Review Article

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20210034

Long term effect of nutrition on thyroid disease

Mohammed Salah Hussein^{1,2}*, Lama Samir Asiri³, Sadeem Wadia Asali⁴, Abdulaziz Mohsin Alawlaqi⁵, Gadeer Sameer Sibah³, Bader Hadi Alshammari⁶, Saltanh Mohammed Gaban³, Alanood Nawaf Almansory⁷, Hind Mousa AlGhamdi⁸, Jinan Hikmat Msallati⁹, Hassan Mohammed Al Dhaif¹⁰, Ali Salem Al Rayshan¹¹

Received: 18 December 2020 **Accepted:** 04 January 2021

*Correspondence:

Dr. Mohammed Salah Hussein, E-mail: dr_msalahali@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Many forms of thyroid diseases have been classified under autoimmune thyroid disease. These include hyperthyroidism or commonly known as Grave's disease, and hypothyroidism commonly identified as Hashimoto's thyroiditis. Many nutritional elements have been linked to the function of the thyroid gland as any disturbance in these elements can lead to the development of relevant thyroid diseases. The most important elements include iodine, iron, selenium, zinc, and soy. In this current manuscript, we aimed to discuss the effect of these nutritional elements on the development of thyroid diseases by reviewing relevant studies in the literature. Although it is widely known that iodine is an essential component for the synthesis and release of these hormones, exaggerated intake of iodine can also lead to the development of hypothyroidism by negative feedback mechanisms. Besides, it can also trigger abnormal autoimmune reactions which can lead to the development of AITD. Selenium is another important factor and evidence shows that it has been associated with Grave's thyroiditis, however, further evidence is needed as recommended by previous investigations. Clinicians should also take care of iron, zinc, and soy levels during management to obtain a better prognosis.

Keywords: Thyroid, Autoimmune, Nutrition, Iodine, Iron, Selenium

INTRODUCTION

Statistics show that the thyroid gland is the commonest organ where autoimmune diseases occur.¹ Research shows that postmortem findings of 40% and 20% of white

males and females in the United States, respectively, indicated the presence of lymphocytic infiltration of the thyroid gland which is also similar to the rates reported by a study from the United Kingdom.² Lower rates by half were noticed in black Americans and Japenese as

¹Department of Gastroenterology and Endoscopy, Dr. Samir Abbas Hospital, Jeddah, Saudi Arabia

²Department of Internal Medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

³College of Pharmacy, Batterjee Medical College, Jeddah, Saudi Arabia

⁴Community Pharmacy, Al-Dawaa Pharmacies, Jubail, Saudi Arabia

⁵Pharmaceutical Care, Ranyah General Hospital, Ranyah, Saudi Arabia

⁶College of Pharmacy, ⁷College of Medicine, University of Hail, Hail, Saudi Arabia

⁸College of Pharmacy, Princess Nourah Bint Abdul Rahman University, Riyadh, Saudi Arabia

⁹College of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

¹⁰College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

¹¹Department of Pharmacy, King Khalid Hospital, Najran, Saudi Arabia

reported by the same study. Hashimoto was the first to report this phenomenon as he also noticed the presence of circulating antibodies against the thyroid gland naming it autoimmune thyroid disease (AITD).³ Many factors as genetics, environment, and nutrition contribute to the development of AITD.⁴

