

Diabetic Kidney Disease

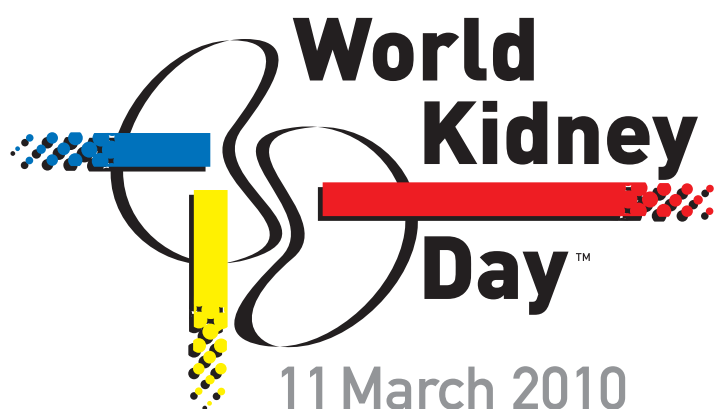
Act Now or Pay Later

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We Must Act on Diabetic Kidney Disease

In 2003, the International Society of Nephrology (ISN) and the International Diabetes Federation (IDF) launched a booklet called *Diabetes and Kidney: Time to Act*¹ to highlight the global pandemic of type 2 diabetes mellitus (DM) and diabetic kidney disease. It aimed to alert governments, health organisations, providers, doctors, and patients to the increasing health and socioeconomic problems due to diabetic kidney disease and its sequelae, end-stage kidney disease requiring dialysis and cardiovascular death. Seven years later, the same message has become even more urgent. World Kidney Day 2010, under the auspices of the ISN and the International Federation of Kidney Foundations (IFKF), together with the IDF, provides yet another chance to underline the importance of diabetic kidney disease, stress its lack of awareness at both public and government levels, and emphasize that its management involves prevention, recognition, and treatment of its complications. Primary prevention of type 2 DM will require massive lifestyle changes in the developing and developed world supported

by strong governmental commitment to promote lifestyle and societal change.

GLOBAL THREAT OF TYPE 2 DIABETES MELLITUS

The 21st century has the most diabetogenic environment in human history.^{2,3} Over the past 25 years or so, the prevalence of type 2 DM in the United States has almost doubled, with 3- to 5-fold increases in India, Indonesia, China, Korea, and Thailand.⁴ In 2007, there were 246 000 000 people with DM in the world, but by 2025, that number is estimated to reach 380 000 000.⁵ People with impaired glucose tolerance, a “prediabetic state” numbered 308 000 000 in 2007 and will increase to 418 000 000 by 2025.⁵ The increase in the prevalence of DM will be greater in the developing countries. In Mexico for example, 18% of its adult population will have type 2 DM by 2025. According to the World Health Organization, China and India will have about 130 000 000 diabetics by 2025 who will consume about 40% of their country’s healthcare budget in addition to reducing productivity and hindering economic growth.

It was against this background that on December 21st 2006, the United Nations General Assembly unanimously passed Resolution 61/225 declaring DM an international public health issue and identifying World Diabetes Day as a United Nations Day, only the second disease after acquired immune deficiency syndrome to attain that status. For the first time, governments have acknowledged that a noninfectious disease poses as serious a threat to world health as infectious diseases like acquired immune deficiency syndrome, tuberculosis, and malaria. The problems of DM are now seen as a major global public health concern, especially in the developing world, which can least afford it. The first step to act on diabetic kidney disease must encompass public health campaigns aimed at preventing the development of type 2 DM.

DIABETIC KIDNEY DISEASE

Diabetes mellitus is now the major cause of end-stage kidney failure throughout the world in both developed and emerging nations.⁶ It is the primary diagnosis causing kidney disease in 20% to 40% of people starting treatment for end-stage kidney disease worldwide.⁷ In Australia, new patients with type 2 DM starting dialysis increased 5-fold between 1993 and 2007.⁸ Between 1983 and 2005, there was a 7-fold increase in new patients starting renal replacement therapy in Japan because of DM, accounting for 40% of all new incidence patients.⁹ Thus, some 30% of the predicted US \$ 1 100 000 000 000 medical costs of dialysis worldwide during this decade will result from diabetic nephropathy.¹⁰

In the United Kingdom Prospective Diabetes Study (UKPDS), the rates of progression of newly diagnosed type 2 diabetics between the stages of normoalbuminuria, microalbuminuria, macroalbuminuria, and renal failure were 2% to 3% per year.¹¹ Over a median of 15 years of follow-up of 4000 participants, almost 40% developed microalbuminuria.¹² In the Developing Education on Microalbuminuria for Awareness of Renal and Cardiovascular Risk in Diabetes Study of 32 208 people from 33 countries with known type 2 DM attending their family doctor, 39% had microalbuminuria and the prevalence increased with age, duration of DM, and presence of hypertension.¹³ About 30% of the UKPDS cohort developed kidney impairment, of which almost 50%

did not have preceding albuminuria.¹² Reduced glomerular filtration rate and albuminuria caused by diabetic nephropathy are independent risk factors of cardiovascular events and death.¹⁴ Therefore, a strategy to detect early diabetic kidney disease by screening for albuminuria as well as reduced glomerular filtration rate is the second step in taking action on diabetic kidney disease.

