



Relationship between Immune Thrombocytopenic Purpura and Thyroid Diseases

İmmün Trombositopenik Purpura ve Tiroid Hastalıkları Arasındaki İlişki

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ABSTRACT

Objective: This study aimed to determine the frequency of thyroid diseases, the positivity rates of anti-thyroid peroxidase antibodies (Anti-TPO-Ab), anti-thyroglobulin antibodies (Anti-TG-Ab), antinuclear antibodies (ANA), and anti-double-stranded deoxyribonucleic acid antibodies (Anti-dsDNA-Ab), and variables related to the frequency of hypothyroidism in patients with immune thrombocytopenia (ITP).

Methods: This retrospective study was conducted between January 2015 and December 2021. A total of 320 patients with newly diagnosed ITP were included in the study. Demographic characteristics, comorbidity status, features of ITP and thyroid diseases, laboratory findings, and mortality information of the patients were retrospectively reviewed. After investigating the thyroid disease and autoantibody frequencies of the patients, we divided the patients into the hypothyroid and no thyroid disease groups.

Results: Fifty-nine (18.4%) patients had thyroid disorders. Anti-TG-Ab positivity was detected in 20.0%, Anti-TPO-Ab positivity in 29.4%, ANA positivity in 16.9%, and Anti-DsDNA-Ab positivity in 4.2% of ITP patients. In total, 42 (13.1%) patients had hypothyroidism. Patients with high age ($p=0.024$), female sex ($p=0.006$), and positive Anti-TPO-Ab ($p=0.009$) had a higher risk of hypothyroidism than other patients.

Conclusion: ITP disease and hypothyroidism may result from a standard pathophysiological process involving Anti-TPO antibodies. Advanced age and female sex also seem to support the coexistence of these two diseases.

Keywords: Immune thrombocytopenia, thyroid diseases, hypothyroidism, antithyroid antibodies, antinuclear antibody, anti-double-stranded deoxyribonucleic acid antibodies

ÖZ

Amaç: Bu çalışma, immün trombositopeni (ITP) hastalarında tiroid hastalıklarının sıklığını, anti-tiroid peroksidaz antikorları (Anti-TPO-Ab), anti-tiroglobulin antikorları (Anti-TG-Ab), anti-nükleer antikorlar (ANA), anti-çift sarmallı deoksiribonükleik asit antikorları (Anti-dsDNA-Ab) pozitiflik oranlarını ve hipotiroidizm sıklığı ile ilişkili değişkenleri belirlemeyi amaçlamıştır.

Gerekle ve Yöntem: Bu retrospektif çalışma Ocak 2015 ile Aralık 2021 tarihleri arasında gerçekleştirilmiştir. Yeni tanı almış 320 ITP hastası çalışmaya dahil edilmiştir. Hastaların demografik özellikleri, komorbidite durumları, ITP ve tiroid hastalıklarının özellikleri, laboratuvar bulguları ve mortalite bilgileri retrospektif olarak incelenmiştir. Hastaların tiroid hastalığı ve otoantikör sıklıkları araştırıldıktan sonra, hastalar hipotiroid grup ve tiroid hastalığı olmayan grup olarak ikiye ayrılmıştır.

Bulgular: Elli dokuz (%18,4) hastada tiroid hastalığı tespit edilmiştir. Anti-TG-Ab pozitifliği %20,0, Anti-TPO-Ab pozitifliği %29,4, ANA pozitifliği %16,9 ve Anti-DsDNA-Ab pozitifliği %4,2 olarak belirlenmiştir. Toplam 42 (%13,1) hasta hipotiroidizm tanısı almıştır. Yüksek yaş ($p=0,024$), kadın cinsiyet ($p=0,006$) ve pozitif Anti-TPO-Ab ($p=0,009$) olan hastalar, diğer hastalara göre hipotiroidizm riski daha yüksek bulunmuştur.

Sonuç: ITP hastalığı ve hipotiroidizm, Anti-TPO-Ab'nin de dahil olduğu ortak bir patofizyolojik sürecin sonucu olabilir. İleri yaş ve kadın cinsiyet de bu iki hastalığın bir arada bulunmasını destekleyen faktörler olarak görülmektedir.

