



## Overview on Thyroid Disorders and Stress

**Arub Adnan Yousef<sup>1\*</sup>, Sultanah Rawi Abdullah Alanazi<sup>2</sup>,  
Fatimah Mofareh Murid Alanazi<sup>2</sup>, Sarah fereih meraid alenezi<sup>2</sup>,  
Ahmed Mahmoud R Abdullah<sup>2</sup> and Mohammed Ghannam Thallab Alharbi<sup>3</sup>**

<sup>1</sup>Department of Internal Medicine, North Medical Tower, Arar, Saudi Arabia.

<sup>2</sup>Northern Border University, Arar, Saudi Arabia.

<sup>3</sup>Internal Medicine Consultant, Prince Mohammed Bin Abdulaziz Medical City, Aljouf, Saudi Arabia.

### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** Several studies have found a link between stress and thyroid disorder, the majority of evidence supporting stress contributing to the start and progression of autoimmune illness is circumstantial, and the mechanisms by which stress impacts thyroid is not fully understood. Study aims to summarize the current evidence regarding relation between thyroid disorders and stress.

**Methodology:** MEDLINE, Embase, CINAHL, Psyc Info, and ASSIA were searched and reference lists of included studies were searched. Studies were included that described relation between stress and thyroid disorders. No software has been utilized to analyze the data. The data was extracted based on specific form that contains (Author's name, publication year, country, methodology and results).

**Results:** The search of the mentioned databases returned a total of 87 studies that were included for title screening. 54 of them were included for abstract screening, which lead to the exclusion of 32 articles. The remaining 22 publications full-texts were reviewed. The full-text revision lead to the exclusion of 13 studies, and 9 were enrolled for final data extraction.

**Conclusion:** There is evidence regarding the association of thyroid disorders with stress. These findings add to the growing literature suggesting that thyroid function changes may be associated with stress.

*Keywords: Hypothyroidism; stress; thyroid disorders; autoimmune disorders.*

## 1. INTRODUCTION

Social development created a new atmosphere for humans, which is accompanied by a rise in stressful life elements. This can result in both adaptation and dis-adaptation of the organism, which can lead to permanent pathological alterations [1]. Many genetic, developmental, and environmental variables influence stress response. Many studies have shown that stresses can alter the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) pathways [2,3]. Thyroid hormones have traditionally been thought to be vital in growth, differentiation, and metabolism. Thyroid hormones also have effects that go beyond development and maturation and are required for appropriate body function in adults. Thyroid hormones also have a significant impact on metabolic control, including oxygen use and carbohydrate, protein, and lipid metabolism [4].

Despite the recognition, the function of stress in the production of pathological alterations in the thyroid gland remains unknown. Numerous research studies have shown that hypothyroidism reduces humoral and cell-mediated immune responses, which may be restored by returning to a euthyroid condition. It suggests that stress may have a role in the start and progression of autoimmune illnesses with unclear mechanisms of action. Autoimmune thyroid diseases (AITD) are the most prevalent autoimmune illnesses, affecting more than 5% of the general public [5]. Hashimoto's thyroiditis (HT), the most prevalent kind of autoimmune thyroiditis, is distinguished by the presence of antithyroid antibodies, both with and without hypothyroid manifestations (e.g. weight gain, fatigue, cold intolerance, hair loss, dry skin, constipation etc.) [6] However stress has not been identified as a risk factor for HT, it is widely known that it affects endocrine and immunological processes that are also involved in HT [7].

Stress alters the release of numerous hormones, which influence immune function by boosting or lowering immunological activity. Thyroid hormones are required for the maintenance of neurotransmitters related with stress, and they also have a substantial influence on immunological response. Hypothyroidism has been linked to thymic growth depression and a

reduction in the number of circulating lymphocytes. Alterations in stress and thyroid hormones, prolactin, cortisol, thyroid stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4), are the primary causes of such changes in the body system [8].

**Study Rationale:** Although several studies have found a link between stress and thyroid disorder, the majority of evidence supporting stress contributing to the start and progression of autoimmune illness is circumstantial, and the mechanisms by which stress impacts thyroid is not fully understood.

