INTERNATIONAL SEVEN JOURNAL
OF HEALTH RESEARCH
ISSN: 2764-9415

Analysis of the association between lipid panel and hypothyroidism in patients at a private laboratory in Jacutinga – MG

Análise da associação entre perfil lipídico e hipotireoidismo em pacientes de um laboratório particular em Jacutinga – MG

DOI: 10.56238/isevjhv2n6-007
Receipt of originals: 10/20/2023
Publication acceptance: 12/13/2023

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ABSTRACT

Introduction: The thyroid gland produces the thyroid hormones triiodothyronine (T3) and thyroxine (T4), which regulate metabolism by transcribing certain genes. Hypothyroidism is characterized by a decrease in the body's metabolic activity due to the low production of important agents for this process, which can cause cases of dyslipidemia. Objective: To analyze the relationship between hypothyroidism and lipid profile in biological samples from patients treated at a private laboratory in the city of Jacutinga, Minas Gerais, Brazil, during 2022. Material and Method: Data were collected from laboratory reports of patients over 18 years of age who simultaneously underwent TSH, free T4, total cholesterol, HDL-c, LDL-c, VLDL-c and triglyceride tests, and after collection, the data were separated according to the presence or absence of hypothyroidism, based on the reference values. The lipid profile of patients with hypothyroidism was also analyzed according to the reference values. The study variables were age and gender. Results: The study included 470 laboratory reports, where 17.66% were characterized as hypothyroidism and of these, 61.45% were females with a mean age of 51 years and 38.55% were males with a mean age of 55 years. Total cholesterol and LDL-c tests showed elevation in 55.42% and 40.96% of hypothyroid patients, respectively. Conclusion: It is concluded that females have a higher incidence of hypothyroidism, especially after 50 years of age. The incidence of elevation in lipid tests was also higher among females.

Keywords: Thyroid, Lipidogram, Dyslipidemias.

1 INTRODUCTION

The thyroid gland is one of the main endocrine glands, located in the anteroinferior region of the neck and composed of lobes that shape it similar to a "butterfly" when observed macroscopically. Microscopically, the thyroid is composed of follicles surrounded by a layer of cells, the thyroid cells (Branca *et al*., 2022). It is responsible for the production of thyroid hormones (HT), triiodothyronine (T3) and thyroxine (T4), which play a considerable role in the body's metabolism and their synthesis and release are coordinated by the hypothalamic-pituitary-thyroid axis (Colaço, 2018; Souza *et al*., 2020).

The regulation of thyroid hormone begins in the hypothalamus by the secretion of thyrotropin-releasing hormone (TRH) synthesized in the paraventricular region. TRH acts on the pituitary gland, in its anterior portion, inducing the release of thyroid-stimulating hormone (TSH) by thyrotrophs. TSH levels are regulated, in turn, by the negative feedback mechanism, i.e., TH concentrations influence its biosynthesis (Feldt-Rasmussen; Effraimidis; Klose, 2021; Feldt-Rasmussen; Klose; Benvenga, 2018).

The synthesis of TH is carried out from thyroglobulin, a molecule formed in the thyroids and composed of the amino acid tyrosine together with iodide ions, which come from the bloodstream. Once inside the thyrocytes, thyroglobulin and iodine travel to the follicular lumen, where they will be stored in the colloid. Therefore, each thyroglobulin molecule has several tyrosine radicals coupled with iodine molecules, where the union of two tyrosines with two iodides each results in a molecule of T4 and two tyrosines, plus one and two iodides, respectively, forming T3 (Bílek *et al*., 2020; Citterio; Targovnik; Arvan, 2019).

Once in the intracellular medium, the concentration of T3 available for binding to thyroid hormone receptors is given by the conversion of T4 to T3, by means of the selenoenzymes iodothyronine deiodases (DIOs), which catalyze the deiodization of the inner and/or outer ring of the T4 molecule. These enzymes are subdivided into: DIO1, DIO2 and DIO3, and DIO1 and DIO3 are located in the plasma membrane, however, the catalytic domain of DIO3 acts by inactivating T4 and T3, producing reverse T3; DIO2 is found in the endoplasmic reticulum and, like DIO1, acts by activating TH (Aranda, 2021; Sabatino *et al*., 2021).

