

CLINICAL STUDY

Natural course of untreated microalbuminuria in children and adolescents with type 1 diabetes and the importance of diabetes duration and immigrant status: longitudinal analysis from the prospective nationwide German and Austrian diabetes survey DPV

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Abstract

Objective: To identify risk factors for the development and progression of untreated persistent microalbuminuria in children and adolescents with type 1 diabetes.

Design and methods: A total number of 683 children and adolescents with type 1 diabetes recruited from the prospective nationwide German and Austrian diabetes survey (DPV) were included in the analysis. Inclusion criteria were onset of type 1 diabetes under the age of 11 years, diabetes duration of more than 1 year and continuous follow-up over 5 years with at least two documented urine analyses per year. Subjects treated with angiotensin-converting enzyme inhibitors were excluded. Risk factors such as sex, body mass index SDS, diabetes duration, HbA1c, total cholesterol, HDL-cholesterol, LDL-cholesterol, systolic and diastolic blood pressure, and immigrant status were analysed by logistic regression.

Results: At baseline (age 10.5 ± 0.1 years, diabetes duration 4.6 ± 2.4 years and HbA1c $7.4 \pm 1.1\%$), 75.6% of children had normoalbuminuria, 15.7% had intermittent microalbuminuria, 8.6% had persistent microalbuminuria and 0.1% had macroalbuminuria. After a follow-up of 5 years, 59.4% of adolescents continued to have normoalbuminuria, 18.4% had progression, 15.2% had regression of microalbuminuria, and in 6.9% of the subjects, microalbuminuria remained unchanged. We found significant associations between persistent microalbuminuria at baseline and during each year of follow-up ($P < 0.0001$). Logistic regression analysis identified diabetes duration and immigrant status as significant factors for microalbuminuria ($P = 0.009$ and $P = 0.009$).

Conclusions: The survey in a real-world setting shows that diabetes duration and immigrant status are risk factors for the development and progression of untreated microalbuminuria in children and adolescents with type 1 diabetes.

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Introduction

Microalbuminuria is a common finding in type 1 diabetes and is found in 30–60% of patients with a diabetes duration of 10–20 years (1, 2, 3, 4). Persistent microalbuminuria is an important predictor of the development of diabetic nephropathy and progressive renal insufficiency in adults with type 1 diabetes (1, 3, 4). Progression to macroalbuminuria or overt diabetic nephropathy occurs in around 25–45% of adults with type 1 diabetes with persistent microalbuminuria over ~10 years (1, 5). Several risk factors, including poor

glycaemic control and a long diabetes duration, have a considerable impact on the rate of progression (1, 4, 6). Furthermore, persistent microalbuminuria is associated with the progression of other diabetes complications such as retinopathy and cardiovascular disease (1, 3, 4). However, risk factors for the development of diabetic nephropathy, including glycaemic control, diabetes duration, hypertension, smoking and hyperlipidaemia, do not explain the risk of nephropathy entirely (1, 4). In particular, only a portion of patients with type 1 diabetes will develop nephropathy irrespective of glycaemic control (1, 2). Family studies with type 1

diabetic siblings have shown that the risk of diabetic nephropathy is three- to four-fold higher if a sibling with diabetes has nephropathy, indicating that genetic factors play an important role (1, 7).

Microalbuminuria is one of the most frequent pathological findings in adolescents with type 1 diabetes. Several cross-sectional studies demonstrated that 6–25% of patients between 15 and 20 years of age develop microalbuminuria (1, 4, 8, 9, 10). Because the natural history of microalbuminuria in adolescents with type 1 diabetes is often not as consistent and clear as in adults, there is ongoing discussion about predictors of persistent microalbuminuria and nephropathy (4, 8, 11, 12, 13). Some studies have shown that half of the probands with type 1 diabetes and microalbuminuria have normoalbuminuria at the end of puberty (4, 11). Only a few longitudinal studies have focused on the natural history of microalbuminuria in adolescents with type 1 diabetes. Furthermore, little is known about the influence of sociodemographic factors on the natural course of untreated microalbuminuria in adolescents with type 1 diabetes. Therefore, the aim was to identify risk factors for the development and progression of untreated persistent microalbuminuria in children and adolescents with type 1 diabetes and childhood onset of diabetes in a real-world setting.