**Study Objective:** The main objective of our study is to summarize the current evidence regarding relation between thyroid disorders and stress.

## 2. METHODOLOGY

**Search strategy:** Search strategies were combined for papers on stress and thyroid, hypothyroidism and stress and thyroid autoimmune disorders with stress together with qualitative methodological filters. MEDLINE, Embase, CINAHL, PsycInfo, and ASSIA were searched from 2000 until April 2021, and reference lists of included studies were searched.

**Study selection:** Studies were included that described relation between stress and thyroid disorders. Papers were included that either focused on hypothyroidism or stress. Papers were excluded that examined other specific objectives. Paired reviewers independently screened titles and abstracts of all identified references. Paired reviewers independently assessed full-text articles. Disagreements were resolved by discussion. Non-English studies were excluded.

**Statistical Analysis:** The data was analyzed without the use of any program. The data was extracted using a specified form that included (Author's name, publication year, country, technique, and results). The data was analyzed by the group members in order to identify the first findings and the modalities for executing the surgical treatment. To confirm the authenticity of the results and to reduce errors, each member's results were double-revised.

### 3. RESULTS

The search of the mentioned databases returned a total of 87 studies that were included for title screening. 54 of them were included for abstract screening, which lead to the exclusion of 32 articles. The remaining 22 publications full-texts were reviewed. The full-text revision lead to the exclusion of 13 studies, and 9 were enrolled for final data extraction (Table 1).

The included studies had different study designs.

Effraimidis, Grigoris et al. reported that; exposure to stress was not different between subjects who developed or did not develop TPO-Ab (study A). No differences were observed in stress questionnaires between hyper-/hypothyroid cases and controls at any time point, but hypothyroid cases had less negative feelings than controls at the time of diagnosis (study B) [9].

Markomanolaki, Zoe S et al. found that; patients in the intervention group demonstrated statistically significant beneficial decrements in the rate change of anti-TG titers and the levels of stress, depression and anxiety as well as better lifestyle scores, compared to the control group [10].

Fukao, Atsushi et al. reported that; T3 has been linked closely to depression and anxiety because of its regulatory effects on serotonin and noradrenalin. It has known that in many cases, the mental symptoms persist even after normalization of thyroid function by treatment. Psychosocial factors including stress have been associated with mental symptoms even after thyroid function normalization in Graves' disease and a combination of mental disorders have been related to the exacerbation of hyperthyroidism [11].

Martin-du Pan, R C. found that; a stress factor has been encountered in 11% cases of Graves' disease and in 6% of Hashimoto's and thyroid nodes. Graves' disease occurred after a pregnancy in 25% of the women in child bearing age versus 10% of the cases of Hashimoto's ( $p < 0.05$ ) and 13% of the thyroid nodes. The role of stressors, if any, in triggering Graves' disease seems to be weak and dubious compared to the role of pregnancy and post-partum [12].

Jung, Sun Jae et al. found significant associations for PTSD only with hypothyroidism.

PTSD was not associated with risk of Graves' hyperthyroidism. Associations were similar in sensitivity analyses restricted to outcomes with onset after 2008, when PTSD was assessed [13].

Bathla, Manish et al. found that; about 63% out of the total patients screened showed some degree of anxiety based on HAM-A. The most common anxiety symptom among the males was depressed mood (70.0%) and among females was anxious mood (92.85%) [14].

A study aimed to detect the possible association between shift work and subclinical autoimmune hypothyroidism by Magrini, A et al. reported that; autoimmune hypothyroidism was diagnosed in 7.7% shift workers and in 3.8% day-time workers with a statistically significant difference: Altered anti- TPO autoantibodies were found in 13.6 percent shift workers and in 8.6% day-time workers [15].

Tolozza, Freddy J K et al. results showed FT3 and TT3 levels were greater in PTSD patients compared to controls. TSH, FT4, and TT4 levels did not differ across groups. In the subgroup study, individuals with combat-related PTSD exhibited greater FT3 and TT3 than controls. Patients with non-combat-related PTSD, on the other hand, had no variations in FT3 or TT3 levels as compared to controls [16].

