Thyroid Dysfunction and Thyroid Autoimmunity in Children with New-Onset Diabetes Mellitus

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Introduction

Type 1 DM (T1DM) are related with other autoimmune disorders. Approximately 25% of patients with T1DM are diagnosed with another autoimmune diseases (AID) such as Hashimoto thyroiditis, Celiac disease, Graves disease, Addison disease, vitiligo, autoimmune hepatitis, myasthenia gravis, and pernicious anemia.[1] The most common AIDs were thyroiditis (24%), gastrointestinal (6%), and collagen vascular diseases (2%).[2] The prevalence of thyroid dysfunction is higher in patients with diabetes mellitus than general population.[3] T1DM and autoimmune thyroid disease share T-lymphocyte mediated immunity, and T-cell infiltration results in dysfunction of the target organ, the pancreatic islet in T1DM and the thyroid in autoimmune thyroid disease.[4] This study was performed to evaluate the prevalence and risk factors of thyroid dysfunction and autoimmune thyroiditis in children with newly developed diabetes mellitus.

Subjects and Methods

We reviewed medical records from 2002 to 2018, retrospectively. The subjects with T1DM and followed for more than 6 months between 2002 and 2018 in a single tertiary center were included in the study. Total one hundred thirty-four patients were diagnosed as having DM at the Department of Pediatrics, Dankook University Hospital. Thirty-one patients who undertook the first TFT at another hospital or performed TFT more than 3 days later after the diagnosis of DM were excluded from the study. A total of 103 patients were included in the study. Sex, onset age, HbA1c, presence of diabetic ketoacidosis (DKA) or thyroid dysfunction, positivity of T1DM-associated antibody (Ab) such as anti-GAD, anti-insulin, and anti-IA2 Ab as well as thyroid autoantibody such as anti-thyroid peroxidase (TPO) and anti-thyroglobulin (TG) Ab were analyzed to find the prevalence and risk factors of thyroid dysfunction and thyroid autoimmunity at the onset of DM. Chi-square, Fisher's exact test, t-test, and logistic regression were used for statistics.

Table 1. Demographic and laboratory data of study subjects

	Total DM		Type 1		Type 2		p value
N	103		57		46		
Sex	Male	Female	Male	Female	Male	Female	
	60	43	38	19	22	24	0.054
DKA	35		32		3		0.000
	Mean	SDS	Mean	SDS	Mean	SDS	
Age at intial visit	11.36	4.17	9.65	4.24	13.49	3.04	0.000
HbA1c	11.6	2.34	12.10	1.80	11.00	2.79	0.025
DM Ab	55		55		0		0.000
GAD Ab	49(48%)	N=102	49(86%)	N=57	0	N=45	0.000
Islet Ab	5(5.3%)	N=93	5(9.8%)	N=51	0	N=42	0.000
Insulin Ab	10(9.8%)	N=102	10(17.9%)	N=56	0	N=46	0.003
IA2 Ab	41(44.1%)	N=93	41(82%)	N=50	0	N=43	0.000
Low total T3	33		29		4		0.000
Low free T4	12		11		1		0.007
Low TSH	10		8		2		0.099
TPO antibody positivity	11(14.7%)	N=75	10(24.4%)	N=41	1(2.9%)	N=34	0.009
TG antibody positivity	13(17.1%)	N=76	9(21.9%)	N=41	4(11.4%)	N=35	0.225
TSHR antibody positivity	0	N=54	0	N=32	0	N=22	
Recent age	15.47	4.13	14.1	4.52	17.08	2.92	
Follow up duration	4.11	3.29	4.52	3.23	3.60	3.36	0.159

Results

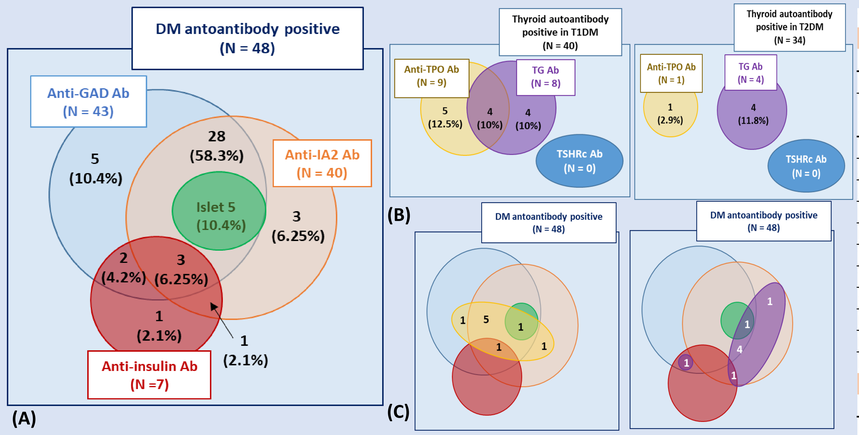

Figure. Diagram of autoantibodies in the subjects
(A)DM autoantibodies
(B)Thyroid autoantibodies
(C)The relationship between DM autoantibodies and thyroid antibodies

