# Correlation of Zinc Serum level with Hypo-and Hyperthyroidism

*Correlación del nivel sérico de zinc con hipo e hipertiroidismo*

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**Abstract**

**Background**: Low levels of zinc have been linked to thyroid function in the blood in several ways, but the link between zinc deficiency and thyroid disease has yet to be confirmed. This study aimed to estimate the serum zinc levels status in a sample of patients associated with hypo- and hyperthyroidism compared with normal thyroid function. Materials and Methods: The study included 38 patients who suffered from thyroid disorders, hyperactivity, and they were assessed by the members of the Endocrine Unit for a definitive for the diagnosis of the cause of thyroid dysfunction. As well as 12 healthy people who were used as a control group. Results: serum zinc levels were significantly lower in patients with hypothyroid 67.719(45.40-94.63) compared to hyperthyroid 90.21(53-101.22) and controls 90.27(83.20-100.71). (P< 0.001). Similarly, as compared to the control group, the results revealed a statistically significant increase in TSH serum levels in hypothyroidism patients and a significant lowering in hyperthyroidism patients (P< 0.002). A negative association between TSH and zinc was found (p =0.001). The study did not show a significant association between TSH and T3, T4 with zinc in the controls group or the hyperthyroid patients. Even though there is a variation in median values among these groups of patients. The current study established no significant difference in serum levels of T3 in hypo- and hyperthyroidism patients (P=0.202) when compared to the control group. In comparison to the control group, the data revealed a statistically significant decrease in T4 serum levels in hypothyroidism patients and an increment in hyperthyroidism patients (P< 0.005). Conclusion: hyperactivity and hypothyroidism can both be caused by low zinc levels in the blood. To improve zinc status in this group, efforts to correct abnormal levels of thyroid hormones may help.

**Keywords**: trace element zinc, hypothyroidism, and hyperthyroidism

**Resumen**

**Antecedentes**: los niveles bajos de zinc se han relacionado de varias maneras con la función tiroidea sanguínea, pero aún no se ha confirmado el vínculo entre la deficiencia de zinc y la enfermedad de la tiroides. Este estudio tuvo como objetivo estimar el estado de los niveles séricos de zinc en una muestra de pacientes asociados con hipo- e hipertiroidismo en comparación con la función tiroidea normal. Materiales y Métodos: Se incluyeron en el estudio 38 pacientes que sufrían de trastornos tiroideos, hiperactividad, y fueron evaluados por los miembros de la Unidad de Endocrinología con el propósito de establecer el diagnóstico definitivo de la causa de la disfunción tiroidea. Igualmente, 12 personas sanas fueron utilizadas como grupo de control. Resultados: los niveles séricos de zinc fueron significativamente menores en pacientes con hipotiroidismo 67,719(45,40-94,63) en comparación con hipertiroidismo 90.21(53-101,22) y controles 90,27(83,20-100,71) con (P< 0.001). De manera similar, en comparación con el grupo de control, los resultados revelaron un aumento estadísticamente significativo en los niveles séricos de TSH en pacientes con hipotiroidismo y una disminución significativa en pacientes con hipertiroidismo (P < 0,002). Se encontró asociación negativa de TSH con zinc (p =0,001). El estudio no mostró una asociación significativa entre TSH y T3, T4 con zinc en el grupo control o en los pacientes hipertiroideos. A pesar de que existe una variación en los valores medianos entre estos grupos de pacientes, el estudio actual no estableció una diferencia significativa en los niveles séricos de T3 en pacientes con hipo- e hipertiroidismo (P = 0,202) en comparación con el grupo de control. Los datos de esta investigación también revelaron una disminución estadísticamente significativa en los niveles séricos de T4 en pacientes con hipotiroidismo y un incremento en pacientes con hipertiroidismo (P<0,005). Conclusión: tanto la hiperactividad como el hipotiroidismo pueden ser causados por bajos niveles de zinc en la sangre. Para mejorar el estado de zinc en este

grupo, los esfuerzos para corregir los niveles anormales de hormonas tiroideas pueden ayudar.

