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# Research Article
# Evaluation of the Lipid Profile and Atherogenic Risk in Hypothyroid Patients

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## Abstract

**Background and Objective:** Hypothyroidism is a common, benign pathology due to a deficiency in the secretion of thyroid hormones by the thyroid. It is often associated with dyslipidemia, thus increasing cardiovascular risk. There is little data relating to a possible correlation between the lipid profile and hypothyroidism despite their high hospital frequencies. Thus, the objective of this study was to evaluate the relationship between lipid profile abnormalities and hypothyroidism. **Materials and Methods:** This is a prospective case-control study involving hypothyroid subjects. The parameters studied were on the one hand age, sex and on the other hand FT4, TSHus and lipid profile. Assays of biochemical parameters were carried out with the Architect Ci 4100 automated system (Abbot). The Spearman test was used to evaluate the correlation. A p-value less than 0.05 was considered significant. **Results:** The current study of 81 hypothyroid patients with a mean age of 41 years and a sex ratio equal to 0.20. Dyslipidemia was found in 67.79% of hypothyroid patients. Hyper LDL-cholesterolemia was the most frequent, affecting 54.32% and hypo-HDLemia was the least frequent, i.e. 22.22%. Analysis of the indices according to the upper normal limits showed an IAP (Log TG/HDL-c) greater than 0.21 in 59.25% of hypothyroids. The Spearman test showed a statistical correlation ($p<0.05$) on the one hand between the parameters of the lipid profile and the thyroid hormones (T4L, TSHus) except HDL-cholesterol and on the other hand between the thyroid hormones and the plasma atherogenicity index. **Conclusion:** The lipid disorders are quite common in hypothyroidism. These abnormalities must be systematically detected at diagnosis and re-evaluated after treatment, due to their strong association with an atherogenic risk.

Key words: Hypothyroidism, lipid profile, dyslipidemia, plasma atherogenicity index, cardiovascular risk

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

The thyroid located at the base of the neck is under the control of Thyroid-Stimulating Hormone (TSH) produced by the thyrotropic cells of the anterior pituitary. It is an important endocrine gland in the human body, due to its ability to produce the thyroid hormones, necessary for proper energy levels and an active life[1]. Thyroid hormones regulate the metabolic process essential for normal growth and development. They increase basal metabolism by stimulating the consumption of oxygen by most cells in the body for energy production and help regulate the metabolism of lipids, carbohydrates and proteins. Dysthyroidism represents a frequent clinical situation in laboratory practice. Their positive diagnosis is based on the TSH assay, the performance of which is widely documented in the literature[2]. Among them, hypothyroidism is the most common thyroid dysfunction, particularly in women. It is defined by an insufficient secretion of thyroid hormones by the thyroid gland, responsible for a state of hypometabolism[3]. It is most often linked to a primary thyroid disorder and more exceptionally to a defect in secretion or activity of pituitary TSH[4]. Thyroid insufficiency can be the consequence of destruction of the thyroid gland, of an autoimmune process with thyroiditis or of an aging process with tissue sclerosis. It can also be the consequence of hormone synthesis disorders of congenital origin[5]. The prevalence in the general population is 0-3% and 3-7% in the United States and between 0-2% and 5-3% in Europe[6]. Hypothyroidism can have significant repercussions on the body, including a disorder of lipid metabolism. Indeed, thyroid hormones (TH) regulate all the main pathways of basic metabolism. They play an important role in the synthesis, metabolism and transport of lipids. Hypothyroidism is a common cause of secondary dyslipidemia, thus amplifying cardiovascular risk and morbidity and mortality[7]. This is linked to the elevation of LDL-cholesterol and blood pressure changes. This risk may be increased by the disruption of homocysteine metabolism under the influence of thyroid hormones[8]. Indeed, the abnormalities observed in total and LDL-cholesterol are associated with changes in thyroid hormone levels in hypothyroidism, because they are significantly improved after thyroxine replacement treatment[9]. In Senegal, there is little data relating to this correlation between the lipid profile and hypothyroidism despite their high hospital frequencies. In this context, this study evaluated the lipid profile and plasma atherogenicity index in patients suffering from hypothyroidism.

## MATERIALS AND METHODS

**Study area:** This is a prospective case-control study, lasting thirteen months from November 4, 2022, to December 15, 2023.