Many forms of thyroid diseases have been classified under AITD. These include hyperthyroidism commonly known as Grave's disease. hypothyroidism commonly identified as Hashimoto's thyroiditis.⁴ The mechanism of hypothyroidism in the latter is that the thyroid gland is destroyed by abnormal activation of an autoimmune cascade leading to a state of impaired synthesis and production of thyroid hormones which can clinically be noticed by the presence of generalized fatigue, constipation, weight gain, reduced tolerability to cold and exercise, depression and dry skin.⁵ It has been estimated that this disease affects around 2% of male and 15% of female patients that are usually aged over 60 years old. 6 Thyroid peroxidase (TPO), which is an essential enzyme for the synthesis of thyroid hormones by oxidation of iodide to iodine, is affected by the presence of antibodies against it in this disease. Similarly, other antibodies have been indicated to attack another protein, namely thyroglobulin (Tg) which is also essential in the process of thyroid hormone synthesis.4 Grave's disease, on the other hand, there is hyperthyroidism which simply refers to a state of increased thyroid hormones leading to a cascade of symptoms as irritability, intolerability to hot weather, weight loss, rapid heartbeats, and abnormal eve looking as ball protrusion, namely Grave's orbitopathy. Unlike Hashimoto's thyroiditis, the antibodies in this disease are directed against the thyroidstimulating hormone receptors leading to further activation and stimulation of the thyroid gland. 4,7,8

Many nutritional elements have been linked to the function of the thyroid gland as any disturbance in these elements can lead to the development of relevant thyroid diseases. The most important elements include iodine, iron, selenium, zinc, and soy. 9,10 In this current manuscript, we aim to discuss the effect of these nutritional elements on the development of thyroid diseases by reviewing relevant studies in the literature.

An extensive literature search of the Medline, Cochrane, and EMBASE databases was performed on 21 December 2020 using the medical subject headings (MeSH) or a combination of all possible related terms. Studies discussing the long term effect of nutrition on thyroid disease were screened for relevant information. We did not pose any limits on date, language, or publication type.

IODINE

Iodine is a major component of the thyroid hormones including thyroxine (T4) and triiodothyronine (T3) and also plays an important role in the synthesis of these hormones within the thyroid follicles. ¹¹ The relationship

between the development of autoimmune thyroiditis secondary to the development of thyroid antibodies in the patient's serum is a complex one as evidence shows that extra or reduced iodine levels below normal might be a trigger or a piece of evidence for the presence of circulating thyroid antibodies.¹² Research also showed that the presence of TPO-antibodies and thyroglobulin (Tg) antibodies have been commonly found in cohorts suffering from AITD irrespective of the frequency of iodine intake, being high, moderate, or low. Iodine deficiency might lead to the development of an accessory thyroid goiter which is considered a foreign antigen leading to the synthesis of thyroid antibodies. 13 On the other hand, many previous studies also showed that excess iodine intake beyond the recommended levels or intake of iodine in large amounts in iodine therapy in previous iodine deficiency-related diseases can also lead to the development of AITD. 14-18 A study from China showed that the prevalence of AITD was found to be 0.5 to 2.8% after the introduction of iodine for three years based on the previous iodine intake of the included patients. 14 Denmark is considered an area with mild to moderate iodine intake at the time when a study was conducted to investigate the 5 year effect of iodine fortification around the country in dietary supplementation. The study authors reported that although the serum iodine and iodine status of the investigated patients were acceptable, the levels of thyroid antibodies have increased by 14-20% from the baseline levels.¹⁸ This effect, however, was deemed to be short-term, and therefore, based on this experience, optimization of iodine in the patients' daily diet has been recommended.¹² The mechanism behind which AITD is initiated is the possibility of the high immunogenicity of the relevant Tg which are rich in iodine and are released and synthesized from the thyroid gland which may alter the immune system against the thyroid tissue. 19,20 Another explanation has also been proposed regarding the abnormal activation of an intracellular adhesion molecule that is usually present within the thyrocytes leading to accelerated tissue inflammation and infiltration.²⁰ This theory has been evidenced by previous animal studies and has been proven to be true.²¹ Excess iodine might also play a role in inhibiting the development of T-regulatory cells and increasing the synthesis and release of T-helper 17 cells that can infiltrate the thyroid gland and can initiate an autoimmune reaction leading to a series of cell necrosis and apoptosis.22

