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

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### Abstract

**Aims/hypothesis.** We aimed to investigate the risk of end-stage diabetic nephropathy due to Type II (non-insulin-dependent) diabetes mellitus in Indo-Asian immigrants from Surinam.

**Methods.** A demographically based case-control study was carried out in Surinamese Indo-Asian immigrants and Dutch Caucasian subjects. All patients with end-stage diabetic nephropathy who had started dialysis between 1990 and 1998 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 Indo-Asians were considered the control subjects.

**Results.** Among Indo-Asian immigrants, the age adjusted relative risk of end-stage diabetic nephropathy was 38 (95% CI 16 to 91) compared with the native Dutch population. The duration of diabetes until the

start of dialysis treatment was similar in both ethnic groups, about 17 years.

**Conclusion/interpretation.** The Indo-Asian subjects had a nearly 40-fold increase in the risk for end-stage diabetic nephropathy due to Type II diabetes, compared with the native Dutch population. This was higher than expected on the basis of the eightfold higher prevalence of diabetes in the Indo-Asian population. The similar duration of diabetes until the start of dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of diabetic nephropathy in the Indo-Asian diabetic population. Early and frequent screening for diabetes and microalbuminuria is recommended in Indo-Asian subjects. [Diabetologia (2002) 45: 337–341]

**Keywords** Diabetic nephropathy, dialysis, end-stage renal failure, diabetes mellitus, Type II diabetes mellitus, Indian, Indo-Asians, Asians, ethnicity.

Type II (non-insulin-dependent) diabetes mellitus is frequently seen in immigrants of Asian Indian descent (Indo-Asians). Three studies in Southall, Coventry and Leicester showed that diabetes occurs three to four times more frequent in those of Indo-Asian origin than among the white population of the United Kingdom [1–6]. In the Netherlands, the increased prevalence of diabetes among Surinam Indo-Asian

immigrants was recently investigated by the local Community Health Service in the city of The Hague. This survey showed an eight times higher prevalence of diabetes in Surinamese Indo-Asian subjects when compared to the general Dutch population [7].

Several hospital-based studies in the United Kingdom have shown a tenfold higher incidence of end-stage renal failure due to diabetic nephropathy in Indo-Asian immigrants compared with the white Caucasian 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 II diabetes mellitus and end-stage renal failure are still lacking in the Indo-Asian population. In several studies, microalbuminuria was more frequent in Indo-

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Asian diabetic patients, which suggests that they are more prone to develop kidney disease [12–14]. There is no evidence that patients of Indo-Asian origin have a higher incidence of high blood pressure or poorer metabolic control which could explain their 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 Indo-Asian and Dutch Caucasian 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 they start 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 II diabetes mellitus, because specific incidence data on end-stage renal failure in Type II diabetes are not known in the Indo-Asian population.

## Subjects and methods

Because of the regional allocation of patients for renal replacement therapy, patients who live in The Hague are therefore treated in only three dialysis centres. Clinical data from all patients who started their dialysis treatment between January 1, 1990 and December 31, 1997 were received from the Renal Replacement Registry Netherlands (RENINE). This registry also contains the diagnosis of end-stage renal failure. Throughout the years a nearly 100% response rate was obtained in the registry. These data were validated using the records of the dialysis centers. The institutional review boards of the Leiden University Medical Center, the Red Cross Hospital, the Medical Center Haaglanden and the Hospital Leyenburg granted ethical approval for the study and the study participants gave their informed consent.

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

**Case group.** We identified all new Indo-Asian and Caucasian dialysis patients with diabetic nephropathy who started their dialysis treatment in one of the three hospitals from 1990 until 1998. Patients living outside of The Hague were excluded. We adjusted for possible immigration for medical reasons, by excluding all Indo-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 (CBS). The term "Indo-Asians" refers to all descendants of emigrants from the Indian subcontinent, like India, Pakistan, Nepal and Bangladesh. The white Dutch population is referred to as "Caucasians". The Hague has 330 000 inhabitants of whom 82% are Caucasian, 10% Indo-Asian and 8% are of another ethnicity. The Hague has about 189 000 Dutch and 15 000 Surinam Indo-Asian inhabitants of age 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 high concentrations of C-peptide in the morning were coded as Type II diabetic patients. Patients who used only insulin with a history of keto-acidosis were coded as patients with Type I (insulin-dependent) diabetes mellitus.

**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 an Indo-Asian ethnicity. The Indo-Asian population has a different age-distribution. Older age groups form a larger proportion of the native Caucasians than in the Indo-Asian population: in the region, approximately 1700 Indo-Asians were older than 60 years of age compared with 76 000 native Dutch inhabitants. Because this leads to an underestimation of the risk for end-stage diabetic nephropathy in the Indo-Asian subjects, we used age-stratification with the Mantel-Haenszel odds ratio in the population of subjects who were 30 years and older. The following age-stratification was chosen: 30 to 49 years, 50 to 59 years and older than 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 Indo-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 1995 to 1998.