Anahtar Kelimeler: İmmün trombositopeni, tiroid hastalıkları, hipotiroidizm, anti-tiroid antikorlar, anti-nükleer antikor, anti-çift sarmallı deoksiribonükleik asit antikorları

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INTRODUCTION

Immune thrombocytopenia (ITP) is an acquired autoimmune disease characterized by isolated decreased peripheral platelet count, which is caused by insufficient platelet production and platelet destruction due to autoimmune antibodies that recognize platelet membrane glycoproteins (1-3). The incidence of ITP has been reported as approximately 1.9-6.4/100000 in children and 3.3-3.9/100000 in adults (4).

Due to changes in the immune response and the development of self-reactive antibodies, ITP and other autoimmune diseases may be present simultaneously (5). It has been shown in previous studies that autoimmune diseases such as antiphospholipid syndrome and systemic lupus erythematosus can coexist with ITP (1, 6). Additionally, various autoimmune thyroid diseases, such as Graves' disease and Hashimoto's thyroiditis, hyperthyroidism, and hypothyroidism, are associated with ITP (5, 7-9). More interestingly, it has been demonstrated that treatment of thyroid disease improves thrombocytopenia (5, 9). Positivity for antinuclear antibody (ANA), anti-double-stranded deoxyribonucleic acid antibodies (Anti-dsDNA-Ab), anti-thyroid peroxidase antibodies (Anti-TPO-Ab), and anti-thyroglobulin antibodies (Anti-TG-Ab)- the latter two defined as anti-thyroid antibodies (Anti-T-Abs)- are more common in patients with ITP than in the general population (10-13). It has been claimed that the presence of these antibodies in ITP patients affects the prognosis of ITP and increases the risk of some comorbidities (14, 15). Anti-T-Abs positivity in patients with ITP has been demonstrated to increase the risk of chronicity (15) and the development of autoimmune thyroiditis (11) and abnormal thyroid functions (8). However, the possible impact of these autoimmune markers on the prevalence, pathophysiology, and management of ITP is still unclear (11).

In this study, our aims were (i) to determine the frequency of thyroid diseases in patients with ITP, (ii) to determine the positivity rates of Anti-T-Abs, ANA, and Anti-dsDNA-Ab in patients with ITP, and (iii) to investigate whether the frequency of hypothyroidism in patients with ITP is associated with antibody positivity, demographic and clinical features, thyroid function tests (TFTs), and laboratory findings.

METHODS

Study Design and Population

This retrospective study was conducted between January 2015 and December 2021 at the Department of Hematology

of University of Health Sciences Türkiye, Bakirkoy Dr. Sadi Konuk Training and Research Hospital. This retrospective study was conducted between January 2015 and December 2021 at the Department of Hematology of University of Health Sciences Türkiye, Bakirkoy Dr. Sadi Konuk Training and Research Hospital. The protocol for this study was approved by the Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (date: 06.12.2021, decision no: 2021-23-16).

A total of 320 patients aged >18 years with newly diagnosed ITP were included in the study. Patients younger than 18 years of age, those with secondary ITP associated with any cause other than thyroid disease(s), and those with known autoimmune diseases other than thyroid diseases were excluded from the study. Demographic characteristics, comorbidity status, ITP and thyroid disease characteristics, laboratory findings, and mortality information of the patients were recorded.

The diagnosis and treatment of ITP were based on the diagnostic criteria and treatment recommendations of relevant guidelines (3).

Laboratory Analysis

Complete blood counts, liver and kidney function tests, and lactate dehydrogenase levels were measured using routine devices (Roche, Cobas 8000, ABD).

TFTs [free triiodothyronine (F-T3), free thyroxine (F-T4), thyroid-stimulating hormone (TSH)], Anti-TPO-Ab, Anti-TG-Ab, and anti-dsDNA-Ab were measured by a chemiluminescence microparticle immunoassay (Roche, Cobas 8000, ABD) according to the manufacturer's protocols.

ANA measurements were performed using an indirect immunofluorescence assay using the HEp-2 Test System (Ipro biosistem, Spain) (15).

