

# Correlation of anti-thyroperoxidase (Anti-TPO) with Anxiety and Depression in Patients with Autoimmune Thyroid Diseases in Kosovo

**Type:** Review Article

**Received:** August 09, 2024

**Published:** September 03, 2024

**Citation:**

Valon Morina., et al. "Correlation of anti-thyroperoxidase (Anti-TPO) with Anxiety and Depression in Patients with Autoimmune Thyroid Diseases in Kosovo". PriMera Scientific Medicine and Public Health 5.3 (2024): 36-42.

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## Abstract

Thyroid hormones are regulators of various physiological processes within the human body, which become particularly evident in case of imbalance. Autoimmune thyroid disease affects about 10% of the population worldwide with an increased incidence in women (Hayter, 2012). The aim is to analyze the reference values of thyroid anti-peroxidase (anti-TPO) and evaluate the relationship between mood disorders such as anxiety, depression and autoimmune thyroid diseases. The correlation of autoimmune thyroid disease with anxiety disorders is significant because it is also the most prevalent mental health problem in women (Rector, 2006), followed by depression. The research was carried out in digestive health institutions in the municipality of Prishtina, namely in the American-Kosovar AmeriKos polyclinic and the Vital Group clinic in Prishtina with a total sample of N-80 female respondents, of which 40 patients with a positive result of Anti-TPO and 40 with a negative Anti-TPO result. The research was carried out based on the qualitative method and the instruments that were used consisted of questionnaires related to anxiety and depression that were determined using the HADS assessment (Zigmond, 1983). The research results show that anxiety and depression have a significant negative strong correlation with people with autoimmune thyroid disease: (alpha = 0.05, P= .002), A -0.4398 and D -0.4608. Based on this research, we can conclude that individuals in the community with autoimmune thyroid disease with positive Anti-TPO may be at high risk for mood disorders, depression and anxiety, the basic factors in normal functioning in life.

**Keywords:** Hypothyroidism; Autoimmune disease; Anti-peroxidase; anxiety disorders; Autoimmune thyroiditis; Depression; Gills; Hashimoto's thyroiditis

## Introduction

This study was undertaken to analyze reference values of thyroid anti-peroxidase (Anti-TPO) and to investigate the relationship between Anti-TPO and mood disorders such as anxiety and depression. Autoimmune thyroid disease may be associated with depression (Fountoulakis KN, 2004) and anxiety (Carta MG, 2002). The reason that prompts the study of this correlation is that autoimmune thyroid disease is more common in women (Hayter, 2012) and anxiety disorders are also the most prevalent mental health problem in women (Rector, 2006). If the antibodies attack the gland and interfere with its normal hormone production process, we are dealing with autoimmune thyroid disease.

The aim of the research is to analyze the reference values of anti-thyroid peroxidase (Anti-TPO) and to evaluate the relationship between mood disorders such as anxiety, depression and autoimmune thyroid diseases, correlations of Anti-TPO values with anxiety, depression in patients with autoimmune thyroid disease and in patients without autoimmune thyroid disease in a community survey. This paper presents the results of the psychiatric and endocrinological cross-assessment.

The immune system protects the body from disease and infection by attacking microbes that enter the body, such as viruses and bacteria. Autoimmune disease is a condition in which the immune system mistakenly attacks healthy cells in organs and tissues. It is not certain what causes autoimmune diseases but in most cases we have a combination of factors such as: genes, which can make you more prone to developing the disease, some are more common in certain ethnic groups, hereditary, from diet such as excess fats (Watson, 2019). Autoimmune diseases refer to problems with acquired immune system responses. Autoimmune diseases can affect almost any part of the body, including: the heart, brain, nerves, muscles, skin, eyes, joints, lungs, kidneys, glands, digestive system, blood vessels. There is no specific test to tell if a patient has a certain autoimmune disease, the symptoms can be confusing, because many autoimmune diseases have similar symptoms.

Autoimmune thyroid disease is by far the most common cause of hypothyroidism and is characterized by the presence of antithyroid antibodies (Kausel, 2021). Some thyroid conditions occur because antibodies attack the gland and interfere with its normal hormone production process. This condition is called autoimmune thyroid disease. Autoimmune thyroid disease affects approximately 10% of the population worldwide with an increased incidence in females (Hayter, 2012). Thyroid disorders include hyperthyroidism, hypothyroidism, thyroid inflammation (thyroiditis), thyroid enlargement (goiter), thyroid nodules, and thyroid cancer (Cleveland Clinic, 2020).

