

Original article / Araştırma**Assessment of psychiatric disorders accompanying Hashimoto's thyroiditis in children and adolescents****Kıvanç Kudret BERBEROĞLU,¹ Işık GÖRKER²****ABSTRACT**

Objective: Hashimoto's thyroiditis is the most common cause of goiter and acquired hypothyroidism in children and adolescents in non-iodine-deficient areas. In our study, it is aimed to determine the psychiatric disorders accompanying Hashimoto's thyroiditis which is a chronic disease in children and adolescents. **Methods:** In order to form the research group, 65 cases who were followed up and treated due to the diagnosis of Hashimoto's thyroiditis in the Pediatric Endocrinology Department of the Trakya University Medicine Faculty were included in the study. In order to form the control group, 65 patients who were evaluated in the General Pediatrics Outpatient Clinic of the Pediatrics Department of Trakya University Medicine Faculty and did not have the chronic medical and neurodevelopmental diseases were include in the study. In the child and adolescent psychiatry outpatient clinic, the Socio-demographic Data Form, the Strengths and Difficulties Questionnaire, Turgay's Scale and the Schedule for Affective Disorders and Schizophrenia for School Age Children were applied to the cases in the research and control groups. **Results:** 38.4% of the cases with Hashimoto's thyroiditis were diagnosed with at least one psychiatric disorder. In our study, the most frequent comorbid psychiatric disorder in children with Hashimoto's thyroiditis was found as Specific phobia with rate of 20%. Specific phobia is followed by attention deficit hyperactivity disorder and depressive disorder with rate of 9.2%. In our study, there were no significant differences between patients with Hashimoto's thyroiditis and healthy volunteers in terms of the attention deficit, hyperactivity, impulsivity, and oppositional defiant disorder. There was no significant difference between the cases with Hashimoto's thyroiditis and the control group in terms of sensation, behavioral, attention deficit and mobility, peer relationships, social behavior and total difficulties scores. **Discussion:** When we evaluate the findings of our study, it can be considered that there was no any adverse effects of Hashimoto's thyroiditis on the children's psychical status. However, due to being the limited number of studies about this subject in the literature, it is necessary to support our findings with other studies conducted about this subject. (*Anatolian Journal of Psychiatry* 2019; 20(2):189-195)

Keywords: Hashimoto's thyroiditis, autoimmunity, psychiatric disorders

Çocuk ve ergenlerde Hashimoto tiroiditine eşlik eden psikiyatrik bozuklukların değerlendirilmesi

ÖZ

Amaç: Hashimoto tiroiditi, iyot eksikliğinin olmadığı bölgelerde çocuk ve ergenlerde, guatr ve edinilmiş hipotiroidinin en sık nedenidir. Çalışmamızda çocuk ve ergenlerde kronik bir hastalık olan Hashimoto tiroiditine eşlik eden psikiyatrik bozuklukların belirlenmesi amaçlanmaktadır. **Yöntem:** Araştırma grubu olarak, Trakya Üniversitesi Tıp Fakültesi Çocuk Endokrinoloji Bilim Dalı'nda, Hashimoto tiroiditi tanısıyla izlenen ve tedavi edilen 65 olgu alınmıştır. Kontrol grubu olarak, Trakya Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Genel Pediatri Polikliniği'nde değerlendirilen kronik tıbbi ve nörogelişimsel hastalığı olmayan 65 olgu alınmıştır. Çalışmaya alınan araştırma ve kontrol grubu olgularına çocuk ve ergen ruh sağlığı ve hastalıkları polikliniğinde Sosyodemografik Veri Formu, Güçler Güçlükler Anketi, Turgay Ölçeği ve Okul Çağı Çocukları için Duygulanım Bozuklukları ve Şizofreni Görüşme

