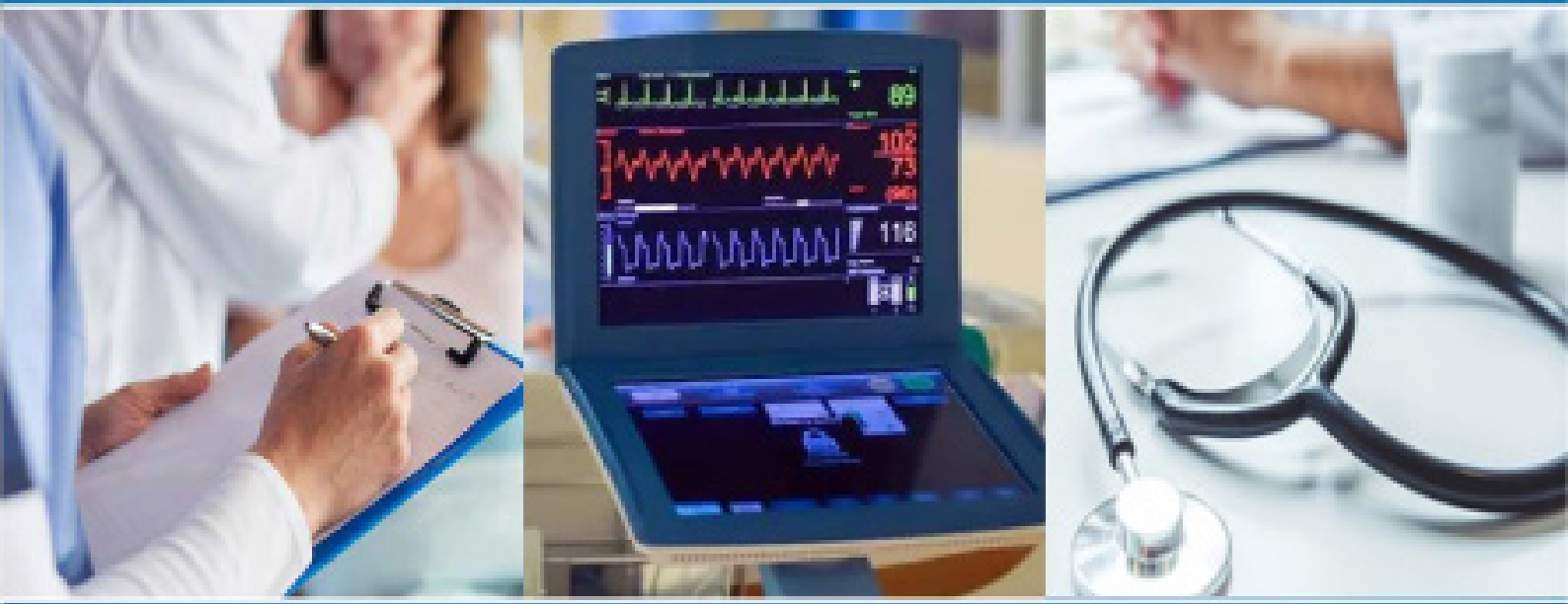
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Original Article

Evaluation of the association between thyroid hormone levels and coronary slow flow in euthyroid patients: a retrospective study

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ABSTRACT

Aims: Coronary slow flow (CSF) is an angiographic phenomenon characterized by delayed distal opacification of coronary arteries despite the absence of obstructive lesions. Although thyroid hormones are known to modulate cardiovascular hemodynamics, their potential association with CSF remains uncertain.

Methods: This retrospective, single-center, observational study included 170 patients (85 with angiographically confirmed CSF and 85 with normal coronary flow). Patients with overt thyroid dysfunction were excluded. Demographic, clinical, and biochemical characteristics were compared between the groups. Thyroid-related parameters (TSH, FT3, FT4, and FT4/FT3 ratio) were analyzed using receiver operating characteristic (ROC) curves and logistic regression to determine their discriminative and independent predictive value for CSF.

Results: Patients with CSF were significantly younger (49.3±10.0 vs. 54.8±11.1 years, p<0.001), predominantly male (72.9% vs. 47.1%, p=0.001), and more frequently smokers (59.0% vs. 36.9%, p=0.021) compared with controls. In multivariable logistic regression analysis, only age remained an independent predictor of CSF (OR 0.95, 95% CI 0.92-0.98, p=0.002). None of the thyroid parameters, including the FT4/FT3 ratio, demonstrated significant discriminative ability for CSF in ROC curve analysis (all AUC <0.60, p>0.05).

Conclusion: In euthyroid individuals, thyroid hormone levels and their ratios were not independently associated with coronary slow flow, whereas younger age and smoking emerged as stronger correlates. These findings suggest that routine thyroid hormone evaluation may not offer additional diagnostic or prognostic value in CSF.

Keywords: Coronary slow flow, thyroid hormones, euthyroid, microvascular dysfunction

INTRODUCTION

Coronary slow flow (CSF) is an angiographic phenomenon characterized by delayed opacification of the distal coronary arteries in the absence of obstructive epicardial stenosis and is most commonly quantified using the thrombolysis in myocardial infarction (TIMI) frame count method.[1] The prevalence of CSF has been reported in approximately 1-7% of patients undergoing diagnostic coronary angiography.[2] Although the exact pathophysiology remains uncertain, accumulating evidence suggests that endothelial dysfunction, microvascular abnormalities, diffuse atherosclerosis, and chronic low-grade inflammation are key contributors.[3,4] Clinically, CSF has been associated with recurrent angina, arrhythmias, myocardial ischemia, and even sudden cardiac death, emphasizing that it is far from a benign angiographic finding.[5,6]

Thyroid hormones exert multiple cardiovascular effects by modulating heart rate, myocardial contractility, systemic vascular resistance, endothelial function, and lipid metabolism.[7] Both overt and subclinical thyroid dysfunctions have been associated with a range of cardiovascular disorders, including coronary artery disease, arrhythmias, and heart failure.[8,9] Beyond these systemic effects, thyroid hormones may also influence coronary microvascular tone and flow regulation through mechanisms involving endothelial nitric oxide synthesis, vascular smooth muscle responsiveness, and tissue oxygen demand.[10,11]

Several studies have examined the potential relationship between thyroid function and coronary flow dynamics, yet the results have been inconsistent. Evrengül et al.[12] reported lower free triiodothyronine (FT3) levels in CSF patients compared with controls, whereas Chen et al.[13] suggested that free thyroxine (FT4) might be associated with CSF, particularly in women. Conversely, other investigations have failed to demonstrate any significant relationship between thyroid parameters and CSF.[14] These conflicting findings raise an important question: do thyroid hormones exert any measurable influence on coronary flow within the physiological (euthyroid) range, or are their vascular effects limited to states of overt dysfunction?

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Given the established cardiovascular actions of thyroid hormones and the lack of clarity regarding their potential influence under normal thyroid function, this study aimed to evaluate the association between thyroid hormone levels and coronary slow flow specifically in a euthyroid patient population. By restricting the analysis to individuals without thyroid dysfunction, we sought to determine whether minor hormonal variations within the normal physiological range hold any clinical or microvascular relevance for CSF.

