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Type I Collagen Cross-Linked C-Terminal Telopeptide as A Predictor Marker of Osteoporosis in Iraqi Thyroid Diseases Patients

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Abstract

Background Adult bone strength and shape are physiologically maintained in large part by thyroid hormones. Thus, there exists a correlation between thyroid diseases and bony outcomes.

Objective To assess the level of type I collagen cross-linked C-terminal telopeptide in Iraqi patients with thyroid disorders and its relationship to other biochemical markers.

Methods Eighty Iraqi thyroid disease patients (40 with hypothyroidism and 40 with hyperthyroidism) were included in this study, aged between 30 and 65 years. Patients were chosen from the Baghdad Teaching Hospital in the Medical City Complex. The 40 individuals in the healthy control group (20 males and 20 females) ranged in age from 30 to 55 years.

Results Among the three study groups, there was a highly significant decrease in vitamin D3 in hypothyroidism and hyperthyroidism compared to control. A statistically significant increase in alkaline phosphatase levels was seen among the study groups (hypothyroidism, hyperthyroidism, and control); however, no statistically significant differences were seen between phosphate and calcium levels. There was a highly significant rise in C-terminal telopeptide (CTX-1) between the groups with hypothyroidism and hyperthyroidism and the control group; similarly, the hyperthyroidism group showed a highly significant increase in CTX-1.

Conclusion There was a substantial increase in type I collagen cross-linked C-terminal telopeptide in hypothyroidism and hyperthyroidism compared to control. This rise could be interpreted as a predictive marker of osteoporosis in thyroid disease.

Keywords CTX-1, hypothyroidism, thyroid hormone, type I collagen cross-linked C-terminal telopeptide, osteoporosis

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List of abbreviations: BMI = Body mass index, CTX-1 = C-terminal telopeptide

Introduction

Osteoporosis is the sixth most prevalent disease worldwide. Life expectancy has increased in an aging culture, making it a significant public health issue. Fractures might result from this circumstance, which would have a negative impact on the person's quality of life as well as their bodily and mental health [(1)]. An imbalance in the activity of osteoclasts and osteoblasts, as well as the disconnection of bone resorption and creation, are the main causes of bone loss [(2)]. Adult bone maintenance and the cycle of bone remodeling

are impacted by clinical thyroid dysfunction. The risk of bone fracture is raised by both reduced and accelerated bone turnover [3]. High bone turnover is caused by excess thyroid hormone.

High bone turnover and bone density loss are connected to osteoporosis and an increased risk of fractures in both overt and subclinical hyperthyroidism [4]. It is well recognized that overt hypothyroidism decreases osteoclastic bone resorption as well as osteoblastic activity, which in turn lowers bone turnover. An increase in bone mineralization would be the outcome of these modifications to bone metabolism [5]. Collagen degradation and bone resorption result in the release of type I collagen cross-linked C-terminal telopeptide (CTX-1) into the bloodstream. Because of its distinct amino acid sequences, CTX-1 is particular to bone and makes about 90% of the bone matrix. It is an end product of bone breakdown that is mediated by osteoclasts and is present in serum, urine [6].

Reduced osteoblast and osteoclast resorption, as well as inadequate turnover of bone or a slowing of the process of bone remodeling, are the outcomes of hypothyroidism. But thyrotoxicosis is distinguished by elevated osteoblast and osteoclast activity, increased bone turnover, and an inefficient bone production cycle. This leads to a remodeling process that expedites resorption [7].

This study aimed to evaluate the CTX-1 level in Iraqi thyroid disorder patients and its relation to other biochemical parameters.

Methods

Study population in this study were 80 Iraqi patients with thyroid disorders, 40 with hypothyroidism, 40 with hyperthyroidism, ranging in age from 30 to 65 years. The 40 individuals in the health control group (20 males and 20 females) for each group range in age from 30 to 55 years Data collection patients chosen from the Baghdad Teaching Hospital's in the Medical City Complex, from November 2023 until the end of April 2024. All information on height, weight, age, sex, body mass index (BMI) was collected.

Blood samples were obtained for laboratory analysis, which involved measuring triiodothyronine (TT3), tetraiodothyronine (TT4), thyroid stimulating hormone (TSH), phosphate (PO_4), vitamin D3, calcium (Ca), and alkaline phosphatase (ALP) as measured by Cobas e411 in Germany. Competitive enzyme Linked Immunosorbant assay (ELISA) was utilized as the determination test for CTX-1.

Statistical analysis

Microsoft Excel 2010 was used for statistical analysis. The data are given as means ± standard deviation (SD). Unpaired student ttest was used to compare between each pair of the study groups. A difference was deemed significant if the P value was less than 0.05, and highly significant if it was less than 0.01.