Excessive iodine might also, in addition to initiating an AITD reaction, cause hypothyroidism. ^{23,24} The story starts as excess iodine has been taken up by the gland leading to increased release of excess thyroid hormones. This leads to the activation of a counter-regulatory mechanism leading to decreasing the synthesis and release of thyroid hormones or in other words hypothyroidism. Moreover, high doses of iodine intake might affect thyroid hormone synthesis and release as such large amounts might affect the organification of the required amounts of iodine to pursue these processes which is called the Wolff Chaikoff

effect. ²⁵ A previous report by Du et al reported that the prevalence of subclinical hypothyroidism was noticed to be higher in areas with increased intake of iodine. Therefore, recommendations should be applied regarding the intake of the recommended daily amounts of iodine which is estimated to be 150 μ g for adults, 220 μ g, and 290 μ g for pregnant and breastfeeding women, respectively. ²⁶ On the other hand, recommendations by the World Health Organization suggest that the optimum daily amount of iodine should be 75 μ g. ¹⁰

SELENIUM

Selenium is a key element that can be profusely found within the thyroid gland as it has been found to take part in many cellular processes within the thyroid gland and also participates in the peripheral synthesis of thyroid hormones.²⁷ Some selenoproteins have been identified to take action in such processes.²⁸ These include deiodinases, glutathione peroxidases, selenoprotein S which has all been found within the thyroid gland.¹⁰ Many thyroid dysfunctional events may occur secondary to selenium deficiency. These include hypothyroidism or subclinical hypothyroidism, thyroid cancer, or enlargement, and AITD or Grave's disease. 29-31 A previous study by Wu et al which was conducted on 6000 Chinese patients, showed that having an adequate selenium status affected the prevalence of thyroid disease in the investigated population, irrespective of iodine levels.³⁰ However, previous studies suggested an adequate intake of iodine was more than enough to reverse the pathological status of the thyroid gland. 14 Previous studies also showed that selenium deficiency will lead to the development of Grave's disease mostly as presented in their populations. 32,33 A previous Chinese study reported a significant negative correlation between selenium levels in their patients' serum and the presence of TPO and Tgantibodies.33 Another case-control Australian study reported that reduced selenium levels in their cases were significantly associated with the severity of an underlying Grave's condition.³⁴ However, selenium levels in Grave's disease might be reduced secondary to the inflammation that the condition induces within the thyroid gland, and therefore, it would not be a healthy judgment that selenium reduction can cause Grave's and not vice versa.35,36 A previous randomized controlled trial (RCT) showed that selenium administration was associated with significant improvement in mild Grave's orbitopathy.⁷ The authors also showed that in these patients, significant improvement of their quality of life, and regression of the disease was noticed, in addition to less frequent improvement of eye disease. Many previous systematic reviews have analyzed the results of the previously published RCT.^{37,38} Wichman et al conducted the most recent one and analyzed 16 RCTs and reported that the results of their analysis showed that selenium supplementation was significantly associated with reducing serum TPO antibodies of the included patients at a follow-up period of 3, 6, and 12 months.³⁷ The authors, however, reported that in chronic AITD, the significant effect was only noticed at three months of follow-up. There are no new big-sized studied to ameliorate this effect, however, promising protocols for big studies have been published and we hope that by the end of the study that further evidence shall be provided.