Design and methods

The German and Austrian diabetes survey (DPV) is a prospective nationwide survey of patients with type 1 diabetes in Germany and Austria. Demographic-, anthropometric- and diabetes-related data of patients with type 1 diabetes are recorded in 271 diabetes care centres. Local data-control authorities and the ethics committee approved data collection and anonymous analysis for study purposes. The participating centres are listed in the appendix. A total number of 33 998 children and adolescents with the onset of type 1 diabetes under the age of 11 years were registered in the survey until March 2010. Inclusion criteria for the present survey were onset of diabetes under the age of 11 years, diabetes duration of more than 1 year and at least two documented urine analyses per year at the age of 11 years according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines (screening for microalbuminuria recommended from age 9 with 5 years of diabetes duration or from age 11 with 2 years of diabetes duration respectively) (14). Exclusion criteria were concomitant diseases such as coeliac disease and treatment with antihypertensive drugs (e.g. angiotensin-converting enzyme (ACE) inhibitors) to avoid effects on urine albumin excretion rate (AER). In total, 2959 children between the age of 10 and 11 years fulfilled the criteria. The present survey included 683 subjects who were followed continuously

from the age of 10 years over 5 years with at least two urine analyses per year. For the rest of the children, no continuous follow-up was available. Body mass index SDS (BMI SDS) and height SDS were calculated using the national reference data in Germany (15).

Assessment of microalbuminuria and macroalbuminuria

Screening for microalbuminuria was performed by the following methods: i) measurement of urine albumin-to-creatinine (UAC) ratio in a random spot urine collection; ii) 24 h collection with creatinine; and iii) timed (e.g. overnight) collection. Microalbuminuria was defined as an increased urine albumin excretion. Thresholds for microalbuminuria were AER ≥ 20 $\mu\text{g}/\text{min}$ or UAC ≥ 2.5 mg/mmol according to the guidelines of the ISPAD and the American Diabetes Association (ADA) (14, 16). No instantaneous consecutive sampling and no specific time interval between urine samples within 1 year were required in the present survey. Macroalbuminuria was defined as AER ≥ 200 $\mu\text{g}/\text{min}$ or UAC ≥ 35 mg/mmol (14, 16). Based on the current guidelines and recommendations, and on the DCCT and EDIC study, persistent microalbuminuria was defined as at least two pathological urine albumin excretions per year (1, 14, 17). Intermittent microalbuminuria was defined as one increased urine albumin excretion and at least one normal urine albumin excretion per year. If only two urine samples were available, and one was pathological and another was normal, classification could not be done and the results were not included in the analysis. Regression to normoalbuminuria from persistent microalbuminuria was defined as AER < 20 $\mu\text{g}/\text{min}$ or UAC ratio < 2.5 mg/mmol in two out of three urine albumin tests in the following year respectively. Albumin and creatinine were measured by centre-specific laboratory methods that had to meet German internal and external quality requirements for laboratory analysis according to the guidelines of the German Medical Association (18).

Risk factors

We analysed the following independent factors for the development of persistent microalbuminuria and nephropathy by logistic regression: sex; BMI SDS; height SDS; diabetes duration; HbA1c; total cholesterol; HDL-cholesterol; LDL-cholesterol; systolic and diastolic blood pressure; and immigrant status.

HbA1c Glycaemic control was assessed as median HbA1c during each year and during the follow-up. Single-centre HbA1c values were standardised mathematically to the DCCT reference range of 4.05–6.05% using the multiple of the mean method (MOM method) (19).

Dyslipidaemia Lipid levels were assessed annually. Dyslipidaemia was diagnosed if at least one lipid parameter was increased and if more than half of the measurements were above the cut-off levels. The cut-off levels were >200 mg/dl for total cholesterol, >130 mg/dl for LDL-cholesterol and <35 mg/dl for HDL-cholesterol.

Hypertension Systolic and diastolic blood pressure was measured according to the current guidelines. Age-specific normal values were obtained from the Task Force on Blood Pressure Control in Children and Adolescents (20). Hypertension was defined as a median value >95th percentile of at least three independent measurements.

Immigrant status The survey provided self-reported information on the place of birth of the parents of the patients. Immigration status was defined as the place of birth of one or both parents in a country other than Germany or Austria.

Statistical analysis

We used SAS 9.1 statistical software for data evaluation and statistical analysis (SAS Institute Inc., Cary, NC, USA). The χ^2 -test was used to examine the associations between the rate of intermittent and persistent microalbuminuria at baseline and during each year of follow-up. Relative contribution of covariates (sex, BMI SDS, height SDS, immigrant status, diabetes duration, median HbA1c, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol, LDL-cholesterol, and intermittent microalbuminuria) to the risk for nephropathy was analysed by multivariate logistic regression. We selected the covariates based on clinical criteria. Odds ratios are reported as point estimates and 95% confidence intervals. Data are presented as medians and interquartile ranges and as means and s.d. where appropriate. Statistical significance was assumed at *P* values of <0.05.