Results

In table (1), there was no significant variation in age or height among the 3 study groups. Weight and BMI were observed to have a significant increase in hypothyroidism when compared with hyperthyroidism and the healthy control group, and, on the other hand, there has been a significant reduction in weight and BMI in hyperthyroidism as compared to the control group.

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Table 1. Anthropometric measurements among study groups (hypothyroidism, hyperthyroidism, and control)

Parameter	Mean±SD			P value		
	Hypothyroidism (G1) N=40	Hyperthyroidism (G2) N=40	Control (G3) N=40	G1 Vs G2	G1 Vs G3	G2 Vs G3
Age (year)	41±14	39.8±18.3	33±13	0.120	0.241	0.06
Weigh (kg)	80.4±14.2	71.6±14.2	75.9±27.5	0.05*	0.05*	0.05*
Height (cm)	166±10	168±10.9	167.37±8.85	0.153	0.025	0.141
BMI (kg/m^2)	28.47±3.92	23.60±3.71	26.27±2.78	0.05*	0.05*	0.05*

*Significant P value ≤0.05

In table (2), TT3 and TT4 concentrations were observed to be significantly lower in hypothyroidism compared to hyperthyroidism and the control group. TSH concentrations were observed to have an extremely significant rise in hypothyroidism when compared with hyperthyroidism and the healthy control group.

Table 2. Thyroid function test among study groups (hypothyroidism, hyperthyroidism, and control)

Parameter	Mean±SD			P value		
	Hypothyroidism (G1) N=40	Hyperthyroidism (G2) N=40	Control (G3) N=40	G1 Vs G2	G1 Vs G3	G2 Vs G3
TT3 (ng/mL)	0.83±0.4	3.78±1.16	1.56±1.1	0.05*	0.05*	0.05*
TT4 (ng/dL)	40.0±37.0	98.47±86.42	83.7±5.64	0.01**	0.01**	0.01**
TSH (µlU/mL)	18.29±21.48	0.39±0.90	2.13±1.25	0.01**	0.01**	0.01**

*Significant P value ≤0.05, ** High significant P value ≤0.01

In table (3), there was a very significant rise in vitamin D3 levels among the 3 study groups. A significant increase in ALP level among 3 study groups, while no statistically significant difference was observed between PO_4 and Ca levels among 3 study groups.

Table 3. Clinical variables among study groups (hypothyroidism, hyperthyroidism, and control)

Parameter	Mean±SD			P value		
	Hypothyroidism (G1) N=40	Hyperthyroidism (G2) N=40	Control (G3) N=40	G1 Vs G2	G1 Vs G3	G2 Vs G3
Vit. D3 (ng/mL)	4.382±14.59	18.7±4.66	27±4.25	0.01**	0.01**	0.01**
ALP (U/L)	33±113	99.45±22.16	69.76±6.72	0.05*	0.05*	0.05*
PO_4 (mg/dL)	2.3±0.6	2.27±0.58	2.8±0.71	0.201	0.145	0.274
Ca (mg/dL)	7.7±1.02	8.26±0.86	7.96±0.65	0.203	0.104	0.221

*Significant P value ≤0.05, ** High significant P value ≤0.01

In table (4), there was a statistically significant rise in CTX-1 in hypothyroidism relative to both hyperthyroidism and control groups, as well as a highly significant rise in CTX-1 in hyperthyroidism relative to the control group.

Table 4. CTX-1 level among study group (hypothyroidism, hyperthyroidism and control)

Parameter	Mean±SD			P value		
	Hypothyroidism (G1) N=40	Hyperthyroidism (G2) N=40	Control (G3) N=40	G1 Vs G2	G1 Vs G3	G2 Vs G3
CTX-1 ng/L	8121±727.22	6089±414.7	968.8±198.25	<0.01**	<0.01**	<0.01**

*Significant P value ≤0.05, ** High significant P value ≤0.01

In table (5), when comparing CTX-1 to vitamin D3, PO_4, and TT3, there was a negative correlation seen in both hypothyroidism and hyperthyroidism. Between CTX-1 and ALP, there is a negative correlation in hyperthyroidism and a positive correlation in hypothyroidism. In both hypothyroidism and hyperthyroidism, there is a positive correlation between CTX-1 and TT4. Between CTX-1 and TSH, there is a positive correlation in hyperthyroidism and a negative correlation in hypothyroidism.

