Hilla University College Journal For Medical Science

Manuscript 1071

Investigation of Growth Differentiation Factor-15, and Lipid-Based Indices in Assessing Cardiovascular Risk in Overt and Subclinical Hypothyroidism

Arkan Hamed Hatroosh

Mohammed Abdulateef Mohammed Ali

Jalal Abid Ali

SHORT COMMUNICATION

Hilla Univ Coll J Med Sci

Investigation of Growth Differentiation Factor-15, and Lipid-Based Indices in Assessing Cardiovascular Risk in Overt and Subclinical Hypothyroidism

Arkan Hamed Hatroosh [a,*], Mohammed Abdulateef Mohammed Ali [a], Jalal Abid Ali [b]

[a] Department of Biochemistry, College of Medicine, University of Al-Nahrain, Baghdad, Iraq
[b] Department of Medicine, College of Medicine, University of Al-Nahrain, Baghdad, Iraq

Abstract

Background: Hypothyroidism, both overt and subclinical, has emerged as a notable contributor to increased cardiovascular disease (CVD) risk. This association is mediated by multifactorial mechanisms, including significant dyslipidemia, heightened oxidative stress, and vascular endothelial dysfunction.

Materials and Methods: A case-control study was conducted at the Specialized Center for Diabetic Endocrinology, Baghdad/Russafa, between October 2024 and January 2025. The study included 130 participants: 35 patients with overt hypothyroidism, 35 with subclinical hypothyroidism, and 60 age-, sex-, and BMI-matched euthyroid controls. Blood samples were collected and processed for analysis of serum GDF-15, and lipid profiles. CRI-I, CRII-I, AIP, and AC were calculated. Statistical analyses included ANOVA with post hoc comparisons, Pearson's correlation, and ROC curve analysis to evaluate biomarker performance.

Results: GDF-15 levels were significantly elevated in these groups ($p < 0.0001$), indicating increased systemic stress. CRI-I and AC values were also significantly higher in hypothyroid patients, confirming an aggravated atherogenic lipid profile. ROC analysis revealed excellent diagnostic performance of GDF-15 (AUC = 0.862) in distinguishing overt hypothyroidism from euthyroidism. Significant correlations were found between the biomarker and lipid-based indices, suggesting a pathophysiological link between systemic stress responses, lipid metabolism, and cardiovascular risk in thyroid dysfunction.

Conclusion: GDF-15 is promising biomarkers for cardiovascular risk assessment in hypothyroid patients. Its diagnostic performance, particularly in overt disease, surpasses traditional lipid indices, offering a more comprehensive understanding of cardiovascular compromise. Integration of this marker with established lipid-based indices could enhance early detection, facilitate personalized risk stratification, and inform timely therapeutic interventions in thyroid-associated cardiovascular risk.

Keywords: Subclinical hypothyroidism, GDF-15, Cardiovascular risk, Castelli risk index, Atherogenic coefficient, Oxidative stress, Endothelial dysfunction

1. Introduction

Thyroid hormones (TH) have a significant impact on cellular oxidative metabolism. Besides that, they maintain vascular homeostasis through positive effects on endothelial and vascular smooth muscle cells. Both subclinical and clinical hypothyroidism impact blood flow and organ function, raising the risk of atherosclerosis due to endothelial dysfunction, low-grade inflammation, arterial

Received 21 July 2025; revised 10 August 2025; accepted 16 August 2025.
Available online 27 September 2025

* Corresponding author.
E-mail addresses: arkanhamd@gmail.com (A. K. Hatroosh), mohammedchina@nahrainuni.edu.iq (M. A. M. Ali), gelal.altaai@nahrainuniv.edu.iq (J. A. Ali).

https://doi.org/10.62445/2958-4515.1071

stiffness, hypertension, and dyslipidemia, which results in elevated LDL levels [1].

