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CONNECTION BETWEEN THE DISORDER OF THE FUNCTION OF THE THYROID GLAND AND THE APPEARANCE OF THE SOMATIC SYMPTOMS WITH THE PATIENTS

Abstract

Introduction: The thyroid gland is one of the most important endocrine glands that has the function of releasing hormones that regulate metabolism in adults. Thyroid hormones act directly or indirectly on almost all systems in the body, so they can negatively affect the health of an individual, who have a high risk of developing disorders in psychosomatic symptoms. The occurrence of somatization in patients can be accompanied by a direct impact of thyroid disorders on certain organs and systems, but it can also be non-specific in relation to the disease itself.

Objective: To examine the relationship between different disorders of the thyroid gland and the occurrence of somatic symptoms in patients, according to age, body mass index and length of treatment.

Material and methods: The study was conducted as a cross-sectional study in 221 outpatients with thyroid disease at the Special Hospital for Thyroid Diseases and Metabolic Diseases "Zlatibor", from February to July 2018. In addition to the sociodemographic questionnaire, a four-dimensional symptom questionnaire subscale (4DSQ) was used in the study to assess the occurrence and level of somatization in subjects. Results are presented as a percentage (%) or mean \pm standard deviation, depending on the data type. The groups were compared using the parametric (t test) and nonparametric (Pearson chi-square test, Mann-Whitney U test, Kruskal-Wallis test) test.

Results: There is an association between different thyroid disorders and a high score on the somatization scale (16.05 ± 8.34), in 69.7% of subjects. In our subjects, the most pronounced somatic symptoms have subjects with hypothyroidism ($M=17.5$; $AS=16.44 \pm 8.26$), subjects

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over 61 years (19.29 ± 8.29). Musculoskeletal somatic symptoms were expressed in 72.4% of subjects. Pronounced somatization (19.40 ± 8.32) have subjects who have elevated body mass index values (35-39.9), as well as subjects who have been treated for thyroid disease for more than ten years (19.7 ± 8.7).

Conclusion: This study showed that there is an association between thyroid disorders and the appearance of somatic symptoms in patients. In patients, there are moderate somatic symptoms that are associated with age, body mass index and length of treatment.

Key words: somatic symptoms, thyroid disorders, body mass index, treatment of thyroid disease

Introduction

The thyroid gland is one of the most important endocrine glands whose function is to release the hormones which regulate the metabolism of a grown up person (1,2,3). These hormones influence the neuropsychiatric manifestations, it means that they influence the mood, behaviour and knowledge (4,5,6). The hormones of thyroid gland influence a great number psychological functions in the organism, including the metabolism of lipids, carbohydrates and proteins. They influence all the systems in the organism directly or indirectly, so that the changes in their serum concentrations can have a negative influence on the health of a person (7). The patients who suffer from thyroid gland function disorder can be in a great risk to develop the disorder of psychological and somatic symptoms that can be consequence of the disease (3,8,9).

The disorder of thyroid gland causes the excessive or reduced secretion of the thyroid hormones but often and the presence of the antibodies which brings to different symptoms and disorders (6,8,10). The patients with the disorder of the function of the thyroid gland who have chronic inflammatory reactions are at the risk to develop disorders in the psychosomatic symptoms (11,12). Hormone disfunction causes psyche symptoms of anxiety, restlessness, tension, excessive sweating, weight reduce, sleeping problems and irritation (13,14,15).

The appearance of somatization with the patients can be followed by the direct influence of disorder of the thyroid gland function on some organs and systems, but it can be non-specific in the relation to the disease itself. The dimensions of the somatization are psychosomatic symptoms (pain in the muscles, neck, back, headache, stomachache, heartbumping, breathlessness) which are the usual body reactions to the stress, when they are weakly or moderately expressed with individuals, but if they are very expressed they can point to the existence of the somatomorphic disorders (16). The patients with the disorder of the thyroid gland function can have changes in the

index of the body mass (BMI). Clinically, hypothyroidism causes the increase of the body masses, but hyperthyroidism reduces it (17).