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Çizelgesi uygulanmıştır. Sonuçlar: Hashimoto tiroiditi olgularının %38.4'üne en az bir psikiyatrik bozukluk tanısı konmuştur. Çalışmamızda çocuklarda Hashimoto tiroiditine en sık eşlik eden psikiyatrik bozukluk %20 ile özgül fobidir. Özgül fobi %9.2 ile dikkat eksikliği hiperaktivite bozukluğu ve depresif bozukluk izlemiştir. Çalışmamızda Hashimoto tiroiditi olgularıyla sağlıklı gönüllüler arasında dikkat eksikliği, hiperaktivite, dürtüsellik ve karşı olma karşı gelme bozukluğu açısından anlamlı bir farklılık saptanmamıştır. Hashimoto tiroiditi olgularıyla kontrol grubu arasında duygulanım, davranım, dikkat eksikliği ve hareketlilik, akran ilişkileri, sosyal davranış ve toplam güçlük puanları açısından anlamlı bir farklılık saptanmamıştır. **Tartışma:** Çalışmamızın bulgularını değerlendirdiğimizde Hashimoto tiroiditin çocukların ruhsal durumu üzerine herhangi bir olumsuz etkisinin bulunmadığı düşünülebilir. Ancak literatürde bu konuda az sayıda çalışma olması nedeniyle bulgularımızın tekrar eden çalışmalarla desteklenmesi gerekmektedir. (Anadolu Psikiyatri Derg 2019; 20(2):189-195)

Anahtar sözcükler: Hashimoto tiroiditi, otoimmünite, psikiyatrik bozukluk

INTRODUCTION

Hashimoto's thyroiditis is the most common cause of goiter and acquired hypothyroidism in children and adolescents in non-iodine-deficient areas. While the incidence of this disease increases in childhood age group, early and mid-term of puberty, it is more rarely seen below four years of age. In addition to the role of autoimmunity in the pathogenesis of the disease, the genetic predisposition and environmental factors are also important.¹ Detection of high thyroid autoantibody levels is important for the diagnosis of Hashimoto's thyroiditis and it was reported that anti-thyroid peroxidase (anti-TPO) positivity may be present in the cases with rate up to 90%.² In a study, it was shown that high levels of thyroid autoantibodies in thyroid diseases are associated with mood disorders as independent of thyroid dysfunction.³

Furthermore, it was reported that the thyroid autoantibody positivity caused also the attention disorders in addition to the mood disorders.⁴

Findings indicating the relationship between thyroid hormone dysfunction and attention deficit hyperactivity disorder (ADHD) were revealed by showing the presence of the ADHD with rate of 46-70% in children with diffuse thyroid hormone resistance.⁵

In our study, it is aimed to determine the psychiatric disorders accompanying Hashimoto's thyroiditis which is a chronic disease in children and adolescents.

METHODS

Sample

In order to form the research group; 65 cases aged between 6 and 18 years who were followed up and treated as outpatients with Hashimoto's thyroiditis between November 2015 and June 2016 in polyclinic of the Pediatric Endocrinology Department of the Trakya University Medicine

Faculty, were included in study. In order to form the control group, 65 cases who were brought to the General Pediatrics Outpatient Clinic of the Pediatrics Department of Trakya University Medicine Faculty by their parents and did not have the chronic medical and neurodevelopmental diseases were include in the study. Ethics approval dated 03.09.2015 was taken from the Local Ethics Committee of Trakya University for the execution of the study (Annex-1).

Data collection tools

The scales such as the Sociodemographic Data Form, the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime (K-SADS-PL), the Strengths and Difficulties Questionnaire (SDQ)-Parent Version, the Child and Adolescent Disruptive Behavior Disorders Screening and Rating Scale based on DSM-IV (Turgay's Scale and DBD-SRS), were applied to the study population. The sociodemographic data form was prepared by taking the opinion of the pediatric endocrine specialists, and it was filled in by the researcher with taking information from the cases, the family and the physician who continued the treatment.