Chaudhuri, Arunima, and Samarjit Koner There was no significant difference in PSLES scores between the two groups, according to the results. There was a substantial positive association between PSS scores and TSH levels, with  $r$  values of 0.97 in G1 and 0.26 in G2, respectively [17].

### 4. DISCUSSION

It is known that various psychosocial factors such as traumas, life events, daily life stressors, social support, and various personality traits affect the occurrence and aggravation of mental disorders in many studies. Thyro-stress is defined as an emotional state, characterized by extreme apprehension, discomfort, or dejection, caused by the challenges and demand of living with thyroid disorders such as hypothyroidism [18]. There is a significant evidence to show that hypothyroidism is usually associated with an impact on psychological health. The physical complaints may impair emotional health and quality of life. However, not much attention has

**Table 1. Author, study region, year of publication, study type, sample size and outcome**

Author	Study Region	Study type	Sample size	Outcome
Effraimidis, Grigoris et al. (2012) [9]	Netherlands	Two nested case-control studies in a prospective cohort	790 euthyroid women	data suggest that stress is not involved in the pathogenesis of AITD.
Markomanolaki, Zoe S et al. (2019) [10]	Greece	Randomized Controlled Trial	60 women with Hashimotos' thyroiditis HT	short-term stress management had beneficial effects on the anti-TG titers, the lifestyle and the psychological status of women with HT.
Fukao, Atsushi et al. 2019 [11]	Japan	Review Article	-	Psychosocial factors including stress and disease awareness as well as biological factors including the effects of thyroid hormones may influence the course of a disease.
Martin-du Pan, R C. (1998) [12]	France	Retrospective study	98 patients with Graves' disease have been compared to 95 patients with Hashimoto's thyroiditis and to 97 patients with benign thyroid nodules (control group)	decrease of immunosuppressive hormones occurring after stress or delivery could induce a rebound autoimmune reaction responsible for the thyroid disease. In Hashimoto's thyroiditis, stress and pregnancies do not seem to have any triggering role.
Jung, Sun Jae et al. (2019) [13]	USA	Longitudinal cohort study	45 992 women	Posttraumatic stress disorder was associated with higher risk of hypothyroidism in a dose-dependent fashion. Highlighted awareness for thyroid dysfunction may be especially important in women with PTSD.
Bathla, Manish et al. (2016) [14]	India	Cross-sectional study	100 patients diagnosed as hypothyroidism	Psychiatric symptoms/disorders are common in patients with thyroid dysfunction.
Magrini, A et al. (2006) [15]	Italy	Retrospective study	220 shift workers and 422 day-time workers	data show a significant association between shift work and autoimmune hypothyroidism.
Toloza, Freddy J K et al. (2020) [16]	-	Systematic Review and Meta-Analysis	10 observational studies included 674 adults (373 PTSD, 301 controls).	There is scarce evidence regarding the association of thyroid disorders with PTSD.
Chaudhuri, Arunima, and Samarjit Koner. (2020) [17]	India	Pilot study	200 newly diagnosed female hypothyroid patients	Females of reproductive age group with clinical and subclinical hypothyroidism faced the same amount of stressful life events. High TSH was positively correlated with high score on Perceived Stress Scale scores

been paid till date to the psychosocial aspects of hypothyroidism [19]. Pelúcio et al. searched 27 and results of 14 studies proved the association of thyroid disease with psychiatric disorders affecting the quality of life. Anxiety and depression disorders were highly prevalent in the population with hypothyroidism [20]. Walsh et al. in a study found no association between thyroid function and psychological well-being [21].

Two case–control studies evaluated the role of stressful events in HT or postpartum thyroiditis. They concluded that stress was not a trigger in either condition [22,23]. A recent population study also did not find a relationship between stressful life events and the presence of anti-TPO antibodies in euthyroid women [24].

The association of stressful life events with the onset of GD was subsequently confirmed by several other case–control studies in different ethnic populations. Recent studies [25,26] suggest that psychosocial factors including emotional stress are related to the onset of GD. Winsa et al. [27] reported the first large population-based case-control study demonstrating a relationship between stress and graves disease GD. Topc et al. [28] reported by a structured interview that according to a stressful life events scale, 45 GD patients had significant differences with respect to 36 healthy controls when negative events number and impact were considered.