Results

Cohort characteristics

In the prospective survey, 683 patients at the age of 10 years were followed longitudinally for 5 years between 1995 and March 2010 with a total of 3415 patient-years of follow-up. The cohort analysed was representative for the 2959 patients between the age of 10 and 11 years and with the onset of type 1 diabetes under the age of 10 years registered in the survey. Age (mean 10.5 vs 10.5 years), diabetes duration (median 4.3 vs 4.3 years), age at diabetes onset (median 6.2 vs 6.1 years), male sex (51.4 vs 51.7%), BMI SDS (mean +0.33 vs +0.38), HbA1c (median 7.3 vs 7.4%), and the percentage of children and adolescents with type 1 diabetes and immigrant status (13.0 vs 14.6%) were comparable.

Baseline characteristics of the 683 follow-up patients are shown in Table 1. At baseline, mean BMI SDS was +0.33, median diabetes duration was 4.3 years and median HbA1c was 7.3% in the whole cohort. In children and adolescents with immigrant status, mean BMI SDS was $+0.49 \pm 0.77$ compared with $+0.31 \pm 0.79$ in those with non-immigrant status. Subjects with immigrant status had a higher median HbA1c of 7.6% (10th percentile 6.2%, lower interquartile 7.0%, upper quartile 8.2% and 90th percentile 8.8%) compared with native-born children (median HbA1c 7.3% with 10th percentile 6.1%, lower interquartile 6.6%, upper quartile 7.9% and 90th percentile 8.86%). Of those subjects with immigrant status, 26% were from Turkey, 35% from Eastern European countries (e.g. Poland, Romania, Ukraine, Belarus), 10% from Southeastern European countries (e.g. Bosnia and Herzegovina), 10% from Northern Africa (e.g. Tunisia) and 19% from various other countries (e.g. Chile). In the present survey, the average number of samples was 3.7 ± 1.5 urine analyses per participant per year. Overall, 44% of the subjects had two urine analyses per year, 27% had three analyses per year and 29% had more than three analyses per year.

Table 1 Baseline characteristics of the cohort.

	All subjects (<i>n</i> =683)		Subjects with microalbuminuria	
	Non-immigrant	Immigrant	Intermittent	Persistent
Number	594	89	107	59
Immigrant status (<i>n</i> (%))		89 (13)	17 (15.9)	9 (15.3)
Age (years) ^a	10.5±0.1	10.5±0.1	10.5±0.1	10.5±0.1
Gender ratio (male/female (%))	51.0/49.0	53.9/46.1	49.5/50.5	30.5/69.5
BMI SDS ^a	+0.31±0.79	+0.49±0.77	+0.33±0.81	+0.35±0.76
Diabetes duration (years) ^b	4.5±3.9	3.8±3.2	4.5±2.5	4.6±2.3
Age at diabetes onset (years) ^b	6.0±4.0	6.7±3.0	6.0±2.5	5.9±2.3
HbA1c (%) ^b	7.3±1.3	7.6±1.2	7.3±1.0	7.3±1.0
Insulin dose (IU/kg) ^a	0.81±0.22	0.86±0.19	0.81±0.21	0.90±0.29
Hypertension (<i>n</i> (%))	7 (1.2)	2 (2.2)	2 (1.9)	0 (0)
Dyslipidaemia (<i>n</i> (%))	104 (17.5)	8 (9)	2 (1.9)	0 (0)

^aData is expressed as mean±s.d.

^bData is expressed as median±interquartile range.

At baseline (mean age 10.5 ± 0.1 years), 75.6% ($n=516$) of children had normoalbuminuria, 15.7% ($n=107$) had intermittent microalbuminuria, 8.6% ($n=59$) had persistent microalbuminuria and 0.1% ($n=1$) had macroalbuminuria. HbA1c levels in subjects with intermittent microalbuminuria were not different from those in subjects with persistent microalbuminuria. Characteristics of children and adolescents with intermittent and persistent microalbuminuria are described in Table 1.