IRON, ZINC, SOY

Iron decreases the efficacy of the thyroid gland to synthesize thyroid hormones as it decreases the activity and action of the TPO.³⁹⁻⁴¹ A previous investigation showed that thyroid hormones were low in women with low iron profiles compared to other patients who exhibited sufficient stores. 42 It has also been reported that iron deficiency can affect the disappearance of symptoms and full recovery in 5-10% of patients suffering from thyroid diseases even after initiating a specific treatment.⁴³ Therefore, it is essential to supplement iron for patients with an iron deficiency that are being treated for thyroid disease. This was indicated by a previous study which reported that significant improvement of symptoms of hypothyroidism was noticed in their included population after iron supplementation as they were suffering from iron deficiency.⁴⁴ In addition to iron deficiency, previous reports also showed that zinc is an important factor for the integrity of the function of the thyroid gland and its deficiency can lead to the development of subclinical hypothyroidism due to its value regarding the activity of the deiodinase II compound.⁴⁵ A previous study on animals showed that zinc deficiency led to a reduction of the thyroid hormones by about 30% from the normal baseline levels. 46 The same effect was also noticed in humans as a previous study showed that normalization of hypothyroidism was noticed in a population with moderate zinc deficiency after being treated with zinc sulfate for 12 months.⁴⁷ Although soy derivatives have shown great benefits in many aspects regarding the cardiovascular system and treating cancer in addition to managing menopausal irregularities, evidence shows that they have harmful effects on the thyroid gland.48 Sathyapalan et al concluded that patients with subclinical hypothyroidism and are being on daily soy supplementation products can easily develop hypothyroidism.⁴⁹ In the same context, Mittal et al reported that in their population of women that were treated with a daily intake of 75 mg of isoflavones, they found that the level of T3 was significantly reduced in these women.⁵⁰

CONCLUSION

Evidence from the reviewed studies in the literature shows that many nutritional components are involved in thyroid hormone synthesis and functions. Although it is widely known that iodine is an essential component for the synthesis and release of these hormones, exaggerated intake of iodine can also lead to the development of hypothyroidism by negative feedback mechanisms. Besides, it can also trigger abnormal autoimmune reactions which can lead to the development of AITD.

Selenium is another important factor and evidence shows that it has been associated with Grave's thyroiditis, however, further evidence is needed as recommended by previous investigations. Clinicians should also take care of iron, zinc, and soy levels during management to obtain a better prognosis.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

REFERENCES

- 1. McLeod DS, Cooper DS. The incidence and prevalence of thyroid autoimmunity. Endocrine. 2012;42(2):252-65.
- 2. Okayasu I, Hara Y, Nakamura K, Rose NR. Racial and age-related differences in incidence and severity of focal autoimmune thyroiditis. Am J Clin Pathol. 1994;101(6):698-702.
- 3. Duntas L, Hiromatsu Y, Amino N. Centennial of the Description of hashimoto thyroiditis-two thought-provoking events. Thyroid. 2013;23.
- 4. Effraimidis G, Wiersinga WM. Mechanisms in endocrinology: autoimmune thyroid disease: old and new players. Eur J Endocrinol. 2014;170(6):R241-52.
- 5. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmun Rev. 2014;13(4-5):391-7.
- 6. Nacamulli D, Petricca D, Mian C. Selenium and autoimmune thyroiditis. J Endocrinol Investig. 2013;36(10):8-14.
- Marcocci C, Kahaly GJ, Krassas GE. Selenium and the course of mild Graves' orbitopathy. N Engl J Med. 2011;364(20):1920-31.
- 8. Brent GA. Clinical practice. Graves' disease. N Engl J Med. 2008;358(24):2594-605.
- 9. Rayman MP. Multiple nutritional factors and thyroid disease, with particular reference to autoimmune thyroid disease. Proc Nutr Soc. 2019;78(1):34-44.
- Mezzomo TR, Nadal J. Effect of nutrients and dietary substances on thyroid function and hypothyroidism. Demetra: Food, Nutr Health. 2016; 11(2):427.
- 11. Koibuchi N. Molecular mechanisms of thyroid hormone synthesis and secretion. Nihon Rinsho. 2012;70(11):1844-8.
- 12. Laurberg P, Cerqueira C, Ovesen L, Rasmussen LB, Perrild H, Andersen S, Pedersen IB, Carlé A. Iodine intake as a determinant of thyroid disorders in populations. Best Pract Res Clin Endocrinol Metab. 2010;24(1):13-27.
- Pedersen IB, Knudsen N, Jørgensen T, Perrild H, Ovesen L, Laurberg P. Thyroid peroxidase and thyroglobulin autoantibodies in a large survey of populations with mild and moderate iodine deficiency. Clin Endocrinol. 2003;58(1):36-42.

