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Relationship between Levels of Thyroid-Stimulating Hormone Greater Than 10 Miu/L with Lipid Profile, Hemoglobin, Hematocrit and Ferritin

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Abstract
Introduction: *thyroid diseases are frequent pathologies in the world population, presenting hypothyroidism as the most common cause of symptoms. In this state, the decrease in hormonal biological activity could cause alterations in routine laboratory tests, which is why some studies have sought to clarify the relationship between various measurable blood analytes and TSH, but the results have not yet been conclusive. The need then arises to evaluate the true utility of some biomolecules in the identification of early stages of these diseases.*
Objective: *Through a retrospective investigation, we sought to understand the relationship of TSH values greater than 10 mIU/L with levels of hemoglobin, hematocrit, ferritin, and lipid profile.*
Materials and Methods: *after searching databases in the period from January to December 2021, a total of 94 patients who met the study criteria were obtained. Subsequently, the relationship between the variables of interest was analyzed, descriptive statistics were calculated and normality tests were applied with a statistical significance of p= 0.05.*
Results: *the prevalence of hypothyroidism was 1,6%, being more frequent in elderly women. A directly proportional relationship between TSH and triglyceride concentration will be appreciated, but a statistically significant relationship between TSH and complete blood count, hematocrit or ferritin was not obtained.*
Conclusion: *elevations in triglyceride levels could be considered an early sign of hypothyroidism, however, it is recommended to carry out larger studies to recover this finding and to clarify the relationship between hematological tests and TSH.*
Keywords: *Hypothyroidism; Lipoproteins; Hypertriglyceridemia; Anemia; Hematocrit; Ferritins*

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I. Introducción

Thyroid diseases have become frequent pathologies in the Colombian population with an approximate prevalence of 10%. According to the Colombian Association of Endocrinology, research has been carried out on thyroid disorders since 1999 [1,2], and although epidemiological studies of the disease remain limited, hypothyroidism is spoken of as the main disorder in its different forms. presentations, with a prevalence of 18.5% [3].

Although the risk of thyroid gland dysfunction is greater at advanced age, in recent years the diagnosis has increased in young subjects. As we well know, thyroid hormones play an essential role in bone growth and brain maturation during childhood and adolescence, so their variations during this period predispose to the appearance of alterations in physical and mental development, often irreversible [4].

The clinical picture of thyroid disorder ranges from the absence of symptoms to the presence of severe manifestations that affect quality of life; emotional lability, sleep disorders, weight gain or loss, fatigue, lethargy and dry skin are some of the most common [5].

Regarding hormonal activity, the gland synthesizes and secretes iodothyronines, with triiodothyronine (T3) and tetraiodothyronine or Thyroxine (T4) being more important from a functional point of view, which regulate basal metabolism and the development of organs and tissues [6]. This dynamic can vary in the population depending on the geographical distribution of where it is located, sex and age.

In this way, the presentation of changes in blood levels of analytes in parallel to the thyroid disorder is plausible. Thanks to the determination of pituitary Thyroid-Stimulating Hormone (TSH), it is possible to make an initial exploration of the function of the hypothalamic-pituitary-thyroid axis in the diagnosis of thyroid disease. After analyzing its levels, the need to perform additional tests is evaluated, such as measuring total and free T3 and T4, Thyroglobulin (TG), antibody titers, ultrasound and scintigraphy.

In conditions with TSH greater than 10 mIU/L, the presence of hypothyroidism must be ruled out, a pathology characterized by the decrease in the biological activity of these thyronines at the tissue level, either secondary to the ineffective production of hormones or resistance mechanisms in the tissues. white [7].

Furthermore, Forero S, et al. [8] mention that the main thyroid abnormalities are initially evident after the measurement of TSH, T3 and T4, ignoring the usefulness of other routine laboratory tests in the early identification of this type of endocrine disorders. The above highlights the importance of designing routine examinations that serve as markers for surveillance and monitoring of thyroid behavior.