The standard reference range for F-T3 was 1.58-3.91 pg/m, (16) F-T4 was 0.7-1.48 ng/d, (16) TSH was 0.35-4.94 mIU/L, (16) Anti-TPO-Ab was 0.00-5.61 IU/mL, (16) Anti TG-Ab was 0.00-4.11 IU/mL, (16) Anti-dsDNA-Ab was >35 IU/mL. (17)

A positive value of Anti-TPO-Ab was defined as Anti-TPO-Ab >5.61 IU/mL, (16) a positive value of Anti-TG-Ab was defined as Anti-TG-Ab >4.11 IU/mL, (16) a positive value of Anti-dsDNA-Ab was defined as Anti-dsDNA-Ab >35 IU/mL, (17) and a positive result for ANA was defined as a titer of $\geq 1:40$. (15)

When selecting laboratory results for inclusion in the study, the time of diagnosis of ITP was taken as a reference.

First, the laboratory results that were studied at the time of ITP diagnosis were used. If absent, the most recently studied laboratory findings before or after the diagnosis of ITP were used.

Thyroid Disease-related Definitions

An F-T4 level lower than the reference range was defined as overt hypothyroidism, and an F-T4 level higher than the reference range was defined as overt hyperthyroidism (18). Subclinical hypothyroidism was defined as TSH levels higher than the reference range with normal serum F-T4 and F-T3 levels in the absence of clinical signs or symptoms (5, 18). Subclinical hyperthyroidism was defined as a normal serum F-T4 and F-T3 level without clinical signs or symptoms and TSH levels lower than the reference range (5, 18).

Patients with single or multiple nodules of 1 cm or more in the thyroid gland on ultrasonography or computed tomography were defined as patients with thyroid nodules (19).

The diagnosis of Hashimoto's thyroiditis was made based on the presence of either Anti-TPO-Ab positivity or decreased echogenicity, heterogeneity, hypervascularity, and small cysts on thyroid ultrasonography, in addition to the clinical symptoms of thyroid dysfunction (20).

Grouping

The "hypothyroidism" group was formed from patients with overt and subclinical hypothyroidism, except for thyroid nodules, thyroid cancer, and thyroidectomy.

Statistical Analysis

All analyses were performed on SPSS v25 (SPSS Inc., Chicago, IL, USA). Histograms and Q-Q plots were used to determine whether continuous variables were normally distributed. Data are given as mean±standard deviation or median (1st quartile-3rd quartile) for continuous variables according to distribution normality and as frequency (percentage) for categorical variables. Between-group analysis of continuous variables was performed using Student's t-test or Mann-Whitney U test, depending on the normality of distribution. Categorical variables were compared between groups using chi-square tests or Fisher's exact test. Multivariable logistic regression analysis was performed to calculate odds ratios (ORs) adjusted for age and sex. The statistical significance was set as $p < 0.05$.

RESULTS

The patients' ages ranged from 19 to 92 (mean age 48.40±18.54), and 231 (72.2%) were female (Table 1).