Progression and regression of microalbuminuria during the follow-up

Out of the 516 children with normoalbuminuria at baseline, 406 (78.7%) had stable normoalbuminuria after a continuous follow-up of 5 years. Of the 59 children with persistent microalbuminuria at baseline, 18 were male (30.5%) and 41 (69.5%) were female. Of these 59 patients, 17 (28.8%) had unchanged persistent microalbuminuria, whereas 42 (71.2%) had regression to intermittent microalbuminuria or normoalbuminuria. Figure 1 depicts the percentages of children with normoalbuminuria, intermittent and persistent microalbuminuria at baseline and after the follow-up of 5 years. In summary, out of the total cohort of 683 children, after the follow-up of 5 years, 59.4% ($n=406$) had stable normoalbuminuria and 15.2% ($n=104$) had regression from intermittent microalbuminuria to normoalbuminuria or from persistent microalbuminuria to intermittent microalbuminuria or normoalbuminuria. Finally, 18.4% ($n=126$) progressed

to intermittent or persistent microalbuminuria and 6.9% ($n=47$) had unchanged intermittent or persistent microalbuminuria.

There was no significant association between intermittent microalbuminuria at baseline and persistent microalbuminuria after the follow-up of 5 years ($P=0.10$). We found significant associations between persistent microalbuminuria at baseline and during each year of follow-up ($P<0.0001$).

Regression analysis

Multivariate logistic regression analysis with the variables sex, BMI SDS, height SDS, immigrant status, diabetes duration, HbA1c, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol, LDL-cholesterol, and intermittent microalbuminuria for the development or progression to microalbuminuria identified diabetes duration and immigrant status as significant risk factors for microalbuminuria ($P<0.01$; see Table 2). The progression rate of microalbuminuria in subjects with type 1 diabetes and immigrant status was significantly higher than that in subjects with non-immigrant status (26 vs 16%, $P=0.03$).

In a second analysis, we analysed prediction factors for the regression of microalbuminuria in children and adolescents with type 1 diabetes. Multivariate logistic regression analysis including the factors sex, BMI SDS, immigrant status, diabetes duration, HbA1c, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol and LDL-cholesterol did not reveal any significant predictors for the regression of microalbuminuria after the follow-up of 5 years.

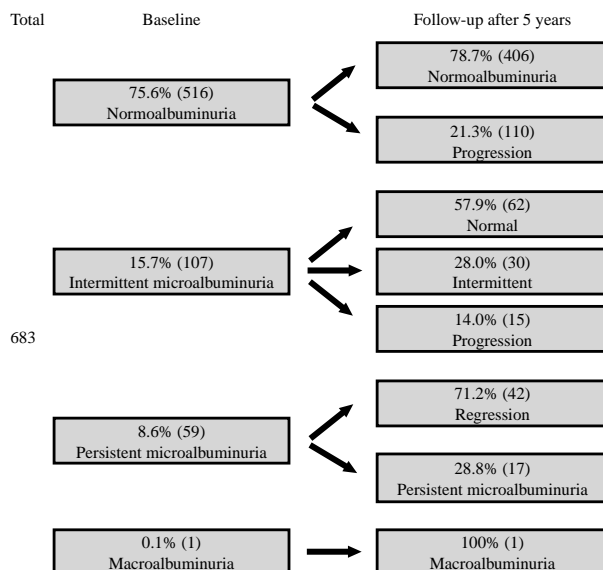


Figure 1 The rates (% and absolute numbers) of the 683 children with type 1 diabetes with normoalbuminuria, intermittent and persistent microalbuminuria at baseline, and the progression and regression of microalbuminuria after a follow-up of 5 years are depicted.

Discussion

To our knowledge, the present survey is the first to demonstrate that immigration status is an independent risk factor for the development of persistent microalbuminuria in children and adolescents with type 1 diabetes. The aim of this survey was to assess the natural history of microalbuminuria without any therapeutic intervention in a real-world setting in order to look for additional risk factors for the development and progression of microalbuminuria. Thus, because of the positive effects of ACE inhibitors on the regression of nephropathy, we excluded children and adolescents with concomitant medication (1, 4, 14). The focus on the natural course of microalbuminuria, the large number of children in the survey in a real-world setting, and the very homogeneous cohort of children regarding age and diabetes duration are major strengths of the present survey. To date, little is known about the development of diabetic complications and comorbidities in type 1 diabetes in different population groups (21, 22, 23, 24). Differences in health status in immigrant and non-immigrant families may explain

Table 2 Logistic regression analysis of risk factors for the progression of microalbuminuria after a follow-up of 5 years.