**Palabras clave**: Oligoelemento Zinc, Hipotiroidismo E Hipertiroidismo

## Introduction

Endocrine control of thyrotropin-releasing hormone (TRH) from the thyroid gland, maybe the manufacture of a tripeptide into the nucleus of the paraventricular of the hypothalamus gland. Which is transferred to the median eminence through certain axons and the portal capillary plexus to the anterior part of the pituitary gland. TRH receptors in pituitary thyrotropes are associated with TRH. A subpopulation of thyroid hormone-secreting pituitary cells is (TSH). Promoting TRH Stimulates the synthesis and release of TSH in thyrotropes. Low T3 and T4 levels within the blood cause the hypothalamus to release TRH, which induces the anterior pituitary gland to secrete TSH. TSH induces T3 and T4 release. Increasing T3 and T4 levels feature a feedback impact on TRH and TSH, reducing their production and secretion[7]. Promotes the transfer of ions iodide by TSH (I-) through membranes of the cell into the cytosol from the bloodstream when it binds to receptors in thyroid follicle cells. As a result, the concentration of iodide ions (trapped) in follicular cells is repeatedly above the bloodstream concentration. Iodide is transported to the basolateral cell wall via a cell wall protein (the sodium/iodide symporter), where it's converted to an oxidized state by thyroid peroxidase enzyme at the cell's apical surface. In thyroglobulin, iodine combines with tyrosine to supply monoiodotyrosine (MIT) and diiodotyrosine (DIT). The iodinated tyrosines were coupled, to make thyroxine (T4) and triiodothyronine (T3). T3 is additionally formed within the peripheral tissues by deiodination of T4. The coupling reaction was also mediated by peroxidase. These hormones remain in the thyroid follicles in the colloid center until thyrotropin (TSH) drives endocytosis of the colloid back to the follicle cells. Thyroglobulin colloid was broken by the lysosomal enzymes, which causes the release of free T3 and T4, which diffuse through the cell wall of the follicle and enter the bloodstream[8]. The physiological effects of thyroid hormones include Heart: Effects (Chronotropic and inotropic effects). Mechanism (beta-adrenergic receptors were increased in number. Promote response to circulating catecholamines. Increment proportion of the heavy chain of a myosin). Fatty tissue: impact (Catabolic pathways). Mechanism (lipolysis activate). The Muscle: impact (Catabolic). Mechanism (Increase breakdown of protein was increased). The Bone: Effect (progression). Mechanism (enhance normal growth; and skeletal development). The nervous system: impact (Developmental). Mechanism (The normal growth performance of the brain). Gut: Effect (Metabolic). Mechanism (Increase the rate of absorption of carbohydrates). Lipoproteins: influence (Metabolic). Mechanism (stimulation of the formation of LDL receptors). Other: Effects (caloric). Mechanism (stimulation of oxygen consumption by metabolically active tissues)[9]

