



# Influence of Thyroid Disorders upon the Incidence and the Severity of Psychosomatic Symptoms in Patients

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## Abstract

**Background:** Thyroid disorders are an area of public health concern worldwide. The study aimed to examine the incidence and severity of psychosomatic symptoms (distress, depression, anxiety and somatization) in patients with hypothyroidism, hyperthyroidism, Graves' disease and Hashimoto thyroiditis in relation to clinically healthy subjects.

**Methods:** This case control study was carried out from Feb to Jul 2019 in Serbia. Total sample consisted of 335 subjects, of both sex. The examined group included patients with thyroid disorders treated at the Special hospital for thyroid gland and metabolism disease. Control group included clinically healthy subjects. The Four Dimensional Symptom Questionnaire a self-assessment questionnaire for psychosomatic symptoms was the measuring instrument. Groups were compared using parametric (t-test) and nonparametric (Pearson chi-square test, Mann-Whitney U test, Kruskal-Wallis test) tests.

**Results:** The incidence of all psychosomatic symptoms was high in patients with thyroid disease. Distress was found in 59.8% of the patients in the examined group comparing to the control group ( $12.8 \pm 8.2$  vs.  $8.9 \pm 8.1$ ). The score of depression was twice higher in the examined group ( $2.05 \pm 2.99$  vs.  $1.23 \pm 2.47$ ). Anxiety was present in 46.2% patients in the examined group, while somatization was found in 69.7% subjects. In hypothyroidism there was no difference between the examined and the control group regarding the level of anxiety, likewise with the level of depression in the control group and subjects with Graves' disease and Hashimoto thyroiditis.

**Conclusion:** Psychosomatic symptoms were significantly more severe in patients with thyroid disorders compared to the control group.

**Keywords:** The four-dimensional symptom questionnaire (4DSQ); Psychosomatic symptoms; Thyroid disorders

## Introduction

Thyroid hormones directly or indirectly affect almost all systems in the body, therefore changes

in their serum levels can have negative effect on human health (1-4). There are numerous psycho-



logical symptoms of anxiety, such as restlessness, tension, increased sweating, weight loss, sleep problems, and irritability connected with the hormonal dysfunction in hyperthyroidism. Patients with hypothyroidism may develop symptoms of depression, lack of interest, feeling tired, lack of motivation, feelings of helplessness and guilt (5-8). Moreover, there is a possibility of developing physiological disorders, and somatic symptoms that are a consequence of the disease itself (3, 9, 10).

Various forms of thyroid disorders have been observed in 5%-10% of the population (11). Hypothyroidism accounts for 60% of thyroid diseases (12) and is up to ten times more frequent in women than in men (13, 14). Hyperthyroidism is up to three times less frequent than hypothyroidism (15, 16).

Many studies have linked thyroid dysfunction with psychiatric symptoms (1, 9, 10, 17,18). There is a statistically significant association between this disease and the development of mental distress, mood disorders, and depression (17, 18). Affective disorders are dominant, namely depression in 33%-43% and anxiety in 20%-39% (10). Depression is one of the most common mental health disorders in the world (11), occurring as a comorbidity in 60% of patients with hypothyroidism (1). People with hypothyroidism may develop depression, while people with hyperthyroidism may develop anxiety (1). The prevalence of depression in hypothyroidism is 20%, while the prevalence of anxiety in hyperthyroidism is 30%-40% (11). Autoimmune diseases of the thyroid gland can result in pronounced psychosomatic symptoms (5, 15, 17).

Research on the prevalence of psychosomatic symptoms in patients with thyroid dysfunction is limited. The Four Dimensional Symptom Questionnaire (4DSQ) could be regarded a useful instrument for discovering these symptoms (19).

We aimed to examine the incidence and severity of psychosomatic symptoms (distress, depression, anxiety and somatization) in patients with hypothyroidism, hyperthyroidism, Grave's disease and Hashimoto thyroiditis in relation to clinically healthy subjects.