- 14. Teng W, Shan Z, Teng X, et al. Effect of iodine intake on thyroid diseases in China. N Engl J Med. 2006;354(26):2783-93.
- 15. Teng X, Shan Z, Chen Y. More than adequate iodine intake may increase subclinical hypothyroidism and autoimmune thyroiditis: a cross-sectional study based on two Chinese communities with different iodine intake levels. Eur J Endocrinol. 2011;164(6):943-50.
- 16. Peng NC, Shi LX, Zhang Q. An epidemiological survey of the prevalence of thyroid diseases in mild iodine deficiency city after salt iodization. Zhonghua nei ke za zhi. 2013;52(1):16-20.
- 17. Zhang JY, Li SM, Leng JL. Changes of the spectrum on thyroid disease after the ten-year implementation of universal salt iodization in Guangxi Zhuang Autonomous Region. Zhonghua liu xing bing xue za zhi. 2013;34(10):970-4.
- 18. Pedersen IB, Knudsen N, Carlé A. A cautious iodization programme bringing iodine intake to a low recommended level is associated with an increase in the prevalence of thyroid autoantibodies in the population. Clin Endocrinol. 2011;75(1):120-6.
- 19. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. Lancet Diabetes Endocrinol. 2015; 3(4):286-95.
- 20. Burek CL, Talor MV. Environmental triggers of autoimmune thyroiditis. J Autoimmun. 2009;33(3-4):183-9.
- 21. Sharma R, Traore K, Trush MA, Rose NR, Burek CL. Intracellular adhesion molecule-1 up-regulation on thyrocytes by iodine of non-obese diabetic.H2(h4) mice is reactive oxygen species-dependent. Clin Exp Immunol. 2008;152(1):13-20.
- 22. Duntas LH. The role of iodine and selenium in autoimmune thyroiditis. Horm Metab Res. 2015;47 (10):721-6.
- 23. Tan L, Sang Z, Shen J. Prevalence of thyroid dysfunction with adequate and excessive iodine intake in Hebei Province, People's Republic of China. Public health Nutr. 2015;18(9):1692-7.
- 24. Sun X, Shan Z, Teng W. Effects of increased iodine intake on thyroid disorders. Endocrinol Metab. 2014; 29(3):240-7.
- 25. Chung HR. Iodine and thyroid function. Ann Pediatr Endocrinol Metab. 2014;19(1):8-12.
- 26. Du Y, Gao Y, Meng F. Iodine deficiency and excess coexist in china and induce thyroid dysfunction and disease: a cross-sectional study. PLoS One. 2014;9 (11):e111937.
- 27. Köhrle J. Selenium and the thyroid. Curr Opin Endocrinol Diabetes Obes. 2013;20(5):441-8.
- 28. Schmutzler C, Mentrup B, Schomburg L, Hoang-Vu C, Herzog V, Köhrle J. Selenoproteins of the thyroid gland: expression, localization and possible function of glutathione peroxidase 3. Biol Chem. 2007;388 (10):1053-9.
- 29. Derumeaux H, Valeix P, Castetbon K. Association of selenium with thyroid volume and echostructure in 35- to 60-year-old French adults. Eur J Endocrinol. 2003;148(3):309-15.