METHODS

Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Batman Training and and Research Hospital Scientific Researches Ethics Committee (Date: 24.06.2018, Decision No: 280118606,429). Given the retrospective nature of the study and the use of anonymized patient data, the requirement for informed consent was waived by the ethics committee.

Study Design and Population

This single-center, retrospective, observational study included a total of 170 patients who underwent diagnostic coronary angiography due to chest pain and suspected ischemic heart disease. Patients were divided into two equal groups: those with coronary slow flow (CSF, n=85) and those with normal coronary flow (n=85). CSF was defined as delayed distal vessel opacification in the absence of significant epicardial stenosis, confirmed by corrected TIMI frame count criteria.

To minimize endocrine and metabolic confounding, the study specifically included only euthyroid individuals. This approach allowed the evaluation of whether small variations in thyroid hormone levels within the physiological range have any measurable impact on coronary flow, independent of overt thyroid dysfunction.

Exclusion criteria were obstructive coronary artery disease, known thyroid dysfunction or use of thyroid-related medications, significant renal or hepatic impairment, active infection or inflammatory disease, and incomplete laboratory data.

Laboratory and Clinical Variables

Venous blood samples were collected after an overnight fast. Standard biochemical parameters including glucose, creatinine, lipid profile, and C-reactive protein were measured using automated analyzers. Thyroid hormones including thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) were measured by chemiluminescence immunoassay. Demographic and clinical characteristics (age, sex, hypertension, diabetes mellitus, hyperlipidemia, and smoking status) were obtained from medical records.

Statistical Analysis

Continuous variables were presented as mean±standard deviation or median (IQR) depending on distribution and compared with students T test or Mann-Whitney U test. Categorical variables were expressed as counts (percentages) and compared using the chi-square test. Receiver operating characteristic (ROC) analysis was performed for TSH, FT3, FT4, and the FT4/FT3 ratio. Logistic regression analysis was used to determine independent predictors of CSF, with results presented as odds ratios (OR) and 95% confidence intervals (CI).

Given the balanced design and sample size, the study was considered to have reasonable sensitivity to detect moderate associations; therefore, the absence of significant relationships is unlikely to reflect a major limitation of statistical power. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 170 patients were included in the final analysis, consisting of 85 patients with coronary slow flow (CSF) and 85 patients with normal coronary flow.

Demographic and Laboratory Characteristics

Baseline clinical and laboratory findings of the study groups are summarized in **Table 1**. Patients in the CSF group were significantly younger than those in the normal flow group (49.3±10.0 vs. 54.8±11.1 years, p<0.001). The proportion of male patients was higher in the CSF group (72.9% vs. 47.1%, p=0.001). The rate of smoking was also significantly higher among CSF patients (59.0% vs. 36.9%, p=0.021). There were no significant between-group differences with respect to diabetes mellitus or hyperlipidemia.

Table 1. Demographic and laboratory characteristics

Variable	Normal flow (n=85)	CSF (n=85)	p-value
Age (years)	54.78±11.12	49.28±9.96	<0.001
Male sex, n (%)	40 (47.1%)	62 (72.9%)	0.001
Hypertension, n (%)	24 (36.9%)	17 (20%)	0.047
Diabetes mellitus, n (%)	25 (30.1%)	16 (18.8%)	0.127
Hyperlipidemia, n (%)	34 (40.5%)	42 (50.6%)	0.247
Smoking, n (%)	24 (36.9%)	36 (59.0%)	0.021
Creatinine (mg/dl)	0.86±0.36	0.86±0.24	0.256
CRP (mg/L)	4.14±7.9	4.46±8.50	0.341
Total cholesterol (mg/dl)	185.49±38.35	179.05±40.15	0.114
LDL cholesterol (mg/dl)	103.11±33.19	98.47±31.50	0.359
Triglycerides (mg/dl)	129.31±57.22	156.26±65.56	0.0024
WBC (x10^3/µL)	7.89±2.32	8.15±2.29	0.364
Platelets (x10^3/µL)	259.80±74.04	244.18±70.84	0.468
TSH (µIU/ml)	1.83±1.69	1.86±1.94	0.971
FT3 (pg/ml)	3.30±0.57	3.41±0.67	0.485
FT4 (ng/dl)	1.38±0.35	1.36±0.40	0.575

CSF: Coronary slow flow, CRP: C-reactive protein, LDL: Low-density lipoprotein, WBC: White blood count, TSH: Thyroid-stimulating hormone, FT3: Free t3, FT4: Free t4

Among laboratory parameters, serum triglyceride levels were significantly higher in the CSF group compared with the normal flow group (156.3±65.6 mg/dl vs. 129.3±57.2 mg/dl, p=0.002), whereas other biochemical and hematologic indices-including glucose, creatinine, and CRP-showed no significant differences. Similarly, thyroid hormone levels (TSH, FT3, and FT4) were comparable between groups (all p>0.05).

Logistic Regression Analysis

Results of the univariate and multivariate logistic regression analyses are presented in **Table 2**. In univariate analysis, younger age (OR 0.94, 95% CI 0.90-0.98, p=0.001), male sex (OR 2.92, 95% CI 1.36-6.26, p=0.006), and smoking (OR 2.51,

95% CI 1.20-5.25, p=0.015) were significantly associated with the presence of CSF.

Table 2. Logistic regression analysis of predictors of coronary slow flow

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age (years)	0.94 (0.90-0.98)	0.001	0.95 (0.91-0.99)	0.007
Male sex	2.80 (1.33-5.91)	0.007	2.20 (0.73-6.60)	0.160
Smoking	2.27 (1.10-4.67)	0.027	0.95 (0.32-2.80)	0.920
FT3 (pg/ml)	1.62 (0.87-3.01)	0.129	1.40 (0.69-2.85)	0.354
FT4 (ng/dl)	0.99 (0.38-2.56)	0.988	0.63 (0.19-2.08)	0.449
TSH (μIU/ml)	1.03 (0.54-1.96)	0.94	0.91 (0.47-1.74)	0.78

OR: Odds ratios, CI: Confidence intervals, FT3: Free t3, FT4: Free t4, TSH: Thyroid-stimulating hormone

Hypertension and triglyceride levels also showed significant associations in univariate analysis but did not remain independent predictors after multivariable adjustment. In the final multivariate model including age, sex, smoking, FT3, and FT4, only age remained an independent predictor of CSF (OR 0.96, 95% CI 0.92-0.99, p=0.030).

When TSH was additionally included in the multivariate model, it did not emerge as an independent predictor of CSF (OR 0.91, 95% CI 0.47-1.74, p=0.78).

ROC Curve Analysis

ROC curves of thyroid parameters are shown in **Figure**. The discriminatory power of thyroid hormones for predicting CSF was poor, with AUC values of 0.50 for TSH, 0.53 for FT3, 0.48 for FT4, and 0.46 for the FT4/FT3 ratio. No clinically relevant cut-off values with adequate sensitivity and specificity could be determined.

