Correlation of Zinc and Magnesium with Thyroid Dysfunction

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Abstract:
Introduction: Thyroid diseases rank as the second most common endocrine disorder worldwide, after diabetes mellitus. Thyroid hormones are essential for growth, neuron development, reproduction, and energy metabolism, influencing the metabolism of all substances, including minerals. Numerous studies have shown that thyroid issues often disrupt mineral metabolism. This study aims to measure serum zinc and magnesium levels in individuals with hypothyroidism and hyperthyroidism and to correlate these levels with serum Triiodothyronine (T٣), Thyroxine (T٤), Free T٣ (FT٣), Free T٤ (FT٤), and Thyroid-Stimulating Hormone (TSH). **Methods**: The study included twenty individuals with hypothyroidism, twenty with hyperthyroidism, and twenty with normal thyroid function as controls. Blood samples were collected to measure serum T٣, T٤, FT٣, FT٤, and TSH using the autoanalyzer method (minividas), while serum zinc and magnesium levels were measured using spectrophotometry. Statistical analysis was performed using SPSS ٢٥ software, employing independent sample t-tests for means and standard deviations, with a significance level of ٠.٠٥ (P value). Pearson correlation was used to determine the relationships between the markers. **Results:** The results showed that serum zinc and magnesium levels were significantly lower (p<٠.٠٠١) in individuals with hypothyroidism and hyperthyroidism compared to controls. There was a notable positive correlation between zinc and magnesium levels and thyroid hormones T٣ and T٤. In hypothyroidism, a negative correlation with serum TSH levels was observed. In hyperthyroidism, zinc and magnesium levels negatively correlated with T٣ and T٤ but positively correlated with TSH. No significant correlation was found between serum zinc and magnesium levels and FT٣ and FT٤ levels. **Conclusion**: This study demonstrates that mineral metabolism is altered in thyroid dysfunction, and dysregulated zinc and magnesium metabolism can lead to various metabolic diseases. Early preventive measures, such as mineral supplementation or hormone replacement therapy, may help manage these secondary conditions.

Keywords: thyroid disorder; zinc; magnesium; endocrine abnormality; hypothyroidism.

علاقة الزنك والمغنيسيوم وخلل الغدة الدرقية

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الخلاصة :

تعد اضطرابات الغدة الدرقية أكثر اضطرا بات الغدد الصماء شيوعًا في العالم بعد مرض السكري. تعتبر هرمونات الغدة الدرقية ضرورية للنمو وتطور الخلايا العصبية والتكاثر وتنظيم استقلاب الطاقة. أنه يؤثر على عملية التمثيل الغذائي لجميع الركائز بما في ذلك المعادن. أظهرت العديد من الدراسات أن استقلاب المعادن يضطرب في كثير من الأحيان في اضطرابات الغدة الدرقية. تهدف هذه الدراسة إلى تقدير مستويات الزنك والمغنيسيوم في الدم في حالات قصور الغدة الدرقية وفرط نشاط الغدة الدرقية وربط كل من العوامل مع ثلاثي يودوثيرونين المصل (T٣)، هرمون الغدة الدرقية (T٤)، **Free T٣ (FT٣)**، **Free T٤ (FT٤)** والهرمون المحفز للغدة الدرقية **(TSH)**، على التوالي. أجريت الدراسة على عشرين حالة من حالات قصور الغدة الدرقية وعشرين حالة من حالات فرط نشاط الغدة الدرقية بناءً على صورة الغدة الدرقية وتم اختيار عشرين حالة من حالات الغدة الدرقية كعناصر تحكم. تم جمع عينات الدم من جميع المرضى لتقدير مصل T٣، T٤، **FT٣**، **FT٤**، **TSH** بطريقة التحليل الذاتي **(minividas)**. بينما تم استخدام الطريقة الطيفية لقياس الزنك والمغنيسيوم في مصل الدم. تم إجراء التحليل الإحصائي باستخدام الإصدار **SPSS ٢٥**، في حين تم استخدام اختبار **t** للعينة المستقلة للجداول ذات المتوسطات والانحراف المعياري. تم استخدام قيمة **P < ٠.٠٥** كمستوى الأهمية. معامل الارتباط يستخدم لإيجاد الارتباط بين العلامات المدروسة باستخدام ارتباط بيرسون. أظهرت نتائج الدراسة أن متوسط مستويات الزنك والمغنيسيوم في الدم انخفضت بشكل ملحوظ (**p<٠.٠١**) في حالات قصور الغدة الدرقية وفرط نشاط الغدة الدرقية مقارنة بحالات الغدة