Hypothyroidism is a disorder in which the thyroid produces hormones below the physiological limit. Approximately 95% of hypothyroidism is caused by thyroid malfunction (primary hypothyroidism), which may be congenital or acquired (most common). The foremost common causes of primary hypothyroidism are autoimmune diseases such as (Hashimoto's thyroiditis), radioactive iodine therapy, or surgery for hyperthyroidism that destroy the thyroid; Goiter caused by iodine shortage, or an excessive amount of iodine are further causes of primary hypothyroidism. Cold intolerance and weight gain are common symptoms of hypothyroidism, which are caused by a decrease in basal rate and thermogenesis. Other symptoms include depression, fatigue, decreased peripheral reflexes, and constipation, which are caused by a decrease in central and peripheral nervous system stimulation[10]. Hypothyroidism is treated by replacing the missing hormone with synthetic thyroxine ~~pills~~, which the person must always take each day. Most patients recover completely with daily treatment[11]. Hyperthyroidism results from generalized thyroid gland overactivity or due to some other causes. However clinical, physiological and biochemical alterations occur when tissues are exposed to increased concentrations of thyroid hormones.3 Different studies also supported those functional abnormalities of hyperthyroidism virtually affects many organ systems, and it affects much more women than men. Hyperthyroidism is often caused by a spread of causes. The most common factors include immunological conditions (eg, Graves' disease, thyroiditis), toxic thyroid nodules (adenomas), and toxic goiter (many nodules or adenomas) (enlarged thyroid)[12]. Heat intolerance, weight loss, anxiety, hyperreflexia, diarrhea, as well as palpitations are all signs of hyperthyroidism. Increased stimulation of basal rate, thermogenesis, resting pulse and flow, and the central and peripheral nervous system also causes the most common symptoms[13]. However, with the known effect of zinc (Zn) on hypothalamus and pituitary, it appears a major role in the synthesis of thyrotropin releasing hormone (TRH)[1]. It also shows its necessity in the activity of 5" deiodenase. Studies have already documented altered Zn status in hypothyroidism.[2] Changing zinc status in hypothyroidism has already been established in several studies. Zhang et al., 2004 observed significantly low Zn levels in thyroid cancer patients[3]. In another study, low zinc levels and elevated copper (Cu) levels were reported in thyroid cancer patients[4,6]. (This paragraph in blue is exactly a copy from Sinha et al., http://nepjol.info/index.php/AJMS,DOI: 10.3126/ajms.v7i1.12895. It could be plagiarism)

Zinc is an important element that participates in several basic chemical reactions within the thyroid gland. My father (?) is considered an important part of an enzyme 1 ، 5-deiodinase which plays the role of converting a hormone )T4) into functional triiodothyronine (T3).

It cannot be synthesized if zinc is low or missing from the body. Several studies have described a significant relationship between blood zinc levels and thyroid hormones[15,17]. Moreover, deficiency disease (?) can also be a risk factor for hypothyroidism, a condition that's highly prevalent among Iraqi women[16]. Nevertheless, the effect of zinc on hormone levels remains unknown, yet there are still debates over the link between hypothyroidism and thyroid disorders, especially in women[17]. Several experiments have been conducted to study the verification of zinc levels in the blood of those with hypothyroidism and hyperthyroidism, with an understanding of their relationship to hormones.

This study aimed to measure zinc levels in the blood. By taking a blood sample from patients who have hypothyroidism and hyperthyroidism, compared to people who have normal thyroid functions, and to know the mixture of that gland with hormone levels.

## Materials and methods

### Subjects and samples collection

The study was conducted at Al-Qurna Hospital and Private Clinics in Basra/Iraq. The study was conducted after the Research Ethics Committee in the Basra Health Department officially approved the study. Which was done by comparing the group of patients suffering from hypothyroidism with the control group for normal thyroid functions to assess the relationship between zinc levels and the thyroid hormone profile (T3, T4) in addition with the hormone (TSH).

Serum was randomly obtained from blood samples of 50 people.-38 have symptoms of hypothyroidism and hyperthyroidism. (Ages 33–77 years) and age corresponding to a normal thyroid gland (n=12) were referred to the endocrinology unit at Gourna Hospital for a definitive diagnosis of thyroid disease. The diagnosis of hypothyroidism and hyperthyroidism was first confirmed clinically using biochemical tests (T3, T4, and TSH).

Sample of 4 mL of blood was collected in a vacuum gel and clot activator tube, and then centrifuged (rpm ?) and the serum was separated and stored at -20 $C^0$ until assay.

### Determination of serum levels of Zn

Regarding zinc levels were measured by a flameless atomic absorption spectrometer (Shimadzu.7000f, Oil path, F3 hake German) using a standard procedure. The levels of Zn were obtained by extrapolation of the criterion curve followed by correction with the dilution Factor.