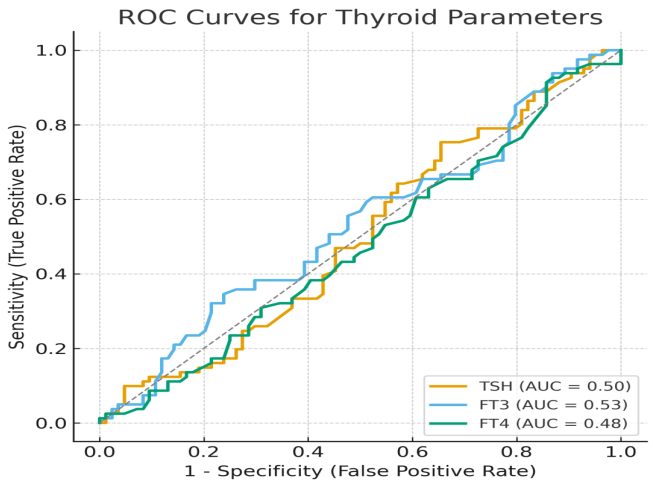


Figure. ROC curves of thyroid hormones (TSH, FT3, FT4, and FT4/FT3 ratio) for predicting coronary slow flow ROC curves are shown for serum thyroid hormone parameters in patients with CSF versus controls. The AUC was 0.50 for TSH, 0.53 for FT3, 0.48 for FT4, and 0.46 for the FT4/FT3 ratio, indicating no significant discriminatory power.

ROC: Receiver operating characteristic, TSH: Thyroid-stimulating hormone, FT3: Free t3, FT4: Free t4, CSF: Coronary slow flow, AUC: Area under the curve

DISCUSSION

In this study, we examined whether thyroid hormone levels are associated with CSF. Patients with CSF were younger, more often male, and more frequently smokers than controls; however, in multivariable analysis only age remained an independent determinant. Thyroid markers (TSH, FT3, FT4, FT4/FT3) did not discriminate CSF status in ROC analyses. In line with prior negative studies, our findings suggest that subtle variations in thyroid hormones within the euthyroid range are unlikely to play a dominant role in CSF pathogenesis.

Previous investigations have reported conflicting results. Evrengül et al.[12] demonstrated lower FT3 levels in CSF patients, while Chen et al.[13] found reduced FT4, particularly in women. In contrast, Madak et al.[14] observed no significant differences in thyroid hormone levels between CSF and control groups. These inconsistencies may stem from population heterogeneity, sex distribution, sample size, or methodological differences.

Importantly, our findings emphasize that in a well-defined euthyroid population, thyroid hormones alone are unlikely to serve as independent predictors of CSF. This is clinically relevant because it highlights that routine thyroid hormone testing may not add diagnostic or prognostic value in daily practice. Instead, traditional cardiovascular risk factors such as younger age, male sex, and smoking remain the major determinants of CSF.

Beyond thyroid hormones, additional mechanisms have been implicated in CSF. Clinical data suggest that CSF is related to microvascular dysfunction, endothelial impairment, and inflammation.[15,16] Furthermore, Razvi et al.[17] emphasized that thyroid hormones can modulate cardiovascular performance through multiple pathways, including vascular tone and myocardial contractility. Vargas-Uricoechea et al.[20] also reviewed the complex effects of thyroid hormones on vascular physiology, noting potential interactions with small-vessel function.[18] Taken together, although thyroid hormones exert significant cardiovascular effects, our results suggest that these influences may not be strong enough to independently determine coronary flow in otherwise euthyroid individuals.

Another key message of our study is that negative results may still have positive implications. By demonstrating the limited role of thyroid hormones, we provide evidence that future research should focus more on the interplay between inflammation, microvascular dysfunction, and novel immunoinflammatory markers. Recently, indices such as the pan-immune-inflammation value (PIV) have shown stronger predictive value for CSF compared with conventional markers.[19,20] Furthermore, retinal and choroidal microvascular alterations in CSF patients, demonstrated by optical coherence tomography angiography, support the concept of generalized microvascular dysfunction.[21] These findings suggest that the contribution of thyroid hormones may be indirect, potentially acting as modulators rather than primary drivers of CSF pathogenesis.

At the experimental level, TSH has been shown to impair endothelial function by altering nitric oxide synthase and vasoactive mediator expression.[22] Although we did not find a direct clinical effect of thyroid hormones, this mechanistic evidence justifies further prospective studies, particularly in populations with subclinical thyroid dysfunction or in those with higher systemic inflammatory burden.

Furthermore, retinal and choroidal microvascular alterations in CSF patients, demonstrated by optical coherence tomography angiography, support the concept of generalized microvascular dysfunction.[23] These findings suggest that the contribution of thyroid hormones may be indirect, potentially acting as modulators rather than primary drivers of CSF pathogenesis. At the experimental level, TSH has been

shown to impair endothelial function by altering nitric oxide synthase and vasoactive mediator expression.[24] Although we did not find a direct clinical effect of thyroid hormones, this mechanistic evidence justifies further prospective studies, particularly in populations with subclinical thyroid dysfunction or in those with higher systemic inflammatory burden.

Limitations

This study has several limitations. First, it was a single-center, retrospective design, which may limit the generalizability of the findings. Second, coronary flow was assessed solely using the TIMI frame count; more sensitive measures of microvascular resistance or endothelial reactivity were not available. Third, only baseline thyroid hormone levels were analyzed, and dynamic variations over time could not be evaluated. Fourth, although patients with overt thyroid disease were excluded, the presence of unrecognized subclinical thyroid dysfunction cannot be completely ruled out. Finally, inflammatory and oxidative stress markers beyond conventional CRP were not assessed, which may have provided additional insight into the link between endocrine and microvascular processes.

CONCLUSION

As a result, our study demonstrates that thyroid hormone levels are not independently associated with coronary slow flow in euthyroid patients. While triglyceride levels were modestly higher among CSF patients, this relationship was not independent after multivariable adjustment. Conventional risk factors such as younger age and smoking remained the dominant determinants of CSF. These results indicate that, within the physiological range, thyroid hormone fluctuations have limited impact on coronary flow, and routine thyroid testing provides minimal additional diagnostic value. Future large-scale, prospective studies should further explore the interaction between thyroid physiology, lipid metabolism, inflammation, and microvascular function to better clarify their collective roles in the pathogenesis of coronary slow flow.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Batman Training and and Research Hospital Scientific Researches Ethics Committee (Date: 24.06.2018, Decision No: 280118606,429).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

Evaluation of cardiovascular, bone mineral, and hematological disorders in chronic hemodialysis patients

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ABSTRACT

Aims: The prevalence of cardiovascular diseases, bone mineral disorders, and anemia in patients undergoing continuous hemodialysis is higher than in the normal population. In addition, due to the ongoing renal parenchymal loss in these patients, there is continuous deterioration in bone mineral metabolism. Anemia, a leading hematological disorder, is considered to be one of the most important and frequent complications leading to compromised quality of life. In this study, we aimed to investigate cardiovascular, bone mineral, and hematological disorders in patients undergoing continuous hemodialysis.

