Diabetic nephropathy in Surinamese South Asian subjects

Chandieshaw, P.K.

Brits-Indische immigranten aan boord van een schip op de Surinamerivier bij Paramaribo, dat hen terug brengt naar Brits-Indië, Suriname, ca. 1890.

Chapter 4

South Asian type 2 diabetic patients have higher incidence and faster progression of renal disease in comparison with Dutch European diabetic patients

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Abstract

Objective

In the Netherlands, South Asians older than 30 years have a nearly 40-fold higher risk for end-stage diabetic nephropathy than Europeans. This higher risk is only partially explained by the reported eightfold higher prevalence of diabetes in the South Asian population. We therefore compared the incidence of microalbuminuria and the progression of renal failure between South Asian and Dutch European type 2 diabetic patients.

Research design and methods

We selected a cohort of 149 South Asian patients who were matched with 155 Dutch European type 2 diabetic patients, by using the registry of an out-patient diabetic clinic. Urinary albumin excretion and creatinine clearance were measured at inclusion and after nearly 5 years follow-up. In each group, about 7% of the patients were lost-to-follow-up and 11% had incomplete follow-up data for final analysis.

Results

Complete follow-up was acquired in 107 South Asian and 94 European diabetic patients. After correction for the younger age of the South Asian patients (12 years), the odds ratio for developing microalbuminuria or macroalbuminuria was nearly 4 in the South Asian type 2 diabetic group. After 5 years follow-up, the loss in glomerular filtration rate was 1.45 times higher (10 ml/min/1.73 m^2) in the South Asian group.

Conclusions

At a much younger age, South Asian type 2 diabetic patients develop more nephropathy and have faster progression of renal failure in comparison to Dutch European diabetic patients.

Introduction

Surinamese South Asian migrants, living in the Netherlands and older than 30 years, have a nearly 40-fold increased age-adjusted risk for end-stage diabetic nephropathy in comparison to their European Dutch counterparts. [1] Several studies in the UK also showed a higher incidence of ESRF 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. Our previous family study in South Asian dialysis patients with type 2 diabetes showed no familiar predisposition for renal disease within the South Asian migrant population. [7] In an earlier study, an eightfold higher prevalence of type 2 diabetes was reported for South Asian migrants living in the Netherlands. [8] However, this higher prevalence of diabetes only partially explains the nearly 40-fold increased risk for end-stage diabetic nephropathy in the South Asian migrants. [1] This gap could be explained by either a higher incidence of nephropathy in the Asian diabetic patients and/or faster progression to end-stage renal disease. A cross-sectional study performed in the UK, showed 1.5 times higher prevalence of microalbuminuria in South Asian diabetic patients compared to native British diabetic patients. [9] This could be an indication for higher incidence of microalbuminuria in the South Asian diabetic patients. Previous follow-up studies revealed conflicting results in the rate of progression of diabetic nephropathy in South Asians versus Europeans. [10,11]

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

Research Design and Methods

Patients

All participants took part in a registry of 1705 diabetic patients who visited the diabetic out-patient clinic of the Haga Teaching Hospital, during the period 1994-1996. After excluding the type 1 diabetic patients, we had 222 South Asian patients and 1201 Dutch European patients with type 2 diabetes. In the registry, we found urinary albumin excretion results in 149 patients of South Asian and, 611 patients of Dutch origin. Among these 611 patients, we performed a matched random sampling of 155 Dutch European patients, matched to the 149 South Asian patients for gender and

level of urinary albumin excretion. The local Medical Ethics Committee of the Haga Teaching Hospital approved the study, and the participants gave informed consent.

Follow-up of the study population

The study population consisted of 149 South Asian and 155 Dutch European type 2 diabetic patients, in total 304 patients. Incomplete follow-up data were obtained in 39 South Asians and 60 Dutch Europeans (see **figure 1**). In each ethnic group, about 11% of the patients had no follow-up investigation done, and in about 2% of the patients the original hospital records could not be retrieved. About 7% of the patients were lost-to-follow-up. At the end of the investigation 10 of the 149 South Asian diabetic patients died (6.7%) versus 30 of the 155 Dutch European patients (19.3%). Three South Asian patients were later excluded; one patient gave no informed consent; one patient became pregnant and one patient had a urine collection date after the inclusion deadline. Of the Dutch European patients, one was excluded because of a missing urine collection date. After exclusion, there were 107 South Asian and 94 Dutch European diabetic patients eligible for analysis. In these patients albuminuria was equally distributed in each ethnic patient group at time of inclusion: about 61% had no microalbuminuria, 28% had microalbuminuria and 11% had macroalbuminuria.

