Golestan University of Medical Sciences
Journal of Clinical and Basic Research
Online ISSN: 2538-3736

Evaluation of the relationship between Hs-CRP and lipid profile in patients with hypothyroidism

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Abstract

Background: Hypothyroidism is a significant contributor to complications in various metabolic and cardiovascular diseases. Thyroid hormones, including lipids, play a crucial role in macromolecule metabolism. C-reactive protein (CRP) is a key marker for cardiovascular diseases and hypothyroidism independently. This study aimed to evaluate serum high-sensitivity CRP (Hs-CRP) levels, lipid profiles, and their relationship with thyroid hormones in patients with hypothyroidism compared to a control group.

Methods: This case-control study included 90 participants (45 hypothyroid patients and 45 healthy controls). Blood samples were collected, centrifuged to separate serum, and analyzed using commercial kits. ELISA measured T3, T4, TSH, and Hs-CRP, while TG, HDL, LDL, VLDL, and total cholesterol were measured by spectroscopy.

Results: The findings revealed higher Hs-CRP levels in hypothyroid patients compared to controls, although not statistically significant (P-value = 0.09). Hs-CRP positively correlated with TSH, T3, and TG but negatively correlated with T4, total cholesterol, VLDL, and HDL in hypothyroid subjects. These correlations were only significant between Hs-CRP and TG and Hs-CRP and LDL *(*P-value < 0.05*)*.

Conclusion: The positive correlation between Hs-CRP and TSH in hypothyroidism highlights a potential link between hypothyroidism and cardiovascular disease.

Article History

Received: 5 March 2024
Received in revised form: 15 April 2024
Accepted: 29 April 2024
Published online: 22 June 2024
DOI: 10.29252/JCBR.8.2.1

Keywords

Hypothyroidism
Lipid metabolism disorders
C-Reactive protein
Cardiovascular disease

Article Type: Original Article

OPEN ACCESS
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Highlights

What is current knowledge?

Established relationships exist independently between thyroid hormone panels and Hs-CRP and lipid profiles in hypothyroidism.

What is new here?

This study concurrently examines the relationship between thyroid hormone panels, Hs-CRP, and lipid profiles in hypothyroidism.

Introduction

Hypothyroidism, a prevalent condition characterized by thyroid dysfunction, often presents with elevated serum thyroid-stimulating hormone (TSH) levels and normal free thyroxine (fT4) levels (1-3). Thyroid hormones exert significant influence on various metabolic pathways, regulating a broad spectrum of metabolic parameters. The thyroid gland notably acts as an effector of lipoprotein metabolism, which encompasses several cardiovascular disease (CVD) risk factors. Consequently, thyroid function can impact overall CVD risk. A linear increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TGs) has been observed even within the normal TSH range. Conversely, a linear decrease in high-density lipoprotein cholesterol (HDL-C) has been noted with increasing TSH levels (4-6). Hypothyroidism is a major cause of secondary dyslipidemia due to the crucial role thyroid hormones play in lipid synthesis (7). Several studies have established a link between subclinical hypothyroidism (SCH) and obesity, dyslipidemia, and metabolic syndrome (8-11).

C-reactive protein (CRP), an acute-phase inflammatory protein activated during inflammatory conditions, serves as a clinical marker for detecting inflammation, infection, and tissue damage (12). Additionally, it has been suggested that CRP levels may be used to assess arterial rigidity and its improvement in hypothyroid patients. However, CRP measurement is not routinely employed for diagnosing thyroid diseases (13). Previous studies have demonstrated the ability of progressive hypothyroid failure to elevate CRP levels, potentially representing an additional risk factor for developing cardiovascular diseases in individuals with hypothyroidism (14). Recent research has highlighted high-sensitivity C-reactive protein (Hs-CRP) as a stronger predictor of CVD among numerous inflammatory markers, even surpassing low-density lipoprotein cholesterol (LDL-C) (15,16). However, conflicting results exist regarding the role of Hs-CRP as a shared risk factor for SCH and coronary artery diseases (17-20).