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

## 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 were not of Caucasian or Indo-Asian ethnicity. Eight patients were excluded because they lived outside the study region comprising The Hague and its surrounding suburbs. One Caucasian and two Indo-Asian patients were incorrectly registered because they did not have diabetes or diabetic nephropathy. Two patients

**Table 1.** Basic characteristics of the selected dialysis population

	Caucasian patients	Indo-Asian patients
<i>n</i>	27	29
Mean age at onset of end-stage renal failure (years)	58.8	53.3
Men (%)	13 (48.1%)	14 (48.3%)
Type II 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%)

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

	Caucasian patients <i>n</i> (%)	Indo-Asian patients <i>n</i> (%)
Diabetes, proteinuria and diabetic retinopathy	20 (74%)	21 (72%)
Diabetes, proteinuria	7 (26%)	8 (28%)

(one Caucasian and one Indo-Asian) had diabetes mellitus only 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 (Table 1).** The basic characteristics of the study population are given in Table 1. There were 27 Caucasian and 29 Indo-Asian patients who started with dialysis treatment due to diabetic nephropathy. The Indo-Asians were slightly younger at the start of the dialysis treatment. The number of female patients predominated slightly in both ethnic groups. Type II diabetes was more present in the Indo-Asian diabetic patients, 93% compared with 67% in the Caucasians diabetic patients (difference 26% with 95% CI 6.4 to 46.5). About 74% of the Caucasian patients and 72% of the Indo-Asian patients had documented proliferative diabetic retinopathy. In about a quarter of the patients, no report of an eye-examination could be found in their medical records. The prevalence of diabetic retinopathy did

not differ between the Caucasian and the Indo-Asian patient groups.

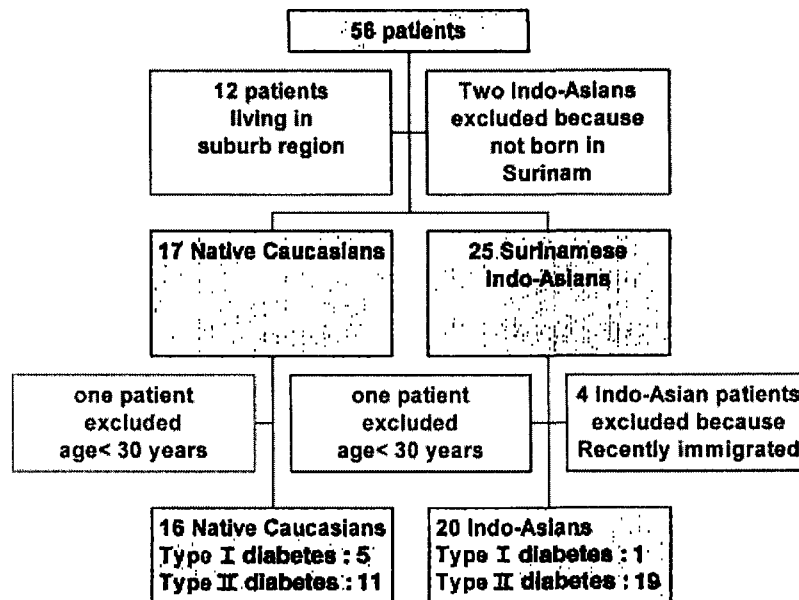
**Diagnosis diabetic nephropathy.** The registered diagnoses were verified by reviewing the medical records of the patients (Table 2). No differences were observed in clinical criteria used to diagnose diabetic nephropathy. All patients had proteinuria. Thirteen patients had had a renal biopsy: seven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

**Type II diabetes mellitus.** There were 18 Caucasian and 27 Indo-Asian dialysis patients with Type II diabetes mellitus. Indo-Asian patients had an earlier age at onset of diabetes than Caucasians: 36 vs 50 years (difference 14 years with 95% CI 6 to 20). Similarly, dialysis treatment started earlier: 67 vs 54 years, (difference 13 years with 95% CI 7 to 21). The duration of diabetes until the start of the dialysis treatment was comparable in both ethnic groups: 16.7 and 17.6 years (difference -0.9 years with 95% CI -6.2 to 4.6).