Antibodies are proteins that the immune system produces to help the system fight infections. Anti-TPO are antibodies that attack the enzyme thyroid peroxidase (TPO), an enzyme in the thyroid gland that helps produce two important thyroid hormones: T3 and T4. Antibodies are associated with Hashimoto's disease and are a sign that the immune system is mistakenly attacking the thyroid gland. These antibodies interfere with TPO function and can lead to hypothyroidism (Shomon, 2021). Hypothyroidism is when the thyroid gland does not produce enough thyroid hormones, it is also called an underactive thyroid (Cleveland Clinic, 2020). This slows down many of the body's functions, such as metabolism. Hypothyroidism can also be caused by: treatment of hyperthyroidism (radioiodine), radiation treatment of some types of cancer, removal of the thyroid. Anti-thyroid peroxidase autoantibodies (Anti-TPO) are considered the most sensitive and specific marker of thyroid autoimmunity (Mariotti S, 1990).

Hashimoto's thyroiditis is the most common autoimmune thyroid disease which is caused by autoimmune inflammation of the thyroid gland and has different clinical stages ranging from euthyroidism to hypothyroidism. It is characterized by high levels of anti-thyroglobulin (Anti-Tg) and antithyroid peroxidase (Anti-TPO) antibodies and the typical hypoechoic pattern of the thyroid gland on ultrasonography (Pearce EN, 2003). The clinical course is variable and spontaneous remission may occur in adolescence (R Loring, 2003). Goiter, menstrual disturbances, short stature, constipation, irritability, and exophthalmos have been reported as the most frequent clinical features of Hashimoto's thyroiditis. In people with Hashimoto's disease, the immune system mistakenly attacks the thyroid (Hopkins Medicine), and this attack damages the thyroid so that it does not produce enough hormones. Hashimoto thyroiditis is often associated with type 1 diabetes and other autoimmune disorders such as celiac disease, type 2 and type 3 polyglandular au-

to immune disorders.

Studies report that patients with autoimmune diseases present a higher risk of developing anxiety and depression (Giynas, 2014). Occasional anxiety is a normal part of life (National Institute of Health, 2023). It is common for people to feel anxious but anxiety disorders involve more than temporary worry or fear, often worsening over time to the point where the feelings interfere with their daily functions. There are several types of anxiety disorders, including generalized anxiety disorder, panic disorder, social anxiety disorder, and various phobia-related disorders, with each type of anxiety disorder having different risk factors (National Institute of Health, 2023).

Some general risk factors include:

- Shyness or feeling uneasy or nervous in new situations in childhood.
- Exposure to stressful and negative events in life or the environment.
- A history of anxiety or other mental disorders in biological relatives.

Anxiety symptoms can be produced or worsened by:

- Certain physical health conditions such as thyroid problems or heart arrhythmia.
- Caffeine or other substances/drugs.

The Hospital Anxiety and Depression Scale (HADS), this self-report scale was developed and found to be a reliable instrument for detecting depressive and anxiety states in an outpatient, medical, inpatient clinic setting. Sometimes the emotional disorder is the result of stress caused by physical disability, but the somatic symptoms that lead to referral to medical and surgical departments may be a manifestation of anxiety or depressive states and have no basis in organic pathology. The HADS was originally developed as a psychometric instrument for identifying depression and generalized anxiety in medical patients in psychiatric treatment, but there was a need to develop a self-rating mood scale specifically designed for use in non-psychiatric hospital wards. The HADS consists of two subscales: the anxiety subscale (HADS-A) and the depression subscale (HADS-D). It is one of the National Institute for Health and Care Excellence (NICE) recommended tools for diagnosing depression and anxiety (B Mykletun, Environ Med 2003).

### **Research question**

1. Which of the mood disorders between depression and anxiety is more pronounced in patients with autoimmune thyroid disease?
2. Do we have significant mood changes in undiagnosed patients with autoimmune thyroid disease?

### **Hypotheses**

H1: Depression preceded by anxiety has a negative expression of presence in patients with autoimmune thyroid diseases.

H2: Anxiety and depression do not correlate with undiagnosed patients with autoimmune thyroid disease.

### **Methodology**

This research was carried out based on the qualitative method, composed through a questionnaire related to anxiety and depression that were determined using the HADS assessment (Zigmond, 1983), where for each variable the necessary analyzes were made to identify the correlation of anti-thyroid peroxidase (Anti-TPO) with anxiety and depression in patients with autoimmune thyroid disease compared with undiagnosed patients with autoimmune thyroid disease.

Participants in this study were a total of N-80 female respondents, N-40 of them patients with autoimmune thyroid diseases residing in different cities of Kosovo and N-40 undiagnosed patients with thyroid disease during the month of January 2022 and June 2022.