## Materials and Methods

The study was designed as a case control study carried out from Feb to Jul 2019 at the Special Hospital for Thyroid Gland and Metabolism Disease Zlatibor, Serbia.

It was carried out in accordance with the ethical principles of the Helsinki Declaration. All respondents gave their informed consent to participate in the study, which was approved by Ethics Committee (code EP-3110/17).

The research involved 355 participants of both sexes, age 18 to 70 years. The examined group consisted of 221 outpatients diagnosed with some of the thyroid dysfunction. Homogenization of the examined group was performed in consideration of various thyroid disorders. Inclusion criteria were the presence of thyroid dysfunction, age over 18 yr, and signed written consent of the subjects. Exclusion criteria were pregnancy and lactation, postpartum period of less than 6 months, cognition or psychiatric disorders at least three months before the study, presence of other comorbidities (other autoimmune and endocrine diseases, malignancies), use of thyrotrophic drugs (amiodarone, lithium, glucocorticoids).

After the examination by an endocrinologist, the subjects were classified in the examined group with thyroid disorders, and the control group without thyroid disorders. The control group consisted of a non-clinical sample of 134 healthy volunteers without any somatic and psychiatric diseases. Examined and control groups were matched by age and gender.

A questionnaire for self-assessment of severity of psychosomatic symptoms was applied, as well as a general sociodemographic questionnaire to collect basic demographic data relevant to our study. All respondents entered general data related to gender, age, body mass index (BMI), marital status, education and employment into the General Sociodemographic questionnaire. There was also a part of this questionnaire related to the type of thyroid disease.

The Four-Dimensional Symptom Questionnaire (4DSQ) is a self-report questionnaire comprising of 50 items distributed over four scales (distress, depression, anxiety and somatization) which are scored separately (19). The reference period is "the past week". The response categories are also worded as normal answers to clinical questions: "no", "sometimes", "regularly", "often", "very often or constantly". The responses are scored as 0 for "no", 1 for "sometimes" and 2 for the other response categories, and the item scores are added up to make the scale scores. The Distress scale contains 16 items and has a score range of 0–32, mild [0-10], moderate [11-20] and severe [21-32]. The Depression scale contains 6 items and has a range of 0–12, mild [0-2], moderate [3-5] and severe [6-12]. The Anxiety scale consists of 12 items and has a range of 0–24; mild [0-7], moderate [8-12] and severe [13-24]. The Somatization scale contains 16 items and has a range of 0–32, mild [0-10], moderate [11-20] and severe [21-32] (19).

The evaluation of results obtained using the questionnaire was carried out in relation to the healthy volunteers, the age of patients and their gender and disease duration. The collected data were verified by the author, coded and entered into a specially formulated database. Results were presented as count (%) or mean  $\pm$  standard deviation, depending on data type. Groups were

compared using parametric (t test) and nonparametric (Pearson chi-square test, Mann-Whitney U test, Kruskal-Wallis test) tests. Cronbach's alpha was used to assess internal consistency within 4DSQ questionnaire. All *P*-values less than 0.05 were considered significant. All data was analyzed using SPSS 20.0 (IBM Corp., Armonk, NY, USA).

## Results

The internal consistency coefficient Cronbach's Alpha 4DSQ (50 items) for patients with thyroid disorders was 0.959, while the values for individual scales were as follows: Distress - Cronbach's Alpha=0.925; Depression - Cronbach's Alpha=0.869; Anxiety - Cronbach's Alpha=0.875; Somatization - Cronbach's Alpha=0.905.

Overall, 355 subjects were divided into the examined group, consisting of 221 (62.2%) with various thyroid disorders, and the control group of 134 (37.8%) subjects without any thyroid disease. The majority of the subjects 203 (91.9%) were female, while the average age was 46.2 years. By comparing the two groups, a statistically significant difference was found regarding income, while there was no statistically significant difference regarding other sociodemographic parameters (Table 1).