Methods: Clinical data of 56 patients receiving continuous hemodialysis at Yüzüncü Yıl University Faculty of Medicine Hospital Nephrology Clinic Dialysis Unit between 01.07.2021 and 01.07.2022 were evaluated retrospectively. Echocardiography), dual-energy X-Ray absorptiometry and laboratory parameters were evaluated for each patient. Demographic characteristics and medications were recorded. Due to the retrospective nature of the study, the sample size was not calculated.

Results: The study included 56 patients undergoing hemodialysis, comprising 26 (46.4%) men and 30 (53.6%) women. Mean duration of hemodialysis was 5.55±5.09 years. Moreover, 92.9% of the patients were receiving medications, with the most common medications including erythropoiesis-stimulating agents (69.6%), phosphorus binders (48.2%), iron supplements (28.6%), active vitamin D supplements (37.5%), and cinacalcet (12.5%). Cardiovascular diseases were detected in 60.7% of the patients, osteoporosis in 41.1%, and anemia in 78.6%.

Conclusion: Cardiovascular disease, bone mineral disorders, and hematological disorders are commonly seen in hemodialysis patients. Hemodialysis patients should be regularly evaluated for complications.

Keywords: Hemodialysis, cardiovascular diseases, osteoporosis, anemia, erythropoiesis-stimulating agent

INTRODUCTION

Chronic kidney disease (CKD) is a common disease with high morbidity and mortality, typically resulting from irreversible damage to kidney function. The overall prevalence of CKD is 10-15%.[1] Renal replacement therapy is recommended for patients with end-stage kidney damage. Hemodialysis is the most common form of renal replacement therapy. End-stage kidney disease is closely associated with cardiovascular diseases (CVD), alterations in bone mineral metabolism, and anemia.[2]

In this study, we aimed to investigate the prevalence of CVD, bone mineral disorders, hematological disorders, and ongoing therapies as well as gender-based differences in patients receiving continuous hemodialysis treatment.

METHODS

Study Design

The study was initiated after obtaining an ethical approval from Van Yüzüncü Yıl Non-interventional Clinical Researches Ethics Committee (Date: 12.05.2023, Decision No: 2023/05-10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Clinical data of 56 patients (30 female and 26 male) that received hemodialysis between July 2021 and December 2022 were retrieved from local databases. Echocardiography (Echo), Dual-energy X-Ray absorptiometry (DEXA), and laboratory parameters were evaluated for each patient. Demographic characteristics and medications were recorded.

Statistical Analysis

Data were analyzed using SPSS for Windows version 26.0 (Armonk, IBM Corp.). Descriptives were expressed as mean, median, standard deviation (SD), minimum, maximum, frequencies (n), and percentages (%). Normal distribution of variables was assessed using Kolmogorov-Smirnov test. Continuous variables with normal distribution were compared between two independent groups using independent samples T test and Mann-Whitney U Test. Categorical variables were compared using Pearson's Chi-squared test and Fisher's exact test. A p-value of <0.05 was considered significant.

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RESULTS

The 56 patients comprised 30 (53.6%) women and 26 (46.4%) men. Mean laboratory values were as follows: urea 134.64±32.42 mg/dl, creatinine 8.59±2.51 mg/dl, hemoglobin 10.82±1.96 g/dl, hematocrit 33.87±5.95%, calcium 8.12±0.68 mg/dl, parathyroid hormone 403.44±282.15 PG/ml, phosphorus 4.79±1.58 mg/dl, and ferritin 966.11±1161.49 ml/NG (Table 1).

Table 1. Laboratory parameters

	Mean	SD	Median	Min-max
Urea (mg/dl)	134.64	32.42	133.3	58.2-224.8
Creatinine (mg/dl)	8.59	2.51	8.7	3.9-17.2
Hemoglobin (g/dl)	10.82	1.96	10.9	5.6-15.1
Hematocrit (%)	33.87	5.95	34.3	19.2-46.4
Calcium (mg/dl)	8.12	0.68	8.1	5.9-10.1
Phosphor (mg/dl)	4.79	1.58	4.9	1.5-11.4
Parathormone (PG/ml)	403.44	282.15	360	21.6-1146.3
Ferritin (ml/NG)	966.11	1161.49	567.6	22-6235.3

SD: Standard deviation, Min: Minimum, Max: Maximum

Table 2 presents the duration of hemodialysis and medications used for each patient. Mean duration of hemodialysis was 5.55±5.09 (range, 0.2-22) years. Moreover, 92.9% of the patients were receiving medications, with the most common medications including erythropoiesis-stimulating agents (ESA) (69.6%), phosphorus binders (48.2%), iron supplements (28.6%), active vitamin D supplements (37.5%), and cinacalcet (12.5%).

Table 3 presents the laboratory parameters of the patients. Mean hemoglobin level was significantly higher in men than in women (11.42±1.83 vs. 10.27±1.95 g/dl; p<0.05). Similarly, mean hematocrit level was higher in men than in women (35.65±5.53% vs. 32.33±5.96%; p<0.05). Nevertheless, no significant difference was found between the two genders with regard to other parameters (p>0.05).

Table 2. Hemodialysis duration and medication use

		Mean	SD	Median	min-max
Hemodialysis duration (years)		5.55	5.09	4	0.2-22
		n			%
Medication use	Yes	52			92.9
	No	4			7.1
ESA		39			69.6
Iron		16			28.6
Phosphorus binders		27			48.2
Active vitamin D		21			37.5
Calcimimetic		7			12.5
Total		56			100

SD: Standard deviation, Min: Minimum, Max: Maximum, ESA: Erythropoiesis-stimulating agents

Of all patients, 78.6% (n=44) had anemia, 60.7% (n=34) had CVD, and 41.1% (n=23) had osteoporosis. Mean duration of hemodialysis was 6 years in men as opposed to 4 years in women. Among male patients, 22 had anemia, 21 had osteoporosis, and 15 had CVD, while 22 female patients had anemia, 19 had CVD, and 12 had osteoporosis. As for medications, 18 of the men were using ESA, 12 were using phosphorus binders, 8 were using iron supplements, and 12 were using active vitamin D supplements, whereas 21 of the women were using ESA, 15 were using phosphorus binders, 8 were using iron, and 9 were using vitamin D (Table 4). No significant difference was found between the duration of hemodialysis and CVD, osteoporosis, anemia, and medication use (p>0.05).