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الدرقية. تم العثور على علاقة إيجابية معنوية بين Zn وMg في المصل مقابل T٣ وT٤، وارتباط سلبي بين الزنك والمغنيسيوم في المصل مقابل TSH لدى مرضى قصور الغدة الدرقية، بينما وجدت علاقة سلبية معنوية بين الزنك والمغنيسيوم مع T٣,T٤ وارتباط ايجابي مع ال TSH لدى مرضى فرط نشاط الغدة الدرقية ولم يكن للزنك والمغنيسيوم علاقة معنوية مع FT٣ وFT٤ في المصل. أظهرت الدراسة الحالية أن استقلاب المعادن يتغير في حالات خلل الغدة الدرقية. واستنتجت هذه الدراسة إلى أن ضعف التمثيل الغذائي للمعادن مثل الزنك والمغنيسيوم يمكن أن يؤدي إلى اضطرابات التمثيل الغذائي المختلفة. يمكن البدء في اتخاذ تدابير وقائية مثل مكملات المعادن أو العلاج بالهرمونات البديلة مبكرًا للسيطرة على هذه الاضطرابات الثانوية.

الكلمات المفتاحية: الغدة الدرقية، الزنك، المغنيسيوم، مؤشر كتلة الجسم.

Introduction

Thyroid disorders encompass a diverse range of illnesses, including hypothyroidism, hyperthyroidism, subclinical hypothyroidism (SH), subclinical hyperthyroidism, structural abnormalities, and malignancies [١]. The thyroid gland secretes hormones that control growth, development, metabolism, and stress reactions. It is a part of the hypothalamic-pituitary-thyroid (HPT) axis. (٢). Markers such as TSH, FT٣, and FT٤ are used to assess thyroid function. Furthermore, there has been a recent surge in interest in the thyroid hormone sensitivity index. These indices offer useful data for elucidating changes in the HPT-axis and thyroid hormone control of local tissue metabolism in a range of normal and pathological conditions.(٣).

Understanding the relationship between thyroid hormone sensitivity and metabolic problems has gained attention in addition to thyroid function. Insulin resistance, type ٢ diabetes (T٢D), and abnormalities in glucose and lipid metabolism have all been reliably predicted by thyroid hormone sensitivity indices in recent years. [٤, ٥]. Additionally, Thyroid dysfunction may give rise to the symptoms and indicators of many illnesses such as the cardiovascular system [٦].

Leafy green vegetables, legumes, nuts, seeds, milk, whole grains, and other foods contain mineral magnesium (Mg) [٧]. Since it is necessary for DNA replication and transcription as well as the activation of adenosine triphosphate (ATP), it plays a role in many aspects of thyroid function. Magnesium is involved in thyroid hormone metabolism and serves as a cofactor for several enzymes and enzymatic processes. Deiodination, which catalyzes the transformation of T٤ into the more active T٣ form, may be indirectly influenced by it [٨]. Magnesium controls the appropriate activity of other nutrients, including vitamin D, which controls calcium and phosphorus (P) homeostasis [٩]. In response to the activation of the TSHR, calcium, diacylglycerol, cAMP, and different phosphate derivatives of myoinositol (phosphatidylinositol and others) are vital secondary messengers that regulate intracellular signaling cascades and are required for the synthesis of TG and H٢O٢ [١٠]. Furthermore, by interacting with inflammation and/or free radicals, which can result in DNA oxidative damage and the development of cancer, magnesium shortage affects carcinogenesis. In contrast to benign nodules, patients with papillary thyroid cancer had lower serum magnesium levels within the usual range, according to a cross-sectional study that examined ٥٧٠٩ patients who had thyroidectomies [١١].

