RESEARCH PAPER

Correlation of Serum Lipid Profile and Inflammatory Markers with Osteocalcin in Thyroid Disorders Patients

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ABSTRACT

Introduction

Thyroid disorders profoundly affect metabolism, bone turnover, lipid profiles, and inflammation. Osteocalcin, a bone formation marker, and sclerostin, an inhibitor of bone formation, are influenced by thyroid hormones. This study aimed to compare serum levels of osteocalcin and sclerostin in patients with hypothyroidism and hyperthyroidism versus healthy controls, and to examine their correlations with thyroid hormones (FT3, FT4, TSH), lipid profiles, and inflammatory markers (CRP).

Materials & Methods

In this cross-sectional study, 180 participants were equally divided into three groups (n=60 each): healthy controls, hypothyroid patients, and hyperthyroid patients. Serum thyroid hormones were measured using chemiluminescence immunoassay (CLIA), osteocalcin via sandwich ELISA, and lipid profiles (Total cholesterol, Triglycerides, LDL-C, HDL-C, VLDL-C, and ratios) along with CRP using automated analyzers. Descriptive statistics and Pearson's correlation coefficients were calculated, with $p<0.05$ considered significant.

Results

Hyperthyroid patients showed significantly elevated osteocalcin (45.3 ± 13.1 ng/mL) and sclerostin (281 ± 31.4 pg/mL), whereas hypothyroid patients had markedly reduced levels (osteocalcin: 3.09 ± 0.452 ng/mL; sclerostin: 28.3 ± 7.38 pg/mL) compared to controls (osteocalcin: 14.6 ± 4.38 ng/mL; sclerostin: 101 ± 28.7 pg/mL). Lipid profiles revealed modest increases in total cholesterol, triglycerides, and LDL-C in hypothyroidism, with minimal changes in hyperthyroidism. CRP levels were comparable across groups. Osteocalcin positively correlated with TSH in controls ($r=0.56$, $p=0.00$) and hypothyroid patients ($r=0.55$, $p=0.00$), and with FT4 in hyperthyroid patients ($r=0.28$, $p=0.03$).

Conclusion

Thyroid dysfunction significantly alters bone metabolism markers, with hyperthyroidism linked to increased bone turnover and hypothyroidism to suppression. Mild dyslipidemia was primarily observed in hypothyroidism. Osteocalcin emerges as a key link between thyroid status, bone metabolism, lipid profiles, and inflammation, highlighting its potential as a biomarker for cardiometabolic complications in thyroid disorders. Further research is needed to explore its therapeutic implications.

Key words: Thyroid disorders, Hypothyroidism, Hyperthyroidism, Osteocalcin, Lipid profile, Dyslipidemia, Inflammatory markers, C-reactive protein (CRP).

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INTRODUCTION

Thyroid disorders are prevalent endocrine conditions that significantly impact systemic metabolism, including lipid profiles and bone turnover [1,2]. These dysfunctions can lead to marked alterations in serum osteocalcin levels, alongside observable changes in lipid parameters such as total cholesterol and low-density lipoprotein [3,4]. Subclinical hypothyroidism, characterized by elevated thyroid-stimulating hormone with normal free thyroxine levels, is particularly associated with dyslipidemia, though findings on high-density lipoprotein and triglyceride levels remain inconsistent [5,6]. Specifically, patients with subclinical hypothyroidism frequently exhibit elevated total cholesterol and low-density lipoprotein cholesterol, alongside decreased high-density lipoprotein cholesterol, indicating a heightened cardiovascular risk [6,7]. Conversely, hyperthyroidism can lead to acquired hypocholesterolemia or an inexplicable improvement in lipid profiles [8]. However, both hyper- and hypothyroidism, whether overt or subclinical, are linked to significant lipid alterations, often including elevated total cholesterol, LDL-C, and triglycerides, which can increase cardio metabolic risk [2,9].

For instance, patients with hypothyroidism commonly present with significantly higher serum levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol compared to healthy controls [10,11]. These lipid disturbances are frequently observed across various thyroid dysfunction states, including both overt and subclinical hypothyroidism, underscoring the pervasive influence of thyroid hormones on lipoprotein metabolism [12,13]. osteocalcin, a bone-specific protein, has also been shown to fluctuate in thyroid disorders, with hyperthyroidism patients exhibiting lower serum osteocalcin levels compared to both hypothyroid patients and healthy controls [1].