Table 1. Summary of patient characteristics and laboratory measurements

Age	48.40±18.54
Sex	
Female	231 (72.2%)
Male	89 (27.8%)
Duration of ITP: years	6 (4-8)
Lymphoproliferative disease	1 (0.3%)
Thyroid disease	59 (18.4%)
Subclinical hypothyroidism	4 (1.3%)
Overt hypothyroidism	38 (11.9%)
Subclinical hyperthyroidism	6 (1.9%)
Overt hyperthyroidism	4 (1.3%)
HT with euthyroidism	2 (0.6%)
Thyroid nodule	3 (0.9%)
Thyroid cancer	1 (0.3%)
Thyroidectomy	1 (0.3%)
Duration of thyroid disease	6.49 ± 4.18
Comorbidities	
Diabetes mellitus	51 (15.9%)
Hypertension	76 (23.8%)
Malignancy (non-hematological)	6 (1.9%)
Hyperlipidemia	20 (6.3%)
Coronary artery disease	26 (8.1%)
COPD	13 (4.1%)
Rheumatic disease	11 (3.4%)
Other	78 (24.4%)
Glucose (mg/dL)	102 (91 - 125)
Urea (mg/dL)	28 (21 - 38)
Creatinine (mg/dL)	0.68 (0.60 - 0.80)
Aspartate aminotransferase (U/L)	19 (15 - 25)
Alanine aminotransferase (U/L)	17 (12 - 26)
Lactate dehydrogenase (IU/L)	210 (172 - 261)
Hemoglobin (g/dL)	12.77 ± 2.08
Hematocrit (%)	38.50 ± 5.76
MCV (fL)	84.29 ± 6.61
WBC (x10 ³)	8.05 (6.26 - 10.00)
Neutrophil (x10 ³)	4.95 (3.68 - 6.83)
Lymphocyte (x10 ³)	2.10 ± 0.96
Eosinophil (x10 ³)	0.10 (0.04 - 0.19)
Platelet (x10 ³)	34.5 (11.0 - 71.5)
TSH (mIU/L)	1.77 (1.04 - 3.00)
F-T4 (ng/dL) (n = 276)	1.09 (0.87 - 1.29)
F-T3 (pg/mL) (n = 196)	2.77 ± 0.97
Anti-TG Ab positivity (n = 40)	8 (20.0%)
Anti-TPO-Ab positivity (n = 51)	15 (29.4%)
ANA positivity (n = 160)	27 (16.9%)
Anti-dsDNA-Ab positivity (n = 120)	5 (4.2%)
Mortality	16 (5.0%)

Data are presented as mean±standard deviation or median (1st quartile-3rd quartile) for continuous variables according to distribution normality and as frequency (percentage) for categorical variables.

ANA: Antinuclear antibody, Anti-dsDNA-Ab: Anti-double-stranded deoxyribonucleic acid antibodies, Anti-TG-Ab: Anti-thyroglobulin antibodies, Anti-TPO-Ab: Anti-thyroid peroxidase antibodies, COPD: Chronic obstructive pulmonary disease, F-T3: Free triiodothyronine, F-T4: Free thyroxine, HT: Hashimoto's thyroiditis, ITP: Immune thrombocytopenia, MCV: Mean corpuscular volume, TSH: Thyroid-stimulating hormone, WBC: White blood cells

Fifty-nine (18.4%) patients were diagnosed with thyroid-related diseases. Anti-TG-Ab positivity was detected in 20.0%, anti-TPO-Ab positivity in 29.4%, ANA positivity in 16.9%, and anti-dsDNA-Ab positivity in 4.2% of the patients. In total, 42 (13.1%) patients had hypothyroidism, 38 (11.9%) of which were defined as overt hypothyroidism, and 4 (1.3%) were subclinical hypothyroidism. The mean age of patients

with hypothyroidism was 54.45 ± 17.61 years, whereas it was 47.38 ± 18.71 years in those without any thyroid disease ($p=0.023$). 90.5% of patients with hypothyroidism and 68.6% of patients without any thyroid disease were females ($p=0.006$). In the hypothyroidism group, the percentage of those with hyperlipidemia ($p=0.033$) and the percentage of those with positive Anti-TPO-Ab ($p=0.039$) were significantly higher than those without any thyroid disease (Table 2).

Table 2. Comparison of patient characteristics and laboratory measurements between groups

