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 ASSOCIATION BETWEEN HASHIMOTO'S THYROIDITIS AND DEPRESSION

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Abstract

Hashimoto's thyroiditis is a disease of the thyroid gland which affects the body in various ways leading to somatic complications. In addition to that, it affects the patient's mental health. The extent of psychiatric diseases in patients with Hashimoto's thyroiditis is not extensively explored. The primary objective of this study was to find the association between Hashimoto's disease and depression in female patients aged 36-50 from North America/Central America. Questionnaires were designed to assess the extent of possible depression in those patients. We compared 115 cases to 188 controls. After analyzing results, we found that relative risk for developing depression in patients with Hashimoto's disease was 1.7202 (95% CI 1.4722- 2.0099, p value < 0.001). Thus, we concluded that Hashimoto's disease is associated with increased risk of development of depression in a given sample.

Introduction

Hashimoto's thyroiditis is a chronic autoimmune disease of the thyroid that destroys thyroid cells by cell and antibody-mediated immune processes¹. It is the most common cause of primary hypothyroidism in North America with prevalence of 4-13% and it affects about 5% of Caucasians at some point in their lives. Hashimoto's disease is estimated to be 10-15 times higher in females than in men and mostly affects women aged from 30 to 50 years [1].

However, surprisingly little is known about its discoverer, Hakaru Hashimoto, who first described the disease in 1912. He presented four patients with a chronic thyroid disorder, which he termed struma lymphomatosa, characterized by diffuse lymphocytic infiltration with germinal centers, fibrosis, parenchymal atrophy and eosinophilic change in some thyroid follicular cells. He summarized the pathological findings in an article which was unrecognized for about two decades: the disease described by Hakaru Hashimoto was considered as the type of Riedel's Thyroiditis. In 1931, Graham and McCullagh used the term "Hashimoto" for the first time in the title of an article, strongly arguing that struma lymphomatosa was indeed distinct from Riedel's thyroiditis [2].

Hashimoto's thyroiditis is a disease which produces a wide variety of symptoms ranging from somatic symptoms such as cold intolerance, loss of energy, hypotension, etc. to psychiatric diseases. One of the mental diseases which is common in patients with Hashimoto's disease is depression. It is a leading cause of disability worldwide affecting more than 264 million people [3]. Despite this, depression is a common condition that often remains undiagnosed and untreated; however, symptoms are more likely to be recognized today than in past decades. The characteristic symptoms of depression include loss of interest in activities that were pleasurable in the past, sadness, irritability, feelings of worthlessness, hopelessness, guilt or anxiety, concerns over death, or suicidal ideation. Associated symptoms may include changes in appetite, weight loss or weight gain, sleep disturbances, psychomotor activity, decreased energy, indecisiveness, or distracted attention [4]. Like autoimmune thyroiditis, depression is a disease which is more common in women [3].

Even though depression is mentioned as the common psychiatric disease in patients with Hashimoto's thyroiditis, there is little evidence proving this association. Meta analysis conducted in 2019 reviewed nineteen studies comprising 21 independent samples with a total of 36 174 participants (35 168 for depression and 34 094 for anxiety). Patients with autoimmune thyroiditis (AIT), Hashimoto thyroiditis, or subclinical or overt hypothyroidism had significantly higher scores on standardized depression instruments, with an odds ratio of 3.56 (95% CI, 2.14-5.94; I² = 92.1%). For anxiety disorders, patients with AIT, Hashimoto thyroiditis, or subclinical or overt hypothyroidism had an odds ratio of 2.32 (95% CI, 1.40-3.85; I² = 89.8%). This meta-analysis establishes the association between Hashimoto's disease and depression and anxiety disorders. It proved that patients with Hashimoto's disease exhibit an increased chance of developing symptoms of depression and anxiety or of receiving a diagnosis of depression and anxiety disorders [1].

Considering the high prevalence of these diseases they have been the major topic for research. There is a lot of literature about depression and Hashimoto's thyroiditis separately in recent years but only few of them studied the association between these 2 diseases. Finding the association between them has social, medical, scientific and economic importance. If association between these 2 diseases will be found and Hashimoto's will be identified as a risk factor for development of depression. Moreover, if awareness of these connections will rise, the patients with Hashimoto's thyroiditis will recognize symptoms of depression and try to seek help. Depression is one of the most commonly not treated and underdiagnosed diseases. Based on the data from the National Health and Nutrition Examination Survey, 2005 to 2008. 58.8% of people with moderate depression (PHQ-9 10-14) have not received nor pharmacological nor mental health professional treatment, 54.9 % of people with moderate severe depression and respectively 36.9 % of people with severe depression [5]. Screening for depressive symptoms in patients with autoimmune thyroiditis might help health care professionals to diagnose depression early and on the other hand will help patients to receive proper pharmacologic and mental health professional help.