	Simple model (confounders adjusted for diabetes duration only)		Complete model (fully adjusted model)	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)
Sex (male vs female)	0.886	(0.600; 1.307)	0.968	(0.563; 1.664)
BMI SDS	0.759 [†]	(0.590; 0.977) [†]	0.840	(0.583; 1.210)
Height SDS	1.034	(0.846; 1.265)	1.185	(0.876; 1.602)
Immigrant status (immigrant vs non-immigrant)	1.803 [†]	(1.064; 3.055) [†]	2.674 [*]	(1.279; 5.590) [*]
Diabetes duration	1.107 [†]	(1.020; 1.200) [†]	1.170 [*]	(1.040; 1.316) [*]
HbA1c	1.009	(0.849; 1.200)	1.018	(0.797; 1.299)
Systolic blood pressure	0.994	(0.973; 1.016)	1.004	(0.971; 1.037)
Diastolic blood pressure	1.000	(0.971; 1.031)	0.997	(0.953; 1.043)
Total cholesterol	0.995	(0.987; 1.003)	1.001	(0.988; 1.014)
HDL-cholesterol	1.004	(0.996; 1.013)	0.995	(0.975; 1.015)
LDL-cholesterol	0.994	(0.983; 1.005)	0.995	(0.981; 1.009)
Intermittent microalbuminuria at baseline (presence vs absence of intermittent microalbuminuria)	0.686	(0.382; 1.233)	0.549	(0.231; 1.305)

* $P < 0.01$; [†] $P < 0.05$.

this newly found and interesting association between immigrant status and microalbuminuria. Principally, there is growing awareness of differences in health status between various population groups (24, 25, 26, 27, 28, 29, 30). The German Health Interview and Examination Survey for Children and Adolescents (KiGGS) conducted from 2003 to 2006 showed that general state of health is estimated to be lower in children with immigrant status compared with those with non-immigrant status (29). Childhood obesity is one example where prevalence differs significantly in population subgroups in Europe and in the USA: prevalence of overweight and obesity is higher in immigrant children compared with native-born children (26, 27). In the present survey, BMI SDS was also higher in children with immigrant status compared with those with non-immigrant status. However, further analysis showed that BMI SDS was not a significant risk factor for the development or progression of microalbuminuria. Disparities in lifestyle and nutrition habits may account for different health status in immigrant and non-immigrant families (24, 30). The KiGGS study reported considerable differences in food intake and dietary habits in children and adolescents with immigrant status compared with those with non-immigrant status (30). Besides health status, confounding factors associated with immigrant status possibly explain the observed association. Immigrant status is strongly associated with low socio-economic status. And then again, socio-economic status is correlated with health status (29, 31). Regrettably, in the present survey, no data about socio-economic status were available. Additionally, in many countries, children and adolescents from immigrant families do not have equal access to health care compared with non-immigrant families. However, in Germany and Austria, health insurance is either compulsory or part of the social security system. Therefore, it is not likely that

different health care access accounts for the observed higher risk of microalbuminuria in children with immigrant status in the present survey. However, the use of health care facilities may well differ between immigrant and non-immigrant families. As one limitation of the present survey, no further data about health status, lifestyle or nutrition habits, socio-economic parameters, and about the use of health care facilities were available. Another reason explaining the association between the development of microalbuminuria and immigrant status is the fact that incidence rates of type 1 diabetes in immigrant and non-immigrant children are different (32). The percentage of children with type 1 diabetes who are not of German descent is smaller (8.3%) compared with the percentage among the general population (15.2%) (32). Causes for this observation are controversial (32). Therefore, incidence of diabetic complications could also be different in immigrant and non-immigrant children. Lastly and importantly, ethnic and genetic differences may have a considerable impact on the development of comorbidities. In type 2 diabetes, South Asians were reported to have a higher risk of developing retinopathy (23). With respect to diabetes in general, the incidence of nephropathy and end-stage renal disease is much higher for some population groups, such as Blacks, Asians and Latinos, compared with Caucasians (21, 22). Several studies have suggested an important genetic influence on nephropathy (1, 4, 7). Some candidate genes, including mutations of the *ACE* gene, have been implicated to play a role (1, 4, 6).