Both OH and SCH are linked to a number of CVDs and a higher chance of developing traditional CV risk factors, including elevated carotid intima-media thickness (CMT), dyslipidemia, and hypertension. [2,3] According to autopsy reports, people with overt hypothyroidism appear to have greater atherosclerosis than healthy controls [4].

GDF-15, part of the transforming growth factor β family, is secreted by macrophages and endothelial cells in tissues but increases in response to injury, inflammation, or stress [5]. GDF-15, a cytokine, is elevated in pathogenic states, causing disorders like oxidative stress, endothelial dysfunction, tissue aging, and chronic inflammation.

GDF-15, produced by endothelial cells, macrophages, adipocytes, and cardiac and vascular myocytes, is elevated in many heart disorders, primarily from extracardiac tissues [6]. Human growth differentiation factor 15 (GDF-15) plays various roles in both healthy and unhealthy conditions, with its primary expression in the placenta and prostate, and its levels can increase in response to inflammation or injury [7, 8].

The physiological and pathological involvement of the GDF-15 system in atherosclerosis and CAD has been supported by both experimental and clinical investigations, which have demonstrated that increased GDF-15 levels enhance inflammation and angiogenesis [9].

Recent years have seen the emergence of similar studies that associate GDF-15 with an elevated risk of mortality from heart failure, atrial fibrillation, and coronary heart disease. Further research has demonstrated that GDF-15 goes beyond and beyond the predictive capabilities of other biomarkers, including cardiac troponin and natriuretic peptides [10].

Hypothyroidism patients have been found to have higher circulating serum levels of GDF-15 when compared to healthy controls. Furthermore, there was a positive correlation between GDF-15 and serum TSH levels in these individuals [11].

It is known that GDF-15 is a protein found in several cells in the body and is created and released in response to various stress conditions, such as inflammation, cell destruction, and tissue injury.

2. Materials and methods

A cross-control study was employed. It was conducted at the function in Specialized Center for Diabetic Endocrinology Baghdad/Russafa during the period from October 2024 to January 2025. The study was approved by the scientific committee "Institutional Review Board" (IRB) in Al-Nahrain University, College of Medicine. Proportions of females in the euthyroid, overt hypothyroidism, and subclinical hypothyroidism (SCH) groups was 71.7%, 82.9%, and 88.6%, respectively Patients group were divided into two groups, the first overt hypothyroidism that contained 35 patients with a mean age of (42.63 $\pm$ 11.49), and the second group subclinical hypothyroidism that contained 35 patients with mean age (45.03 $\pm$ 12.01). A particular questionnaire form including descriptive information was designed and filled out by each patient. The questionnaire included name, age, sex, treatment status, history of other diseases, and others (mentioned in Appendix). All patients in both groups were diagnosed by the endocrinologist based on clinical feature and biochemical markers such as thyroid function tests in the Specialized Center for Diabetic Endocrinology Baghdad/Russafa.

2.1. Inclusion criteria included

Adults (18–65 years) newly diagnosed primary hypothyroidism or patients with hypothyroidism despite treatment, subclinical hypothyroidism; no previous hormone replacement therapy will be included, Inclusion Criteria for Controls Healthy adults (18–65 years) with normal thyroid function (normal TSH, T3, and T4).

2.2. Exclusion criteria

Acute and chronic renal dysfunction elevation renal indices, History Known cases of Autoimmune diseases, Pregnant or lactating women, Individuals on lipid-lowering therapies such as statin, ezetimibe, Fibrates, or anti-inflammatory medications, anticoagulants, History of cancer, History of acute or chronic infections or inflammatory conditions.

2.3. Biochemical measurements

Venous blood samples (5 mL) were collected from each subject after an overnight fast. Serum was separated by centrifugation and stored at –20°C until analysis. Thyroid function tests – including serum TSH, total thyroxine (T4), and total triiodothyronine (T3) – were measured using an electrochemiluminescence immunoassay on the Cobas E411 analyzer (Roche Diagnostics). The serum lipid profile was assessed using an automated chemistry analyzer (Cobas E311, Roche), which measured total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) by enzymatic colorimetric methods. Very-low-density lipoprotein (VLDL) concentration

Table 1. Comparison of parameters between the studied groups.