Procedures

The baseline characteristics of the patients were assessed from the medical record at the inclusion date. Follow-up was completed if the patient had at least four years of follow-up and all required data were present. If values were missing or the patient had not completed the four years follow-up, the investigation was scheduled at the next visit to the out-patient clinic. If patients were deceased before the end date (July 1, 2001) of the investigation, they were stated as such, and otherwise reported as alive. Patients who were discharged from the out-patient clinic were traced by contacting the general practitioner (GP). If the patient was unknown to the GP, we tried to locate the patient by using the registry office or financial records of the hospital. If this was unsuccessful, patients were stated as lost-to-follow-up.

At inclusion we collected from the medical records: date, length, weight, blood pressure, age, gender, ethnicity, first referral date and reason of referral to the out-patient clinic, duration of diabetes, type of diabetes, retinopathy, smoking habits, glycohemoglobin (HbA1c), serum cholesterol, laboratory results for urinary albumin excretion, serum creatinine and creatinine clearance, as well as antidiabetic and/or antihypertensive medication. Acquired cardiovascular disease at start of investigation was registered from the medical records.

At follow-up we collected laboratory test results for urinary albumin excretion (the type of urinary albumin excretion test, spot urine or 24-hour sample was specified), serum creatinine, HbA1c, serum cholesterol, weight, blood pressure and antihypertensive medication. Furthermore, the occurrence of cardiovascular complications during follow-up was registered.