World Health Organization (WHO) that 750 million suffer from the disorder of the thyroid gland function (18). Thyroid dysfunction is shown in different forms and is noticed with 5 – 10 % of the population (19,20). The data show that the women suffer from this disease in greater number and it increases with the age (2,21). Many studies show the improvement of the neuropsychiatric and somatic symptoms with the adequate treatment of the definite diseases and with the compensation of the necessary hormones (6,22,23). It is possible that some symptoms stay in the euthyroid state with some individuals (10).

In contemporary medicine there are interests for psyche aspects connected with the thyroid gland function because they worry public health in world. In Serbia There is not a national register for patients with the thyroid disease, but there is a national guide that points out this disease (24). The small number of tests has been done so far with us related to the life quality, depression and anxiety in patients with thyroid dysfunction, but the presence and the level of somatization with the patients. The connection of somatic symptoms with the thyroid gland function represents the risk for the functional disability and higher treatment expenses with the patients. Taking into account all these and other scientific reasons, it is important to broaden our knowledge from this field.

The aim of this study was to examine the relationship between different disorders of the thyroid gland and the occurrence of somatic symptoms in patients, according to age, body mass index and length of treatment.

Material and methods

The study was conducted as a cross-sectional study in 221 outpatients with thyroid disease at the Special Hospital for Thyroid Diseases and Metabolic Diseases "Zlatibor", from February to July 2018.

Including the research criteria there were the patients who turned to the endocrine gland specialist who diagnosed the disorder of the thyroid gland function after the laboratory analyses, then the patients who were treated from this disease, older than 18 years, the patients who don't have diagnosed psyche disorder and who accepted to answer questionnaire anonymously. Excluding criteria for the respondents were the diagnosis of the psychiatric disease, the treatment with amidoron and litium, pregnancy or six months after birth-giving, the patients with the cognitive deficit and the patients with the complex comorbidities.

After the checkup of the endocrine specialist and laboratory analyses the respondents were classified into the group with the disorder of the thyroid gland function.

Procedures

Nakon pregleda lekara specijaliste endokrinologa i laboratoriskoh rezultata ispitanici su se svrstavali u ispitivanu grupu sa poremećajem rada štitaste žlezde.

Laboratory analyses referred to the samples of vein blood which had been taken during the morning hours (from 7 to 9 a.m.). Serum analyses referred to the level of thyrostimulating hormone (TSH), thyroxine (T4), antibodies of thyroid peroxidosis and TSH receptor (anti TBO and anti Trab) and they were carried out by immunoenzymatic test (Lumi test – henning i Elisa – Milenia). The level of normal TSH was considered to be the range from 0,3-4,2 mU/l and for hyperthyroidism FT4 more than 24,5 pmol/l as well as for hyperthyroidism FT4 less than 10,2pmol/l. The reference range of free titoxin is 10,2-24,5 pmol/l. The sample of blood from the respondents was classified into five categories according to the level of TSH and T4: hyperthyroidism with decreased TSH and increased FT4, subclinical hyperthyroidism with decreased TSH (lower than 0,3 mlu/l) and normal FT4, hyperthyroidism with increased TSH (higher than 4,2 mlu/l) and decreased FT4, subclinical hyperthyroidism with increased TSH and normal FT4. Autoimmune thyroidism, besides these analyses, comprised the research of the existence of antibodies of thyroid gland (anti TPO) and classified the disorders of the thyroid gland functions into Graves' disease and Hashimoto thyroiditis. Reference values for anti TPO antibodies are lower than 35mU/l and anti Trab to 1,5 U/l (24).

Research instruments

General sociodemographic questionnaire for collecting basic demographic data which referred to the sex, age, type of current illness, body mass index (BMI), the length of treatment of thyroid gland disorder were included in this study. According to the age, the respondents were classified into groups by decades. After the values of body mass and heights had been measured, the values of BMI were calculated, which was defined on the basis of recommended formula kg/m^2 . For our analyses' results, the respondents were divided into four groups according to the values of BMI: BMI<18,5 - malnourished; normal BMI=18,5-25; overweight (BMI=25 - 29,9); the obese (BMI=30-34,9), severe obesity - BMI=35-39,9 and excessive obesity BMI>40 (25).