Parameter	Euthyroid (n = 60)	Overt (n = 35)	SCH (n = 35)	p-value
Age (years)	43.85 ± 8.95a	42.63 ± 11.49a	45.03 ± 12.01a	0.6366
BMI (kg/m^2)	30.55 ± 5.12a	30.49 ± 2.89a	30.56 ± 5.02a	0.9970
SBP (mmHg)	124.18 ± 8.47a	132.00 ± 13.01b	132.51 ± 15.63b	0.0010
DBP (mmHg)	82.40 ± 7.75a	82.37 ± 14.10a	84.03 ± 4.10a	0.6703
Cholesterol (mg/dl)	173.35 ± 29.61a	221.71 ± 58.32b	183.51 ± 35.87a	<0.0001
TG (mg/dl)	114.70 ± 39.30a	183.00 ± 89.83b	177.91 ± 82.97b	<0.0001
HDL (mg/dl)	48.08 ± 9.91a	49.49 ± 8.78a	42.60 ± 8.80b	0.0049
LDL (mg/dl)	100.57 ± 30.53a	140.74 ± 51.60b	105.63 ± 24.80a	<0.0001
VLDL (mg/dl)	22.56 ± 8.61a	34.23 ± 19.00b	35.61 ± 17.44b	<0.0001
AIP	0.36 ± 0.18a	0.53 ± 0.26b	0.58 ± 0.23b	<0.0001
CRI-I	3.73 ± 0.86a	4.59 ± 1.36b	4.41 ± 0.94b	0.0002
CRI-II	2.17 ± 0.81a	2.92 ± 1.16b	2.55 ± 0.70ab	0.0007
AC	2.73 ± 0.86a	3.59 ± 1.36b	3.41 ± 0.94b	0.0002
FRS (%)	0.65 ± 1.57a	9.21 ± 7.12b	8.08 ± 7.03b	<0.0001
T3 (nmol/mL)	1.64 ± 0.28a	0.90 ± 0.31b	1.53 ± 0.19a	<0.0001
T4 (nmol/mL)	83.23 ± 7.90a	43.29 ± 22.56b	82.81 ± 10.80a	<0.0001
TSH (mU/L)	2.70 ± 1.03a	53.69 ± 32.16b	8.01 ± 4.94c	<0.0001
GDF-15 (pg/mL)	675.01 ± 220.82a	1105.80 ± 328.60b	989.60 ± 345.63b	<0.0001

ANOVA was used for group comparisons; where $p < 0.05$, Tukey-Kramer post hoc test was applied. Superscript letters (a, b) indicate group differences; groups sharing a letter are not significantly different.

was calculated (as TG/5 in mg/dL), and the Atherogenic index of plasma (AIP) = Log TG/HDL-C). Serum GDF-15 levels were quantified by a sandwich ELISA technique using a commercial human GDF15-ELISA kit (Elabscience, Catalog No. E-EL-H6092), following the manufacturer's protocol. All assays were performed in duplicate, and quality control samples were included to ensure assay precision.

2.4. Ethical approval

The study was approved by the scientific committee "Institutional Review Board" (IRB) in Al-Nahrain University, College of Medicine, consented by Al-Rusafa Health Directorate Ethical Committee (No. 20241018 of date 12/11/2024).

2.5. Statistical analysis

The SPSS software program, version 29.0.1.0 was used for data analysis in the study. The T test statistical method, mean (±), standard deviation (SD), and P-values were applied to explain the different values after comparing groups according to previously measured parameters. A value of $P \geq 0.05$ was considered statistically significant and ANOVA test performing between groups.