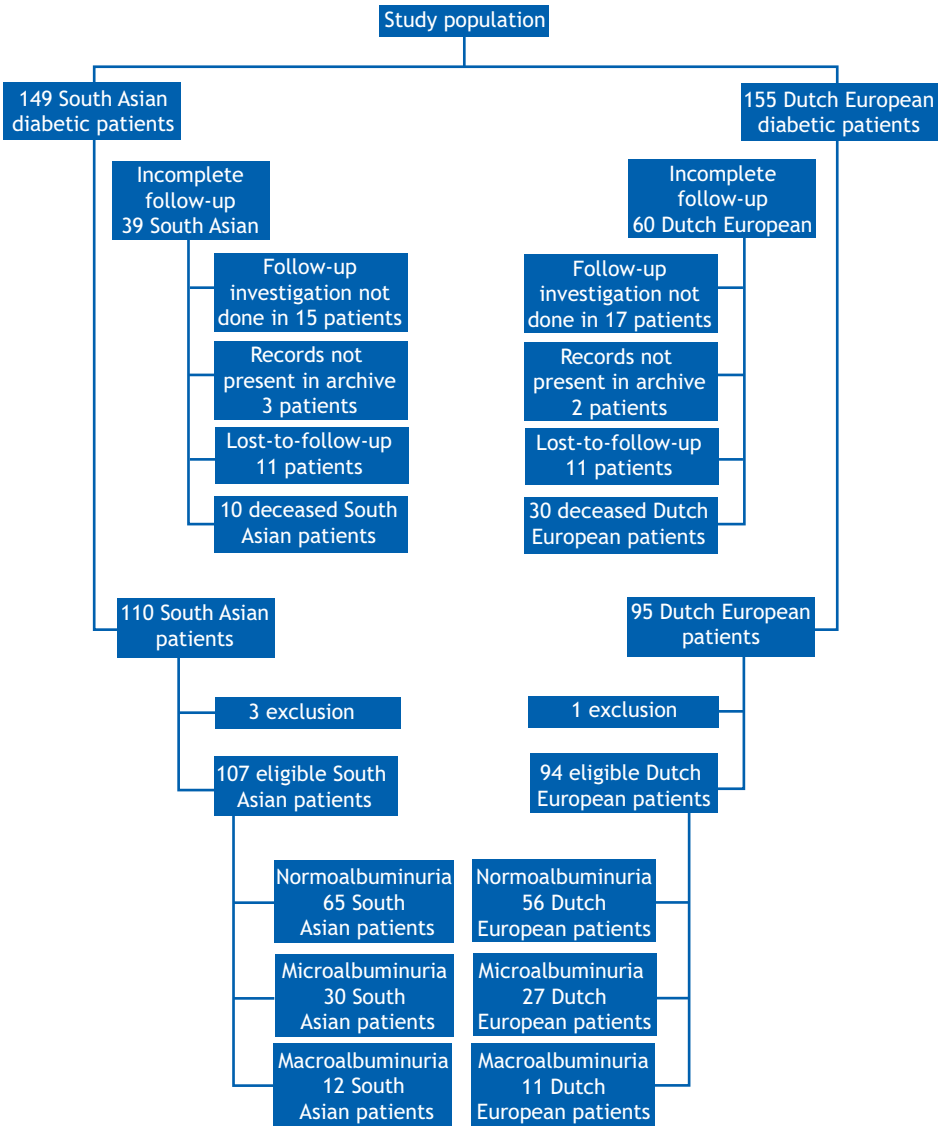

Figure 1: *Follow-up of 149 South Asian and 155 Dutch European type 2 diabetic patients.*

Definitions

Microalbuminuria was defined as albuminuria above 30 mg in a 24-hour urine collection or when using a spot urine collection, an albumin/creatinine ratio above the 2.5 g/mol creatinine in males and above the 3.5 g/mol creatinine in females. *Macroalbuminuria* was defined as albuminuria above 300 mg in the 24-hour urine collection or when using a spot urine collection, an albumin/creatinine ratio above the 36 g/mol in males and above the 40 g/mol in females. The *ethnicity* was self-stated. Patients who were of Dutch native descent were reported as European patients. Migrants who originally descend from the Indian subcontinent (India, Pakistan or Bangladesh) were reported as South Asian patients. If the patient had another ethnicity than South Asian or Dutch European, the patient was excluded for follow-up. *Type diabetes mellitus*: patients who had used oral antidiabetic medication and/or diet for more than one year were coded as type 2 diabetic patients. Patients who used only insulin with a history of keto-acidosis were coded as type 1 diabetic patients. *First referral* was defined as the first presentation of the patient to the out-patient clinic. The *date and reason* of first *referral* to the out-patient clinic was also noted to detect differences in referral for renal disease in the South Asian and Dutch diabetic groups. *Antidiabetic medication* was reported as oral or insulin in combination or alone. *Retinopathy* was defined as proliferative retinopathy necessitating laser coagulation or operation; if no report of the ophthalmologist could be found within one year of inclusion retinopathy was stated as missing report. *Blood pressure, length and weight* were recorded by the treating physician. *Antihypertensive medication* and blood pressure were recorded within 1 month before or after the inclusion date and at the end of follow-up. *Smoking* was classified as never or ever smoked. Loss of renal function during follow-up was compared between the ethnic groups using the creatinine clearance. *Creatinine clearance* was calculated from the 24-hour urine per 1.73 m^2. *Cardiovascular disease* was defined as: coronary heart disease (documented myocardial infarction, PTCA, CABG), cerebrovascular event (TIA, documented stroke, intracranial bleeding) and peripheral vascular complications (documented amputation, re-vascularisation operation)

Laboratory procedures

Laboratory results were taken within one month before or after inclusion date of urinary albumin excretion determination. The urinary albumin excretion at inclusion of the investigation was determined in the 24-hour urine. At follow-up, in the patients without a 24-hour urine collection, spot-urine albumin/creatinine ratio was performed. Urinary albumin and protein were measured by immunoturbidimetric assay on a

clinical chemistry analyzer. Glucose, creatinine, cholesterol and triglycerides and HDL-cholesterol were measured on a clinical chemistry analyzer. HbA1c was measured using the HPLC method with a Variant analyzer (Biorad, Hercules, CA, USA). Variance Coefficient 1.5% at different levels. The reference values for HbA1c are between 4.3 and 6.3%. All the laboratory results at inclusion and most follow-up investigations were done in clinical chemistry laboratory of the Haga Teaching Hospital. Patients who where treated by the GP had their follow-up investigations done in other laboratories. However, an extensive regional interlaboratory comparison study, in which the above mentioned analyses were compared, did not show a clinical relevant difference for the accuracy of the analyses (dr. F. Hudig, personal communication).

Statistics

For statistical comparison of the difference of means, e.g. age, duration of the diabetes, laboratory values between the case - and control group, the Student's t-test was used; the measured difference of the means were expressed with 95% confidence intervals and P-values. Differences of categorical variables like microalbuminuria, medication use, retinopathy, referral reasons were expressed as percentage difference with 95% confidence intervals and as Chi-Square P-values. We used multivariate analysis for correction of differences in risk factors for development of microalbuminuria/ macroalbuminuria, reporting the odds ratio Exp(B) with 95% CI. The decline in creatinine clearance (delta GFR) was calculated per patient. The mean delta GFR was compared between the ethnic groups using the Student's t-test.