Methodology

The study design we chose was retrospective cohort study. Hashimoto's disease was considered as a risk factor for developing depression. To conduct it we decided to use a self-report - Patient Health Questionnaire (PHQ-9) (**Table 1**) which was an easy-to-use questionnaire. Filling these questionnaires took people several minutes. It consisted of 9 questions each having 4 possible answers: not at all, several days, more than half the days or nearly every day. Each of them had their individual score. Not at all - 0 score, Several days -1, more than half the days- 2, nearly every day 3. The sum of points was calculated and according to final results the severity of possible depression was assessed. 0 points- no depression, 1-4 minimal depression, 5-9 mild depression, 10-14 moderate depression, 15-19 moderately severe depression, 20-27 severe depression. Additionally, it involved 5 questions addressing patients' age, gender, ethnicity, geographic location and thyroid disorder. The identity of people who filled the questionnaire was kept anonymous. We posted this questionnaire in the global social online groups where people had various diseases of the thyroid. Next step was to create a new questionnaire for the unexposed cohort control group and compare it to our cases. The questionnaire for controls involved the same questions about age, ethnicity, gender, geographic location and PHQ-9 question. It didn't involve any questions about patient's diseases and was also posted in the global general population social online groups. After receiving results, we filtered them according to inclusion criteria and relative risk was calculated.

Inclusion Criteria

- 1- Age 36-50.
- 2- Gender- female
- 3- Ethnicity - Caucasian
- 4- Geographic location- North America/ Central America
- 5- Diagnosis of Hashimoto's Disease

Controls

Age matched females presenting with symptoms of depressive disorder based on the PHQ-9 questionnaire.

Exclusion Criteria

- 1- Males
- 2- Age below 36 and above 50.
- 3- Geographic location except North America/Central America
- 4- Ethnicity other than Caucasian
- 5- Thyroid diseases other than Hashimoto's Disease

Table 1. PHQ-9 Questionnaire

		Not at all	Several days	More than half the days	Nearly every day
1.	Little interest or pleasure in doing things	0	1	2	3
2.	Feeling down, depressed, or hopeless	0	1	2	3
3.	Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4.	Feeling tired or having little energy	0	1	2	3
5.	Poor appetite or overeating	0	1	2	3
6.	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7.	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8.	Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9.	Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Results

Data of 355 participants was analyzed. The age distribution of cases is the following: 0 to 19 - 1.7%, 20 to 35- 36%, 36 to 50 - 38% and finally 51 + was 24.3%. 97.5 % of participants identified themselves as females, 2.3% as males and 0.3% preferred not to say (**Figure 1**). The most common thyroid diseases our cases had were- Hashimoto’s Disease, Thyroid Nodules, Graves Disease, Goiter, Thyroid Cancer. Our aim was to analyze females aged 36-50 with Hashimoto’s Disease. Out of 346, 114 of them had some degree of depression and were located in North America/Central America.

What gender do you identify as?

355 responses

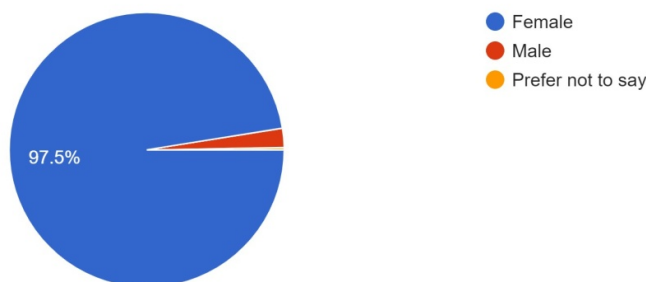


Figure 1. Gender Distribution among cases

More precisely, 1 had no depression, 12 had minimal depression, 39 had mild depression, 37- moderate depression, 14- moderate severe depression, 13- severe depression (**Figure 2**). On the other hand, a total number of 320 controls were studied and only 118 of them fit all inclusion criteria. Out of 118, 50 controls had no depression, 40 had minimal depression, 10 had mild depression, 10- moderate depression, 4 moderate severe depression and 4 had severe depression (**Figure 3**). Relative risk for developing some degree of depression for the exposed group versus unexposed group was 17.20% (RR= 1.7202, 95% CI 1.4722- 2.0099, p value< 0.001). The study demonstrated that exposure to hashimoto's disease is associated with increased disease occurrence.