**Study design:** Patient recruitment and biological tests were carried out in the Biochemistry Laboratory of the University Hospital Center of Fann. Patients monitored for hypothyroidism were included in this study after informed consent. The study did not concern patients with unusable data (unknown diagnosis and missing epidemiological parameters). Blood samples were taken from the subjects by venipuncture at the elbow crease with a tourniquet. Blood was collected in a dry tube for the determination of thyroid hormones (FT4 and TSHus) and lipid profile parameters (total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides). For the assessment of atherogenic risk the indices used are: Total cholesterol/HDL-cholesterol (CT/HDL-c), LDL-cholesterol/HDL-cholesterol (LDL-c/HDL-c), Log (triglycerides/HDL- cholesterol) and dyslipidemia were defined according to the American recommendations of the Adult Treatment Program III (ATPIII) of the National Cholesterol Education Program (NCEP)[10]:

- Hypercholesterolemia (total cholesterol >2 g/L)
- Hypertriglyceridemia (triglycerides >1.5 g/L)
- Mixed hyperlipidemia (total cholesterol >2 g/L and triglycerides >1.5 g/L)
- Hypo HDL-cholesterol (HDL-C<0.4 g/L in men and <0.5 g/L in women)
- Hyper LDL-cholesterolemia (LDL-C>1.3 g/L)

The biochemical parameters were measured using the Architect Ci4100 Analyzer (Abbott).

**Statistical analysis:** Data recording was carried out with Excel software and the exploration was done with XLSTAT 2019. The Spearman test was used for the correlation and the Student's t-test for the comparison of means. A $p<0.05$ was considered significant.

**Ethical consideration:** Patients were included after their informed consent.

## RESULTS

A total of 81 hypothyroid subjects were included in the present study. The average age of the patients was 41±24 years with extremes of 4 and 77 years and the age

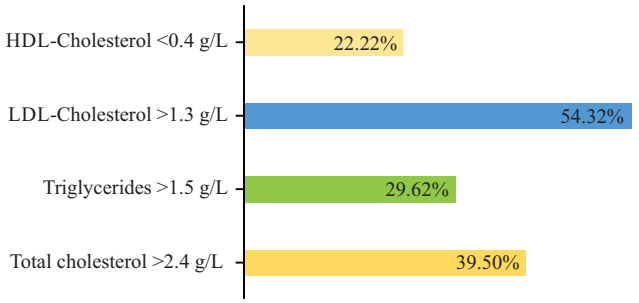


Fig. 1: Distribution of lipid profile parameters in case

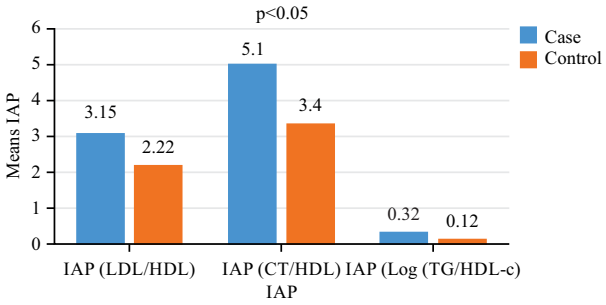


Fig. 2: Comparison of atherogenicity indices between case and controls
IAP: Plasma atherogenicity index

Table 1: Characteristics of the general population

| Characteristics | Case | Control |
|---|---|---|
| Number | 81 | 65 |
| Average age (years) | 41±24 | 43.86±16 |
| Sex-ratio | 0.20 | 0.20 |
| Mean FT4 (pmol/L) | 8.59 | 12.26 |
| Mean TSHus (mIU/L) | 16.88 | 2.17 |

Table 2: Determination of the means of biochemical parameters in cases and controls

| Parameter | Case | Control | p |
|---|---|---|---|
| FT4 (pmol/L) | 8.59 | 12.26 | 0.032* |
| TSHus (mIU/L) | 16.88 | 2.17 | 0.00019* |
| Total cholesterol (g/L) | 2.30 | 1.9 | p<0.05* |
| Triglycerides (g/L) | 1.20 | 0.87 | 0.00022* |
| HDL-cholesterol (g/L) | 0.53 | 0.62 | 0.0024* |
| LDL-cholesterol (g/L) | 1.40 | 1.2 | 0.153 |

*Statistically significant difference (p<0.05), HDL: High Density Lipoprotein and LDL: Low Density Lipoprotein

of the patients. The sex ratio was 0.20. The mean concentrations of FT4 and TSHus in hypothyroid were 8.59 pmol/L and 16.88 mIU/L, respectively (Table 1).

