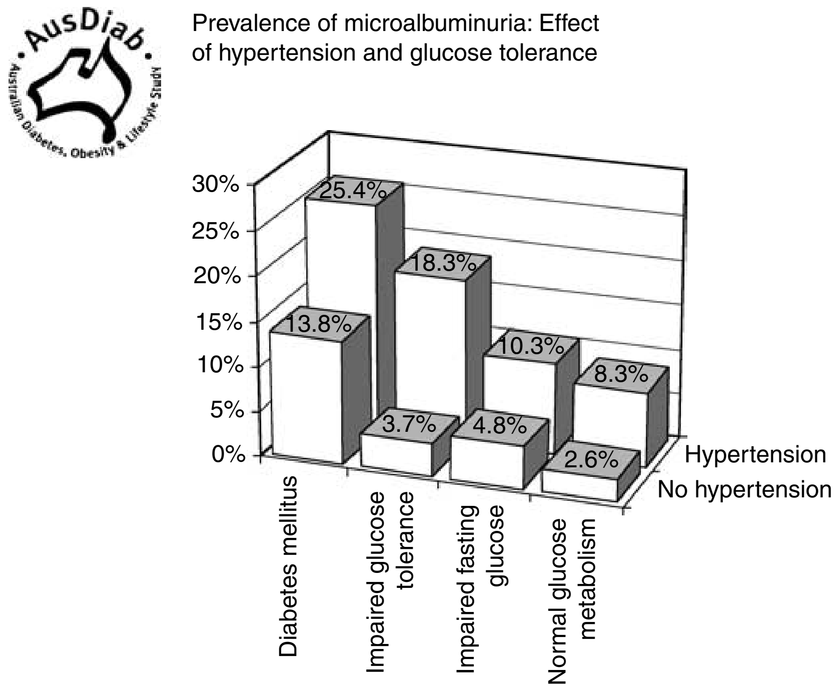

Fig. 1. The effect of glucose tolerance and hypertension on the prevalence of microalbuminuria.

(5.6%), proteinuria (2.4%), albuminuria (5.3% in males and 7.1% in females), and renal impairment, defined by a calculated GFR of less than 60 mL/m, was 12.1%.

This means that 18% of adult Australians had at least one indicator of chronic kidney disease. This is similar to the results of NHANES Study in the United States [7].

The effect of hypertension and glucose tolerance on the prevalence of albuminuria demonstrated an enhancing effect (Fig. 1). With increasing degrees of glucose intolerance there were increasing amounts of albuminuria. However, when the effect of hypertension was also taken into account, microalbuminuria was increased at each degree of glucose intolerance in an incremental fashion, with 25.4% of people with diabetes mellitus and hypertension having albuminuria. This is in keeping with other series, but is less than reported in the recent Demand Project, which showed 49% of 31,470 patients with type 2 diabetes from 34 countries had microalbuminuria as determined by dipstick analysis [8].

The AUSDIAB study also showed a prevalence of microalbuminuria of 6.1% in the general population. Of these, 74% had hypertension either alone (22%) or with glucose intolerance (41%). Thirteen percent had microalbuminuria associated with smoking, urinary infection, hematuria, or renal impairment (GFR <60 mL/m), 13% had isolated microhematuria (Fig. 2). Fifty-three percent of people in the community with microalbuminuria had impaired glucose tolerance. Therefore, of the people testing positive for microalbumunria in the general population, approximately half had glucose intolerance, most of these associated with hypertension. A fourth will be hypertensive alone, and another fourth will have microalbuminuria from other causes, including glomerulonephritis. Thus, on a community basis, microalbumunira is mainly associated with glucose intolerance and hypertension.

PREVALENCE AND INCIDENCE OF END-STAGE RENAL FAILURE

Approximately 30% of patients with diabetic nephropathy eventually progress to end-stage renal failure, and the rest usually die from cardiovascular disease before reaching end stage. All develop microalbuminuria and, subsequently, proteinuria. Therefore, albuminuria is an important risk factor in these patients, and all diabetic patients should have a microalbuminuria assessment yearly [9]. Indeed, albuminuria is strongly associated with progression of kidney disease, in addition to prediction of cardiovascular events not only in diabetic patients, but also in the general community [10, 11]. Thus, the combination of diabetes, hypertension, and chronic kidney disease is now the most common cause of end-stage kidney failure worldwide.

