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ORIGINAL: Association between ABO Blood Groups and Thyroid Dysfunction

Amirhossein Khoshgoeian
Zahra Hosseini-khah
Zahra Kashi
Marzieh Movahedirad
Adele Bahar

Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran
Diabetes Research Center, Mazandaran University of Medical Sciences, Sari, Iran

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Correspondence:
Adele Bahar, Diabetes Research Center, Mazandaran University of Medical Sciences, Sari, Iran.
Email:
doctor_bahar2000@yahoo.com
ORCID: 0000-0002-3254-6230

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ABSTRACT

Introduction: Over the past few decades, numerous studies have been conducted to explore the association between blood groups and thyroid disorders. However, thus far, the findings of these studies have been contradictory. This investigation aims to examine the prevalence of different blood groups among patients with thyroid disorders.

Material and Methods: This study was conducted on 1880 patients who had thyroid disorders including hypothyroidism, hyperthyroidism, and thyroid nodules with or without thyroid dysfunction. These patients were referred to the Endocrine Clinic of Sari in 1400. We extracted and recorded demographic information, which included age, sex, weight, height, presence of thyroid nodule in ultrasound, needle aspiration, and the patient's blood type.

Results: Out of a total of 1880 individuals, 221 individuals (11.8%) were normal, 278 individuals (14.8%) were hyperthyroidism, and 1381 individuals (73.5%) were hypothyroidism. Among the patients, 26.4% of the total subjects had blood group B, 9.8% had blood group AB, 22.3% had blood group A, and 41.4% had blood group O. Furthermore, 8.6% of these individuals were Rh-negative. There was no significant association between thyroid disorders and blood group (P=0.94) as well as Rh (P=0.34). In addition, there was no significant association between thyroid nodule and blood group (P=0.40) and Rh (P=0.17), although a significant relationship was found between nodule and thyroid function (P=0.00001). Also, a significant association between malignancy and thyroid function (P=0.00001).

Conclusion: Individuals with O blood type exhibited a higher frequency of thyroid dysfunction and thyroid cancer compared to those with other blood types.

Introduction

The thyroid is one of the most vascular endocrine glands in the body. It is located in the shape of a butterfly in front of the neck in front of the trachea. This gland under the control of the hypothalamic-pituitary axis and TSH secretion makes T3 and T4 hormones, which play a role in body metabolism.

Thyroid dysfunction may affect several body functions such as growth and reproduction.

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TSH hormone is secreted from the pituitary gland and plays a role in the production of thyroid hormone through negative feedback. As the level of thyroid hormones increases, the secretion of TSH decreases through negative feedback under the control of TRH, and thus the levels of T3 and T4 remain within the normal range (1,2).

Thyroid dysfunction includes a variety of disorders that can affect hormone production as well as the thyroid gland and includes the following: genetic causes: congenital hypothyroidism, congenital hyperthyroidism, inflammatory causes: thyroiditis, autoimmune causes: Hashimoto's thyroiditis, disorder Neoplastic: benign and malignant tumors, nutritional deficiency: endemic goiter, thyroid dysfunction is divided into two main categories: hyperthyroid and hypothyroid (2-6).

Today, the biological and immunological role of blood groups and their relationship with various diseases have been discussed, and a group of diseases associated with ABO blood group phenotypes have been identified, for example, the relationship between blood group A and stomach cancer (2), group A and B blood group with periodontal diseases, O blood group with Hashimoto's hypothyroidism and A and B blood groups with hyperthyroidism (2, 7-9). Also, in Zung's study, the relationship between non-O blood groups and increased risk of myocardial infarction was shown (10).

In the study of Bahar et al., which was conducted on female patients with diabetes, blood group AB had a higher chance of developing CHD and was expressed as a risk factor for developing CHD in women with T2DM (11). Several studies have shown the association of blood groups and diabetes about the role of the immune system in diabetes. Several studies have associated O Rh negative and A Rh positive blood groups with diabetes (12) and some have associated diabetes with A blood groups, AB and Rh positive are related (13).