Comparison of the means between case and controls showed significant differences (p<0.05) for all biochemical parameters except for the LDL-cholesterol fraction (Table 2).

Dyslipidemia was defined according to the American recommendations of the Adult Treatment Program III (ATPIII) of the National Cholesterol Education Program (NCEP) and the analysis of the results showed that 67.79% of hypothyroid patients presented dyslipidemia. The hyper LDL-cholesterolemia is the most common and affects 54.32% of hypothyroids; 39.50% of patients have hypercholesterolemia. Hypertriglyceridemia is found in 29.62% of patients. Hypo-HDLemia is the least common (22.22%) (Fig. 1).

The evaluation of the three indexes used in present study showed higher values in hypothyroids than in controls. Comparison of mean values showed statistically significant differences (p<0.001) (Fig. 2).

Analysis of the indexes according to the upper normal limits showed an IAP (Log TG/HDL-c) >0.21 in 59.25% of patients (Fig. 3).

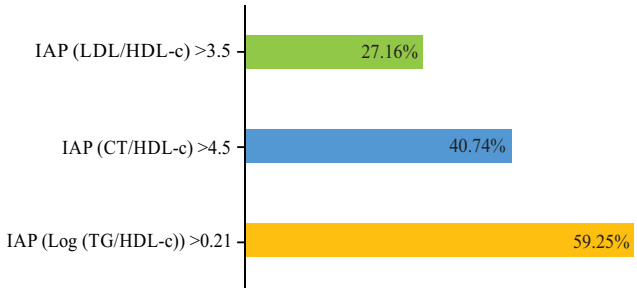


Fig. 3: Distribution of IAP (plasma atherogenicity index) among patients

Table 3: Correlation between lipid profile parameters, IAP and thyroid hormones (FT4, TSHus) in patients

| | TSHus | | FT4 | |
|---|---|---|---|---|
| Parameter | Rho | p | Rho | p |
| Triglycerides | 0.511 | 0.0013 | -0.260 | 0.061 |
| Total cholesterol | 0.231 | 0.001 | -0.402 | 0.003 |
| HDL-cholesterol | -0.113 | 0.418* | 0.098 | 0.482* |
| LDL-cholesterol | 0.440 | 0.001 | -0.300 | 0.029 |
| LDL/HDL | 0.286 | 0.039 | -0.317 | 0.021 |
| CT/HDL | 0.278 | 0.044 | -0.343 | 0.012 |
| Log (TG/HDL) | 0.380 | 0.005 | -0.297 | 0.031 |

CT: Total cholesterol, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, TG: Triglycerides and *Not significant difference (p>0.05)

The evaluation of the correlation by the Spearman test between the parameters of the lipid profile, the plasma atherogenicity indices and the thyroid hormones (FT4, TSHus) in the patients showed statistically significant correlations except for HDL-cholesterol (Table 3).

