Annals of Biomedical and Clinical Research

Original article

ABCR Vol 4; No 2; 2025;64-71

Depression, Anxiety, and Stress in Patients with Hyperthyroid Goiter or Euthyroid Benign Nodular Goiter

Filip Knezović[1], Anamarija Mikulić[2], Jozo Ivanković[2], Ivona Čarapina-Zovko[3], Boris Jelavić[1,2]

[1] School of Medicine, University of Mostar; Mostar, Bosnia and Herzegovina, [2] Department of Otorhinolaryngology, University Hospital Mostar, Mostar, Bosnia and Herzegovina, [3] Department of Psychology, Faculty of Humanities and Social Sciences, University of Mostar, Mostar, Bosnia and Herzegovina

ABSTRACT

Background: A higher incidence of depression, anxiety, and stress was found in patients with hyperthyroidism compared with the general population and patients with nontoxic nodular goiter. It is not clear whether the mental symptoms are related to increased levels of thyroid hormones or thyroid autoimmunity.

Methods: In a cross-sectional study, surgical candidates with hyperthyroidism or euthyroid benign nodular goiter completed a general questionnaire on sociodemographic data, comorbidities, and laboratory findings related to the thyroid disease and the Depression, Anxiety and Stress Scale questionnaire (DASS).

Main findings: Out of all the examined patients (n = 40), 85%, 65%, and 85% of them had depression, anxiety, and stress scores within the normal range. The euthyroid patients had significantly higher scores on the depression (p = 0.013) and stress (p = 0.005) subscales in comparison with the hyperthyroid patients. Compared with males, females had significantly higher scores on the depression (p = 0.046) and anxiety (p = 0.005) subscales. There was no significant relationship between the level of formal education and DASS subscale scores.

Principal conclusion: A small share of the surgical candidates examined for strumectomy had elevated levels of depression or stress. Compared with the hyperthyroid patients, the euthyroid patients showed higher levels of depression and stress. Females had higher levels of depression and anxiety in comparison with males. The levels of examined negative emotional states were not related to the formal education levels of patients.

Key words: hyperthyroidism, euthyroidism, nodular goiter, depression, anxiety, stress

Article processing history:
Received January 8, 2025
Revised April 10, 2025
Accepted August 25, 2025

ORCID IDs of the authors:
F.K. 0009-0001-0022-3744
A.M. 0009-0005-9471-6281
J.I. 0009-0005-0117-260X
I.Č.Z. 0000-0001-6978-5844
B.J. 0000-0002-1952-4192

Corresponding author:
Boris Jelavić
Department of Otorhinolaryngology and Maxillofacial Surgery, SKB Mostar, Bosnia and Herzegovina
E-mail address: slav.boris@tel.net.ba

Cite this article as: Knezović F, Mikulić A, Ivanković J, Čarapina-Zovko I, Jelavić B. Depression, Anxiety, and Stress in Patients with Hyperthyroid Goiter or Euthyroid Benign Nodular Goiter. Annals of Biomedical and Clinical Research. 2025;4:64-71.

https://doi.org/10.47960/2744-2470.2025.2.4.64

INTRODUCTION

Depression and anxiety are often found in patients with chronic diseases, including those with thyroid dysfunction (1). Compared with the general population and patients with other chronic thyroid diseases, an increased prevalence of depression and anxiety has been identified in hyperthyroidism (1–6). It is not clear to what extent depression and anxiety are related to chronic disease per se, or uniquely to hyperthyroidism. In some patients with hyperthyroidism, symptoms of depression and anxiety resolved after thyroid-suppressive treatment, indicating that elevated thyroid hormone levels contribute to depression and anxiety (6, 7). With regard to the monoamine hypothesis, it is important to mention that triiodothyronine (T3) controls the levels and actions of serotonin (8) and noradrenaline (9). Decreased serotonin and noradrenaline concentrations are associated with depression and anxiety, and decreased T3 concentrations can also cause depressive and anxiety disorders (2). A meta-analysis by Aronson et al. showed that the addition of T3 to therapy with tricyclic antidepressants was successful in 25% of cases with refractory depression (10). The action of T3 resulted in increased levels of serotonin and noradrenaline.