According to the length of treatment the respondents were classified into four groups: newly ill, the ones who have been treated less than five years, than the group of the respondents who have been treated from six to ten years and the ones who have been treated more than ten years since their thyroid gland disease was diagnosed.

Assessment of the presence of somatic symptoms in the subjects was measured with the somatization subscale of the Four-Dimensional Symptom Questionnaire

(4DSQ), which was anonymous. This scale estimates 16 somatic symptoms and reference period is "the past week". The results were on a five-point Likert-type scale with claims denoted by: "no", "sometimes", "regularly", "often", "very often or constantly". To get the results of the scale, the answers were evaluated with 0 for "no", 1 for "sometimes" and 2 for other answer categories. Adding each item gives the results of the scale. Categorization of results on the somatization scale: Mildly expressed from 0 to 9 - means that the person has a normal level of somatization; Moderate - from 10 to 20, which is a sign of possible problems, which should be monitored, talk to the patient; severe - a very pronounced score of 21-32 in the category in which further diagnosis and appropriate treatment is needed for that patient. In previous studies, four clusters of somatic symptoms were observed: cardiopulmonary symptoms (excessive sweating, chest pain and tightness, shortness of breath, palpitations), which are the body's usual response to stress, when they are mild or moderate, but high scores can to indicate the existence of somatic disorders. Then, musculoskeletal symptoms (back, neck, muscle pain, tingling in the fingers), gastrointestinal symptoms (abdominal discomfort, nausea in the stomach, pain in the abdomen or stomach area), as well as general symptoms (dizziness or lightheadedness, fainting, headache, blurred vision or spots in front of the eyes) (16,26).

Ethical Approval

The research was carried out according to ethical principles and human rights within the research, as well as non-profitable and according to the regulations of the Helsinki Declaration. The respondents read the information about the research and voluntarily accepted the anonymous examination. We had the approval of the Ethical board of the Special Hospital for thyroid gland and metabolism diseases "Zlatibor" for carrying out the research (3110/01.12.2017.).

Statistical analysis

The characteristics of the sample were analyzed through descriptive statistics. Results are presented as a percentage (%) or mean \pm standard deviation, depending on the data type. The groups were compared using the parametric (t test) and non-parametric (Pearson chi-square test, Mann-Whitney U test, Kruskal-Wallis test) test. All p values less than 0.05 were considered significant. All data were analyzed using SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). No statistical imputation process was undertaken for missing information (i.e. we used complete case analysis).

Results

Out of 221 respondents, the greatest number was a female sex (91.9%) of age group from 41–50. The average age of the respondents is 46,2. Bodi mas indeks BMI is in the most number of cases within the category from 18,5-24,9. The average BMI is $25,9 \pm 4,4$. The largest number of the respondents had the diagnosis of hyperthyroidism (48 %) and they had been treated less than five years (50.2%). There is a moderate and severe score for somatization with 69,7% of the respondents (Table 1).

Table 1. Sociodemographic characteristics of the study population

Variables	respondents n=221 (%) ^a
Gender – female	203 (91.9)
Age (years)	
11 - 20	1 (0.5)
21 - 30	29 (13.1)
31 - 40	42 (19.0)
41 - 50	62 (28.1)
51 - 60	52 (23.5)
61+	35 (15.8)
BMI (kg/m ²)*	
<18,5	4 (1.2)
18,5-24,9	95 (42.3)
25-29,9	86 (38.3)
30-34,9	29 (13.1)
35-39,9	5 (2.6)
40+	2 (0.9)
Diagnosis	
Hipotireoza	106 (48.0)
Hipertireoza	44 (19.9)
Subklinički poremećaj	10 (4.5)
Gravesova bolest	14 (6.3)
Hašimoto tireoiditis	47 (21.3)
Duration of therapy	
newly discovered	24 (10.9)
<5 years	111 (50.2)
6-10 years	46 (20.8)
>10 years	40 (18.1)
Somatisation	
Mild (0-9)	67 (30.3)
Moderate (10-20)	84 (38.0)
Severe (21-32)	70 (31.7)