The present study aimed to evaluate serum Hs-CRP levels, lipid profiles, and their relationship with thyroid hormones in patients with hypothyroidism compared to a control group.

Methods

Sample Collection

This case-control study involved 45 hypothyroid patients and 45 healthy controls recruited at Deziani Hospital in Gorgan, Iran, between November 2022 and February 2023. Data were recorded directly to facilitate study management.

All participants meeting the inclusion criteria provided informed consent. Case and control groups were matched for age and sex. Five milliliters of blood were drawn from each participant without anticoagulant, followed by immediate centrifugation to obtain serum for biomarker analysis.

Inclusion criteria

1. All participants (both hypothyroid patients and controls) were over 18 years old.
2. All patients had hypothyroidism.
3. All patients were newly diagnosed (untreated hypothyroidism).

Exclusion criteria

1. Pregnant and lactating women.
2. Patients with autoimmune diseases.
3. Patients taking steroid supplements.
4. Patients with inherited thyroid disease.
5. Patients with chronic conditions like diabetes mellitus and heart disease.

Experiments

Following sample collection, tubes were centrifuged to separate serum, which was subsequently used for biochemical marker analysis. All markers were measured using commercial kits. ELISA assayed T3, T4, and TSH, while TG, HDL, LDL, VLDL, and total cholesterol were measured by spectroscopy using a Mindray BS-380 automated analyzer (China). Serum Hs-CRP levels were determined using a commercial ELISA kit at a private laboratory, following the manufacturer's instructions.

Chemicals

Kits for determining TSH, T3, and T4 were obtained from Pishtaz Teb Diagnostics. Kits for TG, HDL, LDL, VLDL, and total cholesterol measurement

[DOI: 10.61186/jcbr.8.2.1]

were procured from Pars Azmoon. Hs-CRP levels were quantified using a kit from ZellBio GmbH.

Statistical Analysis

Data analysis was performed using SPSS software (version 18). The Shapiro-Wilk test was employed to assess data normality. Spearman correlation and the Mann-Whitney U test were utilized to evaluate correlations and compare serum Hs-CRP levels and other parameters between groups. Continuous variables are presented as median (interquartile range), and statistical significance is indicated by a P-value < 0.05.

Results

The research involved a total of 90 participants, consisting of 45 patients with hypothyroidism (14 males and 31 females), and 45 individuals without the condition (11 males and 34 females). The results showed a significant difference in the level of thyroid hormone panel between the hypothyroid patients and healthy subjects. The level of TSH in hypothyroid subjects was significantly higher, and T3 and T4 levels were lower than their levels in normal individuals (P-value < 0.05).

According to Table 1, the level of Hs-CRP in hypothyroid patients was higher than that in normal individuals, but this difference was not significant (P-value = 0.09). Also, the components of the lipid profile, including CHO, VLDL, LDL, and HDL in the case, were higher than those in control insignificantly (P-value > 0.05). Measurement of TG level in the control group showed this parameter was higher than in subjects suffering hypothyroidism P-value = 0.9.

Table 1. Levels of lipid profile components, Hs-CRP, and thyroid hormones in case and control

Variables	Case (N=45) Median (inter-quartile)	Control (N=45) Median (inter-quartile)	Test statistic	P-value
T.G (mg/dl)	111 (80, 184.5)	117 (83, 165.5)	- 0.085	0.932
CHO (mg/dl)	185.84 (161, 206)	175.13 (149, 198.5)	1.358	0.178
VLDL (mg/dl)	23 (16.4, 38.9)	22.2 (16.5, 33.1)	- 0.428	0.669
LDL (mg/dl)	98.2 (77.5, 120)	90.8 (75, 106.5)	1.301	0.197
HDL (mg/dl)	48 (40, 56)	46 (38, 51.5)	- 0.840	0.401
T3 (pg/ml)	1 (0.9, 1.2)	1.1 (1.05, 1.4)	- 3.449	0.001
T4 (pg/ml)	7 (6, 8.1)	7.75 (7.2, 8.2)	- 2.396	0.020
TSH (IU/L)	7.4 (6.15, 10.19)	2.2 (1.5, 3.095)	- 8.173	0.000
Hs-RP (mg/dl)	0.65 (0.07, 1.87)	0.39 (0.013, 0.745)	- 1.660	0.097