The Schedule for Affective Disorders and Schizophrenia for School Age Children – Present and Lifetime Version (K-SADS- PL): This form is a semi-structured interview form developed by Kauffman et al. in order to determine the present and past psychopathologies of children and adolescents according to DSM-IV and DSM-III-R diagnostic criteria.⁶

The Strengths and Difficulties Questionnaire (SDQ) - Parent Version: The SDQ contains 25 questions. Some of the statements question the negative, some question the positive behavior features. The questionnaire consists of five sub-titles as emotional problems, attention deficit and hyperactivity, behavioral problems, social behavior, peer problems. As each title is evaluated within itself, the total score of difficulty is the sum of the scores of the others, except from the

the social behavior score. The low score on the subscale of social behavior and the high score on the other subscales indicate the existence of the problem for that area.⁷

The Child and Adolescent Disruptive Behavior Disorders Screening and Rating Scale (DBD-SRS) based on DSM-IV (Turgay's Scale and DBD-SRS): This scale was developed according to the DSM-IV criteria. In the ADHD symptoms group of the scale, there were three items questioning impulsivity, six items questioning hyperactivity and nine item questioning inattention. In the scale, DSM-IV criteria were turned into the question format without changing their contents. Items in the scale are assessed between 0 and 3.⁸

Data analysis

Statistical analysis was performed using the SPSS 23.0 statistical program. Mean, standard deviation, median, lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov Simirnov test. Mann Whitney U test was used for the analysis of quantitative data. Chi-square test was used to analyze qualitative data, and Fischer test was used when chi-square test conditions were not provided. In order to test for the presence or absence of relationships between continuous variables, the spearman correlation analysis was used in the data set which is detected to not fit the normal distribution. Statistical significance level was determined as $p < 0.05$.

RESULTS

The mean age of the cases in the research group was 14.4 ± 3.0 years and the mean age of the cases in the control group was 14.7 ± 1.8 years. Fifty-nine (90.8%) of the cases in the research group were female children and six (9.2%) were male children. Fifty-four (83.0%) of the cases in the control group were female children and 11 (17.0%) were male children. It was found that there was no statistically significant difference between the research group and the control group in terms of age and gender.

It was detected that the maternal education levels and the income level of the family in the control group were significantly higher than the research group ($p < 0.05$).

In the Spearman's correlation analysis, it was detected that there was no correlation between parental education level, the income levels and SDQ total scores of the research and control group.

In research and control group cases, it was detected that there was no significant difference in terms of mother and father's medical history, mother and father's psychiatric disease story, consanguineous marriage, the presence or absence of problem in pregnancies of mothers and delivery methods ($p > 0.05$).

When the time of the births were evaluated in the groups, it was determined that there was a significant difference in the research group in terms of the excess of preterm birth ($p < 0.05$) (Table 1).

Table 1. The Comparison of the research and control groups cases in terms of the pregnancy problem, time of birth, delivery methods

		Research group (n=65)		Control group (n=65)		p*
		n	%	n	%	
Pregnancy problem	Presence	6	9.2	8	12.3	0.571
Time of birth	Term	56	86.1	63	96.9	0.027*
	Preterm	9	13.8	2	3.0	
Delivery methods	Normal	35	53.8	30	46.2	0.380
	c/s	30	46.2	35	53.8	

*: Chi-square test

In our study, the diagnoses according to K-SADS-PL and DSM-5 were evaluated separately and the distributions and percentages of psychiatric diagnosis are shown in table (Table 2).