Several studies have indicated that some patients suffering from hypothyroidism have had a history of anemia in a proportion of 6.1% according to a study carried out by Velásquez P. et al [9]. Furthermore, alterations can be distinguished in the lipid profile, with higher than normal values observed in relation to total cholesterol and triglycerides, increasing the atherogenic risk [10].

In accordance with the above, the objective of this work was to establish the relationship between TSH levels greater than 10 mIU/L with lipid profile, hemoglobin, hematocrit and ferritins, in patients treated in a clinical laboratory in Medellín.

II. Materials and Methods

Type of study: Retrospective study, based on the exploration of the database of patients treated at the ABAD Clinical Laboratory of the city of Medellín in the period of 2021.
Population and sample: The population was made up of patients treated at the ABAD Clinical Laboratory referred for analysis of the thyroid profile. The sample, selected at convenience, was made up of 94 individuals between 4 and 60 years old who had a TSH greater than 10 mIU/L.
Inclusion criteria: Men and women, between 4 and 60 years old with complete medical history.
Exclusion criteria: Patients without complete data, newborns and with other comorbidities.
Data collection: Information on age, TSH value, blood count, lipid profile and ferritin was extracted from the exploration of laboratory databases.

Diagnosis: TSH, ferritin and lipid profile levels were identified in serum samples, obtained by standard procedure and using chemiluminescent methods. To study the results, the biological reference values provided by the manufacturer of each assay were adopted. The determination of hemoglobin and hematocrit was carried out using whole blood with EDTA under standard procedure and electrical impedance techniques. The reference values provided by the manufacturer were adopted for the analysis of results.

Reference values: TSH: 0.45 - 5.33 mIU/L, Hemoglobin (Hb): Women: 12-16 mg/dL, Men: 13.5 -18 mg/dL, Hematocrit (Hct): Women: 36-48 % Men: 40 -54%, Ferritin (Fer): Women: 16- 154 ng/mL Men: 24- 380 ng/mL, Total cholesterol (TC): Desirable: <200 mg/dL, Limit: 200-239 mg/dL, High : >240 mg/dL, HDL Cholesterol (HDL-C): Women: <50 mg/dL, Men: <40 mg/dL, LDL Cholesterol (LDL-C): Normal: <100 mg/dL, Limit: 100-130 mg/dL dL. High limit: > 130 mg/dL. High: >160 mg/dL, Triglycerides (TG): Children from 0 to 9 years: Acceptable: Less than 75 mg/dL, Limit: 75 to 99 mg/dL, High: Greater than 100 mg/dL. Over 10 years - adults: Acceptable: Less than 90 mg/dL, Limit: 90 to 129 mg/dL, High: Greater than 130 mg/dL.

Bioethical Considerations

This research is carried out for academic purposes under the support of the institution's research committee, guaranteeing and respecting the confidentiality of the information, in accordance with resolution 008430 of Colombian legislation, the Declaration of Helsinki and the Council of International Organizations of Medical Sciences. (CIOMS) [11-13].

Statistical Analysis

The results of the tests and the variables were consolidated in a database, for the processing of the data obtained the SPSS© package for Windows™ version 2.0 and Microsoft Excel™ 2007 was used, through which the descriptive statistics of each analyte, obtaining mean, median, averages and standard deviations. In addition,

normality tests were performed with a statistical significance of p=0.05 and crosses of each of the analytes with respect to TSH.

III. Results

170 patients were found, treated in the period of January-December 2021. Of them, 94 met the inclusion and exclusion criteria. 76.6% were female. Overall, a prevalence of disease associated with hypothyroidism was estimated at 1.6%. In children and adolescents between 1 and 17 years of age, the prevalence of thyroid alteration was 0.14%. Figure 1 presents the dispersion of TSH values in relation to sex, and the age of patients with extreme values of the hormone is additionally shown.