Among the pathologies that affect this gland, hypothyroidism comprises the most common hormonal diseases, caused by the reduction in the secretion of thyroid hormones (Colaço, 2018). It can be primary (clinical), central, or subclinical, depending on the values found in TSH and free T4 (FT4) levels (Mavromati; Jornayvaz, 2021). Subclinical hypothyroidism (SCH) is defined by an increase in serum TSH associated with normal FT4, which can progress to the clinical form,

where there is also a decrease in FT4. Central hypothyroidism (CH) occurs when TSH levels are normal or slightly increased associated with low FT4 (Carvalho; Perez; Ward, 2013). Silva *et al*. (2018) state that the main cause of SCH is autoimmunity, manifested by Hashimoto's Thyroiditis.

Due to the decrease in T3 and T4 levels, individuals with hypothyroidism develop alterations in their lipid metabolism, which can lead to cardiovascular and hepatic complications (Chiovato; Mac; Carlé, 2019). The T3 hormone is the active form, which interacts with its receptor and participates in the transcription of specific genes that are essential for the body's metabolism, so its decrease directly affects the synthesis of proteins involved in the most varied physiological processes (Aranda, 2021). This decrease occurs due to thyroid dysfunction, iodine and deiodases deficiency, and also due to changes in the hypothalamus and pituitary gland (Dias *et al*., 2022).

The reduction in T3 and T4 levels results in slowing of metabolism, mainly due to the absence of transcription of several genes involved in metabolic activities, thus hypothyroidism interferes with metabolism (Ritter; Amano; Hollenberg, 2020). Such interference can be detected in the evaluation of the lipid profile (PF), a set of tests that aim to measure the levels of lipids in the blood plasma, in order to monitor and/or diagnose certain diseases. To perform the PF, the following are measured: triglycerides (TG), high-density lipoprotein (HDL-c), very low-density lipoprotein (VLDL), total cholesterol (TC), and calculations are also used to estimate the dosage of low-density lipoproteins (LDL-c) (Dos Santos; Wolf; Pires, 2020; Langlois; Nordestgaard, 2018).

The importance of the proposed theme is based on the study of the complications that hypothyroidism can bring, especially with regard to lipid disorders, which are risk factors for other serious pathologies, such as cardiovascular diseases. For this reason, the evaluated data contribute to the knowledge of patients and health professionals, also allowing the elaboration of future studies on this subject.

Thus, the objective of this study was to analyze the relationship between hypothyroidism and lipid profile in biological samples from patients treated at a private laboratory in the city of Jacutinga – MG during the year 2022, establishing a relationship with age and gender.

2 MATERIAL AND METHODS

The research was carried out by analyzing the relationship between hypothyroidism and lipid profile of patients treated at a private laboratory in the city of Jacutinga – MG in 2022, following as inclusion criteria the laboratory reports of patients over 18 years of age that simultaneously contained all the following tests: free T4, TSH, LDL-c, HDL-c, VLDL-c, Total

Cholesterol and Triglycerides. The exclusion criteria were age under 18 years and not performing all the tests mentioned simultaneously.

After collection, the data were separated according to the presence or absence of hypothyroidism, based on the reference values for this purpose, and the lipid profile of patients with hypothyroidism was analyzed. The study variables were age and gender, emphasizing their prevalence, which was demonstrated by means of graphs and tables. In order to ensure the integrity of the documents and patients, the confidentiality of the information obtained was maintained.

The data were collected in the laboratory's database with the authorization of the Biomedical and Owner Partner, therefore, the research did not require the use of the Free and Informed Consent Form (ICF), since there was no direct contact with the patients.

The research was approved by the ethics committee of the Centro Universitário Fundação de Ensino Octávio Bastos – UNIFEOB/SP under opinion number 6.302.930 and by the Coordination of Research, Extension and Internship (CPE) of the Regional University Center of Espírito Santo do Pinhal (UNIPINHAL) under protocol number 1400.

3 RESULTS AND DISCUSSION

The study included 470 laboratory reports, of which 83 (17.66%) were characterized as having some type of hypothyroidism, based on the reference values shown in Appendix B, namely: Central hypothyroidism (n=1), clinical hypothyroidism (n=1) and subclinical hypothyroidism (n=81). Euthyroid patients corresponded to 82.34% (n=387). These data can be seen in Table 1, which also showed the prevalence of the disease by sex.

Table 1 - Classification of patients according to thyroid function

Thyroid function	Female	Male	Total
Euthyroidism	251	136	**387**
Central hypothyroidism	1	0	**1**
Clinical Hypothyroidism	0	1	**1**
Subclinical Hypothyroidism	50	31	**81**
Total	**302**	**168**	**470**

Source: Author's own (2023).

Corroborating the study by Galeano, Pedrozo, and Ovelar (2020), research has shown that subclinical hypothyroidism is the most common form of hypothyroidism, occurring mainly in females. According to Silva et al. (2018), the main cause of SCH is the autoimmunity observed in Hashimoto's thyroiditis, however, the analysis of autoantibodies was not included in the present study.