	Groups		
	No thyroid disease (n=261)	Hypothyroidism (n=42)	p-value
Age	47.38±18.71	54.45±17.61	0.023
Sex			
Female	179 (68.6%)	38 (90.5%)	0.006
Male	82 (31.4%)	4 (9.5%)	
Duration of ITP: Years	6 (4-8)	6 (5-7)	0.726
Lymphoproliferative disease	0 (0.0%)	1 (2.4%)	0.139
Comorbidities			
Diabetes mellitus	40 (15.3%)	9 (21.4%)	0.441
Hypertension	56 (21.5%)	15 (35.7%)	0.067
Malignancy	2 (0.8%)	2 (4.8%)	0.094
Hyperlipidemia	13 (5.0%)	6 (14.3%)	0.033
Coronary artery disease	19 (7.3%)	6 (14.3%)	0.133
COPD	12 (4.6%)	0 (0.0%)	0.384
Rheumatic disease	6 (2.3%)	3 (7.1%)	0.114
Other	61 (23.4%)	10 (23.8%)	1.000
Glucose (mg/dL)	102 (91-126)	106.5 (95 - 116)	0.479
Urea (mg/dL)	27.1 (21-38)	31.5 (22 - 40)	0.240
Creatinine (mg/dL)	0.68 (0.59-0.8)	0.73 (0.61 - 0.82)	0.438
Aspartate aminotransferase (U/L)	19 (15-25)	21 (16 - 25)	0.785
Alanine aminotransferase (U/L)	18 (12-27)	15.5 (12 - 25)	0.544
Lactate dehydrogenase (IU/L)	214 (179-258)	204.5 (178 - 272)	0.924
Hemoglobin (g/dL)	12.82±2.14	12.60 ± 1.67	0.514
Hematocrit (%)	38.65±5.94	38.15 ± 4.69	0.603
MCV (fL)	84.44±6.65	83.58 ± 6.41	0.434
WBC (x10 ³)	8.13 (6.26-10.20)	7.89 (6.60 - 9.43)	0.676
Neutrophil (x10 ³)	5.02 (3.76-7.13)	4.86 (3.60 - 6.35)	0.385
Lymphocyte (x10 ³)	2.09±0.98	2.15 ± 0.77	0.638
Eosinophil (x10 ³)	0.10 (0.04-0.19)	0.11 (0.05 - 0.19)	0.738
Platelet (x10 ³)	31 (11-69)	39.5 (14 - 81)	0.552
Anti-TG-Ab positivity	6 (24.0%)	1 (12.5%)	0.652
Anti-TPO-Ab positivity	6 (20.0%)	8 (53.3%)	0.039
ANA positivity	20 (15.2%)	6 (33.3%)	0.089
Anti-dsDNA-Ab positivity	3 (3.1%)	2 (15.4%)	0.104
Mortality	13 (5.0%)	2 (4.8%)	1.000

Data are presented as mean±standard deviation or median (1st quartile-3rd quartile) for continuous variables according to distribution normality and as frequency (percentage) for categorical variables.

ANA: Antinuclear antibody, Anti-dsDNA-Ab: antidouble-stranded deoxyribonucleic acid antibodies, Anti-TG-Ab: antithyroglobulin antibodies, Anti-TPO-Ab: antithyroid peroxidase antibodies, COPD: Chronic obstructive pulmonary disease, ITP: Immune thrombocytopenia, MCV: Mean corpuscular volume, WBC: White blood cells

Table 3. Odds ratios for hypothyroidism based on multivariable logistic regression analysis

	Hypothyroidism	
	OR (95% CI)	p-value
Age ⁽¹⁾	1,021 (1,003-1,039)	0.024
Sex, Female ⁽²⁾	4,424 (1,521-12,872)	0.006
Duration of ITP, years ⁽³⁾	0.958 (0.875-1,049)	0.351
Anti-TG-Ab positivity ⁽³⁾	0.753 (0.066-8,631)	0.820
Anti-TPO-Ab positivity ⁽³⁾	9,995 (1,783-56,020)	0.009
ANA positivity ⁽³⁾	2,493 (0.825-7,535)	0.106
Anti-dsDNA Ab positivity ⁽³⁾	5,615 (0.796-39,601)	0.083

⁽¹⁾Adjusted for sex, ⁽²⁾Adjusted for age, ⁽³⁾Adjusted for age and sex, ANA: Antinuclear antibody, Anti-dsDNA-Ab: antidual-stranded deoxyribonucleic acid antibodies, Anti-TG-Ab: antithyroglobulin antibodies, Anti-TPO-Ab: antithyroid peroxidase antibodies, CI: Confidence interval, ITP: Immune thrombocytopenia, OR: Odds ratio

High age was associated with hypothyroidism ($p=0.024$) after adjusting for sex. Females had a 4.424-fold higher risk of hypothyroidism than males (OR: 4.424, 95% CI: 1.521-12.872; $p=0.006$) after adjusting for age. Patients with anti-TPO-Ab positivity had a 9.995-fold higher risk for hypothyroidism than other patients (OR: 9.995, 95% CI: 1.783-56.020; $p=0.009$) after adjusting for age and sex (Table 3).