Results

Incidence of microalbuminuria

In the 65 South Asian and 56 European patients without microalbuminuria (normoalbuminuria) at inclusion, the unadjusted odds ratio for development of micro- or macroalbuminuria in South Asian diabetic patients relative to the European Dutch patients was 2.1 (95% CI 0.84 to 5.1). (**Figure 2**) After correction for the lower age and higher HbA1c values, the adjusted odds ratio for developing micro- or macroalbuminuria increased from 2.1 to 3.9. Without adjustment for higher HbA1c value in the South Asians, the odds ratio for micro- or macroalbuminuria increased to 4.7 (95% CI 1.4 to 16; p-value 0.013) Introduction of other risk factors for microalbuminuria as gender, duration of diabetes showed no significant changes in the adjusted odds ratio. (Table 1)

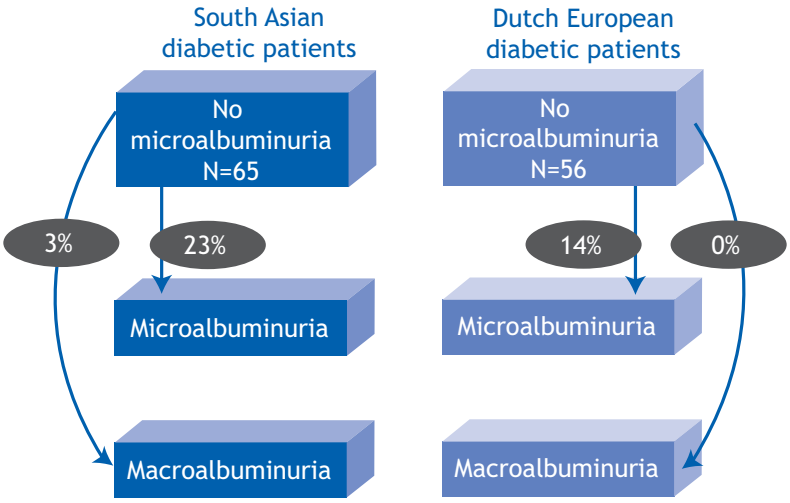

Figure 2: *Incidence of microalbuminuria and macroalbuminuria in South Asian and Dutch European type 2 diabetic patients after 5 years follow-up. The solid arrows show the progression percentage of albuminuria in patients with no microalbuminuria at inclusion.*

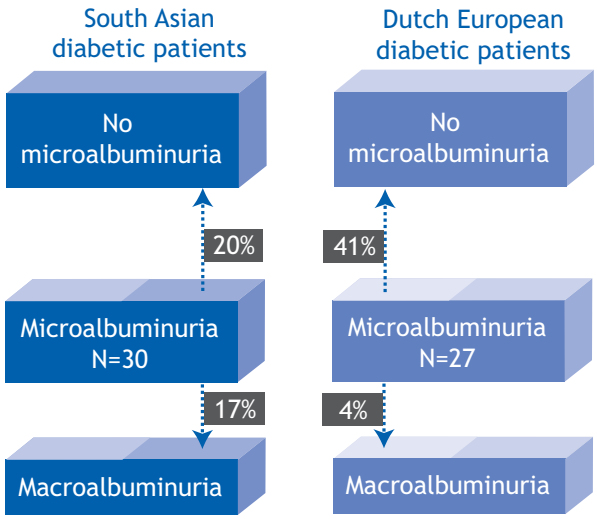

Figure 3: *Evolution of microalbuminuria in 30 South Asian and 27 Dutch European diabetic patients after 5 years follow-up. The dashed arrows show the progression or regression of albuminuria.*

Table 1: *Multivariate analysis for the end-point microalbuminuria/macroalbuminuria in 65 South Asian and 56 Dutch European patients who had no microalbuminuria at inclusion of investigation.*

Model	Exp(B)	95% CI for Exp(B)	P-value
Ethnicity	3.9	1.1 to 14	0.03
Gender	0.9	0.35 to 2.3	0.83
Age	1.05	1.01 to 1.1	0.04
HbA1c	1.2	0.9 to 1.6	0.19
Diabetes duration	0.98	0.9 to 1.05	0.51
Constant	36		0.008

Evolution of microalbuminuria

In the 30 South Asian and 27 European diabetic patients who had microalbuminuria at inclusion of the study, the progression of microalbuminuria to macroalbuminuria was also higher in the South Asian patients. (**Figure 3**) The odds ratio for progression to macroalbuminuria was 5.2 (95% CI 0.56 to 47). European diabetics had a higher tendency for regression to normoalbuminuria. Because of small numbers, we did not include the 12 South Asian patients and 11 European patients with macroalbuminuria in figure 3.