Table 5 presents the medication rates for CVD, osteoporosis, and anemia. No significant difference was found between patients with and without CVD and between patients with and without osteoporosis with regard to medication use (p>0.05 for both). Of the patients with anemia, 81.8% were using ESA, 45.5% were using vitamin D, and 4.5% were using cinacalcet. Moreover, there was a significant difference

Table 3. Laboratory parameters according to genders

	Gender	Mean	SD	Median	min-max	t[a]/Z[b]	p
Urea (mg/dl)	Male	132.9	32.01	128.2	75.9-224.8	-0.370a	0.713
	Female	136.14	33.24	138.6	58.2-200		
Creatinine (mg/dl)	Male	9.15	3	9.2	4.2-17.2	1.564a	0.124
	Female	8.11	1.92	8.2	3.9-12.1		
Hemoglobin (g/dl)	Male	11.42	1.83	11.4	5.6-15.1	-2.361b	0.018*
	Female	10.27	1.95	10.4	6.2-13.5		
Hematocrit (%)	Male	35.65	5.53	36.3	19.2-45.4	2.149a	0.036*
	Female	32.33	5.96	32.6	20.9-46.4		
Calcium (mg/dl)	Male	8.22	0.55	8.3	7.3-9.5	1.032a	0.307
	Female	8.03	0.77	8.1	5.9-10.1		
Phosphor (mg/dl)	Male	4.73	1.4	5	1.5-7.1	-0.223a	0.824
	Female	4.83	1.75	4.7	1.6-11.4		
Parathormone (PG/ml)	Male	441.03	294.85	371	21.6-1146.3	-1.082b	0.279
	Female	372.12	272.12	278.8	32.2-985.2		
Ferritin (ml/NG)	Male	1012.53	1354.76	452.7	27.5-6235.3	-0.526b	0.599
	Female	925.88	986.26	603.2	22-4758.6		

SD: Standard deviation, Min: Minimum, Max: Maximum

Tablo 4. Prevalence of cardiovascular diseases, osteoporosis, and anemia and medication use

		Gender					
		Male		Female			
		Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Z	p
Hemodialysis duration (years)		6.30±5.98	4 (0.3-22)	4.87±4.13	3 (0.2-12)	-0.777	0.437
		n	%	n	%	X^2	p
CVD	Yes	15	57.7	19	63.3	0.186a	0.666
	No	11	42.3	11	36.7		
Osteoporosis	Yes	11	42.3	12	40	0.031a	0.861
	No	15	57.7	18	60		
Anemia	Yes	22	84.6	22	73.3	1.053a	0.305
	No	4	15.4	8	26.7		
Medication	Yes	25	96.2	27	90	0.138b	0.651
	No	1	3.8	3	10		
Medications							
ESA		18	69.2	21	70	0.004a	0.950
Phosphorus binders		12	46.2	15	50	0.083a	0.774
Iron		8	30.8	8	26.7	0.115a	0.735
Vitamin D		12	46.2	9	30	1.221a	0.213
Cinacalcet		4	15.4	3	10	0.041b	0.693

a: Pearson's Chi-square test, b: Fisher's exact test, Note: p-values in bold indicate statistically significant difference (p<0.05). SD: Standard deviation, CVD: Cardiovascular diseases, ESA: Erythropoiesis-stimulating agents

Table 5. Statistical comparison of medications by the prevalence of cardiovascular diseases. osteoporosis. and anemia

	Cardiovascular diseases					
	Yes (n=34)		No (n=22)			
Medications	**n**	**%**	**n**	**%**	**X2**	**p**
ESA	25	73.5	14	63.6	0.618a	0.432
Phosphorus binders	17	50	10	45.5	0.111a	0.740
Iron	9	26.5	7	31.8	0.187a	0.765
Vitamin D	10	29.4	11	50	2.416a	0.161
Cinacalcet	4	11.8	3	13.6	0.042b	0.837
	Osteoporosis					
	Yes (n=23)		No (n=33)			
ESA	14	60.9	25	75.8	1.421a	0.233
Phosphorus binders	11	47.8	16	48.5	0.002a	0.961
Iron	5	21.7	11	33.3	0.893a	0.345
Vitamin D	9	39.1	12	36.4	0.044a	0.833
Cinacalcet	5	21.7	2	6.1	3.024b	0.110
	Anemia					
	Yes (n=44)		No (n=12)			
ESA	36	81.8	3	25	11.835b	0.000*
Phosphorus binders	22	50	5	41.7	0.262a	0.609
Iron	15	34.1	1	8.3	1.933b	0.147
Vitamin D	20	45.5	1	8.3	4.073b	0.021*
Cinacalcet	2	4.5	5	41.7	8.727b	0.003*

a: Pearson's Chi-square test. b: Fisher's exact test. Note: p-values in bold indicate statistically significant difference (p<0.05). ESA: Erythropoiesis-stimulating agents

between patients with and without anemia (p<0.05). The rates of ESA and vitamin D supplement use were higher in patients with anemia, while the rate of cinacalcet use was higher in patients without anemia. Nevertheless, there was no significant difference between these two groups with regard to the use of iron supplements and phosphorus binders (p>0.05).

DISCUSSION

The 56 patients comprised 30 women and 26 men. Among all patients, 78.6% of them had anemia, 60.7% of them had CVD, and 41.1% had osteoporosis. It is known that the prevalence of CVD, bone mineral disorders, and anemia is higher in patients receiving hemodialysis than in the normal

population. Additionally, it is also known that the prevalence of CVD in the hemodialysis population increases in parallel with the increasing frequency of general risk factors for atherosclerosis, particularly including hypertension and diabetes.

It has been shown that a decrease in the estimated glomerular filtration rate (eGFR) is associated with an increased risk of CVD and mortality. Additionally, creatinine levels, which are markers of kidney function, may serve as an indicator of CVD-related mortality, and individuals diagnosed with heart failure have been reported to have more than twice the risk of developing CKD.[3]

The Turkish Public Health Journal, in its 2015 publication, evaluated the studies conducted between 1997 and 2007 and reported that the prevalence of CVD in the normal population aged ≥30 years varied between 4.4-10.9%, with 5.1-17.4% in men and 3.7-8.3% in women.[4] In our study, as consistent with the literature, the prevalence of CVD in men and women receiving hemodialysis was approximately 5-6 times higher than the prevalence in the normal population.

Osteoporosis is a skeletal disorder characterized by deterioration of bone strength, leading to an increased risk of fractures. CKD is an independent risk factor for osteoporosis.[5] The 2017 KDIGO (kidney disease: improving outcomes) guidelines recommend screening with DEXA in patients with CKD, which is a risk factor for osteoporosis (KDIGO, 2017). Osteoporosis is defined as a femoral neck T score of ≤-2.5 standard deviation (SD). In the Third National Health and Nutrition Examination Survey (NHANES III), osteoporosis was twice as common in participants with a glomerular filtration rate (GFR) of <60 ml/min compared to those with a GFR of >60 ml/min. Of note, the prevalence of osteoporosis in patients with stage 3-5 CKD in the Kashmir Valley was reported as 31.8%.[6] According to a study conducted by Festuccia et al.[7] in 2017, the prevalence of osteoporosis in patients with CKD was determined to be approximately 53%. A study conducted at Akdeniz University Faculty of Medicine in 2021 evaluated 74 patients that were receiving hemodialysis and peritoneal dialysis. The authors detected osteoporosis in 13 (35.1%) out of 37 patients receiving peritoneal dialysis and in 19 out of 37 patients (51.4%) receiving hemodialysis.[8] In our study, in line with the literature, osteoporosis was detected in 41.1% of the patients.