During depression, a decrease in serotonin concentration in the brain stimulates the release of thyrotropin-releasing hormone (TRH) from the hypothalamus. TRH is thought to be inhibited by serotonin, resulting in the release of thyroid-stimulating hormone (TSH) from the pituitary gland and the consequent synthesis of thyroxine (T4) and T3 in the thyroid gland. It is known that in depressed patients without thyroid disease, free thyroxine (FT4) concentrations reach the upper limits and decrease to normal values when depressive symptoms improve (8). However, in some patients, mental symptoms persist despite thyroid-suppressive medication, indicating that depression and anxiety may be related to other aspects of hyperthyroidism, such as thyroid autoimmunity (7, 11). Up to one third of such patients cannot return to full-time work, which indicates the need to consider psychological help in patients with hyperthyroidism (11).

The aim of this study was to determine and compare the levels of depression, anxiety, and stress in patients with hyperthyroidism and those with euthyroid nodular benign goiter.

PARTICIPANTS AND METHODS

Participants

The ethics committee of the University Clinical Hospital in Mostar gave consent for the research (Reg. No. 1280/23, March 3, 2023). The participants were surgical candidates for strumectomy who were admitted to the Department of Otorhinolaryngology of the University Clinical Hospital in Mostar from July 1, 2023 to May 31, 2024. The hyperthyroidism group comprised patients with hyperthyroidism, including diffuse toxic goiter (Graves' disease) or toxic multinodular goiter (Plummer's disease) or toxic adenoma, refractory to medical treatment. The euthyroid group included patients with euthyroid benign nodular goiter requiring surgical treatment. The additional inclusion criteria were the participant's informed consent and properly completed questionnaires. The exclusion criteria were Hashimoto's disease, subclinical hyperthyroidism, hypothyroidism, malignant disease of the thyroid or other organs, Graves' ophthalmopathy, inflammation of the thyroid gland, previously established mental illness, the absence of patient consent to participate in research, and incompletely filled questionnaires.

Methods

The general questionnaire on socio-demographic data, comorbid diseases, and laboratory findings related to thyroid diseases was created by the last author. The section on laboratory findings was completed by a doctor.

The Depression, Anxiety and Stress Scale (DASS)

The DASS is a 42-item scale designed for measuring three related negative emotional states of depression, anxiety, and tension/stress (12). DASS-Depression (14 items) focuses on reports of low mood, motivation, and self-esteem, while DASS-Anxiety (14 items) concentrates on physiological arousal, perceived panic, and fear, and DASS-Stress (14 items) relates to tension and irritability. For each of the 42 items, the respondent chooses one of the four offered answers that can be applied to her/him during the past week (from 0 = does not apply to me at all to 3 = can apply to me often or most of the time). For each subscale, the possible range of points is from 0 to 42. Higher scores on each subscale indicate an increasing severity of depression, anxiety, or stress (12). In this study, the adapted Croatian version of the questionnaire was used. Its internal consistency, calculated as Cronbach's α, was quite high: 0.87 for depression, 0.91 for anxiety, and 0.82 for the stress subscale (13). The DASS scale represents a reliable and valid measure for the assessment of unpleasant emotional states in clinical and non-clinical samples.

Study design

The collected data were used as follows:

1. The levels of depression, anxiety, and stress in the whole study group were determined.
2. The hyperthyroidism and euthyroid groups were compared according to the DASS scores on the depression, anxiety, and stress subscales.
3. The relationships between the level of education (measured as years of formal education received) and the DASS scores were examined.

Statistical analysis

The normality of the distribution was tested with the Kolmogorov-Smirnov test. With respect to the distribution and number of compared samples, comparisons of the DASS scores were conducted using the Student's t-test. Correlations between the DASS scores and the years of formal education were examined with the Pearson's correlation coefficient. P-values <0.05 were regarded as being statistically significant. All statistical analyses were performed utilizing SPSS for Windows (Version 13.0; SPSS Inc., Chicago, IL, USA).