A trace mineral, zinc (Zn) is involved in the manufacture and metabolism of thyroid hormones as well as gene expression and cell proliferation. It is also a cofactor for several enzymes that are engaged in other physiological processes [١٢]. Under the effect of environmental trigger events, genetically determined people with autoimmune thyroid diseases (AITD) may lose their tolerance to these thyroid peptides due to impaired intrathymic expression of autoantigens (TSH-R, Tg, and TPO). The autoimmune regulator (Aire) and forebrain embryonic zinc fingerlike protein ٢ (Fezf٢) regulators, which contain zinc , regulate the production of promiscuous gene expression (pGE) tissue-restricted antigens (TRA) TECs genes, which are necessary for the thymus to be able to tolerate self-antigens [١٣]. TSH and TSH-releasing hormone (TRH) are both synthesized using zinc. Furthermore, zinc is a component of T٣ nuclear receptors and a cofactor of type I and II deiodinases, which interfere with the synthesis of thyroid hormones (T٤ and T٣) and influence how these hormones function [١٤].

Materials and Methods

Human serum was collected during the period from October ٢٠٢٤ to March ٢٠٢٥

Collection of Samples:

There were sixty participants, twenty with hypothyroidism, a thyroid condition, of both sexes in the study, twenty patients with hyperthyroidism

and twenty healthy, normal people made up the normal control group, which included people ages ٢٩ to ٦٥. A venous blood sample of ٥ milliliters was obtained from both patients and controls. A simple vial containing a blood sample was filled and incubated for ٢٠ minutes at ٣٧ °C. The clot was removed after incubation, and the remaining material was transferred to a test tube for centrifugation. The samples were centrifuged for ten to twenty minutes at ٣٠٠٠ rpm. The supernatant was collected and stored in a dry, clean test tube so that thyroid hormone and trace elements (Zn and Mg) could be analyzed. Estimates were made for thyroid hormone (T٣, T٤ free T٣, and free T٤), hormone (TSH), and trace elements (Zn and Mg).

Clinical laboratory analysis of groups

Hormonal tests were conducted using the commercially available standardized electro-immunoassay Vidas from BioMérieux, France (Enzyme Linked Fluorescent Analysis). This method was used to measure serum levels of T٣, T٤, Free T٣, Free T٤, and TSH. Serum Zn and Mg levels were tested manually using Medichem kits.

Statistical analysis

Version ٢٤ of the SPSS software was used for statistical analysis. The Spearman test was utilized to look for correlations, the Kruskal Wallis test for remarkable differences, and the Chi٢ test for significant associations. A p-value was deemed statistically significant if it was less than ٠.٠٥.

Results

Anthropometries of Study Groups

There were no statistically significant variations in the ages of thyroid diseases across all categories in the current investigation (P>٠.٠٥). On the other hand, thyroid malfunction (hypo- and hyperthyroidism) formed the basis for this investigation. Table ١ clearly showed that there were no variations in mean baseline BMI between patients with hypothyroidism and hyperthyroidism (٢٧.٧٣±١.٤٢ vs. ٢٦.٣٨±١.٢٧), respectively, with a p-value of ٠.٥٢.

Comparative hormones and trace elements parameter between study groups

The current investigation focused on hypo- and hyperthyroidism, or thyroid malfunction. The primary attributes of the research are displayed in Table ١. Patients with hyperthyroidism (n=٢٠) and hypothyroidism (n=٢٠) are generally included. Additionally, the data suggested a connection between malfunction (hypo-and hyperthyroidism) and the trace element Zn and Mg amounts examined in this investigation.

Table (١) : Anthropometries, trace elements, and thyroid hormone parameters of patient groups and healthy subjects