The baseline values for demographic, clinical and biochemical variables are summarised in **Table 2** for the patients who had no microalbuminuria at inclusion of the study. **Table 3** summarises the baseline values for the patients who had microalbuminuria or macroalbuminuria at the start of the study. The age at which the diabetes was diagnosed was 12 years lower in South Asian diabetic patients than in the European group. The diabetes duration was equal and about 12 years. Patients with microalbuminuria or microalbuminuria at inclusion were relatively older than their ethnic counterparts without microalbuminuria. South Asian patients were shorter but had an equal body mass index (BMI). The urinary albumin excretion rate at inclusion was uniformly distributed between both ethnic groups. Mean serum cholesterol, antihypertensive medication, mean systolic blood pressure values and smoking were lower in de South Asian group. (**Table 4**) Despite the lower cardiovascular risk factors and the younger age in South Asian diabetic patients, there were no differences in cardiovascular complications during follow-up. Renine-Angiotensin System (RAS) blocker usage was higher at the end of the study. There were no differences in RAS-blocker usage between both ethnic groups.

Progression of renal failure

The glomerular filtration rate (GFR) estimated with the creatinine clearance was almost equal at start of the investigation. (**Table 2** and **3**) In the analysis, we excluded 14 South Asian and 14 Dutch European patients because of a missing 24-hour creatinine clearance determination.The duration of follow-up was 5.1 years in the South Asian group and 5.0 years in the European group (difference of 0.1 years with 95% CI -0.21 to 0.35; p-value 0.62).

Table 2: *Normoalbuminuric patients baseline values in 65 South Asian and 56 Dutch European type 2 diabetic patients without microalbuminuria at inclusion.*

	Asian	European	Difference (95% CI)	P-value
Males (%)	41.5	41.1	0.4 (-13.1 to 18.1)	0.95
Age (yrs.)	50.6	63.8	-13.2 (-17 to -9.7)	0.0001
Reasons referral (%) Diabetes	75	61.5	13.5 (-29.8 to 2.9)	0.28
Proteinuria	1.5	1.8		
Follow-up (yrs.)	5.2	5.0	0.2 (-0.23 to 0.47)	0.5
Years after first presentation	4.1	3.2	0.9 (-0.23 to 0.43)	0.5
Known duration of diabetes (yrs.)	9.4	9.2	0.2 (-2.4 to 2.9)	0.85
Age at diagnosis of DM	41.1	54.6	-13.5 (-17 to -9.7)	0.0001
Insulin treatment (%)	60	57.1	2.9 (-14.7 to 20.5)	0.84
HbA_{1c} (%)	8.3	7.4	0.9 (0.43 to 1.5)	0.0001
Proliferative retinopathy (%)	20	14.3	5.7 (-7.6 to 19.1)	0.7
Unknown	10.7	10.8		
Weight (kg)	78.1	77.2	0.9 (-6.0 to 7.9)	0.78
Height (cm)	162	169	7 (-8.6 to -1.4)	0.006
Body mass index (kg/m^2)	29.3	27.9	1.4 (-0.5 to 3.3)	0.148
Body square area (m^2)	1.81	1.86	-0.05 (-0.13 to 0.02)	0.13
Urinary AER (mg/24 h)	11.4	10.8	0.6 (-2.0 to 3.4)	0.62
Urinary creatinine excretion($ml/min/1.73m^2$)	9.3	10.6	-1.3 (-2.7 to 0.16)	0.08
Serum creatinine (µmol/l)	68.7	77.1	-8.4 (-16 to -0.6)	0.03
Creatinine clearance ($ml/min/1.73m^2$)	96	93	3 (-11 to 16)	0.7
Serum-total cholesterol (mmol/l)	5.5	5.7	0.2 (-0.6 to 0.09)	0.16
Ever smoked (%)	16.9	17.9	-1 (-14 to 13)	0.31
Unknown	6.2	14.3		
Antihypertensive treatment (%)	29.2	53.6	-24.4 (-41 to -7.2)	0.007
Systolic blood pressure (mmHg)	135	145	10 (-18 to -3.4)	0.004
Diastolic blood pressure (mmHg)	80.1	80.4	0.3 (-3.4 to 4.2)	0.83

The decline in renal function was 1.45 times higher in South Asian diabetic patient group. (**Figure 4**) After 5 years follow-up, South Asian diabetic patient lost 32 ml/min of their GFR versus 22 ml/min loss in the European patients group (difference of 10 ml/min/1.73 m^2 with 95% CI 0.04 to 20; p-value 0.049).

