Diabetic nephropathy in Surinamese South Asian subjects

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Pas gearriveerde immigranten uit toenmalig Brits-Indië staan voor het immigratiedepot nabij Paramaribo, Suriname, ca. 1915.

Chapter 3

Increased end-stage diabetic nephropathy in South Asian immigrants living in the Netherlands

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Abstract

Objective

To investigate the risk of end-stage diabetic nephropathy due to type 2 diabetes mellitus in South Asian immigrants from Suriname.

Research design and methods

A demographically based case-control study in Surinamese South Asians and Dutch European individuals. All newly started dialysis patients between 1990 and 1998 with end-stage diabetic nephropathy were identified through a national registry of all patients entering a renal replacement program in the Netherlands. The general population of native Dutch and Surinamese South Asians were taken as controls.

Results

Among South Asians, the age adjusted relative risk of end-stage diabetic nephropathy was 38 (95% confidence interval 16 to 91) in comparison with the native Dutch population. The duration of diabetes till start of dialysis treatment was similar in both ethnic groups, about 17 years.

Conclusion

South Asians had a nearly 40-fold increase in the risk for end-stage diabetic nephropathy due to type 2 diabetes mellitus, in comparison with the Native Dutch population. This was higher than expected on the basis of the eight-fold higher prevalence of diabetes the South Asian population. The similar diabetes duration until onset of the dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of diabetic nephropathy in the South Asian diabetic population. Early and frequent screening for diabetes and microalbuminuria is recommended in South Asians.

Introduction

Type 2 diabetes mellitus is frequently seen in immigrants of Asian Indian descent (South Asians). Three studies in Southall, Coventry and Leicester showed that diabetes occurs three to four times more frequent in those of South Asian origin than among the white UK population. [1-6] In the Netherlands, the increased prevalence of diabetes among Surinamese South Asian immigrants was recently investigated by the local Community Health Service in the city of The Hague. This survey revealed an eight times higher prevalence of diabetes in Surinamese South Asians when compared to the general Dutch population. [7]

Several hospital-based studies in the UK have shown a ten-fold higher incidence of end-stage renal failure due to diabetic nephropathy in South Asian immigrants, as compared to the European population. [2;8-11] Because a proportion of patients attended other centres, concerns arose about underestimation of the true incidence in these studies. Furthermore, specific studies on type 2 diabetes mellitus and end-stage renal failure are still lacking in the South Asian population. In several studies, microalbuminuria was more frequent in diabetic South Asians, which suggests that they are more prone to develop kidney disease. [12-14] There is no evidence that patients of South Asian origin have more often a high blood pressure or a poorer metabolic control explaining the early diabetic nephropathy. [2;4;15]

The national registry for renal replacement therapy in the Netherlands offered a unique possibility to study the relative risk of end-stage diabetic renal disease among Surinamese South Asians and Dutch European persons who are living in the city of The Hague. In the Netherlands patients are assigned to a regional dialysis center based on the place of residence of the patient. The overall population figures per region are known and new patients are registered within three months after start of renal replacement therapy. This permitted us to determine the relative risk of end-stage diabetic nephropathy in these two ethnic groups. In this article, we focus on end-stage renal failure due to type 2 diabetes mellitus, because specific incidence data on end-stage renal failure in type 2 diabetes are not known in the South Asian population.

Research design and methods

Clinical data from all patients who started with their dialysis treatment between Januari 1,1990 and December 31, 1997 were received from the Renal Replacement Registry Netherlands (a Dutch acronym: RENINE). These data were validated using the records of the dialysis centers.

Population

In this study, the case group is formed by dialysis patients with ESRF due to diabetes mellitus. The control group comprises the general population in the city of The Hague. The investigated risk factor is an South Asian ethnicity. If this ethnicity would have a higher risk for ESRF due to diabetes mellitus, this would result in an excess of South Asians in the dialysis wards in The Hague.

Case group: we identified all new South Asian and Dutch European dialysis patients with diabetic nephropathy who started their dialysis treatment in one of the three hospitals from 1990 until 1998. Patients living outside the city of The Hague were excluded. We adjusted for possible immigration for medical reasons, by excluding all South Asian patients who migrated to the Netherlands within two years before they started their dialysis treatment.

