



## Research Article

# Association Between ABO Blood Group and Hashimoto Thyroiditis

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### Abstract

**Objectives:** Primary hypothyroidism in iodine-replete areas is commonly caused by chronic autoimmune thyroiditis and is typically manifested as Hashimoto thyroiditis (HT). The association between endocrinological diseases and ABO blood group (BG) has been investigated in very few studies. This study was conducted to investigate whether there is a relationship between HT and ABO BG.

**Methods:** Patients who were followed up in outpatient clinics with a diagnosis of hypothyroidism and who had elevated anti TPO antibodies, decreased T4 and TSH levels above 10 mU/ml were included in the study. Patients who were admitted to the outpatient clinic for any reason, who did not have a diagnosis of HT, and whose BG were checked were included as the control group (CG).

**Results:** 851 HT patients were included in the study. A total of 155977 individuals included as the CG. HT patients BG 0 group consisted of 317 (37.3%) individuals. HT patients with BG 0 had a higher risk of HT (OR 1.18 1.02-1.35 p=0.023).

**Conclusion:** BG 0 was detected more frequently in individuals with HT. We can emphasize that BG 0 is more frequent in diseases associated with autoimmunity and connective tissue origin.

**Keywords:** ABO blood groups, Hashimoto thyroiditis, hypothyroidism

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As the clinical manifestation of thyroid hormone deficiency, hypothyroidism is a common disorder. Unless treated, overt hypothyroidism has multiple, both short-term and long-term, consequences that may cause serious adverse effects on organs. Primary hypothyroidism in iodine-replete areas is commonly caused by chronic autoimmune thyroiditis and is typically manifested as Hashimoto thyroiditis (HT).<sup>[1]</sup> Chronic autoimmune thyroiditis development is related to many factors such as genetic and environmental factors, drugs, infiltration and/or infection, micronutrients (mainly iodine and selenium), immune system defects, and molecular mimicry between microbial and host antigen.<sup>[2]</sup> T cell-mediated inflammatory response failure, lymphocytosed thyroid infiltration, cytokine release, and fibrotic tissue development in the thyroid are among the pathophysiology

of HT development.<sup>[1]</sup> HT should be considered in patients with hypothyroid symptoms if the serum TSH level is elevated, the serum free T4 level is decreased, and the anti TPO antibody is positive. Heterogeneous parenchymal structure on thyroid ultrasonography also supports the HT diagnosis.

Different phenotypes and inherited red cell surface located glycoconjugate structures which have an important function in the pathology and physiology of cells are exhibited by human ABO blood type antigens.<sup>[3]</sup> Among the components of blood group (BG) antigens are red hemoglobin cells, leukocytes, some tissues, plasma proteins, platelets, and different cell surface enzymes.<sup>[4]</sup> The correlation between ABO blood types and a variety of infectious and non-infectious diseases was demonstrated.<sup>[5]</sup> ABO BGs are associated with various infectious diseases, lymphoma, colon, stomach, or pancreatic

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cancers, circulatory diseases, metabolic diseases, and cognitive disorders.<sup>[4]</sup> The ABO BG relationship has been investigated in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis, autoimmune neutropenia as well as HT, an autoimmune disease.<sup>[6-8]</sup> In addition, the relationship between endocrinological diseases and ABO BG has been investigated in very few studies. Within this scope, we planned this study as there is a lack of information on the relationship between HT and ABO BG.

## Methods

The present study was a retrospective review of the files of patients with hypothyroidism who were followed up in internal medicine outpatient clinics of a university hospital. The study was conducted after approval from the local ethics committee. The process of starting levothyroxine treatment was analyzed from the past files of patients who were followed up in outpatient clinics with the diagnosis of hypothyroidism. Inclusion criteria were determined as elevated anti TPO antibodies in blood tests, decreased free T3 and T4 levels and TSH level above 10 mU/ml. The diagnosis of HT was accepted if the same patients had heterogeneous parenchyma with findings compatible with thyroiditis on thyroid ultrasonography. The patients with a diagnosis of HT who continued levothyroxine treatment throughout this period were included in the study. Patients with a diagnosis of subclinical hypothyroidism but who did not develop hypothyroidism in the follow-up was excluded from the study. Patients with a diagnosis of hypothyroidism but whose BG was not studied were excluded from the study. Patients without a diagnosis of hypothyroidism or subclinical hypothyroidism were included in the study as control group (CG). Rh and ABO BG of all individuals included in the study were determined using gel centrifugation method. Prevalence values and information were recorded on the basis of A, B, AB, O BG and Rh antigens of the patients included in the study and the patients in the CG. SPSS (Statistical Package for Social Sciences) Ver.20 software was preferred for statistical analysis. Demographic and baseline characteristics of the patients were expressed with descriptive statistics. In the frequency comparison between groups, the chi-square test was used. The Odds ratio was used for the risk assessment between groups.  $P < 0.05$  was considered statistically significant.

