

South-Asian Type 2 Diabetic Patients Have Higher Incidence and Faster Progression of Renal Disease Compared With Dutch-European Diabetic Patients

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Surinamese South-Asian migrants, living in the Netherlands and aged >30 years, have a nearly 40-fold increased age-adjusted risk for end-stage diabetic nephropathy in comparison with their European Dutch counterparts (1). Several studies in the U.K. also showed a higher incidence of end-stage renal failure in South-Asian diabetic patients (2–6).

There is no clear explanation for the increased risk in South-Asian migrants, who originally descend from the Indian subcontinent. An earlier study showed no familial predisposition for renal disease in South-Asian migrants (7). There is a discrepancy between the reported eight-times higher prevalence of diabetes (8) and the 40-fold higher risk of end-stage diabetic nephropathy (1) in this population. This discrepancy could be explained by either a higher incidence of nephropathy in the Asian diabetic patients and/or faster progression to end-stage renal failure.

We performed a cohort study in South-Asian and Dutch-European type 2 diabetic patients to compare differences in the incidence of microalbuminuria and progression of renal failure between both ethnic groups.

RESEARCH DESIGN AND METHODS

— We used the registry of the outpatient diabetic clinic of the Haga Teaching Hospital during the period of 1994–1996. Ethnicity was by self-report. Migrants who originally descend from the Indian subcontinent were reported as South-Asian. Patients who were of Dutch descent were reported as European. We selected a cohort of 149 South Asian type 2 diabetic patients and matched them for sex and level of urinary albumin excretion with 155 European patients. Urinary albumin excretion and creatinine clearance were measured at inclusion and after 5 years' follow-up. In each group, ~7% of the patients were lost to follow-up and 11% had incomplete follow-up data for final analysis. Mortality was higher in the European patients: 19.3 vs. 6.7% in the South Asians.

All laboratory measurements were done according to ISO 15189 standard procedures. Microalbuminuria was defined as albuminuria >30 mg in a 24-h urine collection or spot-urine albumin-to-creatinine ratio >2.5 g/mol creatinine in male subjects and >3.5 g/mol creatinine in female subjects. Creatinine clearance was calculated from the 24-h urine per 1.73 m².

For statistical comparison of the difference of means, the Student's *t* test was used. Differences of categorical variables were expressed as a percentage with 95% CIs and as χ^2 *P* values. We used multivariate analysis for correction of differences in risk factors for development of microalbuminuria/macroalbuminuria. The decline in creatinine clearance (Δ glomerular filtration rate [GFR]) was calculated per patient.

RESULTS— Complete follow-up was acquired in 107 South-Asian and 94 European diabetic patients. About 61% had no microalbuminuria (*n* = 65 Asians, *n* = 56 Europeans), 28% had microalbuminuria (*n* = 30 Asians, *n* = 27 Europeans), and 11% had macroalbuminuria (*n* = 12 Asians, *n* = 11 Europeans). Serum cholesterol, antihypertensive usage, systolic blood pressure values, and smoking habits were higher in the Europeans. HbA_{1c} (A1C) values were 0.8% higher in South Asians (8.6 vs. 7.8%, *P* = 0.003). South Asians were 12 years younger (52 vs. 64 years in the Europeans, *P* < 0.001). BMI was the same in both ethnic groups (~29 kg/m²).

In 65 South-Asian and 56 European patients without microalbuminuria at inclusion, the unadjusted odds ratio (OR) for development of micro- or macroalbuminuria in South Asian patients compared with the European patients was 2.1 (95% CI 0.84–5.1; *P* = 0.1) (Fig. 1A). After correction for younger age and higher A1C values, the adjusted OR for developing micro- or macroalbuminuria increased from 2.1 to 3.9 (1.1–14; *P* = 0.03). Introduction of sex or duration of diabetes showed no significant changes in the OR.

The loss of GFR estimated with creatinine clearance was 1.45 times higher in South Asians. After 5 years' follow-up, South Asians lost 32 ml/min of their GFR versus 22 ml/min in Europeans (difference: 10 ml · min⁻¹ per 1.73 m²; 95% CI 0.04–20; *P* = 0.049) (Fig. 1B).