## DISCUSSION

A total of 81 hypothyroid subjects were included in the present study. The average age of the study population was 41±24 years with extremes of 4 and 77 years. In addition, most of the subjects included in the current study (40%) were in the age group (20-49 years). This result was corroborated by that of Ezzhara *et al.*[7] in a similar study with an average age of 41.66. Likewise, Abid *et al.*[11] found results comparable to the current study. The occurrence of hypothyroidism is observed at all ages, with a higher frequency in subjects aged between 40 and 50 years old[12]. The sex distribution of the studied population showed a large female predominance with a sex ratio of 0.20. This result thus consolidates what has been found in the literature which reports the high prevalence of hypothyroidism in women. Zoungrana *et al.*[13], in a study carried out in Burkina Faso, found a sex ratio of 0.26. According to Vanderpump *et al.*[14], the prevalence increases with age and reaches up to 16% of women over the age of sixty. Without however asserting that there is a particular link between hypothyroidism and the female sex, this female predominance found in the literature could be explained by the hormonal interactions that women experience at several periods of their life, particularly during menopause[15]. In the present study, the cut-off values adopted by the National Cholesterol Education Program (NCEP) Adult Treatment Program III (ATPIII)[10] to assess lipid abnormalities. Dyslipidemia (whatever its type) was noted in 67.79% of hypothyroid patients. The distribution according to lipid profile showed that hyper LDL-cholesterolemia was the most common, affecting 54.32% of hypothyroids. The 39.50% of patients presented hypercholesterolemia. Hypertriglyceridemia was found in 29.62%. Hypo-HDLemia was the least common with 22.22%. This prevalence of dyslipidemia found in the studied population has been reported in similar studies. In Tunisia, Kechida *et al.*[16] found dyslipidemia in 64.4% of hypothyroid patients in 2018 and hypercholesterolemia was the most common lipid abnormality. In Morocco in 2021, Ezzahra *et al.*[7] in a similar study found a prevalence of dyslipidemia of 91.78% with a predominance of hypo HDL-cholesterolemia (82.12%).

During hypothyroidism dyslipidemia generally manifests as elevated levels of total cholesterol, triglycerides, Low-Density Lipoprotein (LDL) and reduced levels of High-Density Lipoprotein (HDL)[17]. Thyroid hormones (HT) regulate all major pathways of basal metabolism. Indeed, they play an important role in the synthesis, metabolism and transport of lipids[18]. Consequently, hypothyroidism would cause a drop in lipoprotein lipase activity, which could be a

factor in the elevation of triglyceride[19]. The increase in total cholesterol and LDL cholesterol is due to a reduction in the activity of LDL receptors, leading to a reduction in the catabolism of LDL and IDL[20]. Thyroid hypofunction does not seem to have an effect on HDL Cholesterol, which is explained by the expression of apoA-I, leading to a reduction in the synthesis and secretion of HDL by the liver[19]. Thyroid hormones influence all aspects of lipid metabolism, including synthesis, mobilization and degradation, which accelerates the atheromatous process and increases cardiovascular risk[21]. Indeed, plasma concentrations of lipoprotein (a) increase during hypothyroidism and it has been demonstrated that Lp(a) has a thrombogenic and atherogenic effect[19]. A more direct association between hypothyroidism and coronary heart disease has been postulated in other studies, indeed in heart disease, particularly in ischemic heart disease, abnormalities in thyroid hormone levels are common and constitute an important factor to take into account[22]. The assessment of atherogenic risk showed higher values of the three indices (LDL/HDL, CT/HDL) and Log (TG/HDL-c) in hypothyroids compared to controls with a statistically significant difference. The index (Log TG/HDL-c) was greater than 0.21 (upper normal limit) in 59.25% of hypothyroids. Present study result was similar to that of James *et al.*[23], who found triglycerides/HDL-C significantly elevated during subclinical hypothyroidism. Dysthyroidisms appear to impact the cardiovascular system via numerous mechanisms, including dyslipidemia, hypertension, systolic and diastolic myocardial dysfunction, as well as endothelial dysfunction[24]. The Spearman test performed between lipid profile parameters, plasma atherogenicity indices and thyroid hormones (T4L, TSHus) in patients showed statistically significant correlations except for HDL-cholesterol ($p>0.05$).

## CONCLUSION

Results showed that hypothyroidism is often associated with dyslipidemia, in particular hyper LDL-cholesterolemia. These results are consistent with those in the literature regarding the frequency of dyslipidemia during hypothyroidism. This atherogenic lipid profile must be systematically sought when monitoring patients with hypothyroidism to prevent cardiovascular complications.

## SIGNIFICANCE STATEMENT

Hypothyroidism is a common, benign pathology due to a deficiency in secretion of thyroid hormones by the thyroid. It is among the most common endocrinopathies. Hypothyroidism is a common cause of dyslipidemia, thus increasing cardiovascular risk. The objective of this study was to evaluate the relationship between lipid profile abnormalities and hypothyroidism. The results of our study show frequent hyper LDL-cholesterolemia in patients and a positive correlation was found between lipid profile parameters and thyroid hormones. Thus, lipid disorders are common in hypothyroidism and must be sought to assess cardiovascular risk.

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