

RESEARCH ARTICLE

Estimation of Serum Trace metals (Zn and Cu) and Thyroid Hormones in Hypothyroidism

Adil M. Hashim*, Ghadeer H. Al-Ardhi, Ali M. Abd-Alameer

DNA Research Center, University of Babylon, AL-Hila, Iraq

Received: 11th October, 2021; Revised: 09th January, 2022; Accepted: 27th January, 2022; Available Online: 25th March, 2022

ABSTRACT

Hypothyroidism causes clinical and biochemical abnormalities due to Thyroid hormone synthesis is reduced, and thyroid hormone levels in the blood are low. Since, thyroid hormone insufficiency slows numerous metabolic processes, maintaining optimal health needs an adequate quantity of carbs, proteins, and fats and trace elements, macronutrients, and micronutrients. Previous studies compared trace element levels in hypothyroidism patients and healthy people, on the other hand, they had mixed results.

This study is aimed to see if there was a link between changes in blood levels of certain elements (zinc ZN, copper CU) and thyroxine and threonine levels in hypothyroidism patients. We planned to estimate the serum copper and zinc concentration in patient serum compared with healthy person as control. Thyroid hormone levels in the blood were determined using an enzyme immunoassay technique (EIA). The concentration of trace elements, as well as copper and zinc, is determined using the atomic absorption spectrophotometer (AAS) method. We took 25 patient samples with 25 normal subjects and determined the thyroxine, EIA measurement of thyroxine hormone concentration. This study demonstrates that trace elements have a role in a variety of metabolic processes, either as essential nutrients or as cofactors for different enzymes. Leading to hypothyroidism, either directly or indirectly. As a result, the findings show that in hyperthyroidism illness, copper and zinc metabolism is aberrant.

Keywords: Cu, Hypothyroidism, Thyroid hormone, Trace metal, Zn.

International Journal of Drug Delivery Technology (2022); DOI: 10.25258/ijddt.12.1.47

How to cite this article: Hashim AM, Al-Ardhi GH, Abd-Alameer AM. Estimation of Serum Trace metals (Zn and Cu) and Thyroid Hormones in Hypothyroidism. International Journal of Drug Delivery Technology. 2022;12(1):252-255.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The most prevalent pathogenic hormone deficit is hypothyroidism. It can be categorized based on when it first appears (congenital or acquired) and the severity of the endocrine malfunction that causes it (primary or secondary, central hypothyroidism). It's also a prevalent condition that affects more women than males around the age.¹ Serum thyrotropin is used to determine the prevalence of hypothyroidism in communities. Biochemically, The difference between overt and mild hypothyroidism can be detected by the concentration of serum-free thyroxine being below or within the reference range. In congenital instances, iodine deficiency is still common.² Acquired hypothyroidism, on the other hand, is caused by autoimmune thyroiditis (Hashimoto's disease).³ Hypothyroidism is defined as a decrease in thyroid hormone production along with low levels of circulating thyroid hormones. Hyperthyroidism was obtained due to a failing thyroid gland or pituitary gland.⁴ When thyroid hormones were reduced, many metabolic processes were slowed. Hypothyroidism causes slowed mental and physical

performance, thyroid enlargement or goiter, and an increased risk of coronary heart disease.⁵ Hyperthyroidism may have a variety of negative effects on human health, including altering the ovulation process, which can lead to infertility, and slowing cognitive function, which can contribute to depression.⁶ In both sex and age, serum thyrotropin is used to diagnose hypothyroidism, with main cases outnumbering secondary cases.¹ Hypothyroidism (autoimmune "thyroiditis") is caused by autoimmunity against the thyroid gland or other causes. It is characterized by thyroid inflammation followed by progressive degeneration and fibrosis with minimal thyroid hormone production.

As a consequence, When combined with other biochemical markers, trace element testing in biological fluids can be used as a diagnostic or prognostic aid in patients with various hormonal disorders. Thyroid hormones play an important role in the human body's metabolism. After connecting with a specific nuclear receptor, T3/T4 begins transcription of genetic code via mRNA and regulates proteosynthesis in most tissues. Thyroid hormones are involved in the regulation of