RESULTS

During the study period, 72 patients underwent thyroid surgery. Among these, 32 did not meet the inclusion or exclusion criteria. Therefore, 40 patients were included in the statistical analysis. Their mean age was 55 years (54.60 ± 10.65; $\bar{X}$ ± SD). In the whole study group, the patients' ages ranged from 38 to 84 years. The majority of the patients were in the fifth, sixth, and seventh decades of age. There were six (15%) men and 34 (85%) women, with 10 patients in the hyperthyroidism group and 30 patients in the euthyroidism one. The sociodemographic characteristics of both groups are shown in Table 1. In the hyperthyroid group, 40% of patients reported no negative impact of their thyroid disease on the quality of their everyday life during the last four weeks, while the share of such patients in the euthyroid group was 33% (Table 1).

The levels of examined negative states are presented in Table 2. In the whole examined group, the majority of patients had scores within normal ranges. The shares of the patients within the normal range on the depression, anxiety, and stress subscales were 85%, 65%, and 85%, respectively. It is worth noting that all hyperthyroid patients had scores within normal ranges on the depression and stress subscales.

Table 1. Sociodemographic characteristics of surgical candidates with hyperthyroidism or euthyroid benign nodular goiter

Characteristic	Hyperthyroidism group	Euthyroidism group
Age ($\bar{X}$ ± SD)	59.60 ± 17.03	52.93 ± 7.14
Age range (min–max)	38–84	42–66
Male /female	2/8	4/26
Level of formal education: Primary/secondary/higher/high	0/6/4/0	4/18/2/6
Living: Alone/with partner, family	6/4	0/30
Negative impact (subjective) of my thyroid disease on the quality of my daily life during the last 4 weeks: Not at all/a little/somewhat, moderately/fairly/very much	4/2/0/2/2	10/12/6/2/0

Table 2. The levels of depression, anxiety, and stress in patients who underwent strumectomy

	Whole study group	Hyperthyroidism group	Euthyroidism group
The score classification *			
Depression: Normal range/mild/moderate/severe/ extremely severe	34/4/0/2/0	10/0/0/0/0/0	24/4/0/2/0/0
Anxiety: Normal range/mild/moderate/severe/ extremely severe	26/2/12/0/0	8/0/2/0/0/0	18/2/10/0/0/0
Stress: Normal range/mild/moderate/severe/ extremely severe	34/2/2/2/0	10/0/0/0/0/0	24/2/2/2/0/0

*Measured with the Depression, Anxiety and Stress Scale

Table 3. Comparison of the hyperthyroidism group and the euthyroidism group according to the scores of the Depression, Anxiety and Stress Scale

	Subgroup	n	$\bar{X}$	SD	*t* *	*p*
DASS Depression †	Hyperthyroid	10	1.80	2.04	1.54	0.013
	Euthyroid	30	4.87	6.25		
DASS Anxiety †	Hyperthyroid	10	6.00	2.75	0.35	0.726
	Euthyroid	30	6.60	5.17		
DASS Stress †	Hyperthyroid	10	5.40	1.71	1.68	0.005
	Euthyroid	30	9.33	7.28		

* Student's t-test
† Measured with the Depression, Anxiety and Stress Scale (theoretical possible range of scores was from 0 to 42)

The comparisons of the two examined groups in terms of DASS scores are shown in Table 3. The euthyroid patients had statistically significant higher scores on the depression and stress subscales in comparison with the hyperthyroid patients. Compared to males, females had statistically significant higher scores on the depression (t = 1.88, p = 0.046) and anxiety (t = 2.99, p = 0.005) subscales.

There were no significant correlations between the level of education (measured as years of formal education received) and the depression (r = -0.047; p = 0.772), anxiety (r = 0.039; p = 0.11), and stress (r = -0.205; p = 0.204) subscale scores.

DISCUSSION

This research was motivated by studies indicating that a large share of patients with thyroid disease, particularly those with hyperthyroidism, suffer from higher levels of negative emotional states, primarily depression and anxiety (1–11). However, the

results of the current study demonstrated that the majority of the examined patients did not show the expected high prevalence and severity of disability related to depression and stress. Surprisingly, significantly higher levels of depression and stress were found in the euthyroid patients in comparison to the hyperthyroid ones. As many as 40% of the hyperthyroid patients reported no negative impact of thyroid disease on the quality of their daily life during the last four weeks. All hyperthyroid patients had scores within a normal range on the depression and stress subscale, while 80% of them had scores within a normal range on the anxiety subscale.