Table 1 summarizes the descriptive statistics for the variables of interest. The mean and the median; 22.11 and 12.90, respectively, show that TSH elevations are representative for the diagnosis of hypothyroidism.

TSH values were also analyzed with respect to the other analytes (Table 2), and although there was a positive relationship, none was significant (p > 0.05). Triglycerides showed a lower p value than the other analytes (p=0.16).

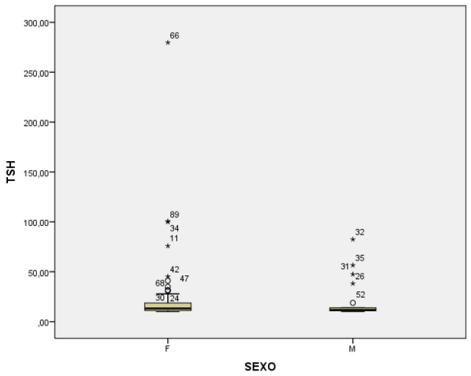

Figure 1: TSH values in mIU/L in relation to sex. Conventions: F; female, M; male, *; age of patient with extreme TSH value.

	Media	Median	Limite Inferior	Limite Superior	DS	Máximo	Mínimo
TSH	22,11	12,90	15,54	28,69	32,08	279,67	10,03
CT	184,6	191,60	172,55	196,65	58,83	303,90	66,99
cHDL	58,18	54,55	54,42	61,94	18,36	148,00	30,20
cLDL	110,97	102,5	103,6	118,34	35,98	205,00	49,00
TG	128,67	99,9	110,28	147,06	89,78	657,8	6,40
Hb	13,99	14,00	13,75	14,23	1,17	16,50	10,80
Hto	41,23	40,65	40,59	41,87	3,13	49,00	34,10
Fer	85,13	64,71	66,59	103,68	90,55	720,90	7,80

Table 1: Descriptive measurements of the determined blood analytes.

Conventions: DS; Standard deviation, HDL-C; high-density lipoprotein cholesterol in mg/dL, LDL-C; low-density lipoprotein cholesterol in mg/dL, TG; triglycerides in mg/dL, Hb; hemoglobin in mg/dL, Hct; hematocrit in %, Fer; ferritin in ng/mL.

	cHDL	cLDL	TG	Fer	Hb	Hto
Pearson correlation coefficient	0,065	0,078	0,146	0,032	0,067	0.014
Value of p	0,537	0,453	0,160	0,761	0,520	0,895

Table 2: Correlation of TSH levels with lipid profile and hematological tests.

Conventions: HDL-C; high-density lipoprotein cholesterol in mg/dL, LDL-C; low-density lipoprotein cholesterol in mg/dL, TG; triglycerides in mg/dL, Hb; hemoglobin in mg/dL, Hct; hematocrit in %, Ferritin in ng/mL

IV. Discussion

According to the Colombian Association of Endocrinology, hypothyroidism is a common disorder in women. Epidemiological studies carried out speak of a ratio of 4 to 10 for each man, in addition, the risk increases with age. The prevalence is around 4.0% [14]. These observations are consistent with our results, where we observed a predominance of the female sex in relation to thyroid alteration.

The prevalence of hypothyroidism in children has remained less than 2.0%, according to the Journal of Pediatric Endocrinology. In recent times, the study of family history of thyroid diseases and goiter has led to more screening tests being performed on minors, increasing diagnoses and thus prevalence figures [15]. Our study reinforces these figures, with a prevalence value of hypothyroidism in children and adolescents of 0.14%.

According to the Colombian journal of endocrinology, diabetes and metabolism [16], a diagnosis of clinical hypothyroidism is considered when TSH values greater than 10 mIU/L coexist in addition to a primary or proper alteration in the thyroid gland. As we well know, in relation to the symptoms, these pathologies often present with imperceptible changes in early stages, as mentioned by several authors such as Quintanilla G. et al [17], however, as the disease progresses they become accentuated and cause nervous, cardiac, metabolic and muscular dysfunction.

