Childhood Diabetes in Germany and Austria

Earlier identification and timely treatment of risk factors may prevent future cardiovascular events.

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Type 1 diabetes is increasingly recognized as an independent risk factor for premature cardiovascular disease (CVD) and elevated cardiovascular death rate in patients aged 20 to 39 years.[1] Postmortem studies in children and youth who died an unnatural death showed that the development of atherosclerotic lesions of the vessel wall starts in childhood, and that there is a close relationship to cardiovascular risk factors. My colleagues and I recently reported on this in *Diabetes Care*.[2]

In the Bogalusa Heart Study[3] and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study,[4] the evaluation of premortal existing risk factors (HbA1c >8%, increased lipids, hypertension, obesity and smoking) verified their unfavorable influence on the progression of atherosclerosis.

Childhood and adolescent diabetes is commonly associated with additional risk factors. Therefore, this cross-sectional analysis of data from the German Diabetes Documentation and Quality Management System DPV was conducted to obtain reliable information on character and prevalence rate, as well as sex differences of potential atherogenic risk factors in 27,358 German children, adolescents and young adults with type 1 diabetes (Table 1).

ATHEROGENIC RISK FACTORS

Overall, 69% of 27,358 patients had one or more analyzed risk factor. The majority of patients showed one risk factor (53%), followed by patients with no risk factors (31%), two risk factors (14%) and three or four risk factors (2%).

The most frequently diagnosed nonlipid risk factor in our patients was HbA1c >7.5%. Poor glycemic control is particularly associated with the development of long-term microvascular complications.[5] Further investigation may show that there is a direct relationship between HbA1c levels and the extent of atherosclerosis.

> Women with type 1 diabetes have an increased risk of CVD that equalizes the advantageous sex difference.

Gerstein et al[6] found that intima-media thickness (IMT) increased 0.026 mm for every 0.9% increase in HbA1c ($P<.0001$). In another study, HbA1c >7.5% was identified as a strong risk factor for progression of coronary artery calcification in type 1 diabetes patients aged 22 to 50 years.[7]

Overweight (90th to 97th body mass index [BMI] percentile or BMI >25 kg/m^2) and obesity (>97th BMI percentile or BMI >30 kg/m^2) are thought to be cardiovascular risk factors with regard to the development of dyslipidemia, hypertension, type 2 diabetes and metabolic syndrome.[8] If obese children become obese adults, one of the long-term consequences may be early atherosclerosis and increased cardiovascular morbidity.[9] Twenty percent of our diabetic population had BMI >90th percentile.

According to the US National High Blood Pressure Education Program, hypertension is defined as systolic blood pressure and/or diastolic blood pressure ≥ 95th percentile by gender, age and height. Blood pressure between the 90th and 95th percentile is designated as prehypertension.[10] In our patients, elevated systolic blood pressure was found in 8.2% and elevated diastolic blood pressure in 3.2%. Hypertension is regarded as an independent atherogenic risk factor and is positively correlated with increased carotid IMT in children and adolescents with type 1 diabetes.[11,12]

TABLE 1. CLINICAL AND LABORATORY CHARACTERISTICS IN PATIENTS WITH TYPE 1 DIABETES

Characteristic	Total number of patients	Frequency of complete records (%)	Value
Age (years)	27,358	100	13.6 ±4.8
Males (%)	27,358	100	51.9
Age at diagnosis (years)	27,358	100	8.3±4.3
Diabetes duration (years)	27,358	100	5.3± 4.4
HbA1c (%)*	26,308	96.2	8.3± 1.8
Any dyslipidemia (%)	19,359	70.8	29± 45
Lipid-lowering therapy (%)	27,358	100	0.4
Total cholesterol (mg/dL)	18,917	69.1	180 ±46
LDL (mg/dL)	11,286	41.3	101 ±39
HDL (mg/dL)	12,811	46.8	61 ±18
Raised systolic blood pressure (%)	25,184	92.1	8.2
Raised diastolic blood pressure (%)	25,178	92.0	3.2
Blood pressure-lowering therapy (%)	27,358	100	2.2
BMI >90th percentile (%)	25,145	91.9	20 ±40
Smoking (%)	19,683	71.9	15.6 ±36.3

*DCCT standardized

Smoking is a commonly accepted independent risk factor for atherosclerosis. The prevalence of smoking, nevertheless, is similar in diabetic patients compared with nondiabetic people.[13] Despite the well-known health risk of smoking, >15% of our type 1 diabetes patients currently smoked.

Total cholesterol serves as a screening parameter for hypercholesterolemia. Values >200 mg/dL (>5.2 mmol/L) were defined as high risk[14] and demonstrable in >26% of our patients.

LDL represents the principal atherogenic lipoprotein fraction. Plasma elevation >130 mg/dL (>3.4 mmol/L) was classified abnormal and concentrations >160 mg/dL (>4.1mmol/L) were used as the reference value for patients at high risk who require lipid-lowering pharmacotherapy if diet and lifestyle changes failed.[14] In our patients, the percentage of LDL >130 mg/dL to 160 mg/dL was 11.8%, and 5.5% had LDL >160 mg/dL.

HDL particles are responsible for the reverse cholesterol transport from the periphery to the liver and have antiatherogenic activities. We considered HDL <35 mg/dL (<0.9 mmol/L) abnormal;[14] this was found in 4.1 % of our diabetic population.

It is known that women with type 1 diabetes have an increased risk of developing CVD and, therefore, equalizing the advantageous sex difference seen in the general population.[15] In our analysis, this is based on increased HbA1c, total cholesterol, LDL and BMI values in females compared with males who were conspicuous by elevated blood pressure and more frequent smoking.