In 1901, Karl Landsteiner (14), a German immunologist, for the first time proved the presence of blood group antigens on red blood cells and antibodies against the same antigens in human serum. He determined that the serum of some people can agglutinate the red blood cells of other people, but it is not effective on the red blood cells of all people, and as a result, he divided people into A, B, AB, and O groups in terms of blood group. In addition to blood group antigen, human red blood cells may also have D antigen, in which case they are called Rh positive. If the red blood cells do not have this antigen, they are Rh-negative.

Previous studies have shown that the ABO blood group system is associated with a variety of cancers, primarily gastric, breast, and pancreatic, as well as cardiovascular disease, type 2 diabetes, infections, peptic ulcers, and several benign diseases. and malignant, including some rheumatological and autoimmune diseases (13,15,16|).

All these findings suggest that there may be an association between the common benign thyroid diseases, especially Hashimoto's thyroiditis, which is the most common thyroid disease and one of the autoimmune diseases, and blood types. However, no study shows the relationship between these diseases and blood groups (15).

Based on our investigations, no study has been conducted in Iran regarding the frequency of blood groups in thyroid patients. This study aimed to evaluate the frequency and correlation of ABO and Rh blood groups in patients with thyroid disorders referred to the endocrinology clinic of Sari in 1400.

Methods

Study population

This cross-sectional study was conducted in patients with a thyroid disorder (including hypothyroidism or hyperthyroidism alone, thyroid nodule alone or thyroid nodule with hypothyroidism or hyperthyroidism and thyroid cancer patients) referred to the endocrinology clinic during 1400.

The sample size was calculated according to the following formula. To calculate the sample size, using the study of Dağdeviren et al. in the years 2012 to 2017 (15) in Turkey

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on patients with benign thyroid disorders, the lowest prevalence was AB blood group at P=0.08 using the following formula and Considering the confidence level of 95% and d=0.02, the number of 707 people was calculated. To increase the power of the study, the number of samples increased to more than two times.

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}}\right)^{2P(1-p)}}{d^2} = \frac{(1 \cdot 96)^2 (0 \cdot 08)(1 - 0 \cdot 08)}{(0.02)^2} = 707$$

The sampling method was based on the purpose and after obtaining informed consent, people who had regular visits and had a complete file were included in the study until the target sample size was reached. All demographic information, including age, sex, weight, height, thyroid nodule, cytology (in case of needle aspiration of the nodule), and pathology (in case of thyroid surgery) as well as the blood type of the patient were extracted from the file and recorded.

To conduct the study, people with hypo or hyperthyroid disorder, thyroid nodules with or without thyroid disorder, as well as thyroid cancer whose disease was diagnosed and confirmed by an endocrinologist, red blood cell surface antigens using antiA and antiB specific antibodies and D specific antibody was done by slide method and ABO blood group and RH positive or negative were determined.

This study was conducted after the approval of the ethics committee of Mazandaran University of Medical Sciences (ethics code: IR. MAZUMS. REC.1400.10503). No intervention was done on the patients and no cost was imposed on the patients. All patient information is kept confidential.

Data analysis

Using SPSS software and descriptive statistics, the frequency was estimated as a percentage and 95% confidence coefficient, T-test and analysis of variance were used to compare quantitative variables, and Chi-Square was used for qualitative variables. Logistic regression and odds ratio (OR) were used to evaluate related risk factors according to disease type. By using the results, can be used as a risk factor in case of differences with the results of blood groups in the community.

Results

Out of the total of 1880 people examined, 221 people (11.8%) were normal, 278 people (14.8%) were hyperthyroid, and 1381 people (73.5%) were hypothyroid. The average age of the examined subjects was 49.44±13.381 years the average body mass index was 28.66±5.35 kg/m2 and the average duration of the disease was 9.98±7.82 years. 88.8% of patients were women. Among the patients, 651 (34.6%) had thyroid nodules with or without thyroid dysfunction. Thyroid peroxidase antibody was positive in 41.4%. In total, 26.4, 9.8, 22.3, and 41.4 percent of people had blood groups B, AB, A, and O, respectively. Of these, 8.6% were Rh-negative (***Tables 1*** and ***2***).