According to the SDQ scores in our study, it was found that there was no significant difference between the research and control groups in terms of affective problem, behavior problem,

Table 2. The diagnosis distributions of the cases in the research group according to K-SADS-PL and DSM-5

	Research group (n=65)		Control group (n=65)		p*
	n	%	n	%	
Diagnosed with at least one disease	25	38.4	32	49.2	0.216
Depressive disorder	6	9.2	6	9.2	1.000
Panic disorder	1	1.5	0	0	1.000
Separation anxiety disorder	4	6.1	3	4.6	1.000
Social phobia	3	4.6	2	3.0	1.000
Generalized anxiety disorder	1	1.5	2	3.0	1.000
Specific phobia	13	20.0	12	15.3	1.000
Obsessive compulsive disorder	3	4.6	8	12.3	0.115
Enuresis	1	1.5	2	3.1	1.000
Attention-deficit/hyperactivity disorder	6	9.2	7	10.7	0.770
Oppositional defiant disorder	4	6.1	6	9.2	0.510
Tic disorder	2	3.0	1	1.5	1.000
Post-traumatic stress disorder	1	1.5	1	1.5	1.000

*: Chi-square test

attention deficit and hyperactivity problem, social behavior problem and total difficulty scores ($p>0.05$) (Table 3).

In our study, it was detected that there was no significant difference between the research and control groups according to the Turgay's Scale ($p>0.05$) (Table 4).

Table 3. The comparison of the Strengths and Difficulties Questionnaire scores of the cases between the research and control groups

	Research group (n=65)	Control group (n=65)	p*
	Mean±SD	Mean±SD	
Affective	1.9±2.2	2.2±2.4	0.637
Behavior	0.8±1.2	1.0±1.5	0.778
Attention deficit and hyperactivity	2.0±2.7	1.6±2.3	0.733
Peer relationship	1.4±1.8	1.8±2.0	0.123
Social behavior	9.4±0.8	9.2±1.3	0.687
Total difficulty	6.2±6.1	6.7±6.1	0.388

*: Mann Whitney U test.

Table 4. The comparison of the cases between the research and control group in terms of attention deficit/hyperactivity, impulsivity and OPD in the according to the Turgay's Scale

	Research group (n=65)		Control group (n=65)		p*
	n	%	n	%	
Attention deficit	6	9.2	7	10.7	0.770
Hyperactivity and impulsivity	4	6.1	3	4.6	1.000*
Oppositional defiant disorder	2	3.0	6	9.2	0.273*

*: Fisher's chi-square test, others chi-square test

DISCUSSION

There are studies supporting and not supporting

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the association of thyroid autoimmunity and some autoimmune markers with various psychiatric disorders such as depression, anxiety and

and ADHD.⁹⁻¹² The aim of our study was to evaluate whether the thyroid autoimmunity causing Hashimoto's thyroiditis lead to psychiatric problems in children and adolescents, and to determine their distribution if it leads to psychiatric disorders.

The brain is a structure that uses thyroid hormone much differently than other organs. The thyroid hormone is specially selected and distributed by the brain. The brain uniquely controls the T4-T3 conversion and very tightly regulates thyroid levels. Normal response to the behavioral stress is provided by the activation of the thyroid system. The increase of thyroid hormone in euthyroid individuals as the result of TSH stimulation, is a helpful factor to get out of depression. If there is a resistance in the thyroid system and this increase is not provided, it is difficult to treat depression. This condition helped explain the association of the Hashimoto's thyroiditis cases in which there is no hypothyroidism and only anti-TPO is positive, with mood disorder.¹³ According to the study conducted by Carta et al. with adult patients in 2004, Anti-TPO positivity was found to be significantly higher in patients with the not otherwise specified (NOS) anxiety disorder, major depressive episode, and NOS depressive disorder than control group.³ In another study conducted by Haggerty and colleagues, it was found that there was no difference in terms of the antithyroid antibodies between patients with unipolar depression and the patients without psychiatric diagnosis in the control group.⁹ In our study, it was found that the depression frequency was 9.2% among patients with Hashimoto's thyroiditis and there was no significant difference between the research and control groups.

According to the results of the twin study conducted by Vonk et al. with adults in 2007, it was shown that the increased anti-TPO levels observed in autoimmune thyroiditis caused genetic predisposition to the development of bipolar disorder.¹⁴ In our study, it was detected that there was no bipolar disorder in any of the research and control group cases we included in the study. This finding may be related to the fact that our study was conducted with children and that our case count is limited.