According to the Table 2, Hs-CRP, it has a positive correlation with TSH T3 and a negative correlation with T4 in subjects with hypothyroidism. All of the correlations were not significant < 0.05).

Table 2. Correlation between Hs-CRP and thyroid hormones and TSH in case and control

Thyroid panel	Hs-CRP			Hs-CRP		
	Case			Control		
	r	P value	N	r	P value	N
T3 (pg/ml)	0.072	0.636	45	- 0.021	0.892	45
T4 (pg/ml)	- 0.095	0.537	45	0.027	0.861	45
TSH (IU/L)	0.141	0.357	45	0.229	0.131	45

Table 3 shows a positive correlation between Hs-CRP and all lipid profile components except HDL. There was a negative correlation between Hs-CRP and HDL. Also, Hs-CRP has a negative correlation with T3. In addition, the correlation of Hs-CRP and TG and VLDL in healthy subjects is significant.

Table 3. Correlation between Hs-CRP and thyroid hormones and TSH in case and control

Lipid profiles	case			control		
	Hs-CRP			Hs-CRP		
	r	P value	N	r	P value	N
T.G (mg/dl)	.014	.926	45	.351	.018	45
CHO (mg/dl)	-.120	.433	45	.124	.415	45
VLDL (mg/dl)	-.082	.593	45	.336	.024	45
LDL (mg/dl)	-.050	.743	45	.183	.230	45
HDL (mg/dl)	-.176	.249	45	-.082	.594	45

Table 4 shows a correlation between thyroid hormone levels and lipid profile in hypothyroidism patients. Statistical evaluation of the result demonstrates the positive correlation between TG, CHO, VLDL, and LDL with T3 and T4, but HDL has a negative correlation with them. In addition, TG, CHO, VLDL, and LDL, with the exception of HDL, have a negative correlation with TSH. The correlation between TG and VLDL with T3 and T4 is significant, and the correlation between other parameters is insignificant.

Table 4. Correlation between thyroid hormone level and lipid profile components in case

Lipid Profile \ Thyroid hormone panel and TSH		T3	T4	TSH
TG (mg/dl)	r	0.451	0.238	- 0.301
	p-value	0.002	0.115	0.045
	N	45	45	45
CHO (mg/dl)	r	0.112	0.165	- 0.166
	p-value	0.463	0.279	0.275
	N	45	45	45
VLDL (mg/dl)	r	0.342*	0.322*	- 0.385**
	p-value	0.022	0.031	0.009
	N	45	45	45
LDL (mg/dl)	r	0.077	0.002	- 0.231
	p-value	0.614	0.992	0.128
	N	45	45	45
HDL (mg/dl)	r	- 0.249	- 0.154	0.208
	p-value	0.098	0.311	0.171
	N	45	45	45

Discussion

This study investigated serum Hs-CRP levels, lipid profiles, and their relationship with thyroid hormones in patients with hypothyroidism compared to a control group. The findings revealed significantly higher TSH levels in hypothyroid subjects compared to controls. While Hs-CRP levels were also higher in hypothyroid patients, this difference did not reach statistical significance.

In contrast to the findings, Jose et al. (2016) found no association between TSH and Hs-CRP in subclinical hypothyroidism (1). The data, however, indicate a positive correlation between Hs-CRP and TSH in hypothyroid patients, aligning with the observations of Shantha et al. (2008), who suggested a potential link between systemic inflammation and subclinical hypothyroidism (20). This is further supported by Czarnywojtek et al. (2014), who investigated the utility of high-sensitivity CRP (Hs-CRP) measurement in distinguishing types of amiodarone-induced thyrotoxicosis (AIT). While they found no significant difference in Hs-CRP levels between AIT types I and II, they did observe a significant negative correlation between Hs-CRP and TSH, a finding that contrasts with the non-significant positive correlation observed in both patient and control groups in the study (13).