Besides the interesting finding that immigrant status is a significant risk factor for microalbuminuria, we confirmed in a real-world setting that a certain percentage of children have microalbuminuria already at a very young age (1, 2, 8, 9, 10, 33). In the present survey, 8.6% of children at the age of 10.5 years had persistent microalbuminuria. Other studies have

reported similar results: the prevalence rate of microalbuminuria was estimated to be 5.9% in children with a mean age of 12.7 years and a diabetes duration of 5.1 years (4). Another study in children (mean age 12.9 years) has revealed that persistent microalbuminuria was present in 9.3% (13). The present survey also showed that intermittent microalbuminuria was not a predictive factor for the progression of microalbuminuria and that in a real-world setting, intermittent microalbuminuria has little prognostic significance in adolescents with type 1 diabetes (1, 4, 12, 14). Regression of microalbuminuria is well described in adults and is estimated to be between 30 and 64% (2, 6, 11, 34). In adolescents with type 1 diabetes, regression rate is even higher (4, 11, 33). Some longitudinal studies have suggested that more than 50% of cases with persistent microalbuminuria in adolescence revert to normoalbuminuria at the end of puberty (4, 11, 13). However, in many longitudinal studies, a certain number of patients do receive treatment with antihypertensive drugs (4, 11, 12, 17, 33, 34, 35, 36). For instance, in the Oxford regional prospective study, cumulative prevalence of regression to normoalbuminuria was 51.9% after ~5 years after the onset of microalbuminuria (33). However, 15% of the subjects with microalbuminuria in this study received treatment with an ACE inhibitor or a β -blocker (33). In the present survey, regression rate of persistent microalbuminuria to intermittent microalbuminuria or normoalbuminuria without ACE inhibitor treatment was estimated at 71.2%. This percentage is comparable to a recently published, small study, where 14 out of 17 patients (82% of patients) who had never received ACE inhibitors underwent spontaneous remission during a follow-up period of 13.1 ± 6.2 years (36).

Many studies have examined risk factors including glycaemic control, diabetes duration, sex, smoking, hypertension and disturbed lipid metabolism to determine and predict diabetic nephropathy (1, 2, 3, 4, 5, 6, 35, 37). Poor glycaemic control is found to be the most important factor associated with faster progression of AER in adolescents and adults with baseline microalbuminuria (1, 2, 3, 4, 5, 35, 38). However, in the present survey we identified diabetes duration but not glycaemic control as predictive for the progression of microalbuminuria. Overall, metabolic control as measured by HbA1c was relatively good in the present survey compared with other studies (HbA1c 7.4% at baseline in the present survey vs 8.7% in the study by Alleyn *et al.* (13) or 9.3% in the Nephropathy Family Study cohort (39)). The small number of patients with poor metabolic control in the present survey possibly explains the reason why we did not observe a significant association between HbA1c levels and the presence of microalbuminuria. Furthermore, other studies showed that abnormal lipid profiles are risk factors for the development of microalbuminuria (36, 39). Especially, lower HDL-cholesterol levels are present in patients with

type 1 diabetes and microalbuminuria (36). However, and in contrast to those studies, we did not observe such an effect. Possible reasons are that in other studies, either age at baseline was higher (e.g. mean age 14.5 vs 10 years in the present survey) or the follow-up period was longer (e.g. 13 vs 5 years in the present survey) (36, 39). Therefore, the effect of abnormal lipid levels is probably more evident in those studies. Subsequently, puberty might influence the development of microalbuminuria (1). The probability of developing microalbuminuria is increased after the onset of puberty (8, 40). Regrettably, as we had no information about pubertal status in the present survey, we did not include this confounding factor in the analysis. Instead, we used height SDS because lower height could represent delayed puberty. Lower height could also indicate prior poor metabolic control or could be an additional risk factor as found by one published study (41). However, we did not observe any significant effect of height as a risk factor for the progression of microalbuminuria in the present survey.

Finally, several limitations of the present survey should be pointed out. A bias towards milder microalbuminuria is possible, because only children and adolescents without medication were included in the study (4). Secondly, continuous follow-up of the study subjects was only 5 years. Because of the limited duration of the study, no assumptions can be made about further progression to macroalbuminuria and overt nephropathy. Lastly, weak to moderate predictors and correlations could possibly not be demonstrated because of limited power.

In summary, the so-far established risk factors for nephropathy in type 1 diabetes do not completely explain the development of micro- and macroalbuminuria (1, 4). We demonstrated for the first time that immigrant status is a relevant risk factor for microalbuminuria and has a considerable impact on the progression of persistent microalbuminuria in children and adolescents with type 1 diabetes in a real-world setting. This finding may be in part due to genetic causes or to modifiable and confounding socio-economic and lifestyle factors associated with health status in immigrant and non-immigrant children. In order to confirm the results of this study and to look for underlying causes explaining the association of microalbuminuria and immigrant status further multicentre studies are needed.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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