Anemia is a leading and frequent complication leading to compromised quality of life in CKD patients.

According to the World Health Organization (WHO), anemia is defined as a hemoglobin level below 12 g/dl in women and below 13 g/dl in men. The most common form of anemia in chronic kidney disease (CKD) is anemia caused by insufficient erythrocyte production due to erythropoietin deficiency. The prevalence of anemia increases with the progression of CKD stages (8.4% in stage 1, 53.4% in stage 5).[9]

A study conducted by Altun et al.[10] evaluated 244 hemodialysis patients and reported the mean hemoglobin as 10.9 g/dl.

When using the WHO's anemia definitions, anemia is detected in 87% of patients with a GFR below 25 ml/min who have not yet started dialysis.[11]

In the CREDIT (chronic renal disease in Turkiye) study conducted in Turkiye, the prevalence of anemia was determined as 12.8% in CKD stage 3, 33.3% in stage 4, and 66.7% in stage 5.[12] In our study, the prevalence of anemia in patients undergoing hemodialysis was 78.6% and the mean hemoglobin value of all patients was found to be 10.82±1.96 g/dl. Moreover, a significant difference was found between the two genders with regard to hemoglobin level ($p<0.05$). These findings were found to be consistent with those reported in the literature.

According to the Social Security Institution Communiqué on Healthcare Practices implemented in Turkiye, an ESA treatment can only be initiated in patients with hemoglobin <10 g/dl, transferrin saturation ≥20%, and/or ferritin ≥100 µg/L and the target hemoglobin value in treatment should be 11-12 g/dl.[13] The 2014 Summary Report published by the Turkish Society of Nephrology Registry demonstrated that 24.04% of hemodialysis patients had previously used ESA but were not currently using it, while 5.36% had never used ESA before and the remaining 70.6% of the patients were currently using ESA.[14] In our study, 69.6% of the patients had a history of ESA use and a significant difference was found between the patients with and without anemia in terms of ESA use ($p<0.05$).

Our study was limited since it was a single-center study and had a relatively small number of patients. Further randomized controlled studies with large numbers of hemodialysis patients are needed to substantiate our findings. We also believe that our findings will shed light on future studies.

Limitations

The most significant limitation of this study is the failure of some patients to attend their scheduled appointments or adhere to regular hemodialysis treatment, which resulted in missing blood test data.

CONCLUSION

Our study clearly showed that the frequency of CVD, osteoporosis, and anemia is higher in hemodialysis patients. Accordingly, hemodialysis patients should be evaluated through a multidisciplinary approach. In these patients, cardiovascular examinations should be performed and bone mineral density should be evaluated at certain intervals, and monthly hemodialysis visits should be made.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Van Yüzüncü Yıl Non-interventional Clinical Researches Ethics Committee (Date: 12.05.2023, Decision No: 2023/05-10).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Review

Coronary artery anomalies: clinical overview, diagnostic strategies, and management

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ABSTRACT

Coronary artery anomalies (CAAs) represent a heterogeneous group of congenital abnormalities involving the origin, course, or termination of the coronary arteries. Although most CAAs are asymptomatic and discovered incidentally, certain variants particularly those with an interarterial or intramural course carry a substantial risk of myocardial ischemia, arrhythmia, or sudden cardiac death. With the advent of multidetector computed tomography and cardiac magnetic resonance imaging, recognition of these anomalies has markedly increased. This mini review summarizes the classification, epidemiology, pathophysiological mechanisms, clinical significance, and current diagnostic and management strategies for CAAs, emphasizing their relevance in contemporary cardiology practice.

Keywords: Coronary artery anomalies, coronary angiography, computed tomography angiography, cardiac magnetic resonance, anomalous aortic origin of coronary artery

INTRODUCTION

Coronary artery anomalies (CAAs) are congenital malformations involving deviations in the origin, course, or termination of coronary vessels, occurring in approximately 0.2-1.3% of the general population on invasive angiography and up to 5% on computed tomography coronary angiography (CTCA).[1,2] Most variants are benign; however, certain configurations, such as anomalous aortic origin of the coronary artery (AAOCA) with an interarterial course between the aorta and pulmonary trunk, have been associated with myocardial ischemia and sudden cardiac death, especially in young athletes.[3,4] Advances in cardiac imaging have led to increasing detection, yet optimal management remains controversial. This review provides a concise overview of CAAs with a focus on diagnostic principles and clinical implications.

CLASSIFICATION

CAAs are typically categorized into three broad groups: (1) anomalies of origin and course, (2) anomalies of intrinsic coronary anatomy, and (3) anomalies of termination.[5] Anomalous origin and course include aberrant origins from the opposite sinus (ACAOS), high take-off from the ascending aorta, single coronary artery, or anomalous origin from the pulmonary artery (ALCAPA or ARCAPA). Among these, left coronary artery arising from the pulmonary artery (ALCAPA) represents a malignant variant with early-onset ischemic cardiomyopathy.[6] Anomalous course refers to interarterial, intramural, retroaortic, prepulmonic, or septal trajectories.[7] The interarterial subtype is of greatest clinical concern because of potential vessel compression during exercise.[8] Anomalies of termination include coronary fistulas draining into cardiac chambers or great vessels, which may lead to volume overload or coronary steal phenomena.[9,10]

EPIDEMIOLOGY

The true prevalence of CAAs varies according to imaging modality and population studied. Autopsy and angiographic series estimate an incidence of approximately 1%, whereas CTCA-based studies report higher frequencies due to improved spatial resolution. In a large multicenter CT study, prevalence reached 5.6%, with most anomalies classified as benign variants.[11] Notably, AAOCA has been identified in up to 0.3% of individuals and accounts for 14-19% of sudden cardiac deaths in young athletes.[12] These data highlight the importance of recognizing high-risk morphologies despite overall rarity.

PATHOPHYSIOLOGY AND CLINICAL SIGNIFICANCE

The clinical manifestations of CAAs range from asymptomatic incidental findings to exertional angina, syncope, arrhythmia, myocardial infarction, or sudden cardiac death.[12,13] Pathophysiological mechanisms include slit-like ostium and acute take-off angle, causing dynamic obstruction during systole; intramural course within the aortic wall, leading to luminal compression; interarterial course, predisposing to external compression between the great vessels during exertion; and coronary steal in fistulous communications.[14-16] In ALCAPA, perfusion of the left ventricle from the low-pressure pulmonary system results in chronic ischemia and

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progressive ventricular dysfunction.[6] Conversely, benign variants, such as retroaortic or prepulmonic courses, typically lack hemodynamic consequences.[17]

DIAGNOSTIC EVALUATION

Echocardiography

Transthoracic and transesophageal echocardiography serve as first-line tools, especially in pediatric patients, offering real-time visualization of coronary origins and proximal courses. However, spatial resolution is limited in adults or complex anatomies.[18]

Computed Tomography Coronary Angiography (CTCA)

CTCA has emerged as the gold standard for anatomical delineation due to its superior three-dimensional resolution, enabling precise mapping of coronary origins, trajectories, and relationships with adjacent structure. The modality is particularly useful in differentiating interarterial and intramural components, which are difficult to appreciate on conventional angiography.[19,20]

Cardiac Magnetic Resonance Imaging (CMR)

CMR complements CT by providing both anatomical and functional assessment, allowing evaluation of ischemia and myocardial viability without radiation exposure[16].