Although the results of research on the association between subclinical hypothyroidism and depressive symptoms are contradictory, it was demonstrated that mood changes and depressive symptoms are a common reason why general practitioners in England prescribe levothyroxine to patients with subclinical hypothyroidism (14). For this reason, Wildisen et al. (15) conducted a systematic review of the literature on the association between subclinical thyroid dysfunction and depressive symptoms. They found no significant difference in the occurrence of depressive symptoms between euthyroid subjects, on the one hand, and patients with subclinical hypothyroidism or subclinical hyperthyroidism on the other.

Bode et al. (16) conducted a systematic review and meta-analysis of 15 studies on the association of subclinical or manifest hyperthyroidism with clinical depression. They noted that, in comparison with euthyroid subjects, patients with hyperthyroidism as a whole have a higher chance of receiving a diagnosis of clinical depression. Furthermore, the association with depression was significantly lower in patients with subclinical hyperthyroidism compared to those with manifest hyperparathyroidism. This gradient in the magnitude of the association between the two degrees of hyperthyroidism, as well as the absence of a relation in subclinical hyperthyroidism in Wildisen's work (15), suggests that it is not autoimmunity that primarily drives the connection, but rather an increase in thyroid hormone levels. This suggests a possible biological link between hyperthyroidism and depression. Differences in the association between women and men have not been established (16).

In a cross-sectional study conducted in Denmark, Bové et al. (4) evaluated the prevalence of depression and anxiety in patients with Graves' disease and those with nodular goiter. The Hospital Anxiety and Depression Scale (HADS) questionnaire was used. Depression and anxiety symptoms were more severe in patients with Graves' disease in comparison to those with nodular goiter. More severe symptoms of depression and anxiety were associated with the presence of comorbidities, while the severity of anxiety symptoms increased with the longer duration of Graves' disease. No significant relationship between the levels of free T4 and anti-thyroid antibodies (TPOAb, TRAb) and the severity of depression and anxiety symptoms in patients with Graves' disease was found, indicating that thyroid function and autoimmune background were not related to the development of depression and anxiety (4).

Demet et al. (5) explored symptoms of depression and anxiety in patients with untreated hyperthyroidism. In comparison with the euthyroid subjects, the scores of the Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were significantly higher in the hyperthyroidism group, but there was no difference in Hospital Anxiety and Depression Scale scores. A study conducted in India (7) reported that patients with hyperthyroidism suffered from moderate or severe anxiety and depression in 40.5% and 50.6% of cases, respectively. Treatment of hyperthyroidism resulted in the improvement of depression and anxiety symptoms, but a significant share of

patients still had psychiatric symptoms after achieving euthyroidism.

Marian et al. (17) presented hyperthyroidism as a cause of depression and psychosis. They stated that thyroid diseases should be considered in the differential diagnosis in patients with depression and psychosis. Early initiation of endocrinological treatment can significantly improve mental symptoms. In some cases, in addition to thyroid disease treatment, psychiatric treatment is also necessary. More radical options such as thyroidectomy may also be considered (17).

In a study conducted in India, Shoib et al. (18) compared the incidence of depression and anxiety between hyperthyroid and euthyroid patients. On the basis of the Mini-International Neuropsychiatric Interview (MINI), HAM-D, and HAM-A, a higher incidence of depression, agoraphobia, anxiety, and suicidal thoughts, as well as panic attacks, was revealed in hyperthyroid patients. Mental symptoms improved in many cases after endocrinological treatment. It is believed that timely treatment can significantly improve the quality of life of these patients (18). Fukao et al. (2) stated that "psychosomatic approaches including antipsychotic drugs and psychotherapies based on the bio-psycho-social medical model are thought to be useful" in Graves' disease patients with mental symptoms as well as hyperthyroidism.