*Author for Correspondence: adilalmaamury@yahoo.com

metabolism.^{7,8} Trace elements influence hormones in a variety of ways, including secretion, activity, and binding to target tissues.⁹ Trace elements have an effect on hormones at work, such as hormone production and activity, as well as hormone binding to the target tissue. On the other hand, hormones have an influence on trace elements such as excretion and transport. Trace elements are required for a variety of biological activities because they serve as activators or inhibitors in enzymatic reactions.⁶ Thyroid hormones, which control proto production in tissue and the pace of metabolic processes,^{10,11} are one of the variables that play an essential role in metabolism. Thyroid hormone deficiency causes several metabolic processes to slow down.⁵ Zinc has a unique role in the enzyme as a catalyzer, contributing to the conversion of thyroxin to its active form (thyronine) as well as gene expression modulation.¹² Zinc is important in the endocrine system because it affects growth and endocrine balance. Zinc deficiency in the body can cause a reduction in thyroid hormone release, which can alter the body's normal metabolism and resting metabolic rate. According to certain research, zinc deficiency is linked to increased hepatic thyroxin-5-monodeiodinase enzyme production, which catalyzes thyroid hormone activation.^{13,14} Thyroid hormone T4 synthesis is stimulated by copper. Copper is the human body's third most frequent trace element, and it helps the thyroid gland produce hormones, absorption, and metabolism. Copper regulates calcium levels by preventing excessive T4 absorption in blood cells,¹⁵ and copper is necessary for phospholipid synthesis, which boosts thyroid hormone production. This action requires copper. Thyroid cancer patients had greater copper levels than healthy people, but they also had lower zinc levels.¹⁶ Thyroid hormones (thyroxine, thyronine, thyroid stimulated hormone) are hormones that control the development and metabolism of the body. Thyroid hormones (T4 and T3) perform the same job, although their speed and degree of action varies. T3 hormone has a 1-day half-life, while T4 hormone has a 7-day half-life. Thyroid hormones are also important in early childhood and pregnancy.¹⁷

MATERIALS AND METHODS

Sample Collection

After an overnight fast, blood samples were drawn from an arm vein with a disposable syringe and allowed to clot in one hour at room temperature. The serum was separated from the clotted blood using a centrifuge at 3000 revolutions for 5 to 10 minutes. To prevent hemolysis, 10 mL of blood was taken aseptically from the ante-cubital vein and transferred to a well-clean, metal-free test tube without any anticoagulant. The plain test tube was kept at room temperature for 20 minutes before being centrifuged for 15 minutes at 2500 rpm. Recentrifugation was done to spin down the residual erythrocytes; then, the serum was transferred to a polyethylene container and stored at freezing temperature for preparation of analysis. Using well-clean auto pipettes, half of the serum was transferred to another metal-free test tube and kept at -20°C after proper labeling and securely packed for measuring trace elements

by Atomic Absorption Spectroscopy (AAS) in different batches.

Instrument

Thyroxin and Thyronin Concentration

The enzyme immunoassay technique was used to determine the concentrations of T3 and T4 in the blood.

Zinc and Copper Determination

A flame atomic absorption spectrophotometer was used to evaluate serum zinc and copper levels. The blood zinc and copper levels were measured after applying absorbencies to a suitable calibration curve for each element created from the standard solution. Samples are preferred to serum for Zn analysis because of possible Zn contamination from erythrocytes, platelets, and leukocytes during clotting and centrifugation.

RESULTS

The result of this study indicates that there is a significant decrease in the concentration of T4 and T3 in patients with hypothyroidism compared with healthy people. At the same time, there is a decrease in the concentration of copper and zinc in patients with hypothyroidism compared with control samples as show in Figure 1 and Table 1.

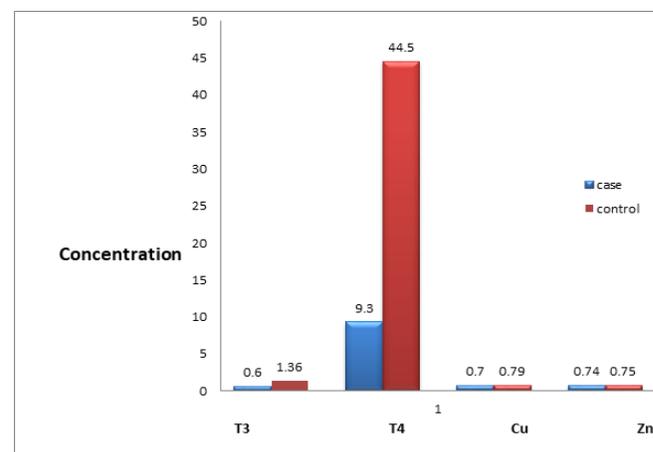


Figure 1: Concentration of heavy metal (Cu, Zn) and thyroid hormone (T3, T4) in samples(n = 25), (p < 0.001)