An added difficulty to overcome is the remarkable lack of awareness among patients about their condition. In population-based surveys, for every known diabetic patient, there is at least one more that is unknown¹⁵; only 8.7% of the general population were able to identify DM as a risk factor of kidney disease.¹⁶ For patients with diabetic kidney disease, very few are aware of their condition with some community surveys putting patients awareness of their disease as low as 9.4%, particularly in those with milder impairment.¹⁷ Thus, public education is the 3rd step required for acting on diabetic kidney disease in the community. The IFKF has a long-term goal for all patients with kidney disease worldwide to not only be aware of their disease, but to actively know for example their blood pressure and the treatment objectives.

MANAGEMENT OF DIABETIC KIDNEY DISEASE

There is little use in screening populations or “at risk” groups unless follow-up is undertaken and effective treatment is begun and assessed.¹⁸ Fortunately, there is evidence that early therapeutic intervention in patients with chronic kidney disease or DM can delay onset of complications and improve outcomes. For example, the UKPDS, Action in Diabetes and Vascular Disease: Preterax and Diamicron-MR Controlled Evaluation, and Steno-2 studies all demonstrated that tight control of blood glucose level, blood pressure (and lipids in Steno-2) significantly reduced incidence and progression of diabetic kidney disease.¹⁹⁻²⁴ In people with type 2 DM, inhibition of the renin-angiotensin-aldosterone system using an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker decreased the progression from normoalbuminuria to microalbuminuria, reduced the progression from microalbuminuria to macroalbuminuria, and slowed the development of end-stage kidney disease.²⁵⁻²⁷ Thus, the use of these drugs is now standard therapy

for patients with diabetic nephropathy as well as glucose, lipid, and blood pressure control. Effective management using evidence-based therapies is the 4th step in tackling diabetic kidney disease.

The 5th step is development of new therapies. Many new agents are now in clinical trials to reduce renal damage and fibrosis, including blockade of formation of advanced glycation endproducts and other signalling pathways. Other novel agents may potentially prove to be effective in large randomized double-blind clinical trials.²⁸

HOW CAN WE ACT NOW?

The steps to be taken are clear: campaigns aimed at (1) prevention of type 2 DM; (2) screening for early diabetic kidney disease; (3) increasing patient awareness of kidney disease; (4) using medications of proven strategy; and finally, (5) researching and trialling of new therapies. The ultimate challenge is to get action from primary healthcare to all higher levels; from the individual patient, to those at risk, in various health jurisdictions, in all countries despite varying economic circumstances and priorities. The problem is a global one and yet requires action at a local level; prevention screening and treatment strategies; education, including increasing awareness both in diabetic patients and those at risk of developing DM; and health priorities and governments. Basic research and clinical trials searching for a new understanding and therapies must be supported.

The United Nations, as noted earlier, recognized the importance of DM in 2006 by establishing a World Diabetes Day. Both the ISN and the IDF are working closely with the World Health Organization to provide increasing understanding of the challenge that diabetic kidney disease poses to world health and healthcare budgets. However, World Kidney Day also provides a focus for other international agencies, government ministries of health, nongovernment organizations, foundations, and academic institutions to come together with national kidney foundations to be involved in the effort to prevent and manage diabetic kidney disease.

The ISN through its Commission for the Global Advancement of Nephrology Research and Prevention Committee has developed the web-based Program for Detection and Management of Chronic Kidney Disease, Hypertension, Diabetes,

and Cardiovascular Disease in Developing Countries (http://www.nature.com/isn/education/guidelines/isn/pdf/ed_051027_2x1.pdf) as a global template involving a detection management and data assessment program which has so far screened some 42 000 people in 25 developing countries and the data are being stored and analyzed at the Kidney Disease Data Center at the committee headquarters at the Mario Negri Institute in Bergamo, Italy. This program can be tailored to any individual country's needs and resources. The IFKF also has a program initiated by the National Kidney Foundation in the United States called the Kidney Early Evaluation Program which is a screening program for people at high risk of kidney disease. The Kidney Early Evaluation Program has now been implemented in many countries and will again screen and manage patients with diabetic kidney disease.

The focus on diabetic kidney disease for World Kidney Day 2010 brings awareness of the magnitude of the problem and ramifications for global health for people with DM and kidney disease. It is therefore time to act and act urgently. It is time for strategies that prevent DM and its sequelae. It is time for programs for healthcare workers to diagnose and treat people with diabetic kidney disease. It is time for governments to pass legislation to enable the DM pandemic to be controlled. After all, diabetic kidney disease, like the epidemics of infectious diseases that have long dominated public health agendas, is potentially preventable. Indeed, March 11, 2010 is time to act on diabetic kidney disease and to sustain that action long after World Kidney Day.

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