Table 3: *Microalbuminuric/macroalbuminuric patients baseline values in 42 South Asian and 38 Dutch European type 2 diabetic patients.*

	Asian	European	Difference(95% CI)	P-value
Males (%)	45.2	39.5	5.7 (-16 to 27)	0.65
Age (yrs.)	54.4	63.7	-9.3 (-14 to -4.5)	0.0001
Reasons referral (%) Diabetes	61.9	78.9	-17 (-37 to 2.5)	0.16
Proteinuria	7.1	5.3		
Follow-up (yrs.)	5.2	5.1	0.1 (-4.2 to 0.5)	0.87
Years after first presentation	4.6	4.3	0.3 (-1.6 to 2.3)	0.73
Known duration DM (yrs.)	11.9	12.3	0.4 (-4.0 to 3.1)	0.56
Age at diagnosis of DM	42.6	51.2	-8.6 (-14 to -3.6)	0.0001
Insulin treatment (%)	64.3	63.2	1.1 (-20 to 22)	0.76
HbA_{1c} (%)	8.9	8.4	0.49 (-0.4 to 1.4)	0.3
Proliferative retinopathy (%)	19.0	13.2	5.9 (-10 to 21.9)	0.56
Unknown	7.1	13.2		
Weight (kg)	83.1	85.8	-2.7 (-15 to 9.6)	0.66
Height (cm)	161	167	-6 (-10 to -1.7)	0.006
Body mass index (kg/m^2)	29.8	30.1	-0.32 (-2.8 to 2.1)	0.79
Body square area (m^2)	1.82	1.93	-0.11 (-0.2 to -0.02)	0.002
Urinary AER (mg/24 h)	431	694	257 (-775 to 249)	0.31
Urinary creatinine excretion (mmol/24 h)	10.8	11.1	-0.3 (-2.1 to 1.5)	0.75
Serum creatinine (µmol/l)	76.3	78.9	-2.6 (-13 to 8.2)	0.63
Creatinine clearance (ml/min/1.73 m^2)	103	94.5	9.1 (-10 to 28.4)	0.35
Serum-total cholesterol (mmol/l)	5.8	6.1	-0.37 (-0.85 to 0.1)	0.12
Ever smoked (%)	19.0	42.1	-23.1 (-43 to -0.03)	0.04
Unknown	7.1	5.3		
Antihypertensive treatment (%)	54.8	76.3	-21.5 (-42 to -1.3)	0.04
Systolic blood pressure (mmHg)	144	159	-15 (-25 to -3.2)	0.01
Diastolic blood pressure (mmHg)	85.5	88.5	-3.0 (-8.5 to 2.4)	0.27

Table 4: *Risk factors for progression of renal failure, antihypertensive usage and cardiovascular complication at the inclusion in 107 South Asian and 94 Dutch European patients with type 2 diabetes mellitus. The values represents means, unless otherwise stated.*