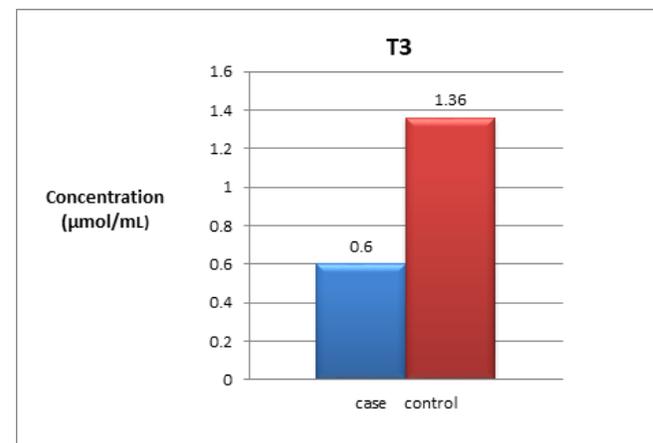


Figure 2: Concentration of T3 hormone in samples (n = 25), (p < 0.001)

Estimation of Serum Trace metals (Zn and Cu) and Thyroid Hormones in Hypothyroidism

Table 1: Concentration of thyroid hormone (T4, T3) and Trace elements (Cu, Zn) in serum sample of patient compared with control.

Group (No.)	Mean	Std.deviation	Std. Error	p-value
T3 (µmol/mL)	Control (n = 25)	1.36	0.40	0.08
	Case (n = 25)	0.6	6.68	1.33
T4 (µmol/mL)	Control (n = 25)	89.60	4.09	0.81
	Case (n = 25)	18.32	3.5	6.51
Cu (ppm)	Control (n = 25)	0.79	0.07	0.01
	Case (n = 25)	0.7	0.04	0.01
Zn (ppm)	Control (n = 25)	0.75	0.07	0.02
	Case (n = 25)	0.74	0.02	0.01

** significant difference at $p \leq 0.01$.

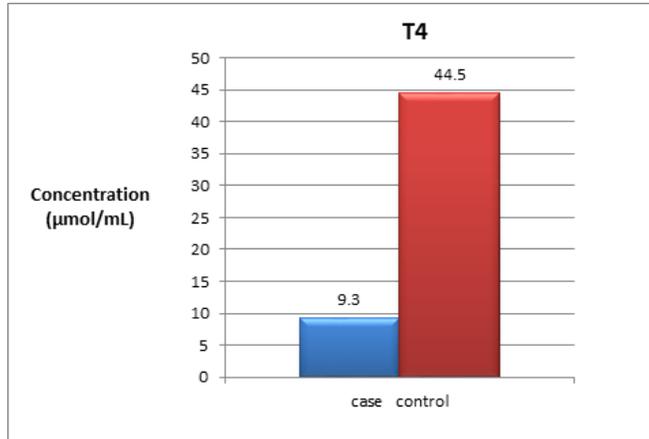


Figure 3: Concentration of T4 hormone in samples (n = 25), ($p < 0.0001$)

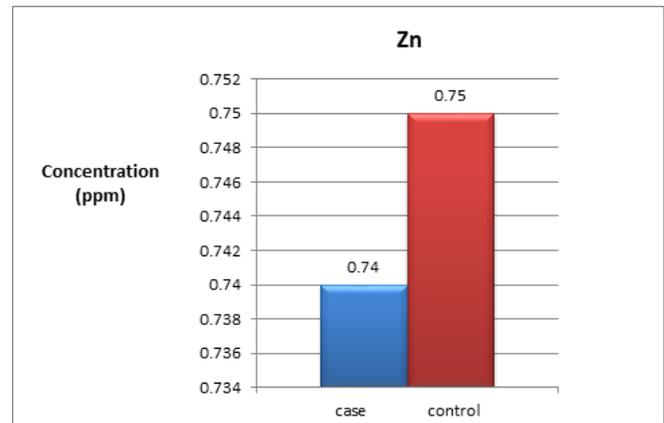


Figure 5: Concentration of Zn in samples (n = 25), ($p < 0.317$)