It is worth noting that in the case of suspected SCH, it is recommended that the TSH measurement be repeated over a period of 3 to 6 months to exclude possible laboratory errors or transient TSH elevation (Sgarbi *et al*., 2013).

The TSH levels of the patients with hypothyroidism can be seen in Table 2, which showed that most of the patients had TSH in the range of 4.5-10 mIU/L, and the majority of females were the majority in both intervals of hormone dosage.

Table 2 - TSH levels of patients with hypothyroidism

TSH (mIU/L)	Female	Male	Total
< 4,5	1	0	1
4,5 - 10	42	28	70
> 10	8	4	12
Total	**51**	**32**	**83**

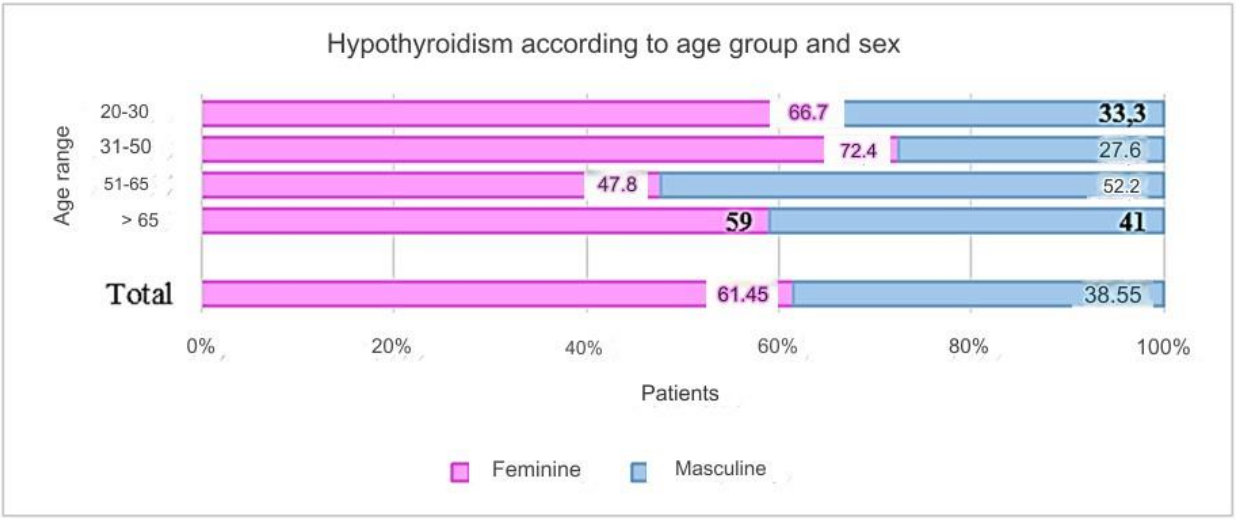
Source: Author's own (2023).

According to Sgarbi *et al.* (2013), SCH can be classified as mild-moderate or severe, according to the risk of progression to the clinical form of the disease, with TSH concentrations higher than 10 mIU/L representing greater chances of this progression. Thus, the TSH range of 4.5–10 mIU/L is considered as mild-moderate SCH. In addition, it is important to emphasize the greater probability of developing other pathologies as TSH levels rise.

Hashimoto (2022) states that 75% of patients with SCH belong to the mild-moderate range in TSH dosage, however, in the present study, of the sample obtained, 97.6% of patients with hypothyroidism were classified as having SCH, and of these, 85.2% (n = 69) fell into the previously mentioned range.

As shown in Graph 1, of the hypothyroidism cases found, 61.45% were female patients (n = 51), while 38.55% were male (n = 32), with the mean age of women being approximately 51 years and men 55 years. The age group with the highest incidence of hypothyroidism in females was 31 to 50 years, while for males it was 51 to 65 years. It is noteworthy that the cases of hypothyroidism found were of patients aged ≥ 20 years.