Krishnamurthy et al. (2022) investigated the role of chronic inflammation in the progression from subclinical hypothyroidism (SCH) to overt hypothyroidism, along with the relationship between hypothyroidism, lipid abnormalities, and cardiac dysfunction. They found that chronic inflammation, assessed by Hs-CRP levels, is a significant risk factor for this progression and is often associated with dyslipidemia (21). Similarly, Ahmad et al. (2018) demonstrated a significant positive correlation between TSH and Hs-CRP in thyroid disorders (22). Sharma et al. also reported elevated Hs-CRP levels in thyroid disorders, with significantly higher levels observed in hypothyroid patients compared to hyperthyroid patients (23).

Further supporting a link between hypothyroidism and cardiovascular disease, Ahmad et al. (2022) showed that Hs-CRP levels were significantly elevated in hypothyroid patients compared to controls and correlated significantly with cardiovascular risk factors, including total cholesterol and high-density lipoprotein (HDL) cholesterol (24). Ganesan et al. (2021) focused on the relationship between Hs-CRP and TSH in subclinical hypothyroidism, finding a significant positive correlation between the two. Their study also noted higher levels of inflammatory markers and lipid profiles in patients with SCH compared to euthyroid individuals, though no correlation was found between Hs-CRP, TSH, and lipid profile. This observation aligns with the study, which also demonstrated a positive, albeit non-significant, correlation between Hs-CRP and TSH (15).

Sharma et al. (2016) specifically evaluated lipid profiles and Hs-CRP levels in patients with SCH, revealing a significant positive correlation between TSH levels and lipids (total cholesterol, LDL-C, triglycerides, and VLDL-C) and Hs-CRP.

In their 2016 study, Sharma et al. found a significant positive correlation between TSH levels and various lipids (total cholesterol, LDL-C, triglycerides, and VLDL-C) in individuals with subclinical hypothyroidism (SCH). Conversely, HDL-C exhibited a non-significant inverse correlation with TSH. Furthermore, a significant positive correlation was observed between TSH and Hs-CRP levels in SCH patients compared to controls (17).

Kshetrimayum et al. (2019) investigated Hs-CRP levels and lipid profiles in adults with hypothyroidism at a tertiary care hospital. They compared thyroid hormone profiles, Hs-CRP, and lipid profiles in newly diagnosed hypothyroid adults to controls and also compared these parameters between subclinical and clinical hypothyroid patients. Notably, they found that dyslipidemia, characterized by elevated total cholesterol and LDL-C, was a common finding in patients with clinical hypothyroidism (CH). Serum Hs-CRP levels were significantly elevated in hypothyroid cases but remained within the normal range in controls. Additionally, significant increases in LDL-C and TG, along with decreased HDL-C, were observed in hypothyroid patients, although the average

[DOI: 10.61186/jcbr.8.2.1]

serum cholesterol was lower in these individuals. The study also revealed a significant positive correlation between TSH and Hs-CRP in hypothyroid cases compared to controls (25,26).

Jublanc et al. (2004) assessed the relationship between circulating C-reactive protein (CRP) levels, thyroid hormone profiles, and cardiovascular risk in hyperlipidemic euthyroid individuals. They reported an association between low free thyroxine (FT4) levels and elevated Hs-CRP but no correlation between FT4 and CRP. This finding is partially consistent with the results, which showed a non-significant negative correlation between FT4 and CRP (27).

Rustam et al. (2021) evaluated osteopontin and Hs-CRP levels in Iraqi patients with hypothyroidism, finding elevated serum levels of Hs-CRP, total cholesterol, triglycerides, LDL-C, VLDL-C, and osteopontin compared to healthy controls. Additionally, they reported a positive correlation between Hs-CRP and both triglycerides and VLDL-C, contrasting with the results, which showed a non-significant positive correlation with TG and a negative correlation with VLDL-C (28).