When we look at the literature, there are studies supporting and not supporting the relation of autoimmunity and anxiety. In a study conducted by Engum et al., it was found that there was no association between thyroid autoimmunity and anxiety.¹⁵ In a study conducted by Carta et al., it

was found that there was a relationship between autoimmune thyroiditis and anxiety.¹¹ In our study, it was seen that the frequency of anxiety disorder was 30.1% in the research and control groups. In our study, the most frequent disorder in psychiatric disorders of the children with Hashimoto's thyroiditis was Specific phobia with rate of 20%. Specific phobia is followed by ADHD and depressive disorder with rate of 9.2%.

In our study, ADHD frequency was found to be 9.2% in the research group and 10.7% in the control group. There was no clinically significant difference between the groups. When we compared the groups with Turgay's Scale, it was detected that there was no clinically significant difference in attention deficit, hyperactivity and impulsivity. When we assessed the two groups in terms of attention deficit/hyperactivity and SDQ scores, it was determined that there was no clinically significant difference between the groups. The prevalence of ADHD in the literature is between the rates of 5% and 16%.^{16,17} The rates of ADHD that we found in our study are consistent with the literature. There are studies in the literature showing the relationship between autoimmunity and ADHD. Glutamic acid decarboxylase 65 (GAD65) antibody was found to be significantly elevated in ADHD cases or patients diagnosed with ADHD.¹² In a study conducted by Chen et al., it was shown that the autoimmune thyroid disease was more common in ADHD cases than in healthy controls.¹⁸

In a study conducted by McLoyd et al., it was shown that the low income level of the family is associated with the child's low intelligence score, impairment in cognitive function, low school achievement and social emotional problems.¹⁹ According to this result, it can be reached the result of that the high income level of the family is a protective factor from psychiatric disorders for children. In our study, it was detected that there was a significant difference between the income levels of the research group and the control group. This difference may be due to the fact that A smaller number of low-income families are included in the research group and there was no significant difference in terms of psychiatric disorder between children with Hashimoto thyroiditis and healthy voluntary children.

In our study, it was found that the rate of school success was significantly higher in the research group than the control group. Studies show that the school success is protective against psychiatric disorders.²⁰ In our study, the high rate of

school success in the research group may be thought to be the one of the factors affecting the not being detected of the difference between the groups in terms of psychiatric disorders.

In a study conducted by Keser and colleagues, the effect of chronic disease presence (diabetes, obesity, asthma, carditis) on psychiatric disorders in children was assessed by applying SDQ and it was detected that the emotional problems were significantly higher in obesity, asthma, and carditis patients. In terms of peer problems, it was found that the obesity and asthma patients had more problems. Patients without chronic disease and patients with carditis had higher scores in terms of positive social behavior.²¹ In another study conducted by Akay et al. according to result of the strengths and difficulties questionnaire, there was no difference between the children with type 1 diabetes, which has autoimmune origin, and the control group in terms of the behavioral problems, hyperactivity, social behaviors, emotional symptoms.²² According to the

assessment with SDQ in our study, there was no significant difference between the cases with Hashimoto's thyroiditis, a chronic disease, and the control group in terms of sensation, behavioral, attention deficit and mobility, peer relationships, social behavior and total difficulties scores.

There are some limitations in our study. First of all, the being low of our sample count limits the generalizability of our study. The second limitation is that our study is cross-sectional and the psychiatric histories of the participants are not considered. Thirdly, the fact that whether the cases in the research group are under drug treatment is not considered.

Performing the follow-up studies by determining the serum autoantibody levels of the cases, including the factors that we mentioned in our limitations of our study, will give more detailed information about the effect of thyroid autoimmunity on psychiatric disorders in children.

Authors' contributions: K.K.B: literature review, sample collection, applying scales, statistics, writing the manuscript; I.G.: finding the subject, conducting research, review the manuscript.

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