Table 2. Incidence of low T3 or low T4 and related factors

Total DM (N=103)										
	Low T3		Non-low T3		p value	Low T4		Non-low T4		p value
N	33		70			12		91		
Sex	M	F	M	F		M	F	M	F	
	24	9	36	34	0.041	6	6	54	37	0.537
	Mean	SDS	Mean	SDS		Mean	SDS	Mean	SDS	
Age at diagnosis (years)	8.79	4.63	12.58	3.38	<0.01	7.8	4.99	11.83	3.87	0.002
Age at initial TFT (years)	8.79	4.63	12.58	3.38	<0.01	7.81	4.99	11.83	3.87	0.002
DKA at diagnosis	23		12		<0.01	10		25		<0.01
Initial HbA1c (%)	12.18	2.06	11.34	2.45	0.09	11.46	2.07	11.63	2.4	0.815
TPO Ab positivity	6	N=25	5	N=50	0.16	2	N=11	9	N=64	0.66
TG Ab positivity	3	N=25	10	N=51	0.53	1	N=11	12	N=65	0.678
GAD Ab positivity	27	N=32	22	N=70	<0.01	11	N=12	38	N=90	0.001
Islet Ab positivity	2	N=29	3	N=64	0.65	1	N=11	4	N=82	0.475
Insulin Ab positivity	5	N=33	5	N=69	0.29	1	N=12	9	N=90	1
IA2 Ab positivity	24	N=29	17	N=64	<0.01	8	N=11	33	N=82	0.055
T1DM (N=57)										
	Low T3		Non-low T3		p value	Low T4		Non-low T4		p value
N	29		28			11		46		
Sex	M	F	M	F		M	F	M	F	
	21	8	17	11	0.349	6	5	32	14	0.478
	Mean	SDS	Mean	SDS		Mean	SDS	Mean	SDS	
Age at diagnosis (years)	8.42	4.35	10.91	3.78	0.025	7	4.33	10.28	4	0.02
Age at initial TFT (years)	8.42	4.35	10.92	3.78	0.025	7	4.33	10.28	4	0.02
DKA at diagnosis	21		11		0.012	10		22		0.016
Initial HbA1c (%)	12.09	1.58	12.1	2.04	0.977	11.96	1.16	12.13	1.93	0.788
TPO Ab positivity	6	N=23	4	N=18	1	2	N=10	8	N=31	1
TG Ab positivity	3	N=23	6	N=18	0.147	1	N=10	8	N=31	0.41
GAD Ab positivity	27	N=29	22	N=28	0.144	11	N=11	38	N=46	0.332
Islet Ab positivity	2	N=27	3	N=24	0.656	1	N=10	4	N=41	1
Insulin Ab positivity	5	N=29	5	N=27	1	1	N=11	9	N=45	0.667
IA2 Ab positivity	24	N=27	17	N=23	0.27	8	N=10	33	N=40	1

Table 3. Positivity of thyroid autoantibody and related factors

Total DM (N=103)										
	TPO Ab positivity		TPO Ab negativity		p value	TG Ab positivity		TG Ab negativity		p value
N	11		64			13		63		
Sex	M	F	M	F		M	F	M	F	
	7	4	35	29	0.746	5	8	37	26	0.181
	Mean	SDS	Mean	SDS		Mean	SDS	Mean	SDS	
Age at diagnosis (years)	7.55	5.1	12.31	3.52	<0.001	11.74	3.94	11.59	4.14	0.905
Age at initial TFT (years)	7.55	5.1	12.31	3.52	<0.001	11.74	3.94	11.59	4.14	0.906
DKA at diagnosis	4		21		1	5		20		0.748
Initial HbA1c (%)	11.6	2.09	11.66	2.33	0.932	12.44	1.5	11.44	2.41	0.156
TPO Ab positivity						4	N=13	7	N=62	0.09
TG Ab positivity	4	N=11	9	N=64	0.09					
GAD Ab positivity	9	N=11	28	N=64	0.02	6	N=13	31	N=63	0.841
Islet Ab positivity	1	N=11	3	N=63	0.482	1	N=13	3	N=62	0.541
Insulin Ab positivity	2	N=11	2	N=64	0.1	2	N=13	2	N=63	0.133
IA2 Ab positivity	8	N=10	25	N=64	0.02	7	N=13	26	N=62	0.432
T1DM (N=57)										
	TPO Ab positivity		TPO Ab negativity		p value	TG Ab positivity		TG Ab negativity		p value
N	10		31			9		32		
Sex	M	F	M	F		M	F	M	F	
	7	3	21	10	1	5	4	23	9	0.429
	Mean	SDS	Mean	SDS		Mean	SDS	Mean	SDS	
Age at diagnosis (years)	7.85	5.27	10.42	3.69	0.093	11.31	4.31	9.37	4.15	0.227
Age at initial TFT (years)	7.85	5.27	10.43	3.69	0.093	11.31	4.31	9.37	4.15	0.227
DKA at diagnosis	4		18		0.469	5		17		1
Initial HbA1c (%)	12.06	1.51	11.99	1.85	0.919	12.63	1.71	11.83	1.75	0.231
TPO Ab positivity						4	N=9	6	N=32	0.185
TG Ab positivity	4	N=10	5	N=31	0.185					
GAD Ab positivity	9	N=10	28	N=31	1	6	N=9	31	N=32	0.028
Islet Ab positivity	1	N=10	3	N=31	1	1	N=9	3	N=32	1
Insulin Ab positivity	2	N=10	2	N=31	0.245	2	N=9	2	N=32	0.204
IA2 Ab positivity	8	N=9	25	N=31	1	7	N=9	26	N=31	0.645

Conclusion

This study showed that low T3 or low T4 was frequently observed at the onset of T1DM and it was statistically significantly associated with the presence DKA. Thyroid autoimmunity was more common in T1DM compared to T2DM, but there was no association between any DM-associated autoantibody and the positivity of thyroid-specific anti-TPO or anti-TG autoantibody in the patients with new-onset T1DM.

References

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