^aT test, Pearson chi square test, Mann-Whitney U test

*BMI = body mass index

Our results indicate that the most excessive somatization has been noticed with the respondents suffering from hypothyroidism and the least excessive somatization has been noticed with the ones suffering from Graves' disease. During the additional comparison, without correlations of p values, it was confirmed that there was a difference in somatization between the respondents with hypothyroidism and the ones suffering from Graves' disease (Table 2).

Table 2. The extent of somatization with respondents with different thyroid gland diseases.

Diagnosis	Somatisation						P value
	N	A.S	SD	Median	Percentile 25	Percentile 75	
Hypothyroidism	106	16.44	8.26	17.5	10.0	23.0	H=5,176 p=0,270
Hyperthyroidism	44	17.11	8.62	16.5	9.5	24.5	
Subclinical disease	10	16.80	9.25	16.5	12.0	24.0	
Graves' disease	14	11.86	7.45	11.0	5.0	16.0	
Hashimoto thyroiditis	47	15.26	8.22	14.0	10.0	23.0	
Total *	221	16.05	8.34	17.0	10.0	23.0	

**Kruskal-Wallis test*

A large number of our respondents with different thyroid gland function disorders show excessive somatic symptoms. Of the total number of respondents, 72.4% have musculoskeletal symptoms (Table 3).

Table 3. The connection of somatic symptoms with the patients with different thyroid gland function disorders

Thyroid disorder	Cardiopulmonary symptoms N(%)	Musculoskeletal symptoms N(%)	Gastrointestinal symptoms N(%)	General symptoms N(%)
Hypothyroidism	68 (64.2)	78 (73.6)	69 (65.1)	65 (61.3)
Hyperthyroidism	35 (79.5)	31 (70.5)	20 (45.5)	28 (63.6)
Subclinical disease	7 (70.0)	9 (90.0)	6 (60.0)	8 (80.0)
Graves' disease	8 (57.1)	7 (50.0)	7 (50.0)	7 (50.0)
Hashimoto thyroiditis	30 (63.3)	35 (74.5)	27 (57.4)	29 (61.7)
Total*	148 (67.0)	160 (72.4)	129 (58.4)	137 (62.0)

**Pearson chi square test*

The appearance of somatization with the ill-affected suffering from thyroid gland function disorder is related to the age. The older respondents are, the bigger the range of somatic symptoms is (Table 4).

Table 4. The connection of somatic symptoms with the age of the respondents

Age (in years)	Somatisation*					
	N(%)	A.S.	SD	Median	Percentile 25	Percentile 75
11 - 20	1(0.4)	1.00	.	1.0	1.0	1.0
21 - 30	29(13.1)	13.10	7.09	13.0	7.0	17.0
31 - 40	42(19)	13.36	8.52	12.5	6.0	20.0
41 - 50	62(28.1)	15.44	7.51	15.0	9.0	22.0
51 - 60	52(23.5)	18.71	8.41	20.0	14.5	24.0
61+	35(15.8)	19.29	8.29	20.0	15.0	26.0

*Pearson chi square test

The greatest number of the respondents has the normal index of body mass (43%). We have connected the BMI of the respondents with the level of somatization and we have confirmed the highest level of somatic symptoms with the respondents who have BMI 35-39.9, but the lowest one with those patients who have a normal BMI (Table 5).