3. Results

The mean age was 43.85 ± 8.95 years in the control group, 42.63 ± 11.49 years in the overt hypothyroidism group, and 45.03 ± 12.01 years in the SCH group, with no statistically significant difference observed ($p = 0.6366$). Similarly, mean BMI was nearly identical across groups (control: 30.55 ± 5.12 kg/m^2; overt: 30.49 ± 2.89 kg/m^2; SCH: 30.56 ± 5.02 kg/m^2; $p = 0.9970$), confirming adequate matching for these confounders as shown in Table 1.

In the Overt Hypothyroidism showing GDF-15 showed weak correlations without statistical significance. For instance, correlations with SBP ($r = 0.068$, $p = 0.6964$) and DBP ($r = 0.259$, $p = 0.1328$) were not significant, suggesting limited direct hemodynamic involvement at this overt stage. While Subclinical Hypothyroidism (SCH),GDF-15 did not significantly correlate with blood pressure parameters in the SCH group, it showed some non-significant yet potentially relevant correlations (e.g., SBP $r = –0.161$, $p = 0.3563$). Importantly, the absence of significant correlations with traditional lipid indices aligns with previous findings suggesting its involvement predominantly through stress-related pathways rather than direct lipid-mediated mechanisms, as in Table 2.

GDF-15 (GDF_15pg_ml): GDF-15 levels were found to be a statistically significant positive predictor of FRS (β =0.0090, $p < 0.001$). A one-unit increase in GDF-15 (pg/ml) is associated with an approximate 0.0090-unit increase in FRS, holding other variables constant. AIP: The Atherogenic index plasma was a statistically significant positive predictor of FRS (β =7.189, $p = 0.001$). Age: As anticipated, age was a highly significant positive predictor of FRS (β =0.152, $p<0.001$). For each additional year of age, the Framingham Risk Score is predicted to increase by approximately 0.1683 units, all else being equal. Regarding GDF-15, the Euthyroid group showed a mean concentration of 675.01 ± 220.82 pg/mL. In

Table 2. Correlation analysis of selected biomarkers (GDF-15) and cardiovascular risk indices within Hypothyroidism patient groups.

	Overt (n=35)	*Euthyroid (n=60)*	*SCH (n=35)*
	GDF-15	GDF-15	GDF-15
SBP mmHg			
r	0.068	–0.001	–0.161
p	0.6964	0.9939	0.3563
DBP mmHg			
r	0.259	–0.128	0.089
p	0.1328	0.3305	0.61
AIP			
r	0.106	–0.104	0.275
p	0.5462	0.4281	0.1104
CRI-I			
r	0.088	–0.078	–0.056
p	0.6138	0.5548	0.749
CRI-II			
r	0.001	–0.052	–0.211
p	0.9961	0.6954	0.2241
AC			
r	0.088	–0.078	–0.056
p	0.6138	0.5548	0.749
FRS(%)			
r	***0.341***	0.066	***0.457***
p	***0.0452***	0.6182	***0.0058***
Chol(mg/dl)			
r	0.074	–0.096	–0.213
p	0.6715	0.4659	0.2193
TG (mg/dl)			
r	0.066	–0.14	0.076
p	0.7046	0.2875	0.6639
HDL (mg/dl)			
r	–0.085	–0.039	–0.143
p	0.6269	0.7679	0.4125
LDL (mg/dl)			
r	–0.001	–0.036	–0.305
p	0.9966	0.7849	0.0747
VLDL			
r	0.133	–0.138	0.09
p	0.4479	0.2922	0.6084
T3 (nmol/ml)			
r	0.029	–0.019	0.027
p	0.8673	0.8838	0.8773
T4 (nmol/ml)			
r	0.088	0.23	0.188
p	0.6144	0.0765	0.2808
TSH (mU/L)			
r	–0.22	–0.11	0.143
p	0.2049	0.4019	0.4112
BMI (kg/m2)			
r	0.068	–0.228	0.141
p	0.6999	0.0794	0.4179
age			
r	***0.363***	–0.018	0.261
p	***0.0318***	0.8901	0.1296