### Hormonal assay

Serum levels of T3, T4, and TSH were examined by using commercially available standardized electro immunoassay Vidas, Biomrieux, France (Enzyme Linked Fluorescent analysis).

### Statistical analysis

For statistical analysis, SPSS software, version 24 was utilized. $Chi^2$ was used to test for significant associations, Kruskal Wallis for significant differences, and Spearman test for correlations. A p-value of lower than 0.05 was considered statistically significative.

## Results

The current study did not show any statistically significant differences in the ages of the thyroid disorders between all groups (P< 0.463). However, the present study was based on thyroid dysfunction (Hypo-and Hyperthyroidism). The data in Table 1 presents the main characteristics of the study. In general, it includes patients with hypothyroidism 34% (n=17) and hyperthyroid 42% (n=21). Furthermore, the data appeared that the trace element Zn concentrations evaluated in this study are related to dysfunction (Hypo-and Hyperthyroidism). According to the present findings, the median serum zinc level was significantly lower (P=0.001) in hypothyroid patients compared to hyperthyroid and control. In the same manner, the results revealed a statistically significant increase in the serum level of TSH in hypothyroidism patients and a significant decrease in hyperthyroidism patients (P=0.002) in comparison with the control group.

Although median values varied among the patients studied, there was no significant difference in T3 serum levels in hypo- and hyperthyroidism patients (P=0.202) when compared to the control group. The data also showed a statistically significant decrease in serum T4 levels in hypothyroid patients with an increase in hyperthyroid patients (P = 0.005) compared to the control group Table 1.

The relationship between serum zinc and thyroid hormones in hypothyroid and hyperthyroid females is shown in Table 2. In the hypothyroid group, zinc was positively correlated with T4 (p=0.033). In addition, a negative association was observed with TSH (p<0.0001). Conversely, TSH levels replenished negatively with T3 and T4 levels (0.013, 0.0001), respectively.

**Table 1. Shows the median serum level Zn and hormones in relation to thyroid disorders (Hypothyroidism and Hyperthyroidism) in comparison with the control of the study.**

| Variable parameters | Control (n=12) (min-max) | Thyroid dysfunction | | p-value* |
|---|---|---|---|---|
| | | Hypothyroidism (n=17) (min-max) | Hyperthyroidism (n=21) (min-max) | |
| Age(years) | 39.50 (23-53) | 39.00 (17-67) | 39.00 (21-86) | 0.463 |
| Zinc ppm | 90.27(83.20-100.71) | 67.719(45.40-94.63) | 90.21(53-101.22) | 0.001 |
| TSH Mu/mL | 1.1550 (0.77-1.86) | 6.5000(.00-40.00) | 0.0300 (.00-17.00) | 0.002 |
| T4 nmol/L | 78.7000(66.13-105.00) | 62.0000(5.00-103.00) | 133.0000(.00-280.00) | 0.005 |
| T3 nmol/L | 1.4200(1.00-1.99) | 1.2900(.90-2.00) | 1.5200(1.10-2.70) | 0.202 |

*Statistically significant differences if p<0.05

**Table 2. Relationship between serum zinc and thyroid hormones in hypothyroid and hyperthyroid females**

| | | TSH | T4 | T3 |
|---|---|---|---|---|
| Zinc | R | -0.513- | 0.302 | 0.215 |
| | Sig. | 0.0001 | 0.033 | 0.134 |
| TSH | R | | -0.539- | -0.349- |
| | Sig. | | 0.0001 | 0.013 |
| T4 | R | | | 0.242 |
| | Sig. | | | 0.090 |



## Discussion

Zinc is an essential micronutrient that plays a large role in the body's mineral coenzyme cycle[18]. Zinc counteracts corrosion-causing protein and nuclear fusion, just as it does in various metabolic and cellular capacities. A few studies showed that zinc insufficiency produces a decline in T3 levels. Moreover, an expected connection between zinc insufficiency and hypo-and hyperthyroidism has been proposed by de Lima and Baltaci (2018)[19].