- 30. Wu Q, Rayman MP, Lv H. Low population selenium status is associated with increased prevalence of thyroid disease. J Clin Endocrinol Metab. 2015;100 (11):4037-47.
- 31. Rasmussen LB, Schomburg L, Köhrle J. Selenium status, thyroid volume, and multiple nodule formation in an area with mild iodine deficiency. Eur J Endocrinol. 2011;164(4):585-90.
- 32. Bülow Pedersen I, Knudsen N, Carlé A. Serum selenium is low in newly diagnosed Graves' disease: a population-based study. Clin Endocrinol. 2013;79 (4):584-90.
- 33. Liu Y, Liu S, Mao J. Serum trace elements profile in Graves' disease patients with or without orbitopathy in northeast China. Biomed Res Int. 2018;2018: 3029379.
- 34. Khong JJ, Goldstein RF, Sanders KM. Serum selenium status in Graves' disease with and without orbitopathy: a case-control study. Clin Endocrinol. 2014;80(6):905-10.
- 35. Hesse-Bähr K, Dreher I, Köhrle J. The influence of the cytokines Il-1beta and INFgamma on the expression of selenoproteins in the human hepatocarcinoma cell line HepG2. BioFactors. 2000; 11(1-2):83-5.
- 36. Nichol C, Herdman J, Sattar N. Changes in the concentrations of plasma selenium and selenoproteins after minor elective surgery: further evidence for a negative acute phase response? Clin Chem. 1998;44(8):1764-6.
- 37. Wichman J, Winther KH, Bonnema SJ, Hegedüs L. Selenium Supplementation Significantly Reduces Thyroid Autoantibody Levels in Patients with Chronic Autoimmune Thyroiditis: A Systematic Review and Meta-Analysis. Thyroid. 2016;26(12): 1681-92.
- Van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H. Selenium supplementation for Hashimoto's thyroiditis. Cochrane Database Syst Rev. 2013(6): Cd010223.
- 39. Dunn JT, Dunn AD. Update on intrathyroidal iodine metabolism. Thyroid. 2001;11(5):407-14.
- Hess SY, Zimmermann MB, Arnold M, Langhans W, Hurrell RF. Iron deficiency anemia reduces thyroid peroxidase activity in rats. J Nutr. 2002;132 (7):1951-5.

- 41. Fayadat L, Niccoli-Sire P, Lanet J, Franc JL. Role of heme in intracellular trafficking of thyroperoxidase and involvement of H2O2 generated at the apical surface of thyroid cells in autocatalytic covalent heme binding. J Biol Chem. 1999;274(15):10533-8.
- 42. Beard JL, Borel MJ, Derr J. Impaired thermoregulation and thyroid function in iron-deficiency anemia. Am J Clin Nutr. 1990;52(5):813-9.
- 43. Wiersinga WM, Duntas L, Fadeyev V, Nygaard B, Vanderpump MP. 2012 ETA Guidelines: The use of L-T4 + L-T3 in the treatment of hypothyroidism. Eur Thyroid J. 2012;1(2):55-71.
- 44. Soliman AT, De Sanctis V, Yassin M, Wagdy M, Soliman N. Chronic anemia and thyroid function. Acta Biomed. 2017;88(1):119-27.
- 45. Betsy A, Binitha M, Sarita S. Zinc deficiency associated with hypothyroidism: an overlooked cause of severe alopecia. Int J Trichol. 2013;5(1):40-2.
- 46. Kelly GS. Peripheral metabolism of thyroid hormones: a review. Alt Med Rev. 2000;5(4):306-33.
- 47. Nishiyama S, Futagoishi-Suginohara Y, Matsukura M. Zinc supplementation alters thyroid hormone metabolism in disabled patients with zinc deficiency. J Am Nutr. 1994;13(1):62-7.
- 48. Tran L, Hammuda M, Wood C, Xiao CW. Soy extracts suppressed iodine uptake and stimulated the production of autoimmunogen in rat thyrocytes. Exp Biol Med (Maywood). 2013;238(6):623-30.
- 49. Sathyapalan T, Manuchehri AM, Thatcher NJ. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: a randomized, double-blind, crossover study. J Clin Endocrinol Metab. 2011;96(5):1442-9.
- 50. Mittal N, Hota D, Dutta P. Evaluation of effect of isoflavone on thyroid economy & autoimmunity in oophorectomised women: a randomised, doubleblind, placebo-controlled trial. Indian J Med Res. 2011;133(6):633-40.

Cite this article as: Hussein MS, Asiri LS, Asali SW, Alawlaqi AM, Sibah GS, Alshammari BH, et al. Long term effect of nutrition on thyroid disease. Int J Community Med Public Health 2021:8:922-6.