Table 1. Frequency of blood groups in patients

Blood group	Frequency (percentage)	Frequency (number)
A	24/9	496
B	20/4	420
AB	10/4	185
O	44/3	779
Total	100	1880

Table 2. Frequency of blood groups in patients with hypothyroidism, hyperthyroidism, and normal thyroid function.

Blood group	Normal	Hyperthyroidism	Hypothyroidism
A	55 24.9%	73 26.3%	368 26.6%
B	45 20.4%	66 23.7%	309 22.4%
AB	23 10.4%	25 9.0%	137 9.9%
O	98 44.3%	114 41.0%	567 41.1%

Relationship between blood groups and thyroid disorders

The frequency of the blood group in normal people was equal to 10.4, 20.4, 24.9 and 44.3 percent respectively for blood group AB< B < A < O. The frequency of the blood group in hypothyroid people was 9.9%, 22.4%, 26.6%

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and 41.1% for blood group AB< B< A< O respectively. The frequency of blood group in hyperthyroid people was equal to 0.9, 23.7, 26.3, and 0.41% respectively for blood group AB< B < A < O. Also, the frequency of Rh-positive in normal, hypothyroid, and hyperthyroid people was 93.2, 90.9 and 92.8%, respectively. Statistical analysis showed that there was no significant relationship between thyroid disorders (hypo and hyperthyroid) with blood group (P=0.94) and Rh (P=0.34).

Relationship between blood groups and thyroid nodule

The frequency of blood group in people with nodules was 8.3%, 22.3%, 26.6%, and 42.9% respectively for AB < B< A< O blood group. And the frequency of Rh positive in people with nodules was 92.6%. Statistical analysis showed that there was no significant relationship between thyroid nodule and blood group (P=0.40) and Rh (P=0.17).

Relationship between thyroid nodule and thyroid function

The frequency of thyroid function disorders (hypothyroid and hyperthyroid) in people with nodules was equal to 51.9 and 17.7%, respectively. Statistical analyses showed a significant difference between nodules and thyroid function (P=0.00001) (***Table 3***).

Relationship between malignancy and blood groups

In patients with thyroid malignancy, the highest frequency was related to blood group O (45.1% with Rh positive percentage of 91.9%). Due to the higher frequency of the O blood group, statistical analysis did not show any significant difference between malignancy and blood groups (P=0.308) and RH (P=0.81) (***Table 4***).

Relationship between malignancy and thyroid function

The frequency of thyroid, hypothyroid, and hyperthyroid dysfunction in people with malignancy was 34.7% and 17.3%, respectively. Statistical analysis showed a significant difference between malignancy and thyroid function (P=0.00001). As shown in ***Table 5***, in patients with malignant thyroid nodules, the thyroid test was normal (48%) and in patients with benign thyroid nodules, the most dysfunction was hypothyroidism (77/4%).

Relationship between types of malignancy and blood groups

Considering that there was no significant relationship between the blood group and malignancy (P=0.673), the frequency of blood groups in papillary thyroid cancer was similar to the normal group and patients with thyroid dysfunction (AB < B< A< O). In patients with

Table. 3. The relationship between hypothyroidism and hyperthyroidism and normal thyroid function in patients with thyroid nodules.