Singh et al. (2021) analyzed lipid profiles, thyroid hormones, and Hs-CRP levels in newly diagnosed hypothyroid individuals and compared them to healthy controls, as well as between subclinical and clinical hypothyroid cases. They observed significantly higher Hs-CRP levels in cases and a significant positive correlation between TSH and Hs-CRP levels. Interestingly, they found lower levels of most lipid profile components in controls compared to cases, with the exception of HDL-C. Conversely, the study showed higher levels of most lipids in hypothyroid individuals, except for TG and total cholesterol.

Jha (2021) focused on thyroid hormone profiles, Hs-CRP, and lipid profiles in newly diagnosed hypothyroid adults, comparing them to healthy controls and between subclinical and clinical hypothyroidism. Hypertriglyceridemia and elevated Hs-CRP levels were more prevalent in clinical hypothyroidism compared to subclinical hypothyroidism. Additionally, serum triglyceride levels were significantly higher in hypothyroid cases compared to controls, and a significant positive correlation was observed between serum TSH and Hs-CRP levels in patients with clinical hypothyroidism (29).

Sumanth Kumar et al. (2020) investigated vitamin D, Hs-CRP, and lipid profiles in newly diagnosed hypothyroid patients. Their findings revealed a positive correlation between Hs-CRP and TSH and a significant negative correlation between HDL levels and TSH in hypothyroid patients (30). These results partially align with the observations, except for the HDL levels, which were higher in the hypothyroid patients and showed a non-significant positive correlation with TSH.

The statistical analysis demonstrated positive correlations between TG and VLDL with TSH, while HDL, LDL, and TG exhibited negative correlations with TSH. However, only the negative correlation between LDL and TSH was statistically significant. Additionally, negative correlations were observed between TG, total cholesterol, VLDL, and LDL (excluding HDL) with T3 and T4, though these correlations were not significant.

Conclusion

In this study, positive correlations were observed between Hs-CRP and TSH, T3, and TG, while negative correlations were noted with total cholesterol, VLDL-C, HDL-C, and T4 in hypothyroid subjects. The positive correlation between Hs-CRP and TSH, as well as TG and LDL-C, suggests a potential role for Hs-CRP as a mediator between thyroid disorders and cardiovascular disease. However, further research with larger sample sizes is needed to confirm these findings due to the lack of statistical significance in most of the results, potentially attributed to the smaller sample size compared to other studies.

Acknowledgement

The authors express their gratitude to Mrs. Nahid Poursharifi for her assistance in the experimental aspects of this study.

Funding sources

This project, registered with the Deputy of Research and Technology of Golestan University of Medical Sciences (Gorgan, Iran) under approval number 113232, was funded by Mr. Ameer Abdulraheem Handhal, an MSc student at Golestan University of Medical Sciences.

Ethical statement

Ethical approval for this study was obtained from Golestan University of Medical Sciences (Ethical number IR.GOUMS.REC.1401.565).

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

Ameer Abdulraheem Handhal: Wrote the proposal and conducted the experimental aspects of the study.
Mahin Gholipur: Collaborated in writing the proposal.
Fatima Mohammadzadeh: Collaborated in the sampling phase of the study.
Somayeh Ghorbani: Performed data analysis.
Safoura Khajeniazi: Supervised the thesis, interpreted results, and wrote the manuscript.

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[DOI: 10.61186/jcbr.8.2.1]

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How to Cite:
Abdulraheem Handhal A, Gholipur M, Mohammadzadeh F, Ghorbani S, Khajeniazi S. Evaluation of the relationship between Hs-CRP and lipid profile in patients with hypothyroidism. *JCBR.* 2024;8 (2):1-4.

[DOI: 10.61186/jcbr.8.2.1]