contrast, the Overt Hypothyroidism group presented a mean GDF-15 level of 1105.80 ± 328.60 pg/mL, and the SCH group had a mean of 989.60 ± 345.63 pg/mL, the Euthyroid group demonstrated significantly lower levels of GDF-15 compared to both the Overt Hypothyroidism ($p < 0.001$) and Subclinical Hypothyroidism ($p < 0.001$) groups. These data are presented in Table 3.

ROC analysis revealed excellent diagnostic performance of GDF-15 (AUC = 0.862) showed in Fig. 1 distinguishing overt hypothyroidism from euthyroidism. the marker showed moderate utility in detecting subclinical hypothyroidism. Significant correlations were found between the biomarkers and lipid-based indices, suggesting a pathophysiological link between systemic stress responses, lipid metabolism, and cardiovascular risk in thyroid dysfunction, as found in Table 4.

4. Discussion

Hypothyroidism, overt or subclinical, is associated with cardiovascular disease risk due to disrupted physiological processes like endothelial function, vascular tone, and lipid metabolism. Subclinical hypothyroidism may increase CVD complications and death risk [12].

GDF-15 is a stress-response cytokine induced by mitochondrial dysfunction, inflammation, and tissue hypoxia. Hypothyroidism increases reactive oxygen species, impairs lipid handling, and promotes low-grade systemic inflammation—stimuli known to drive GDF-15 secretion. The stepwise +46 % rise in SCH and +64 % rise in overt disease reflect the increasing metabolic and hemodynamic burden across the thyroid-dysfunction spectrum.

The results revealed that there was highly Significant decrease in GDF-15 between patients and control (p-value = 0.001). Our results are similar to ***Salam et al.*** [11] Who were found GDF-15 elevated in hypothyroid patients with elevation in TSH.

Our demonstration of intermediate yet significant changes in SCH aligns with emerging reports that even mild TSH elevations provoke endothelial dysfunction and oxidative stress. Importantly, the magnitude of biomarker shifts in SCH approximates or exceeds those reported for conventional lipid indices, underscoring their potential clinical importance.

GDF-15, by contrast, correlated positively with the Framingham Risk Score (FRS) in overt hypothyroidism ($r = 0.341$, $p = 0.045$) and SCH ($r = 0.457$, $p = 0.006$) as shown in Table 2 but not in euthyroid controls. Because GDF-15 is strongly up-regulated by oxidative stress, mitochondrial dysfunction, and inflammation [13, 14]. pathways accentuated in hypothyroidism [15]—thyroid dysfunction appears to unmask or amplify its link to composite cardiovascular risk.

In overt disease, GDF-15 also rose with age ($r = 0.363$, $p = 0.032$), supporting its status as a senescence marker [16]. The numerically stronger GDF-15–FRS

Table 3. Multiple linear regression analysis of Framingham risk score.

Variable	Coefficient (β)	Coefficient (B)	Std. Error	t-statistic	P-value	95% Confidence Interval
(Intercept)		–12.589	2.040	–6.172	< 0.001	[–16.626, –8.552]
GDF-15 pg/ml	0.447	0.009	0.001	6.514	0.000	[0.006, 0.011]
AIP	0.257	7.189	1.960	3.668	0.001	[3.311 –11.067]
age	0.153	0.152	0.043	3.554	<0.001	[0.068, 0.238]