Furthermore, heightened bone turnover, characteristic of hyperthyroidism, often correlates with elevated serum osteocalcin, reflecting its role as a marker for bone formation [1]. This intricate interplay necessitates a comprehensive investigation into the precise correlations between osteocalcin, serum lipid profiles, and inflammatory markers to elucidate the underlying pathophysiological mechanisms in thyroid disorders. This study aims to delineate the intricate relationships between osteocalcin, serum lipid profiles, and inflammatory markers in patients with thyroid dysfunctions, thereby enhancing the understanding of their interconnected roles in disease progression.

MATERIALS AND METHODS

The study conducted in hospital and medical college with the institutional ethical committee approval, total of 180 patients recruited in the study where the participants were divided into three distinct groups: Healthy controls, individuals with hypothyroidism, and those diagnosed with hyperthyroidism each group.

Blood samples were meticulously collected for comprehensive biochemical analysis, including Thyroid hormones, serum lipid profiles, inflammatory markers, and osteocalcin levels, using standardized laboratory protocols. Assessment of thyroid hormones using CLIA method in autoanalyzer. Estimation of osteocalcin using a sandwich enzyme-linked immunosorbent assay kit provided a quantitative measure of this bone-specific protein, while other serum parameters were determined via automated clinical analyzers [1].

The resulting data underwent rigorous statistical analysis to identify significant correlations between thyroid hormone levels, lipid profiles, inflammatory markers, and osteocalcin, facilitating a deeper understanding of their interdependencies in thyroid pathologies.

Results

Table 1:
Correlation of level of Sclerostin and Osteocalcin in thyroid disorders compared to healthy controls. among the study group.

Variable	CONTROL (N = 60)	HYPERTHYROID (N = 60)	HYPOTHYROID (N = 60)
	Mean ± SD	Mean ± SD	Mean ± SD
Age in yrs	39.6 ± 2.42	38.4 ± 4.95	42.7 ± 4.34
FT3	3.00 ± 0.141	5.56 ± 1.66	1.51 ± 0.421
FT4	1.53 ± 0.133	6.63 ± 4.44	0.568 ± 0.235
TSH	2.74 ± 0.539	0.772 ± 1.59	7.51 ± 2.80
Serum Sclerostin	101 ± 28.7	281 ± 31.4	28.3 ± 7.38
Serum Osteocalcin	14.6 ± 4.38	45.3 ± 13.1	3.09 ± 0.452
CRP	4.60 ± 0.913	4.55 ± 0.647	4.42 ± 1.29
T. Chol	187 ± 33.8	192 ± 30.1	196 ± 35.3
TGL	129 ± 53.3	140 ± 43.5	149 ± 48.8
LDL	124 ± 31.2	123 ± 28.5	130 ± 33.3
HDL	41.2 ± 9.62	42.5 ± 15.7	39.7 ± 8.01
VLDL	26.0 ± 10.8	28.0 ± 8.92	29.5 ± 9.91
T. CHDL RATIO	4.94 ± 1.72	4.86 ± 1.26	5.06 ± 1.38
TG / HDL RATIO	4.59 ± 7.83	3.71 ± 1.73	3.87 ± 1.83
LDL/ HDL RATIO	3.62 ± 1.37	3.52 ± 1.11	3.76 ± 1.21