	Asian	European	Difference (95% CI)	P-value
Risk factors				
Age (yrs.)	52.1	63.8	-11.7 (-15 to -8.7)	0.0001
Males (%)	43.0	40.4	2.6 (-11 to 16)	0.71
HbA1c (%)	8.6	7.8	0.8 (0.3 to 1.3)	0.003
Duration of DM (yrs.)	10.4	10.4	0 (-2.2 to 2.1)	0.97
Serum-total cholesterol (mmol/l)	5.6	5.9	-0.3 (-0.58 to -0.02)	0.03
Ever smoked (%)	17.8	27.7	-9.9 (-21 to 1.7)	0.1
Smoking unknown	6.5	10.6		
Antihypertensive usage (%)	39.3	62.8	-23.5 (-36 to -9.7)	0.001
Systolic bloodpressure (mmHg)	138	150	-12 (-19 to -6.0)	0.0001
Diastolic bloodpressure (mmHg)	83	84	-1 (-4.3 to 2.2)	0.52
Antihypertensive medication at inclusion (%)				
RAS-inhibition	27.1	27.7	-0.6 (-13 to 12)	0.64
ß-blockers	12.1	21.3	-9.2 (-20 to 1.2)	0.1
Calcium-blockers	7.5	16.0	-8.5 (-18 to 0.5)	0.08
Alpha-blockers	0.9	1.1	-0.2 (-4.9 to 9.1)	0.4
Diuretics	11.2	30.9	-19.7 (-31 to -8.4)	0.001
Antihypertensive medication at endpoint (%)				
RAS-inhibition	51.4	47.9	3.5 (-10 to 17)	
ß-blockers	16.8	31.9	-15.1 (-27 to -3.2)	0.012
Calcium-blockers	15.0	19.1	-4.1 (-15 to 6.2)	0.43
Alpha-blockers	2.8	3.2	-0.4 (-6.5 to 5.1)	0.87
Diuretics	33.6	43.6	-10 (-23 to 3.4)	0.15
Cardiovascular complications at inclusion (%)				
Ischemic heart disease	14	16	-2 (-12 to 8.0)	0.7
Cerebrovascular accident	7.5	8.5	-1 (-9.3 to 6.7)	0.8
Peripheral vascular disease	0	5.3	-5.3 (-12 to -0.7)	0.02
Cardiovascular complications during follow up (%)				
Ischemic heart disease	12.1	11.7	0.4 (-9.0 to 9.5)	0.92
Cerebrovascular accident	7.5	3.2	4.3 (-1.8 to 10)	0.18
Peripheral vascular disease	0.9	4.3	-3.4 (-7.8 to 1.1)	0.13

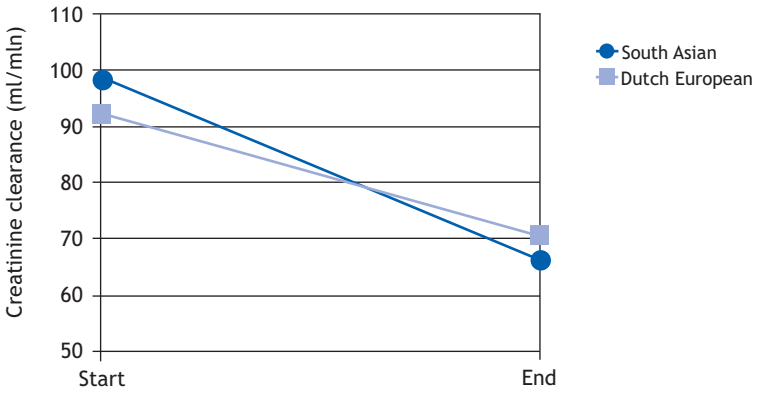

***Figure 4**: Creatinine clearance GFR loss in South Asian (circles) and Dutch European (squares) diabetic patients. Values are shown as mean creatinine clearance, clustered by ethnic group measured at beginning and at end of follow-up period. The GFR declined from 99 ml/min to 67 ml/min for South Asian patients and from 92 ml/min to 70 ml/min for Dutch European patients.*

Discussion

Diabetic South Asian patients have an ethnic susceptibility for developing nephropathy. We found a twice higher incidence of nephropathy and faster loss of renal function in South Asian diabetic patients compared to European Dutch diabetic patients. After correction for the 12 years age difference, the adjusted odds ratio for developing nephropathy increased to nearly 4 for the South Asian type 2 diabetic group. After 5 years follow-up, the loss in glomerular filtration was 1.45 times higher in the South Asian group.

The South Asian population in our study is different from the European Dutch population because at the start of follow-up they were younger and had less cardiovascular complications and used less antihypertensive medication than the European group. Duration of diabetes, time of first referral and reasons of referral were the same in both ethnic groups. Despite the lower blood pressure values, the lesser use of antihypertensive drugs, lower serum total cholesterol and after correction for the higher HbA1c values, we found a 4 times increased odds ratio for developing microalbuminuria or macroalbuminuria in the South Asian diabetic group. The adjusted odds ratio derived after multivariate analysis slightly overestimates the true relative

risk because of the high frequency of microalbuminuria. [12] After correction for the overestimation, the relative risk is still higher in the South Asian group: 2.8 (95% CI 1.08 to 4.9). The higher risk for microalbuminuria was not attributed to differences in RAS blocker usage between the two ethnic groups. However, the use of diuretics was higher in European patients. This could conceal microalbuminuria at inclusion in the European diabetic group, giving in fact an underestimation of the increased risk for microalbuminuria.