Table 5. Correlation coefficient between CTX-1 level and clinical variables parameters in hypothyroidism and hyperthyroidism

Parameter	Hypothyroidism	Hyperthyroidism
CTX-1 vs Vit. D3	-0.392**	-0.128**
CTX-1 vs ALP	0.39*	-0.264*
CTX-1 vs Ca	0.0122	0.05
CTX-1 vs PO_4	-0.320*	-0.1*
CTX-1 vs TT3	-0.16*	-0.24*
CTX-1 vs TT4	-0.068*	0.108*
CTX-1 vs TSH	-0.167*	0.084*

**Correlation is significant at P ≤ 0.01, *Correlation is significant at P ≤ 0.05

In table (6) and figure (1), the receiver operating characteristic (ROC) was employed to assess the accuracy of CTX-1 levels in individuals with hypothyroidism and hyperthyroidism. According to ROC analysis, the CTX-1 level is a highly reliable diagnostic for osteoporosis prediction in patients with hypothyroidism and hyperthyroidism. ROC analysis indicated that CTX level in hypothyroidism patients is an excellent marker for predicting osteoporosis with a predictive cut-off value of 1937.5 U/ml, AUC 0.953, specificity 99%, sensitivity 93%, and P value <0.01, but ROC analysis indicated that CTX-1 level in hyperthyroidism patients is a very good marker for predicting osteoporosis with a predictive cut-off value of 1676.0 U/ml, area under curve (AUC) 0.886, specificity 99%, sensitivity 93%, and P value <0.01.

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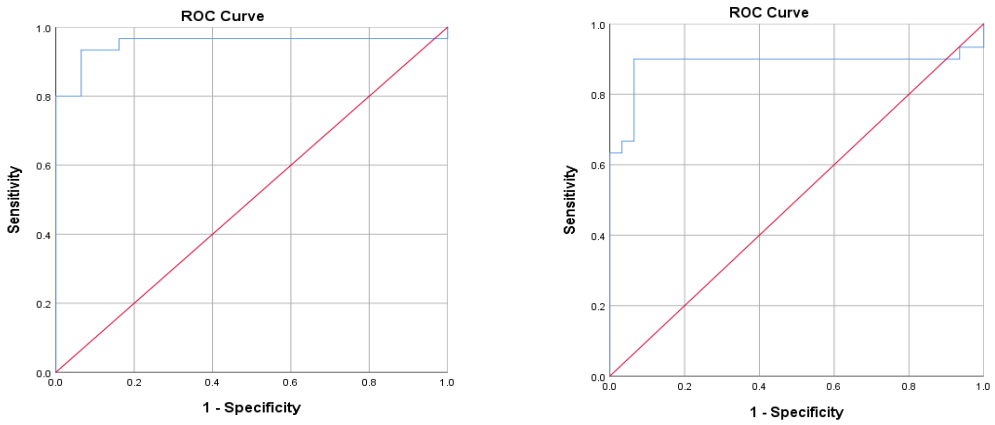
Table (6). Receiver operating characteristic curve data, specificity, and sensitivity of the studied CTX-1 in hypothyroidism and hyperthyroidism groups

Group	Area	Cut off	Explanation	P value	Sensitivity%	Specificity %
Hypo vs control	0.953	1937.50	Excellent	<0.01**	93%	99%
Hyper vs control	0.886	1676.00	Very good	<0.01**	90%	99%



Hypothyroidism vs control **Hyperthyroidism vs control**

Figure 1. CTX-1 level Receiver operating characteristic curve (ROC)

Discussion

The physiological function of thyroid hormones is crucial for preserving the strength and shape of adult bones, which protect critical organs, facilitate movements, house hematopoietic cells, and are essential for maintaining mineral homeostasis [8,9]. As such, there exists a correlation between thyroid disorders and skeletal results; an established factor in fast bone turnover and accelerated bone loss, which increases the possibility of fractures and osteoporosis, is overt hyperthyroidism [10]. Patients with hypothyroidism exhibit higher bone mineralization, while those with hyperthyroidism have increased osteoclast activity and osteoporosis [11].

The fact that the patients in the three groups in the study were within the same age range may have contributed to the lack of significant variations in mean age between the hyperthyroidism, hypothyroidism, and control groups in this study. This is in agreement with studies [12,13].

The BMIs of hypothyroidism, control, and hyperthyroidism differ significantly from one another. This result is explained by the fact that thyroid hormones control thermogenesis and energy metabolism. They also have a major impact on food intake, lipid and glucose metabolism, and fatty acid oxidation. This study supports the research by Sanyal and Raychaudhuri, which indicates that hypothyroidism is linked to a lower metabolic rate and has been linked to a higher prevalence of obesity and an elevated BMI [14]. Reduced levels of T3 and T4, or a minor rise in TSH, will promote the overstuffing of energy stored in adipose tissues, which will ultimately result in an increase in body weight and obesity — a frequent symptom of hypothyroidism [15]. Santini et al. found that the hyperthyroid patient had a lower BMI and most body

composition measurements in comparison with the group of controls [16]. However, their results disagree with those of another study [17], which found no significant differences in the relationship between BMI and small variations within the normal range of thyroid features. As opposed to control groups, there was a significant rise (P = 0.01) in TSH and a significant low (P = 0.01) in T3 and T4 within hypothyroidism, and a significant reduction (p = 0.01) in TSH and a rise (P = 0.01) in T3 and T4 in hyperthyroidism. In people with hypothyroidism, the pituitary gland may release more TSH in an attempt to encourage the thyroid to produce additional thyroid hormones (T3, T4), which could explain their elevated TSH levels. In contrast, people with hyperthyroidism have a decrease in thyroid hormone levels, which leads to a reduction in thyroid hormone output. This aligns with research findings [18,19].