DISCUSSION

The main findings of the current study were as follows: (i) among patients with ITP, 18.4% had thyroid disease, and 13.2% were found to have hypothyroidism (without any known cause); (ii) Anti-TG-Ab positivity was detected in 20.0%, Anti-TPO-Ab positivity in 29.4%, ANA positivity in 16.9%, and anti-dsDNA-Ab positivity in 4.2% of ITP patients; (iii) advanced age, female sex, and Anti-TPO-Ab positivity were determined as independent risk factors for ITP and hypothyroidism to occur in the same patients.

Because autoimmune diseases result from disrupted self-tolerance, the pathophysiological process that causes ITP formation may also trigger other autoimmune or immune diseases, seven and vice-versa. In this context, the most investigated thyroid-related diseases were Graves' disease and Hashimoto's thyroiditis, which are autoimmune diseases of the thyroid (5, 21). In the present study, the incidence of any thyroid disease in patients with ITP was 18.4%, and the incidence of hypothyroidism alone was 13.2%. In a similar study, among patients with ITP, it was reported that the percentage of patients with any thyroid disease was 21.4%, while more specifically, Graves' disease was diagnosed in 3.77%, Hashimoto's thyroiditis in 6.67%, subclinical hyperthyroidism in 0.87%, and subclinical hypothyroidism in 10.1% (5). Although the relationship between autoimmune thyroid diseases and ITP has been investigated (5, 7), the pathophysiological and prognostic link between

these diseases is unknown. One study emphasized that autoimmune thyroiditis was not a prognostic risk factor for chronicity of ITP in the pediatric age (11). A prospective study showed that thyroid dysfunction was not correlated with the duration of ITP or response to treatment (8). The present study specifically examined the relationship between ITP and hypothyroidism, demonstrating a notable association between the conditions. Investigating causal relationships between thyroid dysfunction frequency in patients with ITP compared with the average population may help elucidate the unknown pathophysiological aspects of these disorders.

Anti-TPO-Ab attacks a component of the smooth endoplasmic reticulum of thyroid cells (22). They are the most frequently detected autoantibodies in Hashimoto's thyroiditis and Graves' disease and less frequently in nodular goiter or thyroid carcinoma, and their titers have been used as markers to assess disease activity (23). Anti-TG-Ab recognizes the thyroglobulin molecule. It can often be detected in autoimmune thyroiditis (in 70-80% of patients with Hashimoto's thyroiditis and 30-40% of patients with Graves' disease) and in 10%-15% of patients with non-thyroid autoimmune diseases (21). These two autoantibodies can be detected at varying percentages in many patients with various non-thyroid diseases, including ITP and the healthy population (24, 25). In addition to these two antibodies, we investigated the incidence of ANA and Anti-dsDNA-Ab positivity in ITP patients. The frequency of Anti-TG-Ab positivity was 20.0%, Anti-TPO-Ab positivity was 29.4%, ANA positivity was 16.9%, and Anti-dsDNA-Ab positivity was 4.2% in all ITP patients. Interestingly, these frequencies were 24.0%, 20.0%, 15.2%, and 3.1%, even in those with no thyroid disease. Since there was no healthy control group, we could not compare the findings with the general population's conclusions. Still, our reported percentages are considerably higher than prior data from healthy populations (10, 12, 13). Anti-T-Abs positivity in

patients with ITP ranges from 11.6% to 38% (11). In one study investigating the frequency of autoimmune antibody positivity in ITP patients, 77% of the patients were reported to be positive for at least one of the following autoantibodies: ANA, red blood cell direct antiglobulin test, Anti-TPO-Ab, anticardiolipin antibodies, rheumatoid factor, and lupus anticoagulant. In the same study, the most common positive antibodies were ANA (65%), Anti-TPO-Ab (31%), and red blood cell direct antiglobulin tests (29%) were identified as the most common positive antibodies (15). In summary, it is feasible to suggest that patients with ITP have an increased likelihood of having ANA, Anti-TPO-Ab, Anti-TG-Ab, and Anti-dsDNA-Ab positivity compared with healthy individuals, even if they do not have clinical signs of other autoimmune diseases. The results of the present study support these findings. We believe that if the roles of these markers in the pathophysiology of ITP can be clarified, significant advances in the management of ITP can be achieved.

