

Background/Aims: Little is known about the incidence and clinical consequences of hyperthyroidism in pediatric patients with type 1 diabetes mellitus (T1DM).

Methods: We analyzed the DPV database (Diabetes Prospective Follow-up Registry) to investigate the rate of hyperthyroidism in pediatric T1DM patients, its impact on metabolic control, and potential associations with organ-specific autoantibodies.

Results: Hyperthyroidism was found in 276/60,456 patients (0.46%) and was associated with younger age, shorter diabetes duration, female sex, and reduced body mass index (table 1). Diabetic ketoacidosis (DKA) and hypoglycemia were more frequent in T1DM with comorbid hyperthyroidism, while long-term metabolic control (HbA1c) was similar in both groups. Absolute blood pressure and arterial hypertension rate were elevated in the hyperthyroid patients. Rates of microalbuminuria and diabetic retinopathy were not different (table 2). Thyroid volume and rates of cysts and nodules were higher and echogenicity was decreased (table 3). Thyroid-specific antibodies (TPO, Tg, TR) were associated with hyperthyroidism (table 4).

Conclusion

Hyperthyroidism in children and adolescents with T1DM is rare but significantly more frequent than in children under 18 years without diabetes from Southern Germany.

In most pediatric hyperthyroid T1DM patients, hyperthyroidism tends to be subclinical, showing no or only few clinical signs or symptoms; while it may well have an impact on acute complications of T1DM, such as DKA or hypoglycemia, it has only little influence on long-term metabolic control.

In our opinion, general screening of diabetic children for hyperthyroidism using TR-Ab is not necessary. However, careful clinical monitoring for signs and symptoms of hyperthyroidism and TSH testing should be performed, and if unexplained metabolic deterioration occurs, hyperthyroidism should be considered after other factors have been excluded.

Table 1. Demographic and clinical characteristics of the study population as a whole and by thyroid state

Parameter	Total	Hyperthyroid	Euthyroid	p
<i>Demography</i>				
Patients, n (%)	60,456 (100)	276 (0.46)	60,180 (99.54)	
Age, years	14.35±4.23	12.27±4.09	14.36±4.22	<0.0001
Sex, % male	52.6	34.1	52.7	<0.0001
Height, cm	159.6±20.8	151.9±21.2	159.7±20.8	<0.0001
Height SDS	-0.07±1.1	0.18±1.1	-0.07±1.1	0.0003
Weight, kg	56.9±20.1	48.8±19.1	57.0±20.1	<0.0001
Weight SDS	0.43±1.5	0.43±0.9	0.43±1.5	0.99
BMI	21.45±4.2	20.05±4.1	21.46±4.2	<0.0001
BMI SDS	0.53±1.0	0.41±1.0	0.53±1.0	0.037
<i>Clinical diabetes</i>				
Age at diagnosis, years	8.55±4.3	8.22±4.2	8.55±4.3	0.234
Diabetes duration, years	5.81±4.3	4.07±4.2	5.81±4.3	<0.0001
CT, %	10.1	16.9	10.1	0.0002
ICT, %	61.3	58.5	61.3	0.33
CSII, %	28.6	24.6	28.6	0.15
Insulin dose, IU/kg/day	0.95±0.4	0.92±0.4	0.95±0.4	0.27
Injections per day	5.8±2.3	5.4±2.3	5.8±2.3	0.001
β-Blocker use, %	0.15	3.99	0.14	<0.0001

Significant differences are marked in bold. CSII = Continuous subcutaneous insulin infusion (insulin pump).

Table 2. Metabolic parameters

Parameter	Hyperthyroid	Euthyroid	p
Patients, n (%)	276 (0.46)	60,180 (99.54)	
HbA1c, %	8.4	8.3	0.34
Insulin, IU/kg/day	0.98	0.95	0.21
DKA, episodes/100 patient-years	18.1	7.7	<0.0001
Severe hypoglycemia, episodes/100 patient-years	34.4	17.2	<0.0001
Hypoglycemic coma, episodes/100 patient-years	8.1	4.0	0.026
Cholesterol, mg/dl	165.5	180.5	<0.0001
Arterial hypertension, %	43.7	31.1	<0.0001
Microalbuminuria, %	14.3	14.2	0.97
Retinopathy, %	0.95	1.1	0.90

Age-, sex-, and diabetes duration-adjusted parameters of metabolic control, blood pressure regulation, and the rate of diabetic complications depending on thyroid state. Note the higher rates of DKA and of hypoglycemia in hyperthyroid patients. Significant differences are marked in bold.

Table 3. Thyroid parameters

Parameter	Hyperthyroid	Euthyroid	p
Patients, n (%)	276 (0.46)	60,180 (99.54)	
TSH, μU/ml	1.1	2.2	<0.0001
Thyroid volume, ml	17.1	9.1	0.0006
Thyroid volume-SDS	8.0	3.1	0.0029
Cysts, %	28.5	13.4	0.037
Nodules, %	23.8	6.4	0.004
Decreased echogenicity, %	18.9	77.6	<0.0001

Age-, sex-, and diabetes duration-adjusted thyroid parameters depending on thyroid status. Note the higher frequency of sonographic signs of AIT in the hyperthyroid patients. Significant differences are marked in bold.

Table 4. Organ-specific autoantibodies

Parameter	Hyperthyroid	Euthyroid	p
Patients, n (%)	276 (0.46)	60,180 (99.54)	
TPO-Ab, %	72.5	15.3	<0.0001
Tg-Ab, %	54.1	12.2	<0.0001
TR-Ab, %	25.8	6.1	<0.0001
All thyroid Ab, %	77.1	16.1	<0.0001
β-Cell Ab, %	87.6	85.3	0.47
CD-specific Ab, %	20.0	16.3	0.18
Adrenal cortex Ab, %	9.8	9.3	0.93
Parietal cell Ab, %	17.8	13.9	0.71

Age-, sex-, and diabetes duration-adjusted frequencies of autoantibodies associated with thyroid disease and/or type 1 diabetes by thyroid status. Significant differences are marked in bold. TPO-Ab = Thyroid peroxidase antibodies; Tg-Ab = thyroglobulin antibodies; Ab = (auto)antibodies.