**Table 1:** Sociodemographic characteristics of examined population

Variables	Thyroid disorder		P-value
	Yes (n=221)	No (n=134)	
Age (yr)	46.2 $\pm$ 12.6	45.3 $\pm$ 13.3	0.520 <sup>a</sup>
Gender – female	203 (91.9%)	122 (91.0%)	0.790 <sup>b</sup>
BMI (kg/m <sup>2</sup> )*	25.9 $\pm$ 4.4	25.9 $\pm$ 4.5	0.947 <sup>b</sup>
Education			
Primary (8 years)	20 (9.0%)	18 (13.6%)	0.330 <sup>c</sup>
Middle (12 years)	123 (55.7%)	55 (41.7%)	
High (15+yers)	78 (35.3%)	59 (44.7%)	
Employment			
Yes	114 (53.8%)	70 (57.9%)	0.624 <sup>b</sup>
No	56 (26.4%)	32 (26.4%)	
Retired	42 (19.8%)	19 (15.7%)	
Revenues			
Low	82 (37.1%)	39 (29.1%)	0.031 <sup>c</sup>
Moderately high	120 (54.3%)	73 (54.5%)	
Very high	19 (8.6%)	22 (16.4%)	
Lives in a community	171 (77.4%)	96 (71.6%)	0.225 <sup>c</sup>

\*BMI = body mass index <sup>a</sup>T test <sup>b</sup>Pearson Chi-square test <sup>c</sup>Mann-Whitney U test

A statistically significant difference was observed regarding the rate of severity (mild, moderate, or severe) degree of distress, depression, anxiety, and somatization on the 4DSQ questionnaire (Table 2). Table 3 shows the descriptive data regarding the presence of a certain thyroid disorder

in relation to the examined psychosomatic symptoms in the subjects. There was no statistically significant difference in the incidence and degree of a particular thyroid disorder compared to a psychosomatic disorder alone.

**Table 2:** The severity of psychosomatic disorders according to the 4DSQ score in the examined and control group

Variables	Thyroid disorder		P-value <sup>a</sup>
	Yes	No	
Distress	12.8±8.2	8.9±8.1	<0.001
Mild	89 (40.3%)	89 (67.4%)	<0.001
Moderate	91 (41.2%)	25 (18.9%)	
Severe	41 (18.6%)	18 (13.6%)	
Depression	2.05±2.99	1.23±2.47	0.002
Mild	158 (71.5%)	114 (85.7%)	0.010
Moderate	29 (13.1%)	6 (4.5%)	
Severe	34 (15.4%)	13 (9.8%)	
Anxiety	4.92±5.39	3.54±4.53	0.005
Mild	119 (53.8%)	88 (66.2%)	0.032
Moderate	53 (24.0%)	24 (18.0%)	
Severe	49 (22.2%)	21 (15.8%)	
Somatization	16.05±8.34	11.41±7.24	<0.001
Mild	67 (30.3%)	71 (53.4%)	<0.001
Moderate	84 (38.0%)	44 (33.1%)	
Severe	70 (31.7%)	18 (13.5%)	