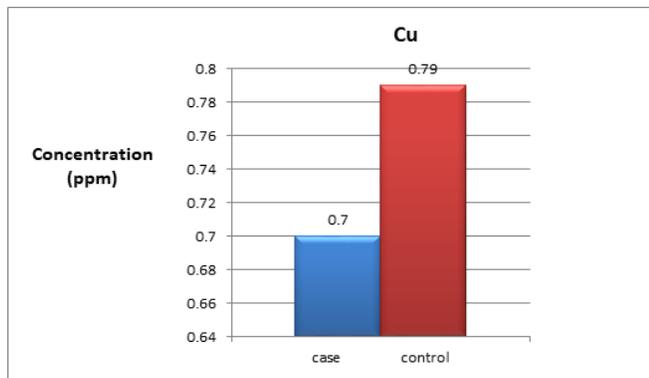


Figure 4: Concentration of Cu in samples (n = 25), ($p < 0.229$)

In this study we found the concentration of T3 hormone in patients sample was (1.36 (µmol/mL)) compared with control samples (0.6(µmol/mL)) Figure 2. Also the concentration of T4 hormone in serum patients sample was highly significant (89.06(µmol/mL)) when compared with healthy control (18.3 (µmol/mL)) Figure 3. While the concentration of copper in serum patients sample was (0.79 ppm) compared with healthy control (0.7 ppm) Figure 4. As for zinc the concentration was (0.75 ppm) in serum patients sample in comparison with healthy control (0.74 ppm) Figure 5.

DISCUSSION

We looked at Zn and Cu levels in hypothyroidism patients' blood and identified a possible connection between thyroid

function and these trace metals. For optimum health, a variety of minerals and trace elements are necessary. Although there are certain co-existing abnormalities, thyroid hormone metabolism is normal.¹⁷ Zinc plays a critical function in protein synthesis and thyroid metabolism.¹⁶ It helps T3 bind to its nuclear receptor and is important in TRH synthesis and activity.¹⁸ In our investigation, we discovered a substantially lower amount of zinc in hypothyroidism patients compared to control participants, which is consistent with Mohammed *et al.*¹⁹ The gastrointestinal absorption of zinc is substantially reduced in hypothyroidism patients, which might explain the lower zinc levels in these individuals.²⁰ A shift in zinc distribution is another possibility; the low zinc level might be due to zinc sequestration by the liver or other tissues.²¹ Thyroid hormone in a variety of forms Zinc deficiency, for example, decreases TRH production and lowers TSH, T4, and T3. It is also required for extrathyroidal T4 to T3 conversion.^{22,23} It is involved in both T3 binding to the nuclear receptor and DNA binding of the receptor.²⁴ TSH has a significant influence on variations in iodine, selenium, and zinc concentrations in normal and altered human thyroid tissues, according to certain studies. Furthermore, Zn excretion through the tubules results have been found in other research.²⁵ Copper is an essential metal because it functions as a cofactor for tyrosinase, a thyroglobulin protein component required for tyrosine synthesis.²⁶ In their studies, the majority of authors found no significant differences in copper levels between hypothyroidism patients and control individuals.²⁷⁻²⁹ There has

been a change in the level. Correct copper levels are required in hypothyroidism patients. Thyroid issues can be prevented with this supplement, and it can also be used to treat them.³⁰