The incidence of patients with end-stage renal disease being treated by renal replacement therapy varies enormously depending on the level of affluence of the country. The highly developed countries such as North America, Europe, and Japan have the highest incident rates of treated end-stage renal failure, whereas the emerging countries have very low incident rates. There are now over 1 million dialysis patients worldwide, with an incidence of about a quarter of a million new patients each year. [12]

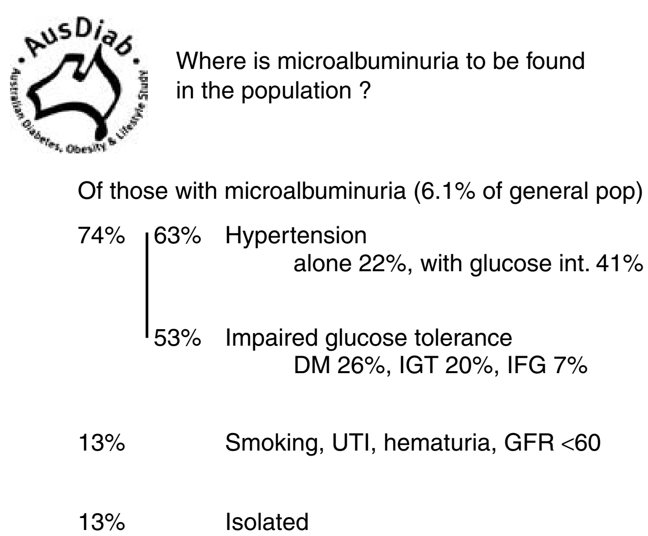

Fig. 2. The significance of microalbuminuria in terms of underlying disease.

The annual incidence of new cases of end-stage renal failure in Hong Kong from their renal registry data demonstrates the worldwide trend of progressively increasing numbers. In 1996, there were 100 patients/million population beginning dialysis in Hong Kong. In the year 2000, this increased to 122 patients, and in 2003, 140 patients/million population began treatment for end-stage renal failure. Similarly, the rates have been increasing in the United States, and with increasing prevalence, it is predicted that by 2010, there will be almost 700,000 dialysis patients in the United States, costing about US$30 million a year for their dialysis treatment [13]. Obviously, treatment of such an ever-increasing burden of end-stage kidney failure cannot be afforded, even in the wealthiest of countries.

CHANGING PATTERNS OF CAUSE OF CHRONIC KIDNEY DISEASE

The major cause of end-stage renal failure in most countries worldwide is now diabetes. Over the past decade, the USRDS figures demonstrate a progressive increase in the number of diabetics entering end-stage renal failure programs. Now, 44% of all incident patients are diabetic (www.USRDS.org), while glomerulonephritis, cystic kidney disease, and hypertension have remained relatively steady as causes of end-stage renal failure over the past decade. This is reflected also in Australia, where the incidence of end-stage renal failure due to diabetes is 25% (www.ANZDATA.org.au), and in the European Registry Data, where the number of diabetics entering end-stage renal failure programs is now between 15% and 33%, while the numbers entering due to glomerulonephritis are 7% to 20% (www.ERA-EDTA-Reg.org/index.55p).

Figures from the Hong Kong Renal Registry also show a progressive increase in the number of diabetics beginning dialysis, which now represents 38% of the incident patients, while only 23% were due to glomerulonephritis. Other countries throughout Asia also have large percentages of their incident end-stage renal failure patients due to diabetes: Pakistan, 42%, Taiwan, 35%, Philippines, 25% and Japan, 37% (USRDS 2003).

This inexorable progressive increase can be gauged by the figures over the past 20 years from the Australian and New Zealand Dialysis & Transplant Registry. Figure 3 demonstrates the relatively steady acceptance rate of type 1 diabetes over this time, but the progressive increase in the number of type 2 diabetic patients being accepted into dialysis programs over the past 2 decades (Fig. 3). Diabetes is now the major cause of end-stage renal failure worldwide in both developed and emerging countries.

THE PANDEMIC OF DIABETES AND CARDIOVASCULAR DISEASE

The prevalence of type 2 diabetes is rising progressively around the world. For example, the diabetes prevalence in Singapore has risen from 2% in 1975 to over 8% in 1998, and this is reflected in many Chinese communities throughout the world. Predictions for the diabetes epidemic in China have indicated an increase for the community prevalence of diabetes from 4% to 10% over the next 10 years. In 2000, a World Health Organization survey showed that 5.2% of Chinese men (12.7 million) and 5.3% of Chinese women (13.3 million) had diabetes. Three fourths were previously undiagnosed. This represents an enormous number of people, as China is the most populous nation in the world. India, the second most populous country, has the most diabetics in the world. This is reflected by an associated high prevalence of cardiovascular disease in India, and coronary deaths are expected to reach 2 million per year by 2010.