<sup>a</sup>Mann-Whitney U test

**Table 3:** Influence of some thyroid disorder on the severity of psychosomatic symptoms in the examined group

Variable		Diagnoses										P value <sup>a</sup>
		Hypo thyroidism		Hyper thyroidism		Subclinical disease		Graves' disease		Hashimoto thyroiditis		
		N	%	N	%	N	%	N	%	N	%	
Distress	Mild	42	39.6	14	31.8	3	30.0	7	50.0	23	48.9	0.400
	Moderate	43	40.6	20	45.5	5	50.0	5	35.7	18	38.3	
	Severe	21	19.8	10	22.7	2	20.0	2	14.3	6	12.8	
Depression	Mild	76	71.7	24	54.5	8	80.0	11	78.6	39	83.0	0.066
	Moderate	15	14.2	10	22.7	0	0.0	1	7.1	3	6.4	
	Severe	15	14.2	10	22.7	2	20.0	2	14.3	5	10.6	
Anxiety	Mild	61	57.5	20	45.5	6	60/0	6	42.9	26	55.3	0.471
	Moderate	28	26.4	10	22.7	1	10.0	5	35.7	9	19.1	
	Severe	17	16.0	14	31.8	3	30.0	3	21.4	12	25.5	
Somatization	Mild	30	28.3	13	29.5	2	20.0	7	50.0	15	31.9	0.371
	Moderate	40	37.7	16	36.4	4	40.0	5	35.7	19	40.4	
	Severe	36	34.0	15	34.1	4	40.0	2	14.3	13	27.7	

<sup>a</sup>The Kruskal Wallis test was used to test the difference between all five groups together. Subsequently, intergroup comparisons were made using the Mann-Whitney U test

We found statistically significant difference between the examined group with hypothyroidism, and the control group regarding psychosomatic symptoms: stress ( $P<0.001$ ), depression ( $P=.010$ ), and somatization ( $P<0.001$ ). Between the control group and the group with hyperthyroidism there was statistically significant difference in all psychosomatic symptoms of stress ( $P=.000$ ), depression ( $P=.002$ ), anxiety ( $P=.016$ ) and somatization

( $P<0.001$ ). In a small number of subjects with Graves' disease comparing to the control group there was statistical significance regarding the anxiety ( $P=.049$ ), while in subjects with Hashimoto thyroiditis statistical significance comparing to the control group was found regarding the level of distress ( $P=.021$ ), anxiety ( $P=.049$ ) and somatization ( $P=.006$ ) (Table 4).

**Table 4:** Psychosomatics characteristics of examined and control group

Variables	Thyroid disorder					Control group (n=134)
	Hypothyroidism (n=106)	Hyperthyroidism (n=44)	Subclinical disease (n=10)	Graves' disease (n=14)	Hashimoto thyroiditis (n=47)	
Distress	12.8±8.1 <sup>a</sup>	14.7±8.8 <sup>a</sup>	12.7±8.5	11.9±8.4	11.6±7.7 <sup>a</sup>	8.9±8.1
Depression	2.0±2.9 <sup>a</sup>	2.8±3.4 <sup>a</sup>	2.3±3.6	2.1±3.6	1.3±2.1	1.2±2.5
Anxiety	4.4±4.9	5.8±6.2 <sup>a</sup>	4.6±5.7	6.3±6.9 <sup>a</sup>	4.9±4.9 <sup>a</sup>	3.5±4.5
Somatization	16.4±8.3 <sup>a</sup>	17.1±8.6 <sup>a</sup>	16.8±9.2	11.8±7.4 <sup>b</sup>	15.3±8.2 <sup>a</sup>	11.4±7.2

Mann-Whitney U test  $P<0.05$  for comparisons between: <sup>a</sup>Healthy control vs thyroid disease and; <sup>b</sup>Hyperthyreosis vs other thyroid disease; other comparisons are not significant

## Discussion

This is the first study in which the 4DSQ questionnaire was applied in patients with thyroid dysfunction, with the internal consistency coefficient Cronbach's Alpha of 0.959. We found no difference in BMI, marital status, education and employment between the examined and control groups.

A higher intensity of distress was observed in the examined group compared to the control group (12.8±8.2 vs. 8.9±8.1). More than a half of the respondents (59.8%) with various thyroid disorders had an elevated score on the distress scale, which indicated that the presence of thyroid disease was an additional source of distress in majority of patients.

The percentage of severe distress was significantly higher in our examined group compared to other studies where the evaluation of psychiatric comorbidity in various thyroid diseases indicated that 48.3% of subjects had neurotic, distress and

psychosomatic disorders, and 26.7% had affective mood disorders (20). The presence of distress can lead to other mood disorders.