Variable parameters	Control	Thyroid dysfunction		P value
		Hypothyroidism	Hyperthyroidism	
Age (years)	٣٦.٣٦±٢.٢٣	٣٧.٠٤±٢.٠٢	٣٧.٧١±٢.٣١	٠.٨٩
BMI I (kg/m٢)	٢٥.٣٦±١.٣٨	٢٧.٧٣±١.٤٢	٢٦.٣٨ ±١.٢٧	٠.٥٢
Zinc µg/dl	٩٨.١ ±١٨.٤ a	٣٥.٩٤ ±٦.٥b	٥٠.٥٠ ± ٥.٨c	<٠.٠٠١
Magnesium mg/dl	١.٩٧± ١.٠١a	٠.٨٩ ± ٠.٣٢b	٠.٦٨ ± ٠.١٧ c	<٠.٠٠١
TSH µIu/mL	٢.٠١ ± ٠.٧٨a	١٦.٧١ ± ٣.٨٥b	٠.٠٨ ± ٠.٠٣c	<٠.٠٠١
T٤ nmol/L	٨٨.٦٨ ± ٢.٦٧a	٥٦.٧٩ ± ٤.٦١ b	١٦٤ ± ١٢.٣٣c	<٠.٠٠١
T٣ nmol/L	١.٢٨ ± ٠.٠٨a	٠.٨٦ ± ٠.٠٦b	٣.٤٢ ± ٠.٧٢ c	<٠.٠٠١
Free T٣ Pmol/l	٥.٣٢±٠.٨٢	٤.١٣±٠.٧٣	٤.٨٩ ±٠.٨٥	٠.٧٦
Free T٤ Pmol/l	١٢.٤٣±٢.١٢	٩.١٥±١.٨٦	١٠.٠١±١.٨٨	٠.٤٨

Values represent mean ± SD; values with nonidentical superscripts (a, b, and c) indicated significant differences between groups (P<٠.٠٠١).

The current results indicate that serum zinc levels were significantly lower (P<٠.٠٠١) in hypothyroid patients compared to hyperthyroid patients and the control group, while serum magnesium levels were significantly lower (P<٠.٠٠١) in hyperthyroid patients (Fig ١ and ٢). Additionally, compared to the control group, there was a statistically significant increase in serum TSH levels in hypothyroid patients and a significant decrease (P<٠.٠٠١) in hyperthyroid patients. The data also showed a statistically significant decrease in blood T٣ and T٤ levels in hypothyroid patients and an increase in these levels in hyperthyroid patients (P<٠.٠٠١).

Relationship between trace element and thyroid hormone of Study Groups

Tables ٢ and ٣ illustrate the correlation between serum zinc and magnesium levels and thyroid hormones in individuals with hypothyroidism and hyperthyroidism, respectively. In the hypothyroid groups, zinc and magnesium levels showed a positive correlation (p<٠.٠٠١) with T٣ and T٤ and a negative correlation (p<٠.٠٠١) with TSH. Conversely, in the hyperthyroid groups, zinc and magnesium levels exhibited a negative correlation (p<٠.٠٠١) with T٣ and T٤ and a positive correlation (p<٠.٠٠١) with TSH.

Table (٢) : Correlations of Zn with hypo and hyper thyroid dysfunctions

parameters	Hypothyroidism r value	P value	Hyperthyroidism r value	P value
TSH	-٠.٨٥٣**	<٠.٠٠١	٠.٨٤٦**	<٠.٠٠١
T٤	٠.٩١٧**	< ٠.٠٠١	- ٠.٨٢٧**	< ٠.٠٠١
T٣	٠.٩٠٢**	< ٠.٠٠١	- ٠.٧٧٣**	< ٠.٠٠١

Correlation** is significant at the <٠.٠٠١ level

Table (٣) : Correlations of Mg with hypo and hyper thyroid dysfunctions

parameters	Hypothyroidism r value	P value	Hyperthyroidism r value	P value
TSH	-٠.٨٥٥**	<٠.٠٠١	٠.٨٨٣**	<٠.٠٠١
T٤	٠.٩٣٦**	< ٠.٠٠١	- ٠.٩٢٥**	< ٠.٠٠١
T٣	٠.٩٠٣**	< ٠.٠٠١	- ٠.٨٧٩**	< ٠.٠٠١

Correlation** is significant at the <٠.٠٠١ level

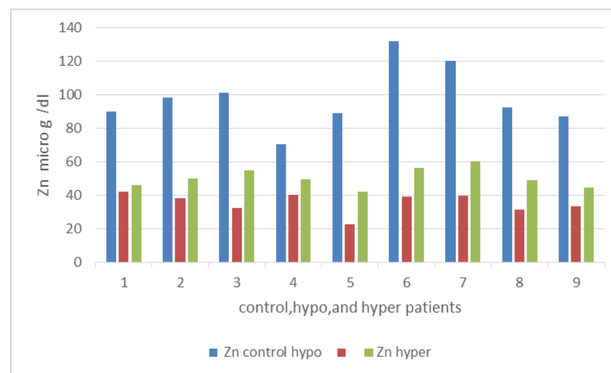

Figure (١) : Differences in serum Zinc levels of thyroid disorder patients and control