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Abbreviations: GFR, glomerular filtration rate.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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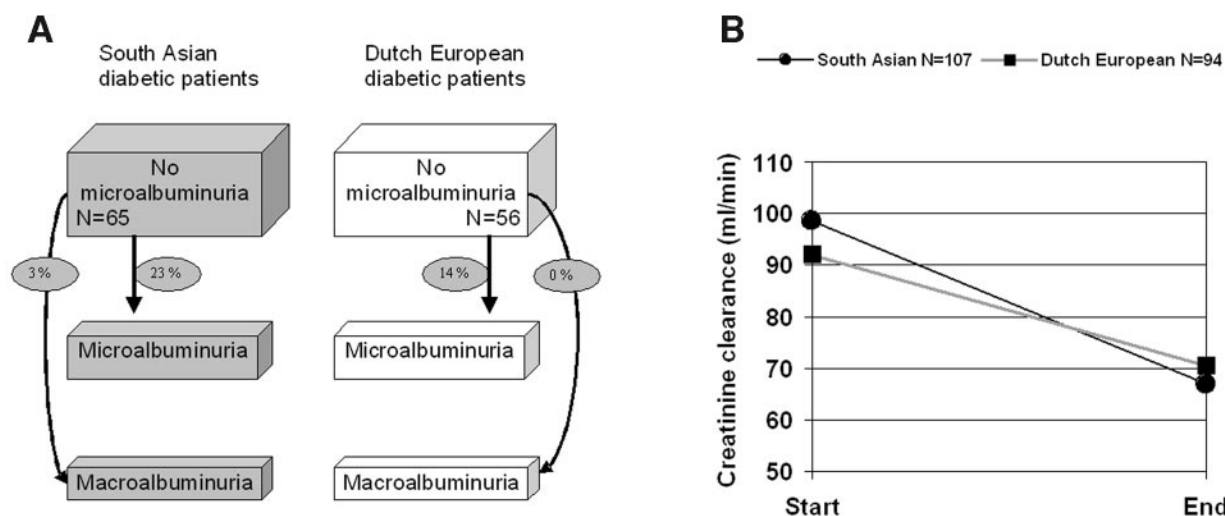


Figure 1—A: Higher incidence of micro- and macroalbuminuria in South-Asian and European diabetic patients after 5 years' follow-up. B: Higher progression of renal failure in South-Asian compared with European diabetic patients.

CONCLUSIONS— At a much younger age, South-Asian type 2 diabetic patients develop more nephropathy and have progressive renal failure in comparison with European diabetic patients. After correction for the younger age of the South Asians (12 years), the OR for developing microalbuminuria/macroalbuminuria was nearly 4 in the South-Asian group. After 5 years' follow-up, the loss in GFR was 1.45 times higher ($10 \text{ ml} \cdot \text{min}^{-1} \text{ per } 1.73 \text{ m}^2$) in the South-Asian group.

The South-Asian population in our study was different from the European-Dutch population at the start of follow-up; they were younger and had less cardiovascular complications and lower blood pressure values with less antihypertensive medication than the European group. The higher risk for microalbuminuria in South Asians was not attributed to differences in renin-angiotensin system blocker or diuretic usage between the two ethnic groups. The adjusted OR, derived after multivariate analysis, slightly overestimates the true relative risk because of the high frequency of microalbuminuria (9). After correction for the overestimation, the relative risk was still higher in the South-Asian group (2.8 [95% CI 1.08–4.9]).

Our study explains the discrepancy between the reported eight-times higher prevalence of diabetes (8) and the 40-fold higher risk of end-stage diabetic nephropathy (1) in the South-Asian population. The lack of familial clustering of renal disease in South-Asian diabetic patients (7)

points to a universal ethnic susceptibility for nephropathy in this population. The best-studied hypothesis is that the high prevalence of insulin resistance drives the high rates of microalbuminuria and ischemic heart disease. High rates of central obesity, elevated fasting blood glucose, and ischemic heart disease have been reported in South Asians when exposed to Western lifestyle, pointing to changes in body composition as causal factor (10,11). However, studies performed in British South-Asian children revealed 50% higher fasting and postload insulin levels, without any differences in central adiposities (12). Recently, insulin resistance has been linked to activity of the innate immune system. For example, inflammatory transcription factors, such as nuclear factor- κ B, which are also involved in the development of target organ damage, may be causally linked to insulin resistance (13). One could hypothesize that increased activity of such systems may have been advantageous to the immigrants in their original environment but that insulin resistance is the price to pay in a Western environment. This ethnic susceptibility for insulin resistance could explain the high risk for type 2 diabetes, coronary disease, microalbuminuria, and renal failure in the South Asians.

We assume that the high risk of end-stage diabetic nephropathy in South-Asian migrants is caused by several factors: the higher prevalence of diabetes, more development of nephropathy, and faster progression of renal failure in diabetic South Asians.

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