General population: this was based on the average population figures in the period 1995 to 1998 derived from the Statistics Netherlands (Central Bureau of Statistics). The term *"South Asians"* refers to all descendants of emigrants including the Indian subcontinent, like India, Pakistan, Nepal and Bangladesh. The white Dutch population is indicated with *"European"*. The Hague has 330000 inhabitants of whom 82% are European, 10% South Asians and 8% have another ethnicity. The Hague has about 189000 Dutch and 15000 Surinamese South Asian inhabitants *with an age of 30 years or older.*

Diagnosis of diabetic nephropathy: patients were selected because they were coded in the RENINE registry as having diabetic nephropathy by their nephrologist. The medical records of all patients were examined for type of diabetes mellitus, presence of proteinuria, diabetic retinopathy and the absence of other causes of nephropathy like infections, tuberculosis, renal stones or obstructive nephropathy. Diabetic retinopathy was defined by proliferative retinopathy necessitating laser treatment.

Type diabetes mellitus: patients who had used oral antidiabetic medication for more than one year or who had a high morning c-peptide level 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.

Statistical analyses

By comparing both populations, we calculated crude odds-ratios as estimates of the relative risks with 95% confidence intervals for the risk factor of having a South Asian ethnicity. The South Asian population has a different age-distribution. Older age groups form a larger proportion of the native Europeans, than in the South Asian population: in the region, approximately 1700 South Asians were aged above the 60 years versus 76000 native Dutch inhabitants. Because this leads to an underestimation of the risk for end-stage diabetic nephropathy in the South Asians, we used age-stratification with the Mantel-Haenszel odds ratio in the population of 30 years and older. The following age-stratification was chosen: 30 to 49 years, 50 to 59 years and above the 59 years. The same age-stratification was used in a previous diabetes prevalence study done by the Municipal Health Service in The Hague to evaluate the higher prevalence of diabetes among the South Asian population. [7] The figures of the inhabitants were based on the census figures of the Statistics Netherlands (CBS) and the Municipal Health Services in the period 1995 to 1998.

The statistical significances in the difference of mean age, duration of the diabetes between the South Asian and Dutch European patients were calculated using the Student's t-test. Differences in type diabetes, dialysis treatment modalities were expressed as percentage difference with 95% confidence intervals.

Results

Study population

From January 1, 1990 to December 31, 1997, there were 94 new patients registered who started with dialysis treatment due to diabetic nephropathy. We excluded 25 patients because they had another ethnicity than Dutch European or South Asian. Eight patients were excluded because they lived outside the study region comprising The Hague and its surrounding suburbs. One European and two South Asian patients were incorrectly registered because they had no diabetes or diabetic nephropathy. Two patients (one European and one South Asian) had diabetes mellitus without proteinuria or a documented diabetic retinopathy. Because no renal biopsy had been done, we excluded these patients from the analysis to prevent misclassification of diabetic nephropathy. After the exclusion, 56 patients entered the study.

Basic characteristics

The basic characteristics of the study population are given in **Table 1**. There were 27 Dutch European and 29 South Asian patients who started with dialysis treatment due to diabetic nephropathy. The South Asians were slightly younger at the start of the dialysis treatment. The number of female patients predominated slightly in both ethnic groups. Type 2 diabetes mellitus was more present in the South Asian diabetic patients, 93% versus 67% in the European diabetic patients (difference 26% with 95% CI 6.4 to 46.5). About 74% of the Dutch European and 72% of the South Asian patients had a documented proliferative diabetic retinopathy. In about a quarter of the patients no report of an eye-examination could be found in the medical records. The prevalence of diabetic retinopathy did not differ between the European and the South Asian patient groups.

Table 1: *basic characteristics of the selected dialysis population*

	Dutch European	South Asians
Total number of patients	27	29
Mean age at onset of ESRF (yrs.)	58.8	53.3
Males number (%)	13 (48.1%)	14 (48.3%)
Type 2 diabetes mellitus (%)	18 (67%)	27 (93%)
Diabetic retinopathy		
No proliferative retinopathy (%)	0	1 (4%)
Proliferative retinopathy (%)	20 (74%)	21 (72%)
No documented visits (%)	7 (26%)	7 (24%)

Diagnosis diabetic nephropathy

The registered diagnoses were verified by reviewing the medical records of the patients (**Table 2**). No differences were observed in clinical criteria used to diagnose diabetic nephropathy. All patients had proteinuria. Thirteen patients underwent a renal biopsy: seven in the Dutch European patient group and six in the South Asian patient group. The histological results were consistent with diabetic nephropathy.