Nodule	Thyroid function			P- value
	Normal	Hyperthyroidism	Hypothyroidism	
Yes	30.4%	17.7%	51.9%	0.00001
No	1.9%	13.3%	84.9%	

Table 4. Relationship between blood groups and thyroid malignancy

Malignancy	Blood group				P- value
	O	B	AB	A	
Yes	45.1%	24.3%	6.4%	24.3%	308.0
No	26.4%	22.3%	9.8%	41.4%	

Table 5. Frequency of thyroid dysfunction in patients with thyroid nodule

Malignancy	Thyroid function			P- value
	Normal	Hyperthyroidism	Hypothyroidism	
Yes	48.0%	17.3%	34.7%	0.00001
No	8.1%	14.5%	77.4%	

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Table 6. Frequency of blood groups in papillary and follicular thyroid cancer

Types of cancer	Blood group				P- value
	O	B	AB	A	
papillary	45.0%	24.4%	5.6%	25%	0.673
follicular	54.5%	27.3%	9.1%	9.1%	

follicular cancer, blood groups O and B were the most frequent (54.5% and 27.3% respectively) (***Table 6***).

In patients with papillary and follicular cancer, the frequency of positive D antigen was 91.3 and 100%, respectively. And there was no significant relationship between Rh and the type of cancer (P=0.306).

Relationship between types of malignancy and thyroid dysfunction

The most laboratory finding in papillary cancer was a normal thyroid test (48.8%) and hypothyroidism was reported in follicular cancer (45.5%). The lowest laboratory disorder was in both types of hyperthyroid cancer (17.5% in papillary and 18.2% in follicular, respectively). Statistical analyses did not show a significant relationship between the types of malignancy and thyroid dysfunction (P=0.690).

Discussion

This cross-sectional study was conducted in 1880 patients with thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroid nodules (with or without thyroid dysfunction).

The findings showed that the highest frequency of blood groups was related to blood group O. This finding was similar to Prakash et al.'s study (2), with the difference that in their study, the frequency order of other blood groups was O, A, B, AB, which was different from the results of our patients. In their study, Murat et al reported a higher frequency of blood group O in patients with Hashimoto's thyroiditis (15), which was similar to the present study. However, the amount of AB blood group was less frequent in autoimmune thyroid disorders, i.e., hypothyroid and Graves, which was also in line with our study.

In this study, the highest frequency of blood group in people with nodules was blood group O, and the frequency of Rh-positive in people with nodules was higher than in people without nodules. Statistical analysis showed that there was no significant relationship between thyroid nodules and blood group and Rh. This finding was similar to Murat et al.'s study without significant association (15).

In another study conducted by Pourfathollah et al. in 2013 in connection with the evaluation of the frequency of blood groups in blood donors of the Iranian Blood Transfusion Organization, the frequency of blood group O is the highest percentage, followed by blood groups A, B, and AB in descending order. The next rank was (17), which was consistent with our study

Various studies have reported conflicting results regarding the association between ABO blood group and thyroid disorders. A study conducted in India on 220 individuals with thyroid gland disorders showed that ABO blood group antigens are associated with thyroid hormone disorders. People with blood type O were more prone to thyroid disorders, followed by "A" and "B". Hypothyroidism was found to be the most common manifestation among blood group O and hyperthyroidism among blood groups A and B, while AB did not show such an association (19). In our study, considering that there was no statistically significant relationship between thyroid function and blood groups and Rh, the result of the frequency of blood groups among patients with thyroid disorders in the aforementioned study was similar to our study. The difference is that in our study, the frequency of blood groups in hyperthyroid patients was similar to hypothyroid patients. In another study conducted in Turkey, ABO and Rh blood groups were investigated in 958 patients with benign thyroid diseases, including autoimmune-mediated thyroid diseases.

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This study showed that the proportion of blood type "O" was significantly higher in patients with hypothyroidism (Hashimoto's thyroiditis). In the non-Hashimoto hypothyroidism group, the proportion of the "AB" blood group was significantly higher (15). Another study focused specifically on the association between ABO blood type and Hashimoto's thyroiditis, showing a slightly increased risk of Hashimoto's thyroiditis in people with blood type "O". However, the odds ratio for blood groups "A", "B" and "AB" was not statistically significant (20). The results of these studies were consistent with our study in terms of the frequency of blood group O in patients with hypothyroidism.