Graph 1 - Cases of hypothyroidism related to gender and age



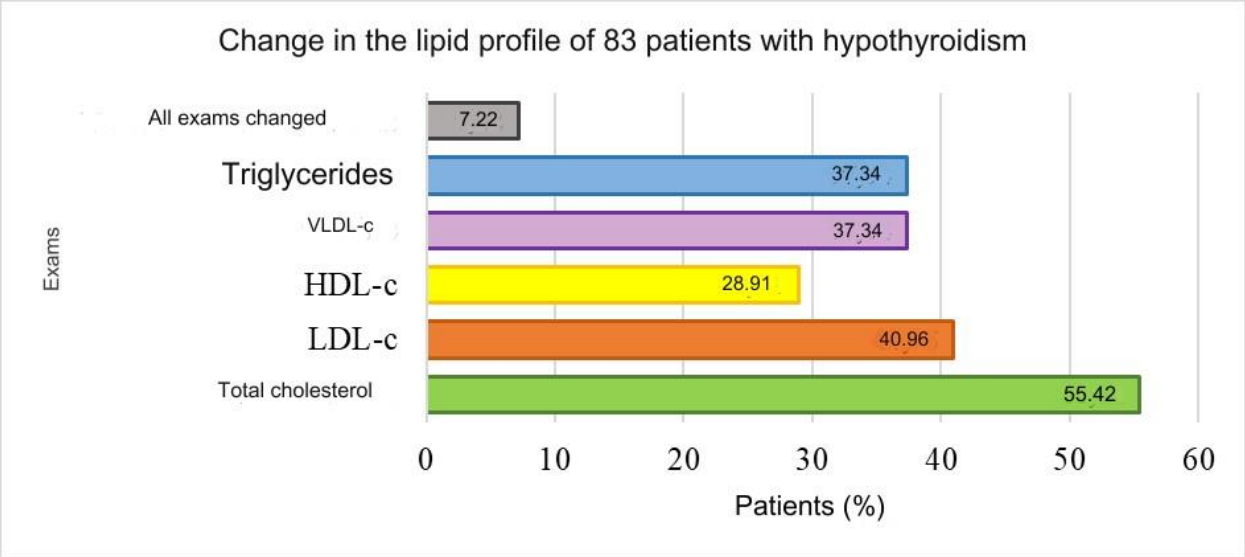
Source: The author (2023)

As in the study by Ejaz *et al*. (2021), the present research revealed that the subclinical form of the disease is associated with advancing age in women, and for females, endocrinological follow-up is recommended, especially after menopause, since hypothyroidism especially affects women in this period, around 45 – 50 years of age, due to hormonal changes (Brenta *et al*., 2013). According to Dula *et al*. (2022), the prevalence of hypothyroidism is lower in males than when compared to females, however, women tend to develop the disease earlier than men, who, in their majority, are diagnosed at 50 years of age.

The third highest incidence of hypothyroidism was in elderly patients (>65 years), however, according to Brenta *et al*. (2013), the maximum serum TSH limit of 4.5 mIU/L may not correspond to the physiological limit of individuals over 80 years of age, since such limits tend to increase with age, leading to overdiagnosis and unnecessary treatments. The authors also emphasize the importance of periodic TSH measurements in patients who present repeated variations between 4.5 and 10 mIU/L in two to three months, in order to confirm thyroid alterations.

The lipid profile of patients with hypothyroidism was analyzed using reference values for fasting adults (Appendix C), thus, as shown in Graph 2, the Total Cholesterol test showed an increase in most patients (55.42%; n=46), followed by LDL-c (40.96%; n=34), triglycerides and VLDL-c (37.34%; n=31) and decreased HDL-c (28.91%; n=24). Alterations in all the tests mentioned were also observed in 7.22% of the patients (n=6).

Graph 2 - Alteration in lipid profile tests in patients with hypothyroidism



Source: The author (2023)

As with the research by Ejaz *et al*. (2021), the present study showed similar results regarding lipid alterations, with serum total cholesterol and LDL-c being the most altered in individuals with hypothyroidism. Paradoxically, the research by Pérez *et al.* (2021) demonstrated a direct relationship between hypothyroidism and hypertriglyceridemia in 37.34% of the cases evaluated. This increase occurs, according to Feingold (2021), due to the suppression of the lipoprotein lipase enzyme, which leads to a decrease in the clearance of triglyceride-rich lipoproteins, causing their plasma increase in hypothyroidism. Another factor that also leads to elevated plasma TG is the increased rate of hepatic secretion of triglyceride-rich VLDL. Also according to the author, HDL-c levels may be decreased in hypothyroidism, even if slightly, which causes the limitation of reverse cholesterol transport, favoring its plasma increase. The cause of the decrease in plasma HDL-c in hypothyroidism is not yet well established, however, according to Su *et al.* (2022), this decrease may be related to the synthesis of dysfunctional HDL particles with an impaired ability to induce the progression of reverse cholesterol transport.