MANAGEMENT OF RISK FACTORS

With regard to the management of additional atherogenic risk factors, there is a considerable discrepancy in juvenile type 1 diabetic patients between the high risk for future cardiovascular morbidity and the low treatment rate of modifiable risk factors such as hypertension and dyslipidemia. Although vascular complications are normally subclinical during childhood and adolescence, cardiovascular risk factors should be given our full attention to reduce risk by optimal metabolic control and lifestyle modification.[16]

Only if these efforts are insufficient is pharmacotherapy a reasonable form of treatment. It must be individualized based on type and number of atherogenic risk factors, family history and existing complications.

Hypertension in children and adolescents with type 1 diabetes may primarily be treated early with angiotensin-converting enzyme inhibitors. These agents have antihypertensive effects and reduce the incidence of microalbuminuria and nephropathy.[17] In addition to hypertension, dyslipidemia is a common concomitant disease in patients with diabetes. The American Diabetes Association strongly recommends lipid-lowering pharmacotherapy for patients with LDL >160 mg/dL but for LDL

between 130 mg/dL and 159 mg/dL only if nutrition therapy and lifestyle changes failed. In any case, the treatment target is LDL <100 mg/dL.[18] So far, in a limited number of children with familial and severe hypercholesterolemia, statins showed good LDL cholesterol-lowering efficacy and a low rate of side effects.[19]

CONCLUSION

This representative analysis demonstrates the high frequency of atherogenic risk factors in children and adolescents with type 1 diabetes and underlines the importance of an early search for these cardiovascular risk factors. Significant sex differences were computed for most of the risk factors. The discrepancy between a high prevalence of cardiovascular risk factors and the low rate of antihypertensive and lipid-lowering treatment deserves special consideration. ■

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CHILDREN WITH DIABETES IN THE UNITED STATES

By Joyce M. Lee, MD

In the United States, at a national level, obesity may be a significant contributing factor to the development of childhood diabetes.

A number of studies suggest that the incidence of type 1 and type 2 diabetes in children is increasing in the United States.[1-3] Furthermore, researchers and policymakers are particularly concerned with large increases in the number of children with type 2 diabetes due to the rising epidemic of childhood obesity.

Because childhood diabetes is a chronic illness that leads to substantial morbidity and mortality,[4] describing the prevalence of diabetes in US children is important for understanding the burden of the disease and its public health implications. My colleagues and I recently published a study in *Diabetes Care* that sought to determine the prevalence of diabetes in US children and to examine the association between the presence of obesity and diabetes.[5]

We used data from the National Survey of Children's Health, a nationwide cross-sectional household telephone survey of 102,363 households conducted in 2003 to 2004. It was sponsored by the Maternal and Child Health Bureau in partnership with the National Center for Health Statistics and the Centers for Disease Control and Prevention (CDC).[6]

The prevalence of diabetes was based on parental report, and type 1 or type 2 diabetes was not specified. Body mass index (BMI) was calculated based on parent-reported weight and height, and children were stratified into three groups based on age- and sex-specific BMI: not overweight if BMI was <85th percentile; overweight if BMI was ≥85th percentile and <95th percentile; and obese if BMI was ≥95th percentile.[7]

We found that the estimated prevalence of diabetes among US children aged <18 years was 3.2 per 1,000 (95% CI: 2.6, 3.7), representing approximately 229,240 children nationally. Table 1 shows the prevalence rates by demographic characteristics in this study. Among children with diabetes, 17% were overweight and 30% were obese.

We evaluated the association between diabetes and weight among school-age children in an analysis stratified by age. Obese children were twice as likely to have diabetes compared with children of normal weight, for the 6- to 11-year age group (OR 2.45, 95% CI:1.31-4.60), and for the 12- to 17-year age group (OR 2.67, 95% CI:1.57-4.56).

The CDC has documented an increasing prevalence of obesity in US children,[8] which is considered the most important risk factor for development of type 2 diabetes in children.[9] This rise in obesity has been accompanied by increases in the numbers of children diagnosed with type 2 diabetes, documented by both registry[10] and retrospective clinic data.[11] In addition, there are recent studies suggesting that childhood obesity may also be a risk factor for the development of type 1 diabetes.[2,12] Our findings suggest that at a national level, obesity may be a significant contributing factor to the development of type 1 or type 2 diabetes in children. Public health interventions to combat the epidemic of childhood obesity are likely necessary for preventing the future burden of diabetes. ■

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TABLE 1. CHARACTERISTIS OF CHILDREN WITH DIABETES: UNITED STATES

	Diabetes Prevalence (95% CI)	P-value	% Among Those With Diabetes	% Among Children in Sample
Overall				
Age		.001		
0 to 5 years	1.3		13%	33%
6 to 11 years	2.5		26%	33%
12 to 17 years	5.6		61%	34%
Gender		.37		
Male	3.4		55%	51%
Female	2.9		45%	49%
Race		.04		
Non-Hispanic white	3.8		73%	61%
African-American	2.2		10%	14%
Hispanic	2.2		12%	18%
Other/Multiracial	2.2		5%	7%
Poverty Status*		.96		
200% of poverty level	3.2		60%	59%
≥200% of poverty level	3.2		40%	41%
Family Structure		.43		
Single Parent	3.5		27%	25%
Two Parent	3.0		73%	75%
Region		.43		
Northeast	2.8		15%	18%
Midwest	3.9		28%	22%
South	2.8		32%	36%
West	3.2		25%	24%
Weight status		.17		
BMI <85th percentile	3.4		53%	61%
85th% ≤BMI <95th percentile	4.3		17%	15%
BMI ≥95th percentile	4.7		30%	24%

*Excludes unknown income

Source: Diabetes Care. *2006;29:420-421.*