Using the Four-Dimensional Symptom Questionnaire, a case control study by Stanić et al. (1) explored the incidence of psychosomatic symptoms in patients with thyroid diseases. In comparison with healthy subjects, a significantly higher incidence of distress, depression, and anxiety in patients with thyroid diseases was identified. Furthermore, thyroid patients exhibited significantly more severe somatization symptoms, which augmented the worsening of their health. Within the group of patients with thyroid diseases, although psychosomatic symptoms were most prominent in patients with hyperthyroidism, a statistically significant difference in symptom severity between examined thyroid disorders was not found. When single thyroid disorders were compared with the healthy subjects, only hyperthyroidism showed a significantly higher severity of all four examined psychosomatic symptoms (1).

The possible connection between hyperthyroidism and mental health conditions was also investigated in the pediatric population. In a retrospective study of the health database of insured members of the United States military between the ages of 10 and 18 in the period from 2008 to 2016, Zader et al. (19) found 2,480 subjects with hyperthyroidism. Most of these patients were between the ages of 16 and 18, with the majority being women (76%). The prevalence of hyperthyroidism in the examined period was 0.95 per 1,000 insured persons. In most cases, the diagnosis of mental health disorders was established before the diagnosis of hyperthyroidism.

A statistically significantly higher incidence of depression, anxiety, attention deficit hyperactivity disorder, and adjustment disorders, as well as bipolar disorder and suicidal thoughts, in addition to self-harm and/or suicide attempts, was identified in patients with hyperthyroidism compared to subjects with normal thyroid function. The nature of this connection is not clear. Symptoms of hyperthyroidism and depression can overlap because hyperthyroidism and depression can cause similar symptoms, such as a loss of appetite and sleep disturbances. The authors recommend that doctors should check thyroid function in patients with positive screening results for depression, anxiety, or other mental disorders. Furthermore, given that their results indicate an increased risk of suicide in the examined patients with hyperthyroidism, they suggest future research to determine the most effective

screening tool for recognizing mental state disorders in hyperthyroid patients (19).

When interpreting the current results, it is important to remember that the DASS is not designed to substitute for a complete psychological evaluation. Utilizing DASS scores to solely verify distinct mood disorders such as depression is not recommended (12). An individual DASS severity rating reflects how far scores are located from average population scores obtained from large, relatively diverse samples; the more distant the score is from the population average, the more intense the symptoms. Patients with DASS scores indicating serious symptoms of depression, anxiety, or stress should be referred to a skilled practitioner with experience in dealing with mood disturbances (12).

Other factors limiting the strength and generalization of the current findings were the small share of males in comparison with females and the limited study sample size, particularly in the hyperthyroid group. Therefore, these findings are considered preliminary. The current research will be continued until a larger adequate sample size is obtained. It is plausible to assume that every disease and hospitalization, particularly surgical admission, can elevate levels of negative emotional states. Therefore, further research on depression, anxiety, and stress levels in all patients admitted to the University Hospital in Mostar, irrespective of underlying pathology, is recommended. Then, these findings in a general inpatient population can be compared with those in patients with a particular disease, for example surgical candidates with thyroid disease.

CONCLUSION

A small share of the examined surgical candidates for strumectomy had elevated levels of depression or stress. Compared with the hyperthyroid patients, the euthyroid patients showed higher levels of depression and stress. Females had higher levels of depression and anxiety in comparison with males. The levels of examined negative emotional states were not related to the formal education levels of patients.

ACKNOWLEDGMENTS

None.

FUNDING

The authors did not receive any financial support for the research, authorship and/or publication of this study.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

FK: acquisition of data, literature review, contribution to study conception and design, supervision, writing the paper; AM: contribution to study conception and design, interpretation of data, literature review, supervision, critical revision of the paper; JI: acquisition of data, literature review, supervision, IČZ: contribution to study conception and design, literature review, supervision, interpretation of data, critical revision of the paper; BJ: study conception and design, supervision, literature review, analysis and interpretation of data, critical review, assistance in writing the paper.

ETHICAL BACKGROUND

Institutional review board statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the University Hospital in Mostar (Reg. No. 1280/23, 3 March 2023).

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Data availability statement: We deny any restrictions on the availability of data, materials, and associated protocols.