The instruments used in this research have been: The HADS questionnaire (Zigmond, 1983) was developed as a psychometric instrument that appears to be reliable for the screening of anxiety and depression with 14 clinically relevant questions in patients attending a medical clinic. It consists of two subscales: the HADS-Anxiety Subscale (HADS-A) and the HADS-Depression Subscale (HADS-D). The advantages of the HADS score are: easy to interpret, provides clear results to indicate the severity of the disorder and is ideal for use as a screening measure. The research was carried out in such a way that the patients answered the questions based on how they felt last week, calculating it from the day of completing the questionnaire.

**Results**

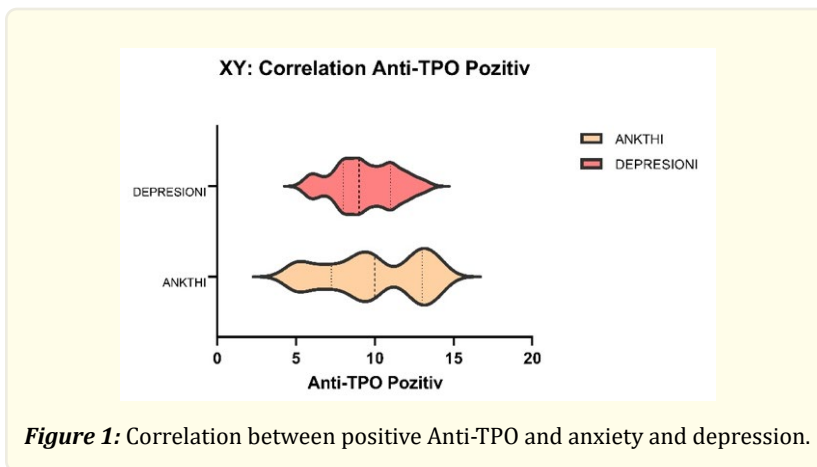
The analyzes that were used to present the results are: correlation and regression analysis through the Spearman test. In the questionnaire addressed to patients on the research of emotion companions, 3 out of 80 individuals (age >18, female gender) who were asked to complete the questionnaire refused to answer.

	<i>Anti-TPO Positiv vs. Anxiety</i>	<i>Anti-TPO Positiv vs. DEPRESSED</i>
<b>Spearman r</b>		
<b>R</b>	-0.4398	-0.4608
95% confidence interval	-0.6661 to -0.1393	-0.6805 to -0.1651
<b>P value</b>		
P (two-tailed)	.005	.003
P value summary	**	**
Exact or approximate P value?	Approximate	Approximate
Significant? (alpha = 0.05)	Yes	Yes
Number of XY Pairs	40	40

\*\*= .002.

**Table 1:** Correlation between positive Anti-TPO with anxiety and depression.

Table 1 shows that Anti-TPO positive with anxiety at 95% confidence interval ranges from -0.6661 to -0.1393, there is weak monotonic negative correlation between the two variables and there is significant relationship P=.005, r =-0.4398 (α= 0.05, significance p< .002). Anti-TPO positive with depression in the 95% confidence interval ranges from -06805 to -01651, there is a weak monotonic negative correlation between the two variables and there is a significant relationship P=.003, r =-0.4608, (α= 0.05, p < .002).



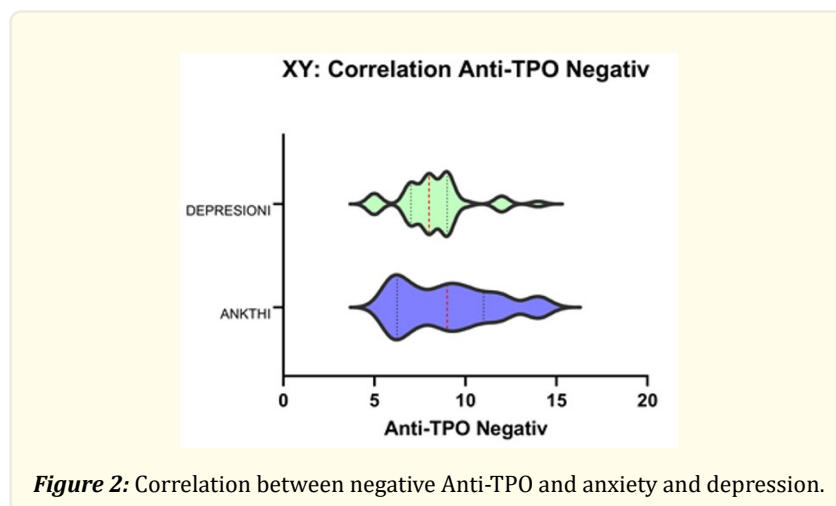
**Figure 1:** Correlation between positive Anti-TPO and anxiety and depression.