INVASIVE CORONARY ANGIOGRAPHY AND FUNCTIONAL TESTING

Conventional angiography remains essential when physiological significance must be assessed. Techniques such as fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) measurements can quantify ischemia in anomalous vessels.[21]

MANAGEMENT STRATEGIES

Therapeutic decision-making depends on anatomical configuration, symptom status, and evidence of ischemia. Low-risk or incidental variants are usually managed conservatively with regular follow-up and activity modification.[22] High-risk configurations particularly AAOCA with an interarterial or intramural course and ALCAPA warrant surgical correction. Surgical options include unroofing of the intramural segment, reimplantation into the appropriate sinus, coronary artery bypass grafting, or ostioplasty.[23,24] Percutaneous closure is reserved for selected coronary fistulas.[25] Recent consensus statements recommend individualized management guided by multimodality imaging, physiological assessment, and patient-specific risk evaluation.[26] Despite increasing recognition, randomized trials are lacking, and most recommendations rely on expert consensus.[27]

CONCLUSION

Coronary artery anomalies encompass a diverse spectrum of congenital abnormalities with variable clinical significance. While most are benign, certain high-risk variants pose substantial risk for ischemic events and sudden cardiac death. Advances in CT and MR imaging have revolutionized detection, yet management continues to rely heavily on anatomical risk stratification and multidisciplinary judgment. Early recognition, appropriate imaging, and tailored treatment remain essential to improving patient outcomes. Future research should focus on prospective multicenter registries and long-term outcome data to better define optimal management pathways.

ETHICAL DECLARATIONS

Referee Evaluation Process

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

From hypothyroidism to Graves' disease during pregnancy: a case of thyrotoxicosis following long-term hypothyroidism

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ABSTRACT

Graves' disease is an autoimmune thyroid disorder characterized by hyperthyroidism, diffuse goiter, and orbitopathy, and it rarely occurs during pregnancy. A 23-year-old woman presented to the emergency department at 20 weeks of her second pregnancy with complaints of palpitations, sweating, and fatigue. She had previously been diagnosed with hypothyroidism by her family physician and had been on levothyroxine therapy. She had also been followed with hypothyroidism during her first pregnancy. Evaluation revealed findings consistent with thyrotoxicosis and positive thyroid autoantibodies, leading to a diagnosis of Graves' disease. Propylthiouracil (PTU) therapy was initiated, and thyroid function was closely monitored throughout pregnancy. Both maternal and fetal outcomes were uneventful, and delivery occurred without complications. The development of Graves' disease during pregnancy in a patient previously diagnosed with hypothyroidism is exceedingly rare. This case highlights the clinical importance of the transition from hypothyroidism to Graves' hyperthyroidism during pregnancy.

Keywords: Graves' disease, pregnancy, hyperthyroidism

INTRODUCTION

Graves' disease is the most common cause of hyperthyroidism in iodine-sufficient regions of developed countries.[1] It results from excessive stimulation of thyroid-stimulating hormone (TSH) receptors by TSH receptor antibodies (TRAb), leading to thyroid hypertrophy, increased hormone synthesis, and consequently thyrotoxicosis, diffuse goiter, and sometimes ophthalmopathy.[2]

Pregnancy represents a physiological state in which the Th1/Th2 balance of the immune system is altered, potentially influencing the course of autoimmune thyroid disorders. Suppression of the autoimmune response during pregnancy and its reactivation in the postpartum period may contribute to the onset of Graves' disease.[3]

The transition from hypothyroidism to hyperthyroidism is extremely uncommon, even among patients with autoimmune thyroid disorders. In the largest 10-year follow-up study of patients with TBAb-induced hypothyroidism, Takasu and Matsushita[4] reported that only 5.9% (2 of 34) of patients developed thyroid-stimulating antibodies (TSAb) and became hyperthyroid, highlighting the rarity of such autoimmune switching.

The mainstay of Graves' disease management involves controlling symptoms and normalizing thyroid hormone levels. Although treatment during pregnancy is generally similar to that in non-pregnant individuals, certain adjustments are required. The goal is to maintain mild maternal hyperthyroidism to prevent fetal hypothyroidism, as the fetal thyroid is more sensitive to antithyroid drugs.[5] Overtreatment with thionamides may lead to fetal goiter and primary hypothyroidism, whereas undertreatment increases the risk of transient central hypothyroidism.[6]

This case represents a rare instance of Graves' hyperthyroidism developing during pregnancy in a patient previously diagnosed with hypothyroidism, emphasizing the importance of vigilant thyroid monitoring in pregnant women.

CASE

A 23-year-old woman presented to the emergency department at 20 weeks' gestation of her second pregnancy with complaints of severe palpitations. Six years earlier, during a routine evaluation at a family medicine clinic, she had been diagnosed with primary hypothyroidism based on an isolated elevation of thyroid-stimulating hormone (TSH) with normal free thyroxine (FT4) levels; thyroid autoantibodies [anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin (anti-Tg), and thyroid-stimulating hormone receptor antibody (TRAb)] were not assessed at that time. Levothyroxine therapy was initiated, and she achieved a clinically euthyroid state on follow-up.

Her obstetric history included two spontaneous pregnancies conceived without assisted reproductive techniques. During her first pregnancy, thyroid autoantibodies (anti-TPO, anti-Tg, TRAb) were assessed for the first time and found to be negative. She remained euthyroid and clinically stable on

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levothyroxine throughout that pregnancy. The early course of her second pregnancy was uneventful, with normal fetal growth and routine obstetric monitoring.

At 21 weeks' gestation, however, she presented to the emergency department with severe palpitations, excessive sweating, and fatigue, though. Initial laboratory evaluation demonstrated suppressed TSH and markedly elevated FT4 and free T3 levels. Endocrinology consultation confirmed thyrotoxicosis secondary to Graves' disease. Thyroid autoantibody testing performed at presentation was positive, including elevated TRAb levels, indicating autoimmune stimulation. Considering the maternal and fetal risks associated with uncontrolled thyrotoxicosis during pregnancy, treatment with propylthiouracil (PTU) was initiated. The patient responded favorably, with gradual clinical improvement and normalization of thyroid hormone levels.

Thyroid ultrasonography revealed diffuse gland enlargement with increased vascularity, while ophthalmologic examination showed no evidence of Graves' orbitopathy. The remainder of the pregnancy was uneventful, and the patient delivered a healthy infant at term. Postpartum endocrinology follow-up demonstrated stable thyroid function.