**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 Indo-Asians were excluded because they were not descendants of Surinamese Indo-Asian immigrants, and four Indo-Asian patients were excluded because they had immigrated to the Netherlands within two years before starting dialysis treatment. Two patients were left out of the calculation because they were younger than 30 years at the start of renal replacement therapy. A total of 16 Caucasian and 20 Indo-Asian patients were included (Fig. 1). The crude and age-adjusted relative risks with 95% CI are given in Table 3. The crude relative risk for end-stage diabetic nephropathy overall was 16.2 for Indo-Asians, with a 95%-CI of 8.15 to 30.3. There was a slight increase with Type I diabetes but the numbers are very small. The largest risk of nephropathy is caused by Type II diabetes with a 21.6-times higher incidence in the Indo-Asian group. The

**Table 3.** Relative risk for end-stage renal failure due to diabetes mellitus in Caucasian and Indo-Asian inhabitants older than 30 years of age. Age corrected relative risk was calculated using the Mantel-Haenszel method. (95% CI are given in brackets)

	Crude relative risk	Age-corrected relative risk
Overall risk of end-stage renal failure due to diabetes mellitus	16.2 (95% -CI 8.15 to 30.3)	21.7 (95% -CI 10.1 to 42.7)
Relative risk in Type I diabetes	2.52 (95% -CI 0.29 to 21.6)	Not given because of small numbers
Relative risk in Type II diabetes	21.6 (95% CI 10.3 to 45.7)	37.7 (95% CI 15.6 to 91.2)



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

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 21.7 (95% CI 10.1 to 42.7). This was mainly due to Type II diabetes giving an age-adjusted relative risk of 37.7 (95% CI 15.6 to 91.2).

## Discussion

We determined the relative risk of end-stage renal failure due to diabetes mellitus between Surinamese Indo-Asian immigrants and native Dutch Caucasian persons older than 30 years, who are living in the city of The Hague. The Surinamese Indo-Asians, originally descended from the Indian subcontinent. Due to the former colonial ties with the Netherlands, a relatively young Indo-Asian migrant population settled in the Netherlands. In this population, the age-adjusted relative risk for end-stage renal failure due to both types of diabetes was increased 22-times. End-stage renal failure due to Type II diabetes was almost 40-fold increased in the Indo-Asian population. Also a slight increase in Type I diabetes was noted in this population but the numbers were too small to draw conclusions.

We were in a unique position to carry out 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. We could identify them by using the national registry for renal replacement ther-

apy. We validated 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 done. There were no differences in the criteria used to diagnose diabetic nephropathy in both ethnic groups. To avoid missing any patients with diabetic nephropathy because of incorrect registration of the renal diagnosis we cross-checked the hospital registries. We chose 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 Indo-Asian patients who immigrated to the Netherlands within two years before onset of renal replacement therapy. The Indo-Asian population had a different age-distribution. Because of this we did an age correction using the Mantel-Haenszel method. The age-corrected relative risk for end-stage renal failure due to Type II diabetes was 38 compared to native Caucasians. We calculated a similar diabetes duration of about 17 years in both ethnic groups. Indo-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 Indo-Asian population, but might also be a reflection of the younger age distribution in the Indo-Asian population. We cannot exclude that more Indo-Asians died from cardiovascular disease before starting their dialysis treatment than in the Caucasian group. This would underestimate the risk in the Indo-Asian population.

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

ly, 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 done in the United Kingdom calculated the risk in the population of subjects older than 15 years of age, whereas we included only persons aged 30 and older because the risk of end-stage diabetic nephropathy is negligible 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 Indo-Asian immigrants originating from different parts of the Indian subcontinent [16]. Unlike the Indo-Asian people in the United Kingdom, Surinamese Indo-Asians originally descend from a restricted area in Northern India, the West-Bihar and the former United Provinces. So the Indo-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 II diabetes in the Indo-Asian population. A recent survey done by the Municipal Health Service showed an eightfold higher prevalence of diabetes among the Indo-Asian population in The Hague [7]. In addition, large population studies in the United Kingdom show a three to four times increased risk for diabetes among the Indo-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 II diabetic nephropathy among Indo-Asian people. Additional factors should therefore be considered such as a more aggressive course of diabetic disease or a higher incidence of nephropathy in the Indo-Asian Type II diabetic population. The similar diabetes duration until the start of dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of diabetic nephropathy in the Indo-Asian diabetic population.

**Conclusions.** We found a close to 40-fold higher risk of end-stage diabetic nephropathy due to Type II diabetes mellitus in Surinamese Indo-Asian immigrants compared to native Dutch individuals. The eight-times higher prevalence of diabetes in the Indo-Asian general population only partially explains the increased risk of end-stage diabetic nephropathy in Indo-Asian people. The similar diabetes duration until the start of dialysis treatment in both ethnic groups supports the hypothesis of a higher incidence of diabetic nephropathy in the Indo-Asian diabetic population. Therefore, early and frequent screening for diabetes and microalbuminuria is recommended in Indo-Asians.

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