## Results

A total of 851 patients with HT diagnosed by blood tests and ultrasonographic examination findings were included in the study. Patients who were previously admitted to the internal medicine outpatient clinic and whose BG was checked from the files of patients without an HT diagnosis were included in the study as the CG with support from hospital data pro-

cessing. The CG consisted of 155977 patients, while the total number of patients was 156828 individuals. The BG and Rh distributions of the CG and HT are shown in Table 1.

Among the patients diagnosed with HT, those with BG O were 317 (37.3%). The risk of HT was higher in patients with BG O compared with CG patients with BG O (OR 1.18 1.02-1.35  $P=0.023$ ). There is no statistical difference when other BGs of patients diagnosed with HT are compared with CG. The odds ratio and p values of other BGs in patients diagnosed with HT are shown in Table 2. Figure 1 shows that the distribution of BGs of CG included in the study was similar to the Turkey Kizilay Center data in the country in general.

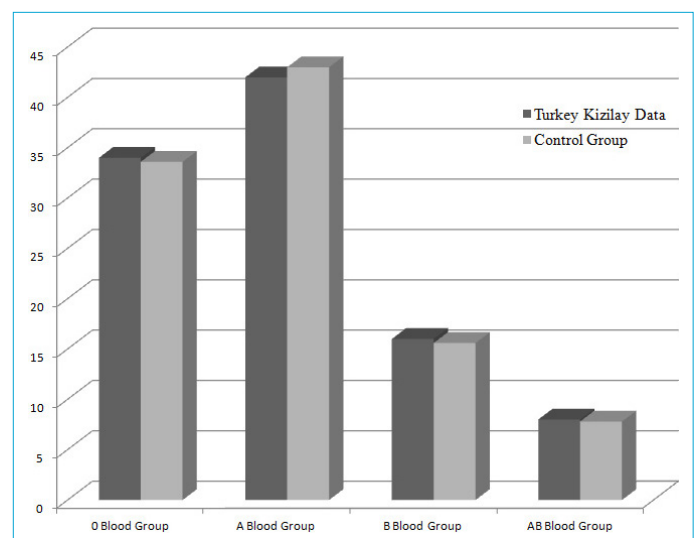
**Table 1.** ABO/Rh blood group distribution in patients with Hashimoto thyroiditis and in controls.

Blood Group	Control Group	HT Group
O	52327 (33.6)	317 (37.3)
A	67127 (43)	361 (42.4)
B	24314 (15.6)	116 (13.6)
AB	12209 (7.8)	57 (6.7)
Rh+	136306 (87.4)	750 (88.1)
Rh-	19671 (12.6)	101 (11.9)

HT: Hashimoto thyroiditis.

**Table 2.** Odds ratio of ABO/Rh blood groups in hypothyroidism

Blood Group	Odds Ratio (95% CI)	p
O	1.18 (1.02-1.35)	0.023
A	0.98 (0.85-1.12)	0.717
B	0.86 (0.70-1.04)	0.116
AB	0.85 (0.65-1.11)	0.221
Rh	1.07 (0.87-1.32)	0.515



**Figure 1.** The distribution of blood groups at Turkey Kizilay Center and control group.

## Discussion

The present study is the first study to investigate the ABO BG relationship in HT patients. In the study we found that BG 0 is more common in HT individuals. Previously, Toft et al. detected that in patients with Graves' disease, the transfer of ABO BG antigens to saliva was significantly more common compared to the CG.<sup>[9]</sup> In this study, ABO antigens were detected at normal levels in salivary secretion in HT patients. In the same study, the frequency of any ABO BG was not investigated and the number of cases was quite limited (60 individuals with Graves' disease and 21 individuals with HT).