Two previous studies conducted by Pan [29] and Rossana [30], respectively, did not find association between life events and the development of thyroid dysfunction which was on the live with one study in our results by Effraimidis, Grigoris et al. [9] who reported that stress is not involved in the pathogenesis of AITD.

Abnormal thyroid function is prevalent among women and has been linked to increased risk of chronic disease. Women have major roles to play in the collective social well-being. Stress may lead to early aging and death or sometimes in reduced levels of performances in females. Jung, Sun Jae et al. [13] evaluated trauma exposure and PTSD symptoms in relation to incident thyroid dysfunction and found that PTSD is associated with higher risk of hypothyroidism in a dose-dependent fashion. Chaudhuri, Arunima, and Samarjit Koner also found that females of reproductive age group with clinical and subclinical hypothyroidism faced the same amount of stressful life events [17].

## 5. CONCLUSION

There is evidence regarding the association of thyroid disorders with stress. These findings add to the growing literature suggesting that thyroid function changes may be associated with stress.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Chrousos GP. Stress and disorders of the stress system. *Nat Rev Endocrinol.* 2009;5 (7):374–81.
2. Kyrou I, Chrousos GP, Tsigos C. Stress, visceral obesity, and metabolic complications. *Ann NY Acad Sci.* 2006; 1083:77–110.
3. Li B. et al. Establishment and comparison of combining disease and syndrome model of asthma with “kidney yang deficiency” and “abnormal savda”. *Evid Based Complement Alternat Med* 2013;658364.
4. Mizokami T, Wu Li A, El-Kaissi S, Wall JR. Stress and thyroid autoimmunity. *Thyroid.* 2004;14(12):1047-55. DOI: 10.1089/thy.2004.14.1047. PMID: 15650357.
5. Bagnasco M, Bossert I, Pesce G. Stress and autoimmune thyroid diseases. *Neuroimmunomodulation.* 2006;13(5-6): 309-17. DOI: 10.1159/000104859. Epub 2007 Aug 6. PMID: 17709953.
6. Hadj-Kacem H, Rebuffat S, Mnif-Féki M, Belguith-Maalej S, Ayadi H, Péraldi-Roux S. Autoimmune thyroid diseases: Genetic susceptibility of thyroid-specific genes and thyroid autoantigens contributions. *Int J Immunogenet.* 2009;36:85–96.
7. Chrousos GP, Elenkov IJ. Interactions of the endocrine and immune systems. In: DeGroot LJ, Jameson JL (eds.), *Endocrinology*, Saunders Elsevier, Philadelphia, PA. 2006;1:799–818

