Diabetes Could Cost You Your Kidneys, Act Now!

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The title of this editorial is the slogan given by the International Diabetes Federation (IDF) and World Health Organisation (WHO) as the theme of this year’s World Diabetes Day to draw the attention of the physicians and the patients towards the consequences of diabetic nephropathy, encourage early detection and evaluation and try to prevent what is essentially a preventable disease.

Diabetic nephropathy is clinically defined by the presence of persistent proteinuria of > 500 mg/day in a diabetic patient who has concomitant diabetic retinopathy and hypertension and in the absence of clinical or laboratory evidence of other kidney or renal tract disease. Nearly 30% of chronic renal failures in India are due to diabetic nephropathy.1

INCREASED PREVALENCE OF DIABETIC NEPHROPATHY IN SOUTH ASIANS

The prevalence of diabetic nephropathy in type 2 diabetic subjects is reported to be 5-9% from various Indian studies.2-4 Racial differences in the prevalence of diabetic renal disease have been reported. In a recent study by Young et al,5 it was observed that Asian subjects had significantly (p < 0.01) higher prevalence (52.6%) of diabetic end-stage renal disease (ESRD) when compared with the Caucasians (36.2%). Recently, Shaw et al showed that migrant Asian Indians had 40 times greater risk of developing ESRD when compared with the Caucasians.6

Patients with diabetic nephropathy, especially with type 2 diabetes, have a high cardiovascular risk. The risk for cardiovascular disease (CVD) was 3-fold higher in South Indian nephropathic subjects when compared with their non-nephropathic counterparts.7

Thus, in type 2 diabetes, many patients may not reach end-stage renal disease due to premature death from CVD.

The pathogenesis of diabetic nephropathy is multifactorial and genetic susceptibility has been proposed to be an important factor. The exact cause of diabetic nephropathy is unknown, but various mechanisms that are postulated are hyperglycemia (causing hyperfiltration and renal injury), AGE and activation of cytokines.

Hyperglycemia also may activate protein kinase C, which may contribute to renal disease and other vascular complications of diabetes.

Familial aggregation of diabetic nephropathy in South Indian type 2 diabetic subjects has been demonstrated. It was found that proteinuria was present in 50% and microalbuminuria in 26.7% of the siblings of probands with diabetic nephropathy.

Early Diagnosis of Risk Factors for Diabetic Nephropathy

Diabetic patients with microalbuminuria (MAU) are at a high risk for developing overt nephropathy and cardiovascular complications. Early screening for MAU in diabetic patients allows for aggressive intervention with a view to prevention of ESRD.

The following are key issues in the medical care for patients with diabetic nephropathy.

Glycemic control

In both type 1 and type 2 diabetes, hyperglycemia has been shown to be a major determinant of progression of diabetic nephropathy.

In the UKPDS study,9 more than 4000 patients with newly diagnosed type 2 diabetes were observed over 15 years, showed that with 12 years of blood glucose control, there was a risk reduction of 33% in the onset of microalbuminuria, 34% risk reduction in proteinuria and 74% risk reduction in two-fold increase of plasma creatinine.

ANTIHYPERTENSIVE TREATMENT

Hypertension is the single most important factor that accelerates the progression of diabetic renal disease.

Recently, several trials (IRMA, INDT, MARVAL etc) conducted respectively in microalbuminuric and nephropathic type 2 diabetic subjects have shown that treatment with angiotensin receptor antagonist (ARB) is renoprotective and slow the progression of glomerulopathy.10,11 This protection is independent of reduction in blood pressure with minimal drug-specific serious adverse events. Similar protection was seen with ACE inhibitors.

The IRMA trial showed that treatment with irbesartan reduced in a dose-dependent manner, the number of patients attaining the primary end-point of developing overt nephropathy. Similarly the IDNT trial showed that the risk of developing the primary end-point (doubling of serum creatinine and onset of ESRD) in the irbesartan 300 mg group was 20 times lower than the placebo group and 23 times lower
than the amlodipine treated group. Viberti in the Landmark MARVAL trial showed the same effect with Valsartan when compared to Amlodipine.17

Losartan, Irbesartan and Valsartan all ARBs. were found to be renoprotective, independent of its beneficial effect in lowering 24 hour blood pressure in patients with type 2 diabetes and persistent microalbuminuria.

In a recent study by Herman et al.,13 it was shown that treatment with losartan in type 2 diabetic patients with nephropathy reduced the incidence of ESRD and resulted in decrease in cost associated with ESRD. Losartan and the conventional therapy reduced the number of days with ESRD by 33.6 per patient over 3.5 years when compared with the placebo and conventional therapy group.

According to the study by Rossing et al.,14 dual blockade of renin angiotensin system using both angiotensin converting enzyme inhibitor (ACEI) and ARB provides superior short term renoprotection independent of systemic blood pressure changes in comparison with maximally recommended doses of ACEI in patients with type 2 diabetes as well as nephropathy.

Early screening for microalbuminuria is the key for early detection of the devastating complication. Once identified, intensive treatment to control the blood sugar should be the primary objective. A target blood pressure of < 130/80 as recommended by the Joint National Committee VII15 should be achieved in all diabetic patients. This can be attained using novel drugs like angiotensin converting enzyme inhibitor (ACEI) and ARBs.

Intensified multifactorial treatment are useful in slowing the progression of nephropathy. In the Steno type 2 diabetes randomized study, it was shown that intensive treatment with a stepwise implementation of behaviour modification, pharmacological therapy targeting hyperglycemia, hypertension, dyslipidaemia and microalbuminuria lowered the rate of progression to nephropathy (OR = 0.27) when compared with a conventional therapy. Thus the treatment strategy should not only aim at attenuating high blood sugars and blood pressures but also treat comorbid conditions associated with diabetic nephropathy.16

Given the worldwide rise in diabetes and its complications, investments in prevention looks to be the most logical choice for diabetic kidney disease and healthcare sustainability.

**References**