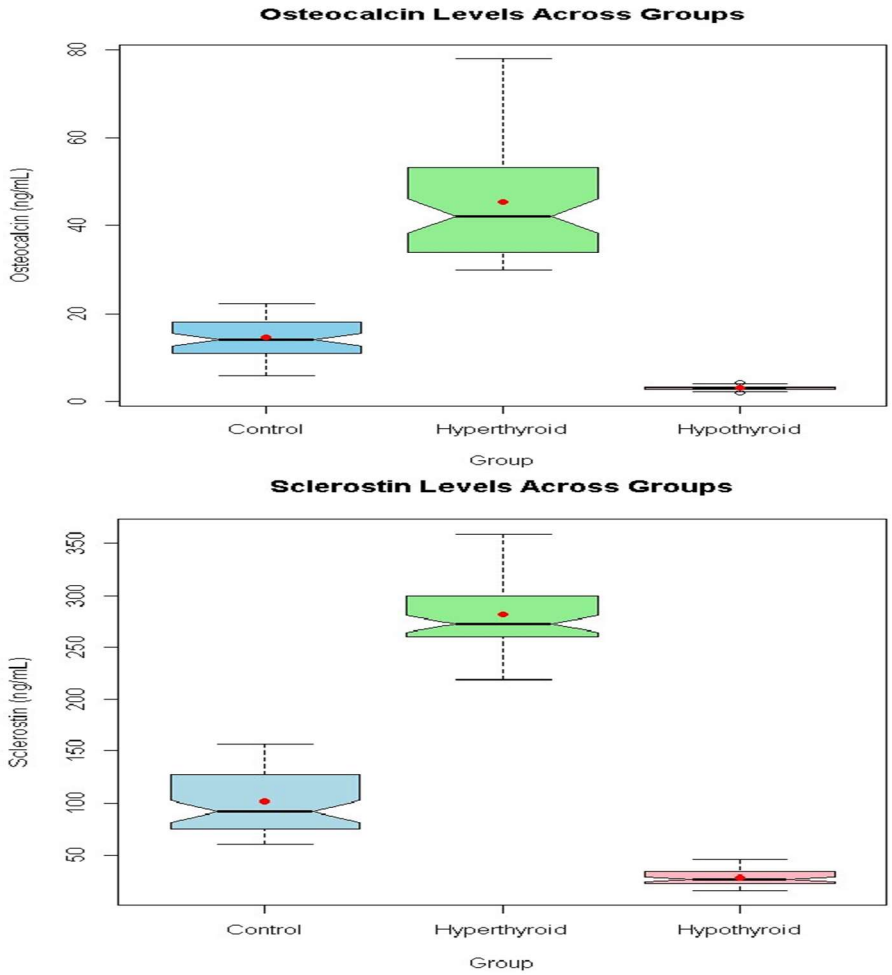

Figure-1 Association of Osteocalcin and sclerostin levels among groups.

Table 2: Correlation Coefficients and p-Values between Thyroid Hormones (TSH, FT3, FT4) and Biomarkers (Sclerostin, Osteocalcin) across groups.

Group	Biomarker	FT3		FT4		TSH	
		r	p Value	r	p Value	r	p Value
Control	**Sclerostin**	-0.09	0.52	0.1	0.46	-0.05	0.74
	Osteocalcin	-0.21	0.11	0.02	0.91	0.56	0.00
Hypothyroid	**Sclerostin**	-0.11	0.43	-0.04	0.78	-0.02	0.86
	Osteocalcin	-0.21	0.11	-0.07	0.59	0.55	0
Hyperthyroid	**Sclerostin**	-0.15	0.25	0.19	0.16	0.12	0.37
	Osteocalcin	-0.06	0.63	0.28	0.03	-0.21	0.12

These results analyze serum Sclerostin and Osteocalcin levels in patients with thyroid dysfunction compared to healthy controls. There are a total of 180 subjects, and each group had 58 participants. The aim was to compare Sclerostin and Osteocalcin levels across groups, to find the association with thyroid hormones (FT3, FT4, TSH), and evaluate their utility as biomarkers for thyroid dysfunction.

Descriptive statistics were analysed across all groups as depicted in table 1. For age, the control group had a mean of 39.6 ± 2.42 years, hypothyroid had 42.7 ± 4.34 years, and hyperthyroid had 38.4 ± 4.95 years (median 38, IQR 6.75, p=0.0525, marginally normal). These results indicate higher Sclerostin and Osteocalcin in hyperthyroid, lower in hypothyroid, with thyroid hormones reflecting group definitions.

DISCUSSION

The present study investigated the intricate relationships among thyroid hormone levels, serum lipid profiles, inflammatory markers, and osteocalcin, a critical biomarker of bone metabolism, across various thyroid dysfunction states. Our findings indicate significant alterations in lipid parameters, including total cholesterol and low-density lipoprotein, in both hyperthyroid and hypothyroid individuals, consistent with previous studies [10,14]. For instance, hyperthyroid patients often exhibit reduced total cholesterol and LDL-C, while hypothyroid patients typically present with elevated levels of these lipids (Table-1) [6]. Moreover, thyroid hormones play a crucial role in the regulation of skeletal system development and growth, stimulating both bone formation and resorption, which can lead to thinning of mineralized bone tissues. Specifically, osteocalcin levels, reflecting bone formation, have been observed to differ significantly between hypothyroid and hyperthyroid patients compared to healthy controls, reinforcing the thyroid gland's influence on bone metabolism [1].