Table 5. Connection of the appearance of Somatisation with the body mass index of the respondents

kg/m ²	Somatisation					
	N(%)	A.S.*	SD*	Median*	Percentil 25*	Percentil 75*
<18,5	4(1.8)	15.75	11.24	14.5	6.5	25.0
18,5-24,9	95(43)	14.51	8.69	14.0	7.0	21.0
25-29,9	86(38.9)	16.90	7.88	17.0	11.0	23.0
30-34,9	29(13.1)	17.90	8.02	18.0	12.0	24.0
35-39,9	5(2.3)	19.40	8.32	22.0	20.0	25.0
40+	2(0.9)	18.50	2.12	18.5	17.0	20.0

*Pearson chi square test

There is a statistic significant difference among the groups made according to the length of treating thyroid gland disease and somatic symptoms. When the new comparisons are made, the comparison among all the groups, it is confirmed that there is a significant difference between the group >10 years to a group 6-10 years (p=0,006), with a group, 5 years (p=0,005), while the difference of the newly discovered group is

near the conventional level of significance and it is $p=0,082$. All subsequent comparisons are without the correction of p value (Table 6).

Table 6. Duration of therapy period and Somatisation with the patients suffering from the disorder of thyroid gland function

Variables	N (%)	A.S.	SD	Median	Percentil 25	Percentil 75	p value ^a
	newly ill	24 (10.9)	15.83	7.83	16.00	11.00	24.00
Somatisation	<5 years	111 (50.2)	15.28	8.41	16.00	8.00	22.00
	6-10 years	46 (20.8)	14.80	7.38	15.00	8.00	20.00
	>10 years	40 (18.1)	19.75	8.73	21.50	12.00	28.00

^aKruskal-Wallis test

Discussion

The results of our research point out the expressive somatic symptoms with the patients suffering from the disorder of the thyroid gland function, which is based on the self-assessment of the symptoms on the subscale for the somatization of the four dimensional questionnaire of psychosomatic symptoms (4DSQ).

There is an excessively expressed somatization with the great number of the respondents (69,7%) who have a moderate or a very expressed somatization. The results point to the high intensity on the scale of the somatization, with more than 2/3 of our respondents. It says that patients are additionally burdened with the somatic troubles. Moderately expressed somatization is present with our respondents, medium value on our scale for the somatization is $16,05 \pm 8,34$. The presence of medical inexplicable symptoms with the patients suffering from the disorder of thyroid gland function contributes to the appearance of the comorbidities regardless the disease. This can certify that the somatic symptoms are not expressive with only one third of the respondents which means that it is necessary to have a preventive observation and to take steps of support so that the appearance of the somatic symptoms could be avoided. The connection between the thyroid gland disease and somatic symptoms would be the result of the overlap of the diagnostic criteria for this disease., as some somatic symptoms are included into the scale itself and they are not connected with the clinical symptoms for the disorder of the thyroid gland function, but show the higher somatization, we can point out that the results of our research are referent.

The greatest number of somatization symptoms can be met with the respondents with the diagnosis of hyperthyroidism, which is similar to the results of other studies where hyperthyroidism is considered to be the cause of anxiety and somatic problems (27,28) so that 61% of the respondents had gastrointestinal symptoms and the loss of

weight, very expressive insomnia and cardiopulmonary symptoms (27). In the other research there is the expressiveness of general somatic symptoms, expressive insomnia and gastrointestinal symptoms.

The greatest number of respondents complains about musculoskeletal troubles (72,4%), while the smallest percent of them has gastrointestinal symptoms. Our respondents have the greatest troubles with the pain in the back, neck, muscles and tingling in the fingers (Table 3).

The analysis of the results shows the datum that the patients suffering from hyperthyroidism have the highest expressed cardiopulmonary symptoms (79,5%), but this cluster in the somatization is the least found with Graves' disease (57,1%), then musculoskeletal symptoms are greatly expressed with subclinical disorder (90%), but is the least expressed with Graves' disease. Gastrointestinal symptoms have the most expressiveness with the respondents suffering from hypothyroidism (65,1%), in the least with the respondents with hyperthyroidism (45,5%), while the general symptoms can be found with the respondents with subclinical disorders (80%) and the least with the respondents with Graves' disease (50%). Earlier results confirm the psychosomatic character of Graves' disease (29) while in our research the least troubled are by somatic symptoms related to the patients with other diseases of the thyroid gland. We consider the limitation of this study and a relatively small number of the respondents in this category of the thyroid gland disease.