Teumer et al. examined thyroid diseases with a TSH-based genetic risk score.<sup>[10]</sup> A significant relationship between elevated Graves' and subclinical thyroid disease risk and clinical complications with the genetic risk score. Over 70,000 individuals from 22 cohorts, detected 42 loci for circulating TSH levels within the reference range were included in the study. Compared to the individuals with a low genetic risk score, the ones with a high TSH-based genetic risk score had a 2.5-fold increased odds of hypothyroidism.<sup>[10]</sup> In this study by Teumer et al. ABO BG was not evaluated and TSH-based genetic risk score was analyzed.

Autoimmune diseases and ABO BG have been investigated in numerous studies. According to Nik et al., Lupus patients with the BG B and Rh-positive group had more coombs-positive autoimmune hemolytic anemia and arthritis.<sup>[8]</sup> No relationship between ABO BG and Rh and rheumatoid factor and anti-cyclic citrullinated peptide seropositivity was found in this study. Additionally, no difference was found in the distribution of BG in RA and SLE patients.

In another study carried out by Cildag et al., while the patients with BG A had more stypondyloarthropathy, Behçet's diseases, vasculitis, undifferentiated connective tissue disease, and RA, while the patients with BG 0 suffered more from familial Mediterranean fever, systemic sclerosis, SLE, and Sjögren's syndrome.<sup>[11]</sup> As in our study, Cildag et al. detected BG 0 more frequently in familial Mediterranean fever, SLE, systemic sclerosis, and Sjögren's syndrome. The common point of these diseases in which BG 0 is detected more frequently is that they have connective tissue disorders. The fact that the thyroid gland is a connective tissue layer is shown with the histological examination of normal thyroids.<sup>[12]</sup> Considering that HT is also a tissue disorder, the higher frequency of BG 0 in our study may be explained. The most important limitation of this study is the lack of a CG. On the other hand, there are other studies with contradictory results. In a study conducted by Collet et al., ABO BG distribution was not different from the general population in systemic sclerosis patients.<sup>[6]</sup>

In the meta-analysis by Francini et al. on ABO BG, hypercoagulability, and cardiovascular risk, individuals with BG 0 had significantly lower levels of von Willebrand factor and factor VIII.<sup>[13]</sup> Therefore, it was emphasized that cardiovascular diseases were less common in individuals with BG 0. It was also found that upper gastrointestinal bleeding is more frequent in individuals with BG 0 because they are more prone to bleeding.<sup>[14]</sup> Many studies have also been conducted between ABO BG and cancers. In the study investigating the relationship between stomach cancer and ABO, it was found that stomach cancer was found to be more common in BG A individuals as a result of a 35-year follow-up of more than 1 million donors.<sup>[15]</sup> In a study investigating the ABO association of pancreatic cancer, higher risk of pancreatic cancer was identified in individuals with non-0 BG.<sup>[16]</sup> According to Xie et al., a 14% decreased risk of developing squamous cell carcinoma and a 5% decreased risk of developing basal cell carcinoma were found in individuals with BG 0.<sup>[17]</sup> Individuals with non-0 BG have been reported to have an increased risk of developing certain cancers, especially gastric and pancreatic cancers.<sup>[18]</sup>

The most important limitation of our study is that it was single centered and conducted only in the Turkish population. The fact that the CG of our study included a large number of individuals and was similar to the Turkey Kızılay Center data reduced these limitations considerably.

In conclusion, BG 0 was found to be more frequent in individuals with HT in our study. BG 0 was found to be more frequent in SLE, systemic sclerosis and Sjögren's syndrome, which are connective tissue diseases as well as autoimmune diseases. We can emphasize that BG 0 is more frequent in diseases associated with autoimmunity and connective tissue origin.

## Disclosures

**Ethics Committee Approval:** Local Ethics Committee Approval for this study was obtained from University of Health Sciences, Kocaeli Derince Training and Research Hospital, Clinical Research Ethics Committee (Decision no: 2020/13, decision date: 23.01.2020).

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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