It is known that the decrease in the activity of the T3 hormone affects lipoprotein metabolism as a consequence of the decrease in lipid catabolism. Apparently, there is a slowdown in the processing of cholesterol and triglycerides at the intrahepatic level, which is reflected in high concentrations in the blood [17].

In this research, a direct relationship between TSH and TG levels was found, approximately 14%. This relationship was also observed, although to a lesser extent, with the patients' TC and LDL-C levels. In other research works, such as that of Montaño M. [18], they mention that free fatty acids, instead of being used by the cell as fuel, are diverted towards the synthesis of LDL-C, which increases the atherogenic risk in the patient. They also indicate that the most affected population is females, with 66.4% of cases and that TG are affected in 64.4%, being more common in adult patients.

If we talk about other studies and research, we find information that reaffirms the results obtained; For example, in the study carried out by Villalba M, et al. [19] it is mentioned that when analyzing the TSH values with the lipid profile and Hb, only a correlation was obtained with the TG levels corresponding to 65%, likewise, they express that women with clinical hypothyroidism (TSH >10 mIU/L) show a 5-fold higher risk of suffering from hypertriglyceridemia, and that postmenopausal women are the most affected, which confirms that the adult population adds predisposing risk factors.

Additionally, it can be noted that the hypothyroid patient has a greater risk of developing metabolic syndrome. According to several organizations, high triglyceride levels are one of the critical points for the diagnosis of the syndrome, adding glucose intolerance, diabetes, high blood pressure and obesity. In a study carried out by Diaz D, et al. [20], where they analyzed the metabolic status of patients admitted to a hospital unit, they found that 41% suffered from metabolic syndrome and 6.0% presented hypothyroidism and metabolic syndrome together. It is therefore appropriate to apply therapeutic strategies aimed at carrying out physical activity and adopting low-fat diets, since they have a direct link with the reduction of triglyceridemia.

It has also been mentioned that hypothyroidism can have consequences at the level of erythropoiesis, affecting hemoglobin, hematocrit and ferritin. However, the studies carried out in Colombia on this topic are limited. A study carried out in India demonstrated the existence of mild hemoglobin variations, with a frequency of 18.0%, in patients with hypothyroidism and normocytic-normochromic or microcytic-hypochromic anemia may occur [21]. If contrasted with our research, there was no significant statistical relationship between THS and Hb, Hct or Fer. This lack of association may be linked to early stages of hypothyroidism and factors that affect iron metabolism and absorption. According to Martin D. et al [22], coronary heart disease, heart failure and COPD have common pathophysiological mechanisms, which converge in the alteration of ferritin values, after which anemia occurs. Therefore, it is important to consider these interferences. Iron deficiency is also related to low levels of T3, according to Tanver H, et al. [23], showing statistically significant figures in which women have a higher prevalence of iron deficiency (28.5%).

Our study allowed us to notice thyroid alterations linked to the dose of levothyroxine used to control hypothyroidism, so it is necessary to monitor the patient and their respective routine for taking the medication. The manual of thyroid pathology [24] states that it is essential to take the drug daily, on an empty stomach and with water, at least one hour before breakfast. Furthermore, it is extremely important that the patient is not consuming other drugs that may modify their absorption or effect such as omeprazole, ferrous sulfate, and aluminum hydroxide [25].

V. Conclusion

Currently, there is an increase in the need for early surveillance of thyroid disorders. This study demonstrates that there is a positive trend between elevations in TSH and triglycerides, which is why one could consider using hypertriglyceridemia as signs of hypothyroid disease. Thus, in clinical practice, cases of hyperlipidemia could be evaluated from endocrinology with the thyroid profile in order to verify the functioning of the neuroendocrine axis and make a timely therapeutic intervention. With the sample used, no association was observed between the levels of TSH and hemoglobin, hematocrit and ferritin. It is recommended to carry out larger studies to clarify the relationship between hematological tests and TSH.

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