Our research-detected problems with depression with a twice higher score in the examined group compared to the control group (2.05±2.99 vs. 1.23±2.47). Almost a third of our subjects (28.5%) had symptoms of depression, which differs from other study where 15% of subjects with thyroid disorders had symptoms of depression (21).

The anxiety symptoms in our subjects with thyroid disorders were significantly more prominent in relation to the control group (4.92±5.39 vs. 3.54±4.53), indicating that thyroid disease associated with increased distress levels resulted in increased level of anxiety in the examined group. Anxiety symptoms were detectable in almost half of the examined group (46.2%). Such a high percentage of subjects with anxiety symptoms was also found in another study (22). The percentage of the participants with thyroid disease who had

symptoms of anxiety was significantly lower (9, 10).

The results demonstrated a high intensity on the somatization scale in more than 2/3 of the subjects indicating that the subjects were additionally burdened with somatic problems. This study confirms that in patients with thyroid disorder, the presence of severe distress, depression and anxiety leads to increased severe somatization compared to the control group ( $16.05 \pm 8.34$  vs.  $11.41 \pm 7.24$ ;  $P < 0.001$ ). Patients with thyroid disorders had severe symptoms of somatization, which contributed to the deterioration of their health.

In the examined group, the intensity of psychosomatic symptoms was not significantly different between subjects with various thyroid disorders (Table 3). Psychosomatic symptoms were the most pronounced in subjects with hyperthyroidism. Our results indicate that the degree of distress is most pronounced in subclinical thyroid disorders, but with a small number of subjects. The subjects with hyperthyroidism, 68.7% had a moderately high to very high distress score. This large percentage of subjects with symptoms of distress indicates that the presence of hyperthyroidism contributes to the occurrence of severe distress in patients.

Our research demonstrated that in various thyroid disorders, moderate or severe symptoms of depression were found in a small percentage of respondents (Table 3). Among our respondents with Graves' disease 78.6% had no symptoms of depression. We found severe symptoms of depression in 28.4% of our subjects with hypothyroidism, which is similar to some other studies (10, 23, 24). Other studies also demonstrated that symptoms of depression were more pronounced in subjects with hyperthyroidism (24.8%) compared to subjects with hypothyroidism (18.2%) (21). Unlike our research, the data from the literature show that a higher incidence rate of depression has been confirmed in hypothyroidism than in hyperthyroidism (1). Moreover, there are some results opposite to ours, which indicate that patients with hypothyroidism have more severe depression (29.4%) compared to subjects with hy-

perthyroidism, with more than half had moderate depression, while only 6.3% severe depression (22). Some studies with a limited number of subjects confirmed high levels of anxiety and depression in subjects with thyroid disorders but did not confirm a link between diagnoses of hypothyroidism and depression, nor a link between the high levels of anxiety in hyperthyroidism (25). In various thyroid disorders, when measured by the 4DSQ questionnaire, the symptoms of anxiety were more intense than the symptoms of depression. Contrary to our research results, 50.6% of newly diagnosed patients with reduced thyroid function had a psychiatric disorder, of which depression rate was 20%, followed by anxiety rate of 12% (10). When compared to subjects with hypothyroidism, a higher percentage of subjects with hyperthyroidism had a higher anxiety score. Similar results are found in previous studies where anxiety was detected in 47% of subjects with hypothyroidism, and in 56.2% of subjects with hyperthyroidism (22). Symptoms of hyperthyroidism combined with those of anxiety, such as restlessness, and nervousness can indicate the connection between the two diseases.