	<i>Anti-TPO Negative</i> vs. <i>Anxiety</i>	<i>Anti-TPO Negative</i> vs. <i>DEPRESSED</i>
<b>Spearman r</b>		
<b>r</b>	-0.1201	-0.06304
95% confidence interval	-0.4239 to 0.2080	-0.3755 to 0.2623
<b>P value</b>		
P (two-tailed)	.461	.699
P value summary	ns	ns
Exact or approximate P value?	Approximate	Approximate
Significant? (alpha = 0.05)	No	No
Number of XY Pairs	40	40

**Table 2:** Correlation between negative Anti-TPO with anxiety and depression.

Table 2 shows that the negative Anti-TPO with anxiety in the 95% confidence interval ranges from -0.4239 to 0.2080, there is a weak monotonic negative relationship between the two variables and there is no significant relationship  $r = -0.1201$ , ( $\alpha = 0.05$ ,  $p < 12$ ).

Anti-TPO negative with depression at 95% confidence interval ranged from -0.3755 to 0.2623, there is a weak monotonic negative relationship between the two variables and no significant correlation  $r = -0.06304$ , ( $\alpha = 0.05$ ,  $p < 12$ ).



**Figure 2:** Correlation between negative Anti-TPO and anxiety and depression.

## Discussion

The purpose and hypotheses of this research are mainly focused on the thyroid factor in the identification of the presentation of mood change anxiety, (Carta MG, 2002). and depression as an influence on life functioning, mainly to analyze the reference values of thyroid anti-peroxidase (anti-TPO) and to evaluate the relationship between mood disorders. (Fountoulakis KN, 2004). The present study shows an association between the presence of mood disorder and anti-TPO in a general population sample that was not selected from medical or psychiatric health institutions. The first hypothesis where depression preceded by anxiety has a negative expression of presence in patients with autoimmune thyroid diseases in the analysis of the correlation between mood changes such as depression and anxiety in patients with autoimmune diseases has a strong and significant negative correlation that shows a relationship of strong among them, which contradicts the hypothesis presented before the data analysis. Depression is more pronounced than anxiety in

patients with autoimmune thyroid disease. The results support the research findings (Benros et al., 2011, Benros et al., 2013). In the second hypothesis, anxiety and depression do not correlate with undiagnosed patients with autoimmune thyroid disease, it has been proven on the basis of correlation analysis that anxiety and depression have a weak negative correlation with undiagnosed patients with autoimmune thyroid disease and have no significant correlation, which shows us that we have no significant difference mood in undiagnosed patients with autoimmune thyroid disease. The results support the research findings (Onofriichuh et al, 2020).

It is important to carry out other research that explains the mood changes without therapy and those in therapy of patients with autoimmune diseases to identify the patient's condition to see the differences that may exist compared to similar research in other countries. developed. At the end of this research, we see that it is necessary for every health institution to measure mood changes during the treatment of people with autoimmune thyroid disease. If these findings are confirmed, they would constitute a more important public health issue, due to the high risk attributed to it. It should be noted that the potential of the study is diminished by the small sample size, therefore, the generalizability of the findings is quite limited.

### **Conclusion and Recommendations**

In conclusion, the results found in this study show a high prevalence of anxiety and depression in patients with autoimmune thyroid disease, anti-TPO positive. The study suggests that individuals in the community with autoimmune thyroid disease with positive Anti-TPO may be at high risk for mood disorders, which may lead to high social risk. Psychiatric disorders and autoimmune reaction seem to be in cooperation and in the same abnormality in the immuno-endocrine system. Based on previous research the HADS scale was an efficient screening instrument and a number of points are given so that the proportion of false positives or false negatives is minimized. For routine clinical use, the scale may be a useful tool for assessing change in a patient's emotional state, as well as for assessing the presence or absence of clinically relevant levels of anxiety and depression. It is recommended that within each health level that provides health services, an adequate space is promised in a group of several health-educational or counseling professionals, so that this group of professionals has the responsibility in the correct and direct orientation of the patient for receiving the various requests that have to health services. This is also the best way to maintain the level of quality of health care and reliability in the provision of health services. Such persons who have a lack of information about the proper access to health services need real health education about the proper referral for their treatment. The most frequent participation in trainings that are organized around health education, promotional and informative activities of health and illness, debates with professionals and experts in this field, media programs with awareness and clear messages about health, appropriate access to institutions of different levels health, a systematic screening for mood disorders in anti-TPO+ subjects and a systematic evaluation for thyroid disease and thyroid autoimmunity in subjects with mood disorders are advised.

### **Acknowledgement**

We would like to acknowledge the contribution of proofreading the article of Prof. Ass. Dr. Florim Gallopeni from the Heimerer College, for the critical review of this manuscript.

### **Statement of Interests**

The authors declare no conflict of interest

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