Elevated osteocalcin levels are commonly observed in hyperthyroidism (Table-2,Fig-1) aligning with increased bone turnover and resorption processes in these patients [15]. Conversely, hypothyroidism is generally associated with decreased osteocalcin levels (Table2, fig-1), reflecting a reduction in bone remodeling activity [1]. These contrasting observations highlight the complex and differential impact of thyroid hormone imbalances on bone metabolism and calcium homeostasis [16]. Furthermore, the direct influence of thyroid hormones on osteoblastic and osteoclastic activity underscores the necessity of maintaining euthyroid status for optimal bone health. The strong positive correlation between sclerostin concentrations and free thyroxine in individuals with thyroid dysfunctions further emphasizes the hormonal regulation of bone metabolism [17]. Thyroid dysfunction, particularly hyperthyroidism, is recognized for its detrimental effects on bone mass, leading to a heightened risk of fragility fractures due to accelerated bone turnover [18].

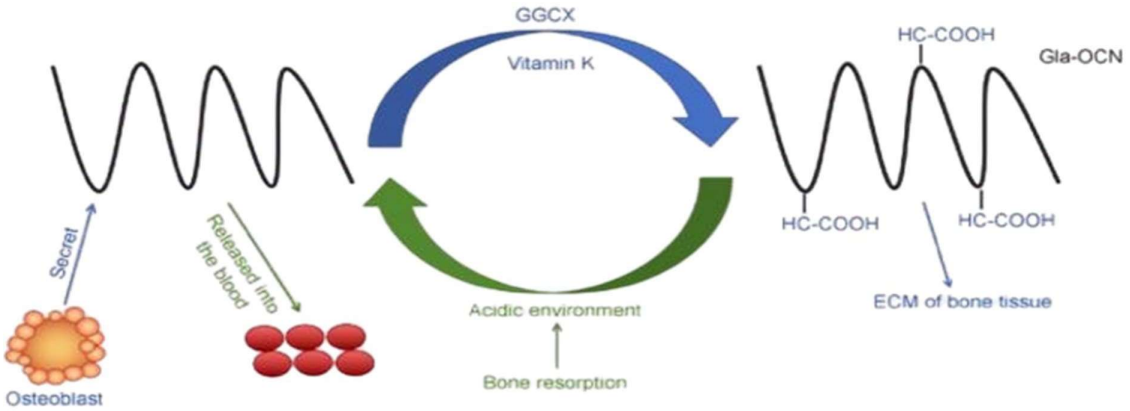

Figure-2: Carboxylation and decarboxylation of osteocalcin

Osteocalcin from osteoblasts will be in decarboxylated form will get converted to carboxylated form in the presence of vitamin K and gamma glutamyl carboxylase (GGCX). The carboxylated active form will help in the bone mineralization formation of hydroxyapatite (Fig- 2). When there is metabolic imbalance due to thyroid dysfunction or lack of GGCX and vitamin K may also result in increase in the decarboxylated form of osteocalcin. It shows a strong correlation with dyslipidemia has been observed, there is a significant reduction in lipid profile when there is high osteocalcin levels were observed in blood stream [19–21]. Studies have demonstrated that decarboxylated osteocalcin exerts protective effects by reducing visceral fat accumulation and hepatic lipid deposition [21]. Beyond its associations with dyslipidemia, osteocalcin also modulates other endocrine and metabolic pathways (Fig-3), including glucose homeostasis and insulin sensitivity, functioning as an endocrine hormone [17,20,22]. Specifically, decarboxylated osteocalcin stimulates insulin secretion from pancreatic β-cells and enhances insulin sensitivity in peripheral tissues, highlighting its broad metabolic impact beyond bone regulation [22].