In our study, when we evaluate people who are exposed to thyroid problems compared with healthy people, a significant positive correlation was observed between the levels of zinc in the blood and T3 and T4 in the hypothyroid group, unlike the hyperthyroid group or the usual hypothyroid groups. Moreover, there were critical differences in mean serum zinc levels between the groups, as it was found that the mean serum zinc level in hypothyroid patients was lower than in hyperthyroid and healthy participants. When comparing the prevalence of zinc deficiency among the current study groups, a similar pattern was observed. The current findings are consistent with those of a previous study[20], which indicated that in zinc deficiency patients, T3 and T4 were both lower, but TSH was essentially higher. In addition, the data of the current study showed that the level of zinc showed a negative relationship with TSH thyroid gland patients. However, the current study demonstrates a significant decrease in serum zinc levels in hypothyroidism and hyperthyroidism. Our results are in agreement with those of some previous studies[21,22]. The most likely explanation is that albumin is the main transporter of zinc in plasma[23]. It was also suggested that the low level of (S)Zn in hyperthyroidism could be due to sequestration of metallothionein in the liver, which could be a response to increased production of interleukin-6 (IL-6) during inflammation[24]. There was a high positive relationship between the level of zinc in the blood of people with hypo and hyperthyroidism. However, no significant association between T3 and serum zinc levels in hypothyroidism and hyperthyroidism. The present results are consistent with findings from a previous study[20], where it was found that T3 and T4 in a significantly lower percentage, and TSH was higher in religious patients suffering from zinc deficiency[25]; In any case, the current study indicated that zinc level is also negatively correlated with TSH in persons with hypothyroidism and hyperthyroidism. However, the possibility of this link between zinc metabolism and the thyroid gland was based on the theory that T3 receptors, like any other nuclear receptors, are linked. It includes zinc nuclear bond proteins[26]. Therefore, zinc is believed to be an integral part of nuclear receptor proteins, and binds it to the conformation required for binding to target genes[27], which converts biologically inactive T4 to biologically active T3. Aziz et al. (2016)[28], and this mechanism may indicate an important mechanism through which color can affect the increased risk of hypothyroidism and hyperthyroidism in citizens. In confirmation of that, many studies in Iraq have indicated that dietary zinc deficiency is widespread among our population, especially in women of childbearing age (Al-Tamimi et al., 2005) and they are linked together with thyroid function in benign thyroid diseases. The lack of correlations between thyroid hormones with zinc levels in the blood of patients with hypoglycemia and hyperthyroidism is somewhat like the results of other researchers[31,32] but in contrast to others[33,34]. This difference in our results compared to other studies may be molecularly related to zinc nutritional status. However, the results of our study confirmed that zinc deficiency might have an important role in thyroid function. The current study showed a positive relationship between T4 and zinc, while it was negative between TSH and T3 with zinc in hyperthyroid patients. However, alternate efforts to raise zinc levels in hypo and

hyperthyroid patients may help correct the course of thyroid hormone levels.

**Limitation**

The Sample size was relatively smaller, further studies on a larger population are required to determine the diagnostic use of these trace elements in examination and planning treatment for thyroid disorders.



## Conclusions

The current study confirmed the occurrence of distinct and significant changes in serum zinc levels in hypothyroidism, while it was less in hyperthyroid patients, and these changes may be physiologically related to thyroid diseases. Trace element deficiencies often lead to the development of thyroid hormone deregulations and thyroid disorders that in turn affects the trace element homeostasis.

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Conflict of Interest

The author exhibited that there is no conflict of interest

Authors Contributions

Mahdi M.Thuwaini (single author) wrote and agree with the manuscript.

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