DISCUSSION

This case demonstrates a rare occurrence of Graves' disease emerging during pregnancy in a patient with a prior diagnosis of hypothyroidism. Transition from hypothyroidism to Graves' hyperthyroidism has been described only in a limited number of reports, and to our knowledge, there are very few cases documented during pregnancy.[7,8] The underlying pathophysiology remains unclear, but it may involve immune modulation due to lymphocytic infiltration, fibrosis, and follicular damage of the thyroid gland. Although elevated anti-TPO antibody levels generally indicate progressive irreversible hypothyroidism, in some cases, follicular regeneration followed by the dominance of stimulating autoantibodies may result in hyperthyroidism.[7]

McDermott et al.[9] reported two female patients who, similar to our case, developed thyrotoxicosis after an initial diagnosis of primary hypothyroidism. Up to 2014, only 37 such cases of hypothyroidism converting to hyperthyroidism had been reported.[10] Autoimmune thyroid diseases are more common in women,[2] and the predominance of female patients in published cases supports the hypothesis of gender-related differences in immune response.[7,8,10]

Although the precise cause of hyperthyroidism following hypothyroidism is uncertain, it has been proposed that the shift between thyroid-stimulating and thyroid-blocking antibodies plays a central role.[11] During pregnancy, immune modulation characterized by a shift from Th1 to Th2 dominance leads to suppression of cell-mediated immunity and enhanced humoral activity. This shift may reduce autoimmune attacks during pregnancy but rebound postpartum, possibly triggering the transition from hypothyroidism to hyperthyroidism.[2] Physiological immune tolerance changes during pregnancy may enhance TRAb production, leading to abrupt thyrotoxicosis or Graves' disease. In support of this mechanism, Aranyosi et al.[12] reported a case diagnosed with Graves' disease at 20 weeks of gestation, complicated by orbitopathy.

Selection and dosage of antithyroid drugs during pregnancy are crucial for maternal and fetal safety. Methimazole has teratogenic potential; therefore, PTU is preferred during the first trimester.[13,14] In our patient, thyrotoxicosis detected in the second trimester was successfully controlled with PTU therapy.

The sudden development of Graves' hyperthyroidism during pregnancy in a patient with a history of hypothyroidism is a rare phenomenon. This transition may be influenced by shifts in the balance between thyroid-stimulating and blocking antibodies, as well as pregnancy-related alterations in immune response. This case emphasizes that clinicians should monitor not only TSH levels but also the patient's antibody profile and clinical symptoms. Regular assessment of thyroid function and autoantibodies during pregnancy facilitates the early detection of potential autoimmune transitions, thereby contributing to the protection of both maternal and fetal health.

CONCLUSION

This case illustrates that Graves' disease may develop during pregnancy in women with a prior history of hypothyroidism. Early diagnosis and appropriate antithyroid therapy are crucial for safeguarding maternal and fetal well-being. Monitoring thyroid function tests alongside autoimmune markers throughout pregnancy allows for the timely identification of potential autoimmune shifts.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Letter to the Editor

Letter to the Editor: comment on "Frailty scoring systems in clinical practice: are we underdiagnosing?"

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Dear Editor,

Frailty has emerged as one of the most critical geriatric syndromes influencing morbidity, hospitalization rates, treatment tolerance, and overall survival and has emerged as one of the most critical determinants of adverse outcomes in older adults, yet it remains inconsistently identified in daily medical practice.[1] Although populations are aging globally, the detection of frailty has not kept pace with clinical need. Frailty is no longer viewed as a vague geriatric concept but rather as a measurable, prognostically significant syndrome characterized by diminished physiological reserves and reduced resilience to stressors.[2]

Despite the availability of frailty assessment tools for nearly two decades, screening remains sporadic, and underdiagnosis persists in outpatient clinics, emergency departments, and inpatient settings.[3] This disconnect between knowledge and practice has implications for mortality, hospitalization duration, functional decline, and healthcare utilization.

Multiple validated instruments, such as the fried frailty phenotype, Clinical Frailty Scale (CFS), Edmonton Frail Scale, and FRAIL questionnaire, have been proposed; yet, integration into internal medicine workflows is far from standardized.[4] Each tool offers different levels of feasibility, sensitivity, and clinical applicability. Although these tools are validated and relatively simple to administer, they are not consistently integrated into internal medicine, cardiology, oncology, nephrology, or primary care settings. Most clinicians acknowledge frailty as a concept but do not routinely document it or formally measure it before making diagnostic or therapeutic decisions. One of the biggest obstacles to early frailty detection is still the gap between awareness and action.

Frailty is frequently overlooked due to time constraints, insufficient training, and an overemphasis on chronological age rather than biological vulnerability. In many institutions, frailty scoring is seen as optional rather than essential. As a result, patients with subtle functional decline or low physiological reserve are often categorized as "fit" or "stable" based solely on basic laboratory tests, vital signs, or self-reported independence. Without formal scoring, these individuals undergo invasive procedures, polypharmacy, or aggressive treatments without adequate risk adjustment. The absence of systematic screening prevents proactive interventions such as nutritional support, physiotherapy, medication review, or shared decision-making based on functional status.[5]

Failure to identify frailty promptly has direct consequences on patient outcomes. Hospitalizations become longer, complication rates rise, and recovery after acute illness or surgery is often delayed. Inappropriate medication regimens, increased risk of delirium, and higher rates of institutionalization are frequently observed in frail individuals who were never assessed formally.[6] Moreover, when frailty is not documented, multidisciplinary interventions are either postponed or never initiated. Treatment goals may not align with the patient's physiological capacity, leading to emotional distress for both patients and families. Ultimately, the health system absorbs higher costs due to preventable adverse events and prolonged care needs.

Given these preventable risks and the systemic burden they create, a structured approach becomes indispensable. Frailty scoring should not be viewed as an additional administrative step but as a clinical necessity. Integrating these tools into admission protocols, outpatient evaluations, and preoperative assessments can transform care planning. When clinicians routinely incorporate frailty scores, they are better equipped to individualize therapies, adjust drug dosages, and determine realistic rehabilitation targets. Hospitals and academic centers that embed frailty assessments into electronic health records and clinical algorithms report improved outcomes and more efficient resource allocation. Making frailty screening part of standard internal medicine practice would increase awareness, guide multidisciplinary collaboration, and improve continuity of care.

Frailty is not merely a geriatric concept but a cross-disciplinary determinant of prognosis and treatment tolerance. Underdiagnosis persists because scoring systems are not routinely applied, despite being practical and valid. To close this gap, healthcare providers must adopt a proactive approach by incorporating frailty assessment into everyday clinical workflows. Education, institutional protocols, and simple screening steps can significantly improve recognition

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rates. By normalizing frailty scoring in internal medicine and related specialties, we can better align treatments with physiological reserve, reduce complications, and improve the quality of life for older adults.

Sincerely,

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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