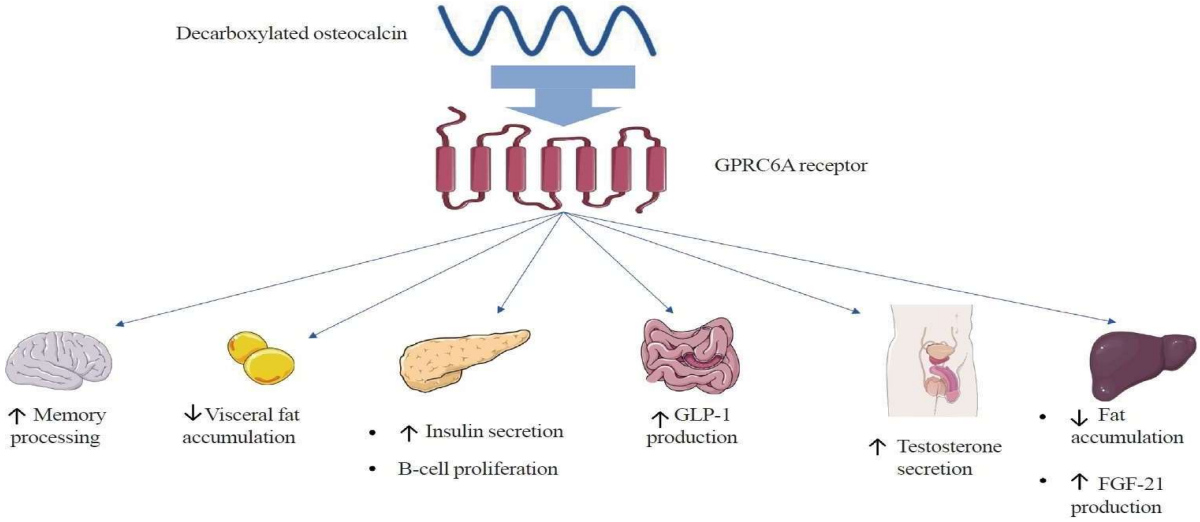

Figure-3: Actions of decarboxylated osteocalcin on different systems

Furthermore, chronic inflammation, often associated with thyroid dysfunction, can exacerbate metabolic derangements, potentially influencing osteocalcin's regulatory functions and lipid metabolism [1,17]. The interplay between inflammatory markers and thyroid hormones can further disrupt the delicate balance of bone remodeling and lipid metabolism, contributing to the complex pathophysiology observed in these conditions [23,24].

Role of osteocalcin on inflammation CRP levels Specifically, osteocalcin has been shown to inversely correlate with inflammatory markers such as C-reactive protein, suggesting its involvement in mediating anti- inflammatory responses and maintaining metabolic homeostasis. This interaction implies that osteocalcin may serve as a crucial link between bone metabolism, inflammation, and broader metabolic health, offering potential therapeutic avenues for managing thyroid-related complications [25]. Consequently, further investigation into osteocalcin's role as a mediator between inflammation and metabolic dysregulation in thyroid disorders could reveal novel therapeutic targets. This is supported by studies indicating that decarboxylated osteocalcin can decrease inflammatory factor secretion and mitigate inflammation via the PI3K/Akt/NF-κB signaling pathway [26].

Therefore, osteocalcin's function extends beyond bone metabolism to encompass a comprehensive role in maintaining metabolic and inflammatory balance [27,28]. Beyond these anti-inflammatory effects, decarboxylated osteocalcin also plays a significant role in energy metabolism, influencing glucose homeostasis and fat mass regulation [29,30]. In this paper we concentrated on establishing the correlation of osteocalcin levels in thyroid disorder with dyslipidemia and inflammation, in the further research contribution we will discuss the role sclerostin with detailed mechanism.

CONCULSION

Overall, our investigation highlights the intricate interplay between thyroid hormones, lipid metabolism, inflammatory markers, and osteocalcin, emphasizing the multi-faceted impact of thyroid dysfunction on systemic physiological processes.

Further research is warranted to elucidate the precise molecular mechanisms underpinning these interactions and to explore the potential of osteocalcin as a diagnostic or therapeutic target in thyroid-related metabolic complications. Specifically, osteocalcin's role in stimulating insulin synthesis, enhancing beta-cell proliferation, and improving insulin sensitivity further underscores its potential as a metabolic marker in conditions like diabetes. This comprehensive understanding could pave the way for novel interventions aimed at mitigating the cardio metabolic risks associated with thyroid disorders.

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