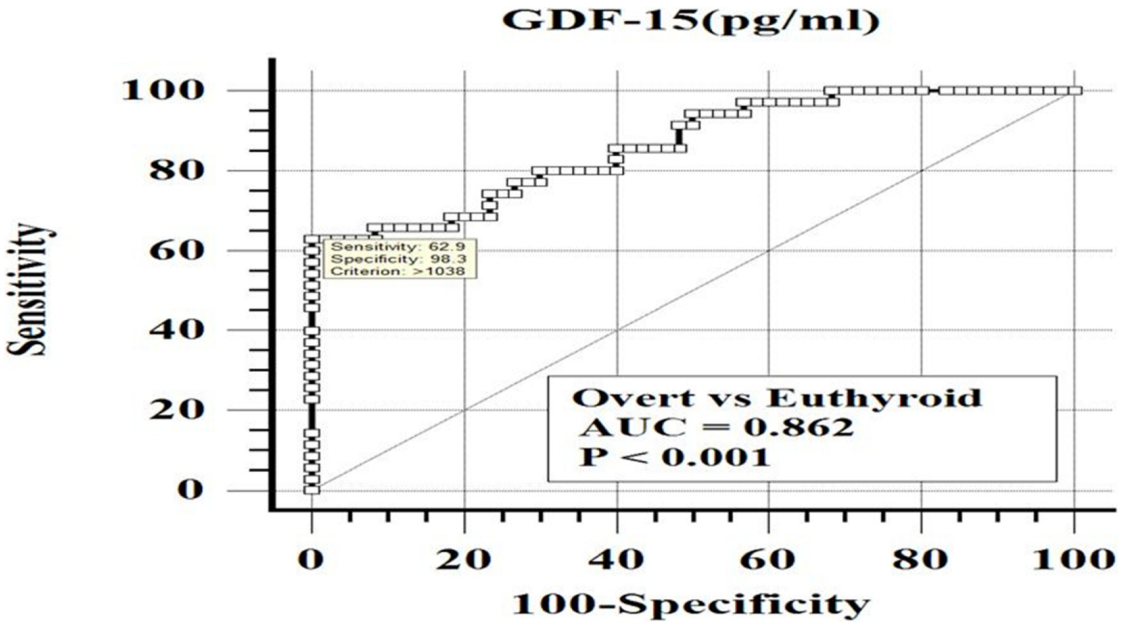

Fig. 1. Receiver operating characteristic curves for GDF-15 in distinguishing overt hypothyroidism from euthyroid stat.

coupling in SCH suggests the cytokine begins to rise early in the disease continuum, paralleling incremental cardiovascular risk before full metabolic imbalance sets in.

This study aimed to investigate the determinants of the Framingham Risk Score (FRS), a widely used predictor of 10-year cardiovascular disease (CVD) risk. The findings of the multiple linear regression analysis demonstrated that the proposed model accounted for approximately 49.1% of the variance in FRS, underscoring the significance of the selected clinical and biomarker variables in explaining cardiovascular risk.

Multiple Linear Regression Analysis of GDF15 shows the correlation between GDF15 and FRS% appears as a one-unit increase in GDF-15 (pg/ml) is associated with an approximate 0.0084-unit increase in FRS, holding other variables constant, although it is more likely to reflect disease-related physiological stress rather than age or obesity [17] Growth Differentiation Factor-15 (GDF-15) is a strong positive predictor of FRS, linked to inflammation, oxidative stress, and cardiovascular outcomes, suggesting it could be a potent biomarker..

AIP was also positively and significantly associated with the dependent variable ($\beta = 0.226, B = 6.312, P = 0.001$), underscoring the contribution of atherogenic dyslipidemia to cardiovascular risk. Given that AIP reflects the balance between triglycerides and HDL, its independent predictive value supports the importance of lipid profile management, and this consistent with its established role as an indicator of dyslipidemia and atherogenic risk.