REFERENCES

1. Tunbridge WMG, Evered DC, Hall R, *et al.* The spectrum of thyroid disease in community; Whickham survey Clin Endocrinol (oxf). 1977;7:115-125.
2. Delange F, de Benoist B, Pretell E, Dunn GT. Iodine deficiency in the world :where do we stand at the turn of the century? Thyroid. 2001;11:437-447.
3. Lafranchi S. Congenital hypothyroidism: etiologies, diagnosis, and management. Thyroid. 1999;9:735-740.
4. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clarck F, *et al.* The incidence of thyroid disorders in the community. Clin –endocrinol –oxf. 1995 Jul;43(1):55-68 .
5. Sarks MI, Ocampo E. Subclinical thyroid diseases. AM. J. Med. 1996;100:216-223.
6. Salomons N. Trace Element in clinical Nutrition: Parenteral 2 ed edition Philadelphia. 1993. pp 150-183.
7. Wartofsky L. The scope and impact of thyroid disease. Clin-Chem bjan. 1969;42(1):121-124
8. Meng W. Diagnosis and therapy of hypothyroidism in adulthood Z-Arztl-Forbild –Jena. 1996 Feb;90(1):43-49.
9. Henkin RI. Trace elements in Endocrinology. Medical clinics of North America. 1976;60:779.
10. Kvicala J, Zamarazil V. Effect of iodine and selenium upon thyroid function. Ce4nt-euro-J-public Health. Jun 2003;11(12):107-113.
11. Yanagisawa H. Zinc deficiency and clinical practice. JMAJ. 2004;47(8):359-364.
12. Cole ch, Waddel RW. Alteration in intercellular sodium concentration and ouabain-sensitive ATP ase in erythrocytes from hyperthyroid patients. J clin Endocrine Metab. 1976;42:1056-1036.
13. Maret W. Zinc in human Disease MET LONS LIFE SCI. 2013;13:389-414.
14. Rashid NF, Abed BA, Abas TA. Relationship between some trace elements, lipid profile and hypothyroidism. AJPS. 2010; 8(2):127-138.
15. Khuran IM, Choudhry KS. Mohammed k Islam N. Clinical presentation of hypothyroia case control analysis J ayub Med Coll ABBOTTED. 2013;15:45-49.
16. AL-Sayer H, Mathewtc AS, Khourshed M, AL-bader A, Behbehane A, *et al.* serum changes during thyroid cancers. MOL Cell Bioche. 2004;260:1-5.
17. Yen PM. Genomic and non genomic actions of thyroid hormones. In: Braverman LE, Utiger RD eds. Werner, and Ingbars The Thyroid a fundamental and clinical text.philadelphia :Lippincott Williams and Wikins. 2005;135-150.
18. Zimmermann MB, Kohrle J The impact of iron and selenium deficiency on iodine and thyroid metabolism: Biochemistry and relevance to public health. Thyroid. 2002;12(10): 867-878.
19. Arthur JR, Nicol F, Beckett GJ. Selenium deficiency, thyroid hormone metabolism, and thyroid. 236S-239S.
20. Pekary AE, Lukaski HC, Mena I, Hershman JM. Processing of TRH precursor peptides in rat brain and pituitary is zinc-dependent. Peptides. 1991;12:1025-1032.
21. Baloch S, Memon AR, Hayat AS, Masood N. Evaluation of serum copper and zinc in hypothyroidism patients. ARPN J Sci Technol. 2013;3(3):316-318.
22. Yoshida K, Kiso Y, Watanabe T, Kaise K, Kaise N, Itagaki M. Erythrocyte zinc in hyperthyroidism: reflection of integrated thyroid hormone levels over the previous few months. Metabolism. 1990;39(2):182-186.
23. Pekary AE, Bhasin S, Smith V, Sugawara M, Swerdloff RS, *et al* Thyroid hormone modulation of thyrotrophin-releasing hormone (TRH) and TRH-Gly levels in the male rat reproductive system. J Endocrinol. 1987;114(2):271-277.
24. Pekary AE, Lukaski HC, Mena I, Hershman JM. Processing of TRH precursor peptides in rat brain and pituitary is zinc dependent. Peptides. 1991 Sep 1;12(5):1025-1032.
25. Anselmet A, Bismuth J, Torresani J. Triiodothyronine nuclear receptor: Role of histones and dna in hormone binding. Biochimica et Biophysica Acta (BBA)-Gene Structure and Expression. 1983 Apr 15;739(3):291-300.
26. Baltaci AK, Mogulkoc R, Belviranli M. Serum levels of calcium, selenium, magnesium, phosphorus, chromium, copper and iron-their relation to zinc in rats with induced hypothyroidism. Acta Clin Croat. 2013 Jun 1;52(2):151-156.
27. Adedapo KS, Sonuga AA, Afolabi AO, Amosu A. Interaction of some selected trace elements with thyroid hormones in patients with goiter in Ibadan, Nigeria. J Scient Res Rep. 2014;3(22):2875-2883.
28. Baloch S, Memon AR, Hayat AS, Masood N. Evaluation of serum copper and zinc in hypothyroidism patients. J Sci Technol. 2013;3:316-318.
29. Al-Juboori IA, Al-Rawi R, A-Hakeim HK. Estimation of serum copper, manganese, selenium, and zinc in hypothyroidism patients. IUFS J of Bio. 2009;68(2):121-126.
30. Rashid NF, Abed BA, Abas TA. Relationship between some trace elements, lipid profile and hypothyroidism. Al-Mustansiriyah Journal of Pharmaceutical Sciences (AJPS). 2010 Dec 1;8(2): 127-138.