The prevalence of diabetes in the Asian Pacific area is variable but increasing. In the highlands of Papua New Guinea, there is virtually zero incidence of type 2 diabetes, but on relocation to urban cities in Papua New Guinea, the prevalence rises to 16%. Nauru, a small island state in the Pacific, has a prevalence of 42% of type 2 diabetes among the adult population. The global projection by the International Diabetes Federation predicts that the number of diabetics in the world will rise from 189 million today to 224 million in the year 2025 [3], an increase of 72%. Furthermore, the International Diabetes Federation has predicted an increase in diabetic numbers of 88% in South America, 59% in North America, 18% in Europe, 98% in Africa, 97% in the Middle East, and 91% in Asia over the next quarter of a century. Thus,

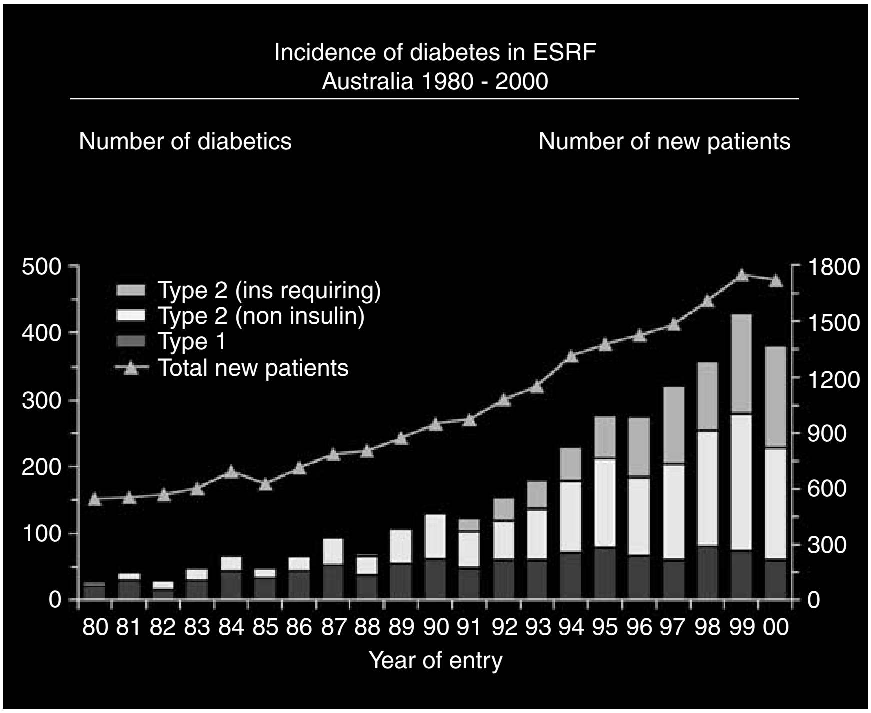

Fig. 3. Incidence of diabetes in ESRF Australia, 1980 to 2000.

diabetes will drive the future epidemics in cardiovascular and renal disease. This additional burden of progressive chronic kidney disease due to the diabetes pandemic will constitute one of the greatest medical challenges of the 21st century.

In addition, the explosion in the number of people with diabetes has enormous economic implications. The cost affects individuals and families, as well as health services and also national productivity. Individual families are greatly affected. Studies from India have estimated that as much as 25% of the family income may be devoted to diabetes treatment of an adult. The cost of diabetic care ranges from 2.5% to 15% of national health care budgets. The global cost of diabetes is now $150 billion, and will double by 2025. By then, countries with a high prevalence of diabetes, such as China and India, may be spending up to 40% of their health care budget on diabetes and its complications. In addition, the cost of death and disability due to chronic disease is profound, and will reduce productivity, particularly in the emerging world, and significantly reduce economic growth.

WHAT CAN BE DONE?

We have a great challenge to communicate the magnitude of the diabetic, cardiovascular, and chronic disease kidney problem to communities and to governments worldwide [14]. The International Society of Nephrology is responding to this challenge by forming partnerships with other appropriate societies, such as the International Diabetes Federation, with agencies and foundations such as the World Health Organization, the World Bank, and the Rockefeller Institute [15], in order to influence global and national health policy and decision makers as to the enormity of this chronic disease problem. It will also require a concerted approach from individual practitioners, nephrologists, and diabetic and cardiovascular physicians. Detection and prevention programs, including screening of communities for diabetes, hypertension, and chronic kidney disease have to be implemented in order to avert this enormous problem of chronic disease. Lifestyle changes, modification of the ill effects of sweeping globalization, and massive community education will be needed. This ISN Hong Kong Prevention Congress is one such initiative to provide a multidisciplinary approach to the chronic disease problem, particularly within the Asian Pacific area. However, the discussions and outcomes are world encompassing.

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