Type 2 diabetes mellitus

There were 18 Dutch European and 27 South Asian dialysis patients with type 2 diabetes mellitus. South Asian patients had an earlier age at onset of diabetes than Caucasians: 36 versus 50 years (difference 14 years with 95% confidence interval 6 to 20). Similarly, dialysis treatment started earlier: 67 versus 54 years (difference 13 years with 95%

confidence interval 7 to 21). The duration of the diabetes until the start of dialysis treatment was comparable in both ethnic groups: 16.7 and 17.6 years (difference -0.9 years with 95% confidence interval –6.2 to 4.6)

Table 2: *Diagnostic criteria for diabetic nephropathy in 56 patients with end-stage renal failure.*

	Europeans Number (%)	South Asians Number (%)
Diabetes, proteinuria and diabetic retinopathy	20 (74%)	21 (72%)
Diabetes, proteinuria	7 (26%)	8 (28%)

Relative risk of end-stage diabetic nephropathy

To calculate relative risks, we made a comparison with the population of *30 years and older* living in the city of The Hague. When looking at the relative risk for end-stage diabetic nephropathy, we excluded 12 patients because they lived in the suburbs of The Hague. For the final analysis two South Asians were excluded because they did not descent from Surinamese South Asian immigrants, and four South Asian patients were excluded because they had immigrated to the Netherlands within two years after start of dialysis therapy. Two patients were left out of the calculation because they were younger than 30 years at start of renal replacement therapy. A total of 16 European and 20 South Asian patients were included (**figure 1**). The crude and age-adjusted relative risks with 95% confidence intervals are given in **Table 3**. *The crude relative risk* for end-stage diabetic nephropathy overall was 16.2 for South Asians, with a 95%-confidence interval of 8.1 to 30.3. When looking at type 1 diabetes there was a slight increase, but the numbers are very small. The largest risk of nephropathy is caused by type 2 diabetes: 21.6-times higher incidence was noticed in the South Asian group. The *age-adjusted relative risk* using the Mantel-Haenszel method over the three age-strata showed an overall relative risk for end-stage diabetic nephropathy of 21.6 (95% confidence interval 10.1 to 42.7). This was mainly due to type 2 diabetes giving an age-adjusted relative risk of 37.7 (95% confidence interval 15.6 to 91.2).

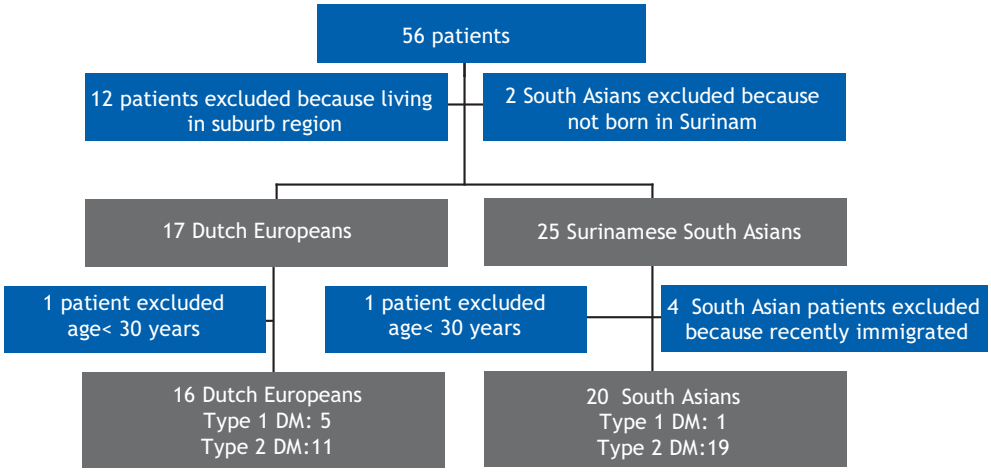

***Figure 1**: Flow diagram of the study population used for the incidence calculations.*

***Table 3**: Relative risk for end-stage diabetic nephropathy in Dutch European and South Asian inhabitants above the age of 30 years. Age corrected relative risk was calculated using the Mantel-Haenszel method. (95% confidence intervals are given in brackets).*

	Crude relative risk	Age-corrected relative risk
Overall risk ESRF due to diabetes mellitus	16.2 (95%-CI 8.1 to 30.3)	21.7 (95%-CI 10.1 to 42.7)
Relative risk in type 1 diabetes	2.52 (95%-CI 0.3 to 21.6)	Not given because of small numbers
Relative risk in type 2 diabetes	21.6 (95%-CI 10.3 to 45.7)	37.7 (95%-CI 15.6 to 91.2)

Discussion

We determined the relative risk of end-stage renal failure (ESRF) due to diabetes mellitus between Surinamese South Asian immigrants and native Dutch European persons older than 30 years, who are living in the city of The Hague. The Surinamese South Asians, originally descended from the Indian subcontinent. Due to the former colonial bounds with the Netherlands, a relatively young South Asian migrant population settled in the Netherlands. In this population, the age-adjusted relative risk for ESRF due to both types of diabetes was 22-times increased. ESRF due to type

2 diabetes was almost 40-fold increased in the South Asian population. Also a slight increase in type 1 diabetes was noted in this population but the numbers were too small to draw conclusions.