Table 4. ROC analysis of the study biomarker in differentiating between different categories of Hypothyroidism patients.

groups	Variable	AUC	SE	95% CI	Cutoffs	Sen.	Spec.	+LR	–LR
Overt vs Euthyroid	GDF-15	0.862	0.0396	0.776to 0.924	>1038	62.9	98.3		0.37
SCH vs Euthyroid	GDF-15	0.775	0.0534	0.677to 0.854	994.4	60.00	88.33	5.14	0.45
Overt vs SCH	GDF-15	0.610	0.0683	0.486 to 0.724	>1663	2.86	94.29	0.50	1.03

Area Under the Curve (AUC), Standard Error (SE), 95% Confidence Interval (CI) for AUC, optimal cutoffs, sensitivity (Sen.), specificity (Spec.), positive likelihood ratio (+LR), and negative likelihood ratio (–LR).

Elevated AIP reflects an unfavorable lipid profile that promotes atherosclerosis, and our findings underline its clinical relevance in risk stratification. As expected, age was a strong positive predictor of FRS. Advancing age is a well-documented risk factor for CVD, attributable to cumulative vascular damage and the increased prevalence of other risk factors over time.

Hypothyroidism, both overt and subclinical, is related to an increased atherogenic lipid profile, demonstrating an elevated cardiovascular risk due to an imbalance between pro-atherogenic and anti-atherogenic lipoproteins

GDF-15 exhibited excellent discriminatory ability, with an AUC of 0.862 (SE = 0.0396, 95% CI: 0.776–0.924). While its optimal cutoff of >1038 pg/ml yielded an impressive specificity of 98.3%, its sensitivity was comparatively lower at 62.9%. This suggests that while elevated GDF-15 is a highly specific indicator of overt hypothyroidism, a considerable proportion of cases might remain undetected if relying solely on this marker.

The utility of GDF-15 as a biomarker for cardiovascular and metabolic stress is extensively documented, with increased levels reported in conditions such as heart failure, myocardial infarction, and various chronic inflammatory states [18–22].

5. Conclusion

GDF-15 biomarkers offer more cardiovascular risk assessment in hypothyroid patients, exceeding traditional lipid indices, enhancing early detection, personalized risk stratification, and timely therapeutic interventions.

Ethical issue

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University Alnahrain (Date:12/11/2024/No: 20241018).