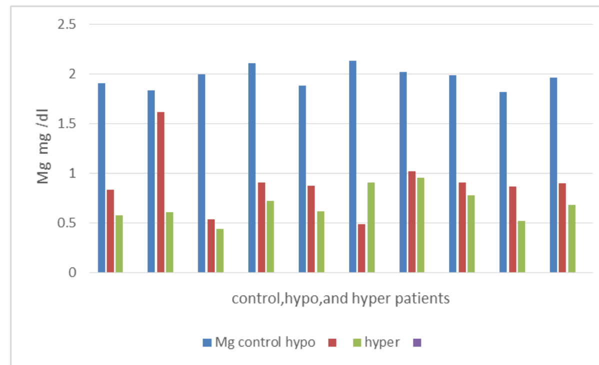

Figure (٢) : Differences in serum Mg levels of thyroid disorder patients and control

Discussion:

levels of zinc and magnesium in the blood as well as T٣ and T٤ were found to be significantly positively correlated in our study when individuals with thyroid issues were compared to healthy individuals for the hyperthyroid group. Furthermore, it was discovered that the mean serum zinc level in hypothyroid patients was lower than in hyperthyroid patients and healthy participants, indicating significant variations in mean serum zinc and magnesium levels across the groups. However, it was discovered that compared to people who were hypothyroid and in good health, hyperthyroid patients had meant serum magnesium levels that were lower.

Furthermore, the results of this investigation demonstrated that in hypothyroid patients, the levels of zinc and magnesium exhibited a negative correlation with TSH and a positive correlation with T٣ and T٤. Nonetheless, the current study shows that both hyperthyroidism and hypothyroidism are associated with a considerable drop in serum zinc and magnesium levels. The most plausible theory is that albumin serves as the primary zinc transporter in plasma. Additionally, it was proposed that the sequestration of metallothionein in the liver, a possible reaction to increased interleukin-٦ (IL-٦) production during inflammation, could account for the low Zn level in hyperthyroidism [١٥].

Furthermore, since iodine uptake by thyroid cells is mediated by a sodium-iodide cotransporter that requires a mitochondrial energy source, a prior study demonstrated that inhibition of mitochondrial oxidative phosphorylation may result in decreased iodine uptake by thyroid cells . Thyroid cells use less iodine when they are deficient in magnesium, which lowers thyroid hormone synthesis and triggers the release of thyroid-stimulating hormone (TSH). Magnesium is an enzyme cofactor that is essential to mitochondrial oxidative phosphorylation and ATP synthesis. According to animal studies, thyroid cells' uptake of radioactive iodine can be greatly increased by supplementing with magnesium, but a shortage in the mineral has the opposite effect . Deficits of magnesium, selenium, and the antioxidant coenzyme Q١٠ can cause decreased mitochondrial function in hyperthyroidism, which is indicative of an inflammatory process linked to alterations in the musculoskeletal system [١٦].

There were certain restrictions on this investigation. First, however, serum magnesium and zinc levels remain the most practical and representative indicator in a large-scale epidemiological study. Second, the study did not investigate the consumption of magnesium and zinc from food. More thorough information on the nutritional status of magnesium might have been acquired if the nutritional questionnaire, serum magnesium and zinc levels, and zinc analysis were all done at the same time.

Conclusion

Thyroid autoimmunity and tumors are correlated with several trace elements that are crucial to thyroid metabolism and function. Evidence also points to possible interactions between Zn and Mg as well as a potential link between anomalies in trace elements and thyroid iodine uptake. Avoiding trace element deficiencies may decrease diseases linked to those deficiencies as well as increase the efficiency of other trace elements. Because of interactions between trace elements, the prevalence of shortages in certain elements may lessen the efficacy of ongoing public health initiatives. In the meanwhile, more study on thyroid-related trace elements is necessary to improve clinical diagnosis and future thyroid disease treatment plans.

Conflict of interests: The authors declared no conflicting interests.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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