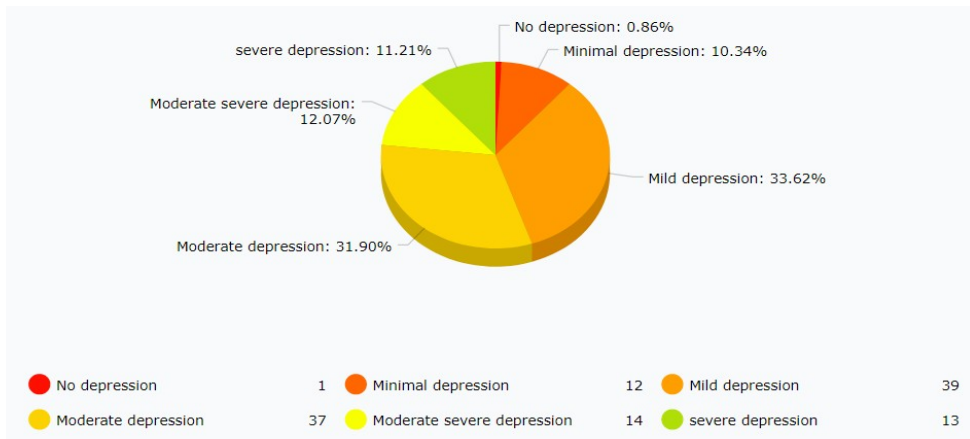


Figure 2. Distribution of severity of depression among cases

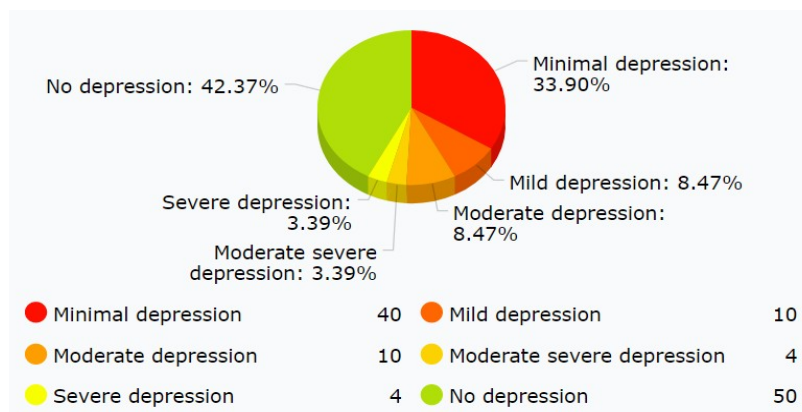


Figure 3. Distribution of severity of depression among controls

Discussion

Association between Hashimoto’s disease and depression is an important topic for both patients and physicians, but because of lack of precise information it remains underexplored. Multiple studies have already aimed to explore the link between thyroid diseases and depression. Even though it’s believed that there’s a positive relationship between those two, some of these studies showed conflicting results further proving that more thorough research about this association is needed. Researches that took place in the Netherlands [6], Norway [7] and Korea [8], did not show the significant relationship between thyroid diseases and depression, meanwhile studies held in Brazil [9] showed a significant association. Disparity of results should be attributed to regional, socioeconomic and lifestyle differences.

First studies which researched the association of thyroid disease and brain function were conducted by Marangell and Callahan using PET paradigms [10]. Interestingly, Hendrick and colleagues noticed a high occurrence of hypothyroidism among patients with therapy-resistant depression [11]. Despite these indications, no direct association between particular alterations in brain regions because of thyroid disease and the development of a depressive disorder was found yet.

Considering the importance of this topic, our study aimed to explore the association of Hashimoto’s disease and depression in 36-50 years old Caucasian females from North America/Central America. Results of our study proved a significant relationship between Hashimoto’s disease and developing a different degree of depressive disorders (RR= 1.7202, 95% CI 1.4722- 2.0099, p value < 0.00) which once again demonstrates the significance of accessing mental health problems in the patients with Hashimoto's thyroiditis.

Different degrees of depression were assessed in these patients, most common being mild depression making up 33.9 % of all cases. Only 1 patient had 0 score (no depression) on the PHQ-9 questionnaire while a total of 114 patients had some degree of it (minimal depression- 10.41%, moderate- 32.17%, moderate severe- 12.17%, severe- 11.30%).

Our results might have various implications for physicians and patients. It is known that depression is one of the most common diseases and people affected with it seek for help without knowing

the possible root cause of their disease. Besides mental dysregulation, depression can be caused by various diseases including Hashimoto's disease. Depression associated with a thyroid disease requires different treatment than usual depression. Besides typical levothyroxine treatment, selenium supplementation can help to reduce the amount of thyroid antibodies and improve mood or well-being [12].

Additionally, patients with AIT and no symptoms of depression must be aware of the vulnerability to develop psychiatric issues. As a consequence, both a screening for psychiatric symptoms is advisable in patients with AIT and a test for AIT is recommended in patients with depression. Recognizing this association can help with early identification of depressive disorders, help to educate these patients about the possible risks and provide an early treatment, which can further decrease the burden for the people with this condition.

Our study was conducted with a sample of sufficient size. We managed to investigate depression in a diverse group of patients with a variety of thyroid disorders, different age groups and ethnicities. We respected the privacy of our study participants and the answers and personal data of the cases and controls were kept private, giving them maximum chance to give honest answers.

Even though we tried minimizing the limitations of our study, there are still some topics we have to address. Our study was held in a closed online group for people with thyroid problems. We believe there are more people in need of help and compassion in these types of groups, which in itself might increase the incidence of mood disorders. Hence our research was likely affected by a sampling bias. Moreover, conducting online surveys has its disadvantages. Having face to face conversation with a patient while filling the questionnaire is more reliable and less prone to errors.

To conclude, there is known association between Hashimoto's disease and depression, but not enough evidence proving this association is available. Based on our research results we found that relative risk for developing depression in patients with Hashimoto's disease was 1.7202 (95% CI 1.4722-2.0099, p value < 0.001). Thus, we concluded that patients with Hashimoto's disease are at increased risk for developing depression.

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