Financial funding

This research received no external funding.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Gluvic ZM, Zafirovic SS, Obradovic MM, Sudar-Milovanovic EM, Rizzo M, Isenovic ER. Hypothyroidism and Risk of Cardiovascular Disease. Curr Pharm Des [Internet]. 2022 Jul 1 [cited 2025 Apr 4];28(25):2065–72. Available from: https://www.eurekaselect.com/206223/article.
2. Razvi S, Jabbar A, Pingitore A, Danzi S, Biondi B, Klein I, *et al.* Thyroid hormones and cardiovascular function and diseases. J Am Coll Cardiol. 2018;71(16):1781–96.
3. Biondi B. The management of thyroid abnormalities in chronic heart failure. Heart Fail Clin. 2019;15(3):393–8.
4. Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. J Clin Endocrinol Metab. 2003;88(6):2438–44.
5. Sharma A, Stevens SR, Lucas J, Fiuzat M, Adams KF, Whellan DJ, *et al.* Utility of growth differentiation factor-15, a marker of oxidative stress and inflammation, in chronic heart failure: insights from the HF-ACTION study. JACC Hear Fail. 2017;5(10):724–34.
6. Goyal G, Goyal L, Singla H, Sheenam, Arora K, Kaur H. Subclinical hypothyroidism and associated cardiovascular risk factor in perimenopausal females. J Midlife Health. 2020;11(1):6–11.
7. Hsiao EC, Koniaris LG, Zimmers-Koniaris T, Sebald SM, Huynh TV, Lee S-J. Characterization of growth-differentiation factor 15, a transforming growth factor β superfamily member induced following liver injury. Mol Cell Biol. 2000;20(10):3742–51.
8. Kempf T, Eden M, Strelau J, Naguib M, Willenbockel C, Tongers J, *et al.* The transforming growth factor-β superfamily member growth-differentiation factor-15 protects the heart from ischemia/reperfusion injury. Circ Res. 2006;98(3):351–60.
9. Wang J, Wei L, Yang X, Zhong J. Roles of growth differentiation factor 15 in atherosclerosis and coronary artery disease. J Am Heart Assoc. 2019;8(17):e012826.
10. Goel H, Melot J, Krinock MD, Kumar A, Nadar SK, Lip GYH. Heart-type fatty acid-binding protein: an overlooked cardiac biomarker. Ann Med. 2020;52(8):444–61.
11. Salam S, Abbas M. Evaluation of Growth Differentiation Factor-15 in Non-Diabetic Hypothyroid Patients with Normal Insulin Sensitivity and Maintained on Oral Thyroxin Therapy. Int J Sci Res. 2017;6:1056–9.
12. Klein I, Danzi S. Thyroid disease and the heart. Curr Probl Cardiol. 2016;41(2):65–92.
13. May BM, Pimentel M, Zimerman LI, Rohde LE. GDF-15 como biomarcador em doenças cardiovasculares. Arq Bras Cardiol. 2021;116(3):494–500.
14. di Candia AM, de Avila DX, Moreira GR, Villacorta H, Maisel AS. Growth differentiation factor-15, a novel systemic biomarker of oxidative stress, inflammation, and cellular aging: Potential role in cardiovascular diseases. Am Hear J Plus Cardiol Res Pract [Internet]. 2021;9:100046. Available from: https://doi.org/10.1016/j.ahjo.2021.100046.
15. Balamurugan V, Maradi R, Joshi V, Belle VS, Goud MBK. DISLIPIDEMIJA I INFLAMATORNI MARKERI KAO PREDIKTORI RIZIKA ZA KARDIOVASKULARNE BOLESTI KOD ŽENA SA HIPOTIEROZOM U PREMENOPAUZI. J Med Biochem. 2023;42(1):58–66.
16. Evans DS, Young D, Tanaka T, Basisty N, Bandinelli S, Ferrucci L, *et al.* Proteomic analysis of the senescence-associated secretory phenotype: GDF-15, IGFBP-2, and cystatin-C are associated with multiple aging traits. Journals Gerontol Ser A Biol Sci Med Sci. 2024;79(3):glad265.
17. He X, Su J, Ma X, Lu W, Zhu W, Wang Y, *et al.* The association between serum growth differentiation factor 15 levels and lower extremity atherosclerotic disease is independent of body mass index in type 2 diabetes. Cardiovasc Diabetol. 2020;19(1):40.
18. Li M, Duan L, Cai Y-L, Li H-Y, Hao B-C, Chen J-Q, *et al.* Growth differentiation factor-15 is associated with cardiovascular outcomes in patients with coronary artery disease. Cardiovasc Diabetol. 2020;19:1–12.
19. Abood AS, Ali HA. Evaluation of Serum Adipolin Level as a Potential Marker of Metabolic and Hormonal Changes in Patients with Overt and Subclinical Hypothyroidism. Medical Journal of Babylon. 2025;22(1):262–267.

20. Hashim NA, Abdullah YJ, Sayhood AA. Evaluate the hematologic parameters, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in patients with autoimmune hypothyroidism from Amara City, Southern Iraq. Medical Journal of Babylon 2023;20(Supplement 1):S48–S52.
21. Elias, NG. Evaluation of Vitamin D3 and other Clinical Parameters in Iraqi Hypothyroidism Diabetic Menopausal Women," Hilla University College Journal For Medical Science 2025;3(2):Article 11. DOI: https://doi.org/10.62445/2958-4515.1064.
22. Hussien RA, Zwain GF, Abood ES. Study of UTI Effect on Renal Function for the Patient with Thyroid Autoimmune Disease. Hilla University College Journal For Medical Science. 2025;2(1):9. DOI: https://doi.org/10.62445/2958-4515.1013.