This research indicates that more than half of the subjects with various thyroid disorders have moderate or very severe somatization symptoms, with the most severe somatization symptoms found in subjects with subclinical disorders, followed by subjects with hypothyroidism (71.7%). A slightly fewer subjects with hyperthyroidism (70%) had severe somatization symptoms. This result is similar to those in other studies, where hyperthyroidism is considered a risk factor in the development of anxiety and somatic disorder (26, 27). In previous studies, 61% of subjects with hyperthyroidism had gastrointestinal symptoms and weight loss (14), as well as severe insomnia and cardiovascular symptoms (26). There were pronounced general somatic symptoms, i.e. severe insomnia and gastrointestinal symptoms (1). When diagnosing and treating patients with thyroid disorders, it is necessary to pay special attention to mental and physical problems in order to prevent and/or treat somatic problems timely and adequately.

Compared to other studies dealing with the presence of psychosomatic symptoms related to various thyroid diseases, we noticed that our results differed regarding the observed incidence of depression and anxiety in these patients and the control group (Table 4). The incidence of depression and anxiety in hypothyroidism we recorded was similar to that in other studies (1, 3, 23, 24), for example where the rate of anxiety (63%) was higher compared to depression (60%) in subjects with hypothyroidism (1), but there were also some opposite results (7, 28).

In subjects with hypothyroidism, the level of severe anxiety compared to the control group did not show significant difference, which is contrary to other studies where the level of anxiety was increased (46.1%) in subjects with hypothyroidism (3, 22). A population-based study demonstrated an association with depression and thyroid dysfunction, as well as an association between hypothyroidism and anxiety (13). However, this is not the case in our study.

In subjects with hyperthyroidism, our results like results of other studies confirm that anxiety and depression are frequent comorbidities in comparison to the control group (14, 23, 25, 26). In our subjects, intense symptoms of anxiety rather than depression were more frequently related to hyperthyroidism, which is different from the results of other authors where 40% of subjects with hyperthyroidism had problems with depression, but there was no difference regarding anxiety between the study and control group (29). Contrary to our results, in 3790 respondents in Germany no association was found between mental disorders and physical complaints in newly diagnosed patients with hyper and hypothyroidism, moreover lower incidence of anxiety was observed in hyperthyroidism (7).

Our results confirm that Graves' disease and Hashimoto thyroiditis may be linked with more severe psychosomatic symptoms, as found in the results of other studies (5, 15, 17, 30-32). Both the results of our study and those of other studies that we found in the literature indicated that there was a high anxiety rate in subjects with Hashimoto thyroiditis (17). Our results were

similar with those where an increased level of anxiety was found in 18% of subjects with Graves' disease (31).

In our subjects with Graves' disease and Hashimoto thyroiditis, there was no significant statistical difference between the groups regarding the symptoms of depression, which is opposite to the data in the study where an increased level of depression was found compared to the control group (12, 16, 32). There was a higher level of anxiety and depression in subjects with Hashimoto thyroiditis, which was similar to our results, but they also confirmed a difference in depression level between the study and control group, which was opposite to our study (32). Our results did not confirm that Hashimoto thyroiditis had an effect on the development of depression in the examined group compared with the control group.

Our results differ from the results in other studies where depression was confirmed in patients with Hashimoto thyroiditis (17, 32, 33), i.e. there was an increased level of depression and a higher rate of severe depression, same as with the level of distress compared to the control group ( $16.5 \pm 6.5$  vs.  $3.6 \pm 3.17$ ) (30). The data indicating that Hashimoto thyroiditis represents a risk for developing depression is opposite to our results (12).

## Conclusion

Psychosomatic symptoms were significantly more severe in patients with thyroid disorders compared to the control group, which was assessed by the 4DSQ questionnaire. A holistic and individual approach is needed for every patient with thyroid dysfunction, because this disease can lead to psychiatric comorbidity, and thus damage other organs and systems in the body.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or

submission, redundancy, etc.) have been completely observed by the authors.

## Financial source

This study had no financial support.

## Conflict of interest

All authors declare that there is no conflict of interest.

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