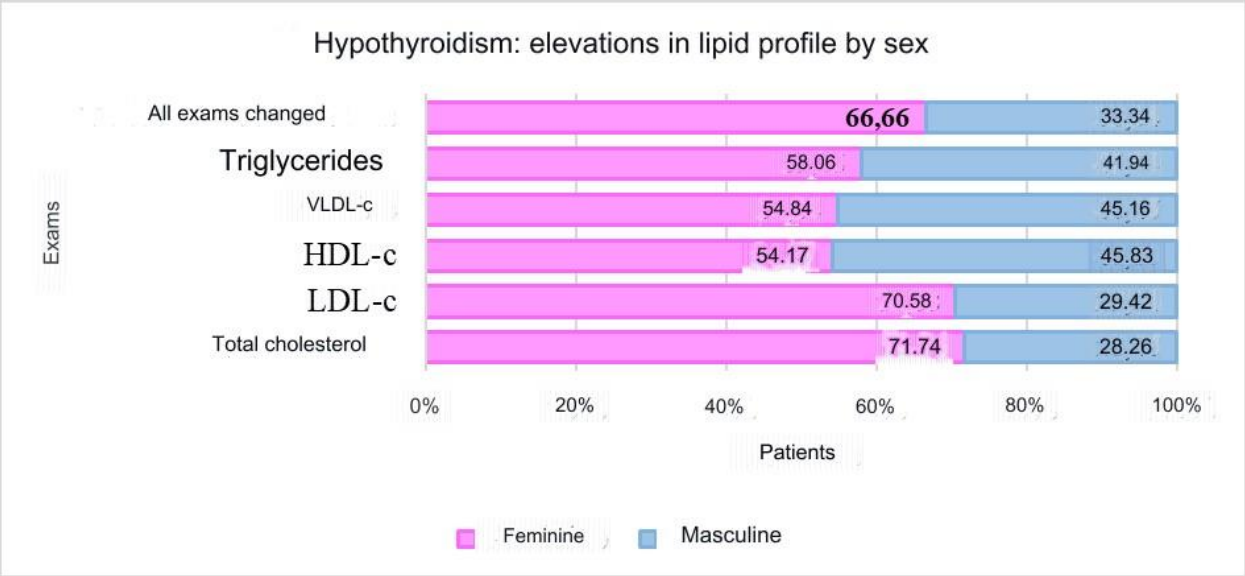
According to the study by Xu (2014), carried out through a meta-analysis involving 41,931 adults with the aim of evaluating changes in the lipid profile of individuals with the subclinical form of hypothyroidism, it was found that the levels of TC, LDL-c and TG were significantly higher compared to euthyroid patients. In addition, HDL-c levels were significantly lower in patients with subclinical hypothyroidism compared to euthyroid patients.

According to Yanai and Yoshida (2021), dyslipidemia secondary to hypothyroidism is mainly caused by the decrease in hepatic LDL-c clearance, due to the decrease in transcription of

the genes responsible for the production of LDL-c receptors in the liver, leading to the plasma accumulation of this lipoprotein. In addition, there is a decrease in the enzyme 7-alpha-hydroxylase, which converts cholesterol into bile acids, which results in its accumulation.

Graph 3 details the relationship between lipid profile elevation and gender in patients with hypothyroidism. It was observed that females showed a higher elevation in relation to males in all examinations.

Graph 3 - Relationship between Lipid Profile and gender of patients with hypothyroidism



Source: The author (2023)

In agreement with Karthick's study *et al.* (2013), the present study revealed a greater susceptibility of females to suffer elevations in plasma lipids, especially in the context of hypothyroidism, characterizing a form of secondary dyslipidemia.

4 CONCLUSION

Hypothyroidism emerges as a significant risk factor for the development of dyslipidemias. The prevalence of the disease in its subclinical stage is higher than when compared to the clinical disease, predominantly affecting the female sex, due to the hormonal fluctuations that occur throughout the life of women. Advancing age is also a risk factor for hypothyroidism. However, it is crucial to point out that the increase in thyroid-stimulating hormone (TSH) levels in individuals over the age of 80 may be a physiological response. Therefore, healthcare professionals must take an individualized approach in order to avoid overdiagnosis and the implementation of unnecessary treatments.

Changes in the lipid profile are a striking feature in the context of hypothyroidism. Plasma lipids are elevated when thyroid hormones are decreased, due to the absence or decrease in transcription of genes that encode factors essential for lipid metabolism. The levels of total cholesterol and LDL-c are particularly affected, due to the reduction of their conversion into bile acids and the decrease in uptake by hepatic receptors, respectively, favoring the onset of cardiovascular diseases, which are related to the high number of deaths in Brazil and worldwide.

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