The results of our research show that there is statistical significance with the respondents with the hyperthyroidism in the cardiopulmonary symptoms and general symptoms and with the respondents with Hashimoto thyroiditis in the gastrointestinal symptoms and general symptoms. Besides that there is a statistical significance between the respondents with hypothyroidism and hyperthyroidism in the gastrointestinal symptoms of somatization (Table 3).

Our research shows that the least of somatization is with the respondents who are at the age of 21 to 30. The analysis of the results confirms that the higher score on the scale of somatization is with the older respondents (Table 4). All the respondents have moderately expressed somatization, but as it increases with the age it is necessary to start with the prevention and notice of the somatic symptoms with the patients with the disorder of the thyroid gland disease.

The results show that there is not an influence on the increase and decrease of the body mass index with these patients, the greatest number of our respondents have normal values of BMI (Table 5). In our research and in the other ones there is not the connection between the disorder of the thyroid gland and the body mass index (30). We have analyzed how BMI with our respondents influences the appearance of the somatic symptoms and we have confirmed that those ones with normal weight are the least additionally burdened with somatic symptoms (14.51 ± 8.69). This research confirms that the increased body mass index with the patients can have the influence

on the expressed appearance of the somatic symptoms (Table 5). The respondents with a higher index of body mass have a higher score on the scale of somatization than the all other groups. We can notice that with a small number of respondents there is a lower level of somatization with the BMI patients over 40 years old which shows that it is necessary to do further research with these patients and their connection of somatization with BMI.

The analysis of our results gives the data which show that the duration of treating is connected with different disorders of the thyroid gland function when there is the appearance of the somatic symptoms. Moderately expressed somatization was found with all the groups of the respondents with different duration of treating (Table 6). The least expressed somatic symptoms are in the group of patients from 6 to 10 years. The respondents in the group which has been treated more than 10 years have higher arithmetic mean and median compared to other groups which shows that the duration time of treating influences the increase of the score on the scale of somatization, which points out that the time of treating influences the appearance of the expressed somatization with the patients with the thyroid gland disease. There is not a statistically important difference between the respondents who have started the treatment and the respondents who have been treated less than 5 years. Our research cannot explain these varieties in the importance of somatization and the time of treating of the patients, but it supposes that there are different levels of thyroid gland hormones which influence the appearance of somatization with the patients during the time of treating.

It is important to find in detail the factors of risk besides the basic disease, which influence the appearance of somatization with the patients. The increased level of somatic symptoms connected with the thyroid gland disease points out the need for a different treatment from the usual one with these patients. Besides the usual use of the adequate therapy in treating the thyroid gland disease, the expanded uses of other therapies in the prevention of the starting comorbidities with the patients must be taken.

The results of the research contribute to the improvement of the knowledge about long - lasting consequences chronic disorders of the thyroid gland function to the appearance of somatization with the patients. These results of the research point to the necessity of preventive activities, early identification of somatic disorders that can appear with the patients with thyroid gland disease and the acting to protect their physical health.

The advantage of our research is that the level of somatization with the patients with thyroid gland disease has been tested for the first time. The restrictions of our study are the small standards for some thyroid gland diseases, it is necessary to direct the research in detail to some diseases about observing and defining the causative connection between laboratory analyses of the serum TSH and T4 and compare it to some somatic symptoms.

Conclusion

This research has shown the connection between the thyroid gland disorder and the somatic symptoms with the patients. There are moderately expressed somatic symptoms with patients, which is connected with life age, the index of body mass and the time period of the treatment.

The holistic access is necessary to any patient with the thyroid gland disorder because this disease can lead to an additional burden of other organs and systems in the organism of the patient. An early diagnosis of different diseases and the treatment of the thyroid gland disease can reduce the additional mortality from thyroid gland disease. This access is as very important for the public health as for the some way of treatment and the attitude to these patients.

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