REFERENCES

1. Stanić G, Snežana M, Ignjatović DR. Influence of thyroid disorders upon the incidence and the severity of psychosomatic symptoms in patients. Iran J Public Health. 2022;51:1798-806.
2. Fukao A, Takamatsu J, Arishima T, Tanaka M, Kawai T, Okamoto Y, et al. Graves' disease and mental disorders. J Clin Trans Endocrinol. 2020;19:100207.
3. Brandt F, Thvilum M, Almind D, Christensen K, Green A, Hegedüs L, et al. Hyperthyroidism and psychiatric morbidity: evidence from a Danish nationwide register study. Eur J Endocrinol. 2013;170:341-8.
4. Bové KB, Watt T, Vogel A, Hegedüs L, Bjoerner JB, Groenvold M, et al. Anxiety and depression are more

prevalent in patients with Graves' disease than in patients with nodular goitre. Eur Thyroid J. 2014;3:173-8.
5. Demet MM, Ozmen B, Deveci A, Boyvada S, Adigüzel H, Aydemir O. Depression and anxiety in hyperthyroidism. Arch Med Res. 2002;33:552-6.
6. Trzepacz PT, McCue M, Klein I, Greenhouse J, Levey GS. Psychiatric and neuropsychological response to propranolol in Graves' disease. Biol Psychiatry. 1988;23:678-88.
7. Chopra R, Kalaria T, Gherman-Ciolac C, Raghavan R, Buch HN, Kar N. Impact of hyperthyroidism and its treatment on the outcome of mental health, occupational functioning, and quality of life: a naturalistic, prospective study. Indian J Psychiatry. 2023;65:586-94.
8. Kirkegaard C, Faber J. The role of thyroid hormones in depression. Eur J Endocrinol. 1998;138:1-9.
9. Mason GA, Walker CH, Plange Jr AJ. L-triiodothyronine: is this peripheral hormone a central neurotransmitter? Neuropsychopharmacology. 1993;8:253-7.
10. Aronson R, Offman HJ, Joffe RT. Triiodothyronine augmentation in the treatment of refractory depression: a meta-analysis. Arch Gen Psychiatry. 1996;53:842-8.
11. Fahrenfort JJ, Wilterdink AM, van der Veen EA. Long-term residual complaints and psychosocial sequelae after remission of hyperthyroidism. Psychoneuroendocrinology. 2000;25:201-11.
12. Parkitny L, McAuley J. The Depression Anxiety Stress Scale (DASS). J Physiother. 2010;56:204.
13. Reić Ercegovac I, Penezić Z. Skala depresivnosti, anksioznost i stresa (DASS). In: Proroković A, Ćubela Adorić V, Penezić Z, Tucak Junaković I, eds. Zbirka psihologijskih skala i upitnika, Svezak 6. Zadar: University of Zadar; 2012:15-22.
14. Allport J, McCahon D, Hobbs FD, Roberts LM. Why are GPs treating subclinical hypothyroidism? Case note review and GP survey. Prim Health Care Res Dev. 2013;14:175-84.
15. Wildisen L, Del Giovane C, Moutzouri E, Beglinger S, Syrogiannouli L, Collet TH, et al. An individual participant data analysis of prospective cohort studies on the association between subclinical thyroid dysfunction and depressive symptoms. Sci Rep. 2020;10:19111.
16. Bode H, Ivens B, Bschor T, Schwarzer G, Henssler J, Baethge C. Hyperthyroidism and clinical depression: a systematic review and meta-analysis. Transl Psychiatry. 2022;12:362.
17. Marian G, Nica EA, Ionescu BE, Ghinea D. Hyperthyroidism - cause of depression and psychosis: a case report. J Med Life. 2009;2:440-2.
18. Shoib S, Ahmad J, Wani MA, Ullah I, Tarfarosh SFA, Masoodi SR, et al. Depression and anxiety among hyperthyroid female patients and impact of treatment. Middle East Curr Psychiatry. 2021;28:26.
19. Zader SJ, Williams E, Buryk MA. Mental health conditions and hyperthyroidism. Pediatrics. 2019;144:e20182874.