These conflicting results may be due to differences in the study population, sample size, and genetic and environmental factors. More research is needed to better understand the relationship between the ABO blood group and thyroid disorders and to clarify existing contradictions.

The exact mechanism of association between ABO blood group and thyroid disorders, especially hyperthyroidism and hypothyroidism, is not fully understood. However, there are some possible explanations.

Thyroid disorders, such as hyperthyroidism (Graves' disease) and hypothyroidism (Hashimoto's thyroiditis), are often caused by autoimmune responses, where the immune system mistakenly attacks the thyroid gland. ABO blood group antigens have been shown to play a role in immune responses, so they may be involved in autoimmune thyroid disorders (2, 21). Also, some genetic factors may be associated with an increased risk of thyroid disorders. Studies have shown that people with blood type "O" are more prone to thyroid disorders, while blood types "A" and "B" are more associated with hyperthyroidism (2, 21). The secretion of thyroid hormones, which are responsible for regulating the body's metabolism, is controlled by thyroid-stimulating hormone (TSH), which is secreted from the pituitary gland. ABO blood group antigens may affect TSH binding and activity, leading to an imbalance in thyroid hormone levels and causing thyroid disorders (2). In addition to the mentioned cases, ABO blood group antigens are also involved in inflammation and tissue damage processes. Differences in ABO blood group antigens may influence the inflammatory response in the thyroid gland and contribute to the development of thyroid disorders (2).

Several studies have been conducted on the association between ABO blood group and thyroid cancer. In a study that investigated the distribution of ABO blood groups and Rh factor in benign and malignant thyroid nodules, it showed that there was no significant difference in the distribution of ABO blood groups and Rh factor between benign and malignant thyroid nodules. 22). Another study of 2996 patients found that the ABO blood group was not associated with malignant thyroid disease compared to benign thyroid disease (21). Also, Tam et al.'s study showed that there was no significant difference between ABO blood groups and Rh factor in patients with benign and malignant thyroid disease. However, patients with malignant disease were more Rh-positive compared to patients with benign disease (23). In another study, the distribution of the ABO/Rh blood group in patients with papillary thyroid carcinoma (PTC) was evaluated, and the results showed that the distribution of blood groups in PTC patients is not significantly different from the general population (21). In general, the results of these studies were in line with our study. Overall, the results of these studies suggest that there may be an association between ABO blood group and thyroid cancer, but the evidence is not conclusive. More research is needed to better understand the relationship between ABO blood group and thyroid cancer.

In our study, no significant relationship between thyroid dysfunction and malignancy was observed. Given that there is no direct causal relationship between thyroid cancers and thyroid disorders, some studies have shown that people with a history of thyroid

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disorders may be at a slightly increased risk of developing thyroid cancer. For example, one study found that people with a history of hyperthyroidism or hypothyroidism had a slightly higher risk of developing thyroid cancer than people without a history of thyroid disorders (24). This study was in line with our study in terms of the relationship between performance and malignancy. A systematic review and meta-analysis reported that thyroid dysfunction is associated with an increased risk of thyroid, breast, and prostate cancers. Hyperthyroidism was associated with a higher risk of thyroid, breast, and prostate cancers, whereas hypothyroidism was associated with a higher risk of thyroid cancer only in the first 10 years of follow-up (25).

Conclusion

However, thyroid cancer and thyroid disorders are two distinct diseases that affect the thyroid gland, while there is no direct relationship between them. The overall risk of thyroid cancer in patients with thyroid dysfunction is still relatively low, and most people with thyroid disorders do not develop thyroid cancer. Studies with a larger sample size are needed to investigate the relationship between dysfunction and thyroid cancer.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Authors' contributions

All authors contributed to the study conception and design. All authors conceived, designed, supervised the research and acquiredthe project funds. Material preparation, datacollection and analysis were performed by Amirhossein Khoshgoeian.all authors read and approved the final manuscript.

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