We were in an unique position to perform a demographically and geographically defined population study. In the Netherlands, patients with end-stage renal failure are assigned to a dialysis facility based on their place of residence. All patients with ESRF who live in the city of The Hague are therefore treated in only three dialysis centers. We could identify them by using the national registry for renal replacement therapy (RENINE). This registry also contains the diagnosis of end-stage renal failure (ESRF). Throughout the years a nearly 100% response rate was obtained in the registry. We verified the diagnosis of diabetic nephropathy by reviewing the medical charts. Most patients had proteinuria and diabetic retinopathy. In only a few patients a renal biopsy was performed. There were no differences in the criteria used to diagnose diabetic nephropathy in both ethnic groups. It might be argued that we missed some patients with diabetic nephropathy because of incorrect registration of the renal diagnosis. We therefore performed a crosscheck with the hospital registries, which revealed no missed patients. We choose the period until 1998, to ensure that the nephrologist's diagnosis of diabetic nephropathy was not influenced by the study hypothesis. We carefully corrected for immigration for medical reasons by excluding all South Asian patients who immigrated to the Netherlands within two years before onset of renal replacement therapy. The South Asian population had a different age-distribution. Older age groups, which form a large section in Dutch European population are almost absent in the South Asian population. Because this underestimates the risk for end-stage diabetic nephropathy in South Asians, we performed an age correction using the Mantel-Haenszel method. The age-corrected relative risk for ESRF due to type 2 diabetes was 38 compared to Dutch European. We calculated a similar diabetes duration of about 17 years in both ethnic groups. South Asians were 13 years younger at the onset of the dialysis treatment. This age difference could be explained by the younger age at which the diabetes started in the South Asian population, but might also be a reflection of the younger age distribution in the South Asian population. We cannot exclude that more South Asians died from cardiovascular disease before startingdialysis treatment than in the European group. This would underestimate the risk in the South Asian population.

In two hospital-based studies done in the UK, the centre-specific incidence was a tenfold higher for end-stage diabetic nephropathy in the migrant South Asian population. [8;10] The difference with our study is explained by the study design.

Firstly, our study was a demographically and geographically defined population study. This prevented underestimation of the risk by missing patients which were treated in other hospitals. Furthermore, the studies performed in the UK, calculated the risk in the population above the age of 15 while we used only persons aged 30 and above, since the risk of end-stage diabetic nephropathy is neglectible below that age. When we calculated the risk in our population also from the age of 15 years and older the relative risk was similar. Finally, there are differences in disease patterns of South Asian immigrants originating from different parts of the Indian subcontinent. [16] Unlike the South Asians in the UK, Surinamese South Asians originally descend from a restricted area in Northern India, the West-Bihar and formerly United Provinces. So the South Asian population of the Netherlands is probably more homogeneous than in other studies.

The increased risk of end-stage diabetic nephropathy could be explained in part by the increased prevalence of type 2 diabetes in the South Asian population. A recent survey done by the Municipal Health Service showed an eightfold higher prevalence of diabetes among the South Asian population in The Hague. [7] In addition, large population studies in the UK show a three to four times increased risk for diabetes among the South Asian migrant population. [1-6] However, this higher prevalence of diabetes does not fully explain the close to 40-times increased risk for end-stage type 2 diabetic nephropathy among South Asians. Additional factors should therefore be considered such as a more aggressive course of diabetic disease or a higher incidence of nephropathy in the South Asian type 2 diabetic population. The similar diabetes duration until onset of the dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of diabetic nephropathy in the South Asian diabetic population.

Conclusion

We found a close to 40-fold higher risk of end-stage diabetic nephropathy due to type 2 diabetes mellitus in Surinamese South Asian immigrants when compared to native Dutch individuals. The eight-times higher prevalence of diabetes in the South Asian general population only partially explains the increased risk of end-stage diabetic nephropathy in South Asians. The similar diabetes duration until onset of the dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of

diabetic nephropathy in the South Asian diabetic population. Early and frequent screening for diabetes and microalbuminuria is recommended in South Asians.

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