8. Kav Vedhara, Jeremy Miles, Paul Bennett, Sue Plummer, Deborah Tallon, Emily Brooks, Lone Gale, Katherine Munnoch, Christa SchreiberKounine, Clare Fowler, Stafford Lightman, Alistair Sammon, Zenon Rayter, John Farndon, An investigation into the relationship between salivary cortisol, stress, anxiety and depression. *Biological Psychology*. 2003;62:89-96.
9. Effraimidis, Grigoris et al. Involvement of stress in the pathogenesis of autoimmune thyroid disease: a prospective study." *Psychoneuroendocrinology*. 2012;37(8): 1191-8.  
DOI:10.1016/j.psyneuen.2011.12.009
10. Markomanolaki, Zoe S et al. "Stress Management in Women with Hashimoto's thyroiditis: A Randomized Controlled Trial." *Journal of molecular biochemistry*. 209;8 (1):3-12.
11. Fukao, Atsushi, et al. Graves' disease and mental disorders. *Journal of clinical & translational endocrinology*. 2019;19 100207.  
DOI:10.1016/j.jcte.2019.100207.
12. Martin-du Pan, RC. "Rôle déclenchant des stress émotionnels et des accouchements. Dans la survenue de 98 cas de maladie de Basedow, comparés à 96 cas de thyroïdite de Hashimoto et 97 cas de nodules thyroïdiens" [Triggering role of emotional stress and childbirth. Unexpected occurrence of Graves' disease compared to 96 cases of Hashimoto thyroiditis and 97 cases of thyroid nodules]. *Annales d'endocrinologie*. 1998;59(2):107-12.
13. Jung, Sun Jae, et al. "Posttraumatic stress disorder and incidence of thyroid dysfunction in women." *Psychological medicine*. 2019;49(15):2551-2560.  
DOI:10.1017/S0033291718003495
14. Bathla, Manish et al. "Prevalence of anxiety and depressive symptoms among patients with hypothyroidism." *Indian journal of endocrinology and metabolism*. 2016;20(4):468-74.  
DOI:10.4103/2230-8210.183476
15. Magrini A, et al. "Shift work and autoimmune thyroid disorders." *International Journal of immunopathology and pharmacology*. 2006;19,4 Suppl: 31-6.
16. Toloza, Freddy JK, et al. "Association of Thyroid Function with Posttraumatic Stress Disorder: a Systematic Review and Meta-Analysis." *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists* . 2020;26(10):1173-1185.  
DOI:10.4158/EP-2020-0104
17. Chaudhuri, Arunima, and Samarjit Koner. A study of correlation of perceived stress and thyroid function among females in a rural population of reproductive age group." *Medical Journal of Dr. DY Patil Vidyapeeth*. 2020;13.1:30.
18. Khare, Mayuri, Poonam Singh, and Vinod Singh. "ISSN 2320-138X ISSN 2320-138X."
19. Kalra S, Verma K, Balhara YP. Thyro-stress. *Indian J Endocrinol Metab*. 2017; 21:632-3.
20. Pelúcio L, Nardi AE, Ornelas AC, Levitan M. Psychiatric disorders and quality of life in patients with hypothyroidism: A narrative review. *J Depress Anxiety*. 2016;5:241.
21. Walsh JP, Ward LC, Burke V, Bhagat CI, Shiels L, Henley D, et al. Small changes in thyroxine dosage do not produce measurable changes in hypothyroid symptoms, well-being, or quality of life: Results of a double-blind, randomized clinical trial. *J Clin Endocrinol Metab*. 2006; 91:2624-30
22. Martindupan RC. Triggering role of stress and pregnancy in the occurrence of 98 cases of Graves' disease compared to 95 cases of Hashimoto's thyroiditis and 97 cases of thyroid nodules. *Ann. Endocrinol. (Paris)*. 1998;59:107 – 112.
23. Oretti RC, Harris B, Lazarus JH, et al. Is there an association between life events, postnatal depression and thyroid dysfunction in thyroid antibody positive women? *Int. J. Soc. Psychiatry*. 2003;49: 70 – 76.
24. Streder IGA, Prummel MF, Tijssen JGP, et al. Stress is not associated with thyroid peroxidase autoantibodies in euthyroid women. *Brain Behav. Immunity*. 2005;19: 203 – 206.
25. Fukao A, Takamatsu J, Miyauchi A, Hanafusa T. *Endocrine diseases*. iConcept Press; 2014. Stress and thyroid disease. ISBN: 978-1-922227-78-2.
26. Mizokami T, Wu Li A, El-Kaissi S, Wall JR. Stress and thyroid autoimmunity. *Thyroid*. 2004;14:1047–1055.
27. Winsa B, Adami HO, Bergström R, Gamstedt A, Dahlberg PA, Adamson U. Stressful life events and Graves' disease. *Lancet*. 1991;338:1475–1479.

28. Topcu CB, Celik O, Tasan E. Effect of stressful life events on the initiation of Graves' disease. *Int J Psychiatry Clin Pract.* 2012;16(4):307–311. Epub 2011 Dec 5.
29. Pan RM-D. Triggering role of stress and pregnancy in the occurrence of 98 cases of Graves' disease compared to 95 cases of Hashimoto thyroiditis and 97 cases of thyroid nodules. *Annales d Endocrinologie.* 1998;59(2):107–112.
30. Oretti RG, Harris B, Lazarus JH, Parkes AB, Crownshaw T. Is There an Association between Life Events, Postnatal Depression and Thyroid Dysfunction in Thyroid Antibody Positive Women? *Int J Soc Psychiatry.* 2003;49(1):70–76.

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