In an earlier study, we found a nearly 40-fold increased risk for end-stage diabetic nephropathy in the South Asian population living in the Netherlands. [1] Our study explains the gap between the reported 8-times higher prevalence of diabetes [8] and the 40-fold higher risk of end-stage diabetic nephropathy in the South Asian population. Our previous reported family study in South Asian dialysis patients showed no familiar predisposition for renal disease within the South Asian population. [7] The lack of familial clustering of renal disease in South Asian diabetic patients points to an universal genetic or environmental susceptibility for nephropathy in this population. We assume that the nearly 40-fold higher risk of end-stage diabetic nephropathy in South Asian migrants is caused by several factors: first the 8-times higher prevalence of diabetes in South Asians, secondly more development of nephropathy and finally, a faster progression of renal failure in the South Asian group.

Our findings could have been confounded by the higher mortality in the European population, probably explained by the older age. The same phenomenon was described earlier by Mather et al. [13] After 11 years follow-up 33% of the South Asian patients died (mean age 55 years) versus 57% of the older European diabetic patients (mean age 67 years). Since microalbuminuria is an independent risk factor for cardiovascular mortality, [14,15] this could give lower microalbuminuria levels in the studied population at the end. Nevertheless, during the follow-up, cardiovascular disease was equal in both ethnic groups. Furthermore, we matched the European patients for urinary albumin excretion and gender at start of the investigation. Finally, after age-adjustment, the higher risk for microalbuminuria still persisted. Other limitations of our study concern the patient group who was discharged from the out-patient clinic and taken into the care of the general practitioners. First, follow-up measurements for urinary albumin excretion and creatinine clearance were not frequently done by the GP. Another problem we encountered was that the follow-up measurements of the discharged patients were done in different laboratories. However, the patients of both ethnic groups were equally distributed over the laboratories and also the method of albuminuria testing was equally distributed over the South Asian and European diabetic patients groups.

Our cohort study complements the cross-sectional studies performed by Mather et al. [9] and Chowdhury et al. [16] Both studies found higher prevalence rates of microalbuminuria in South Asian diabetic patients versus British European diabetic patients. Two studies showed conflicting results with regard to renal loss in South Asian migrants. The study of Koppiker et al. [10] showed no difference in loss of renal function. However, another study of Earle et al. [11] found a higher progression of renal failure in South Asians versus British diabetic patients. The conflicting results of the previous studies are understandable, because both studies could only utilize the serum creatinine values as determinant for renal function loss, making these studies less sensitive for detecting differences in renal failure. We therefore used creatinine clearance in the 24-hour urine, which is a better estimate of renal function. Using serum creatinine value alone is especially hazardous in migrant populations because of the differences in muscle mass. We did not use calculated GFR method, like Cockcroft-Gault estimation or simplified MDRD-formula because these have not been validated South Asian patients. [17] The results calculated by Cockcroft-Gault or simplified MDRD formula revealed also a high progressive loss in GFR in the South Asian diabetic group. (data not given).

What could be the pathophysiologic mechanism leading to more nephropathy in South Asian diabetic patients?

Higher microalbuminuria does not always implies renal disease, but can also be a marker for endothelial damage. One of the hypothesis could be a common ethnic susceptibility for endothelial dysfunction within the South Asian population, leading to more microalbuminuria and ischemic heart disease. We therefore took cardiovascular complications into account, which were not different between the groups. This was observed despite the younger age, less hypertension and lower serum cholesterol values in the South Asians. McKeigue et al. reported unusually high coronary heart disease rates in people originating from the Indian subcontinent. [18,19] In a cross-sectional study in the UK, Cappuccio et al. showed that the classical Framingham risk equations underestimate the risk for myocardial infarction. [20] It is difficult to prove this hypothesis because our study was not designed to detect differences in endothelial dysfunction.

Conclusion

South Asian type 2 diabetic patients develop more nephropathy and have faster progression of renal failure in comparison to European diabetic patients. Classic risk factors for development of microalbuminuria and progression of renal failure do not explain this higher risk in South Asian diabetic patients. Our study confirms the hypothesis of a general genetic or environmental susceptibility for nephropathy among South Asian diabetics. As South Asian patients develop these complications insidiously at a much younger age, we recommend general practitioners to screen for diabetes and renal failure in every South Asian migrant above the age of 30 years.

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