We also investigated the risk factors for hypothyroidism in patients with ITP. For this purpose, we compared the data of patients with ITP and hypothyroidism (before, simultaneously, or after ITP) with those who had ITP but not thyroid disease. Consequently, advanced age, female sex, and Anti-TPO-Ab positivity were found to be independent risk factors for hypothyroidism in patients with ITP. In this retrospective study, pediatric patients diagnosed with chronic ITP were examined. It was reported that no significant correlation was observed between the positivity of Anti-T-Abs and clinical phenotype and biochemical profile (immunoglobulin levels, bleeding diathesis, frequency of immunosuppressive therapy, hypothyroidism, and duration of chronicity) in chronic ITP patients (11). In another retrospective study, female sex and ANA positivity were found to be associated with the presence of thyroid disease in patients with ITP (5). Mousa et al. (24) reported a significant relationship between Anti-T-Ab positivity and the development of relapse and the presence of low platelet count. However, no significant results were reported concerning the effects of sex and age. In another study, none of the participants with Anti-TPO-Ab positivity were found to have clinically apparent thyroid disease at baseline or during follow-up. However, thrombosis was significantly associated with lupus anticoagulant and ANA positivity, while a lower likelihood of remission was associated with Anti-TPO-Ab positivity (15). In another study, no significant difference was found between the Anti-T-Ab levels of patients with newly diagnosed ITP, persistent ITP, and chronic ITP; however, Anti-T-Ab positivity was determined to be associated with low platelet count

at baseline and ITP relapse risk during 1-year follow-up in children with ITP (24). Many immunological factors play a role in the pathophysiology of ITP. Some autoantibodies in patients with ITP appear to affect the clinical severity, transient or permanent nature of ITP, or development of other diseases. Advanced age and female sex may also affect the course of ITP and its association with comorbid disorders like hypothyroidism. ITP and hypothyroidism may be caused by a common pathogenic mechanism, possibly through the involvement of Anti-TPO antibodies. Further investigation of this possible pathophysiological scenario could contribute to the management of both diseases. It may be beneficial to recommend that patients with ITP, especially elderly individuals and women with anti-TPO-Ab positivity, be followed up with TFTs and Anti-T-Ab measurements to prevent the development of overt hypothyroidism.

Several limitations of this study should be considered when interpreting the results. First, given the retrospective nature of the study, test results for all markers and TFT were unavailable for all patients. Thus, there was a lack of homogeneity in the testing of autoimmune markers and TFT. Alcohol use and smoking status were not assessed and may have affected the results. The timing of antibody quantification was not consistent in all patients. Because autoantibody levels may change over time, (11) future studies may benefit from performing measurements in a prospectively planned manner. The absence of a healthy control group without ITP is also a limitation that prevents reliable comparisons with healthy subjects. Lastly, to establish a cause-effect relationship between ITP and hypothyroidism, the longitudinal relationship between the diseases should be evaluated, which necessitates prospective designs or highly accurate record keeping.

CONCLUSION

Data from the current study revealed that the overall frequency of thyroid diseases and hypothyroidism and the percentages of positivity for Anti-TG-Ab, Anti-TPO-Ab, ANA, and Anti-dsDNA-Ab were higher in ITP patients than in the literature in which healthy subjects were examined. We also determined that advanced age, female sex, and Anti-TPO-Ab positivity were independently associated with hypothyroidism in ITP patients. Further studies are required to confirm our findings and identify common pathophysiological pathways and autoimmune markers of ITP and thyroid-related diseases. These relationships could contribute to the better management of ITP and related autoimmune thyroid diseases.

ETHICS

Ethics Committee Approval: The protocol for this study was approved by the Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (date: 06.12.2021, decision no: 2021-23-16).

Informed Consent: Since this study was retrospective, patient consent was not required.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: D.Y., E.G., F.A., Concept: D.Y., E.G., K.A., F.A., Design: D.Y., E.G., K.A., F.A., Data Collection or Processing: K.A., F.A., Analysis or Interpretation: E.G., F.A., Literature Search: E.G., Fa.A., F.A., Writing: E.G., Fa.A.

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