A significant variation (P <0.01) was seen in the concentrations of vitamin D3 between the study groups, which agrees with the outcomes of Mackawy et al., who discovered that individuals suffering from hypothyroidism and hyperthyroidism had hypovitaminosis D. Their findings also suggested a significant correlation between the severity and degree of the disease and serum vitamin D deficiency. This relationship has two possible causes. First, inadequate intestinal absorption of vitamin D could be the cause of the low vitamin D levels. Second, improper vitamin D activation may occur in the body [20]. Additionally, insufficient calcium intake from food and elevated bone turnover in hyperthyroid individuals result in elevated calcium levels, which have a detrimental effect on PTH hormone release and vitamin D synthesis [21]. Vitamin D maintains the necessary mineralization of the skeleton by controlling the metabolism of calcium and phosphate [22].

Between the research groups, there was no discernible variation in Ca or PO_4 levels. This may be explained by the fact that many hypothyroid individuals have thyroid hormone levels within the normal range; only their TSH level is increased, and there is a lack of epidemiological information regarding changes in Ca or PO_4 levels or because they have been taking calcium and phosphate supplements as well as thyroid medication. Thyroid hormones are important for mineral and metabolic activities, thermogenic maintenance, and cellular development in our bodies. When it comes to bone mineral density, osteoporotic fractures, and serum Ca or PO_4 levels, hyperthyroidism is to blame for some of these problems, while hypothyroidism is known to lower these levels [23]. Current study results concerning Ca or PO_4 is in agreement with [24] and in disagreement with previous studies [25,26].

Patients with hyperthyroidism and hypothyroidism had serum ALP levels greater than those of the control group, according to the current study. A rise in osteoblastic activity is the cause of elevated ALP. This study's findings agree with Priya and Prathyusha study [27] who found that out of the 36 hyperthyroid individuals, 15 showed higher levels of blood alkaline phosphatase activity. Patients with thyroid disorders (hypothyroidism and hyperthyroidism) have higher levels of ALP compared to controls because membrane-bound glycoprotein ALP is widely known to be a potential osteogenic marker of calcification and bone formation. In order to deposit an elevated amount of phosphate at the outer layer of the osteoblast cell throughout bone formation, osteoblasts release ALP [28].

Between the study groups, there was an extremely significant variation (P <0.01) in the CTX-1 concentrations. According to several studies, an extremely significant rise in CTX-1 was observed in hypothyroidism when compared to the control and hyperthyroidism groups, and a highly significant increase in CTX-1 in hyperthyroidism when compared to the control group [29,30]. Osteoclasts secrete a variety of proteolytic enzymes that can degrade the organic matrix of the bone, discharging calcium and a variety of collagen breakdown products into the serum. CTX-1 is among the products that degrade collagen [31]. The adult bone maintenance cycle and the bone remodeling cycle are impacted by clinical thyroid disease. The risk of bone fracture is increased by both decreased and accelerated

bone turnover. High bone turnover is caused by excess thyroid hormone [32]. The fast bone turnover and bone density loss connected to both overt and subclinical hyperthyroidism have been associated with osteoporosis and a higher chance of fractures. In overt hypothyroidism, slower bone turnover additionally elevates the possibility of bone fractures [33]. On the other hand, it is unknown how subclinical hypothyroidism and fracture risk are related to bone density reduction. Subclinical hypothyroidism and bone loss have been linked in some research; however, there has been no correlation found in other studies investigating fracture risk or bone loss [34]. In order to assess TSH's contribution to bone metabolism independently of T3 and T4, Heemstra et al. employed CTX-1 as a marker for bone turnover. They discovered an inversely proportional association between CTX-1 and TSH. While bone markers should rise in conjunction with a decrease in TSH, low TSH levels may indicate hyperthyroidism [35]. There remains controversy regarding the relationship between bone turnover indicators and TSH concentration with regard to fragility fracture risk.

TSH increases osteoblast differentiation, as demonstrated by [36]. Tsai et al., on the other hand, previously only observed a small amount of cAMP activation, TSH binding, and TSHR expression among human osteoblasts, leading them to postulate that TSH is unlikely to play a physiological role within osteoblast blood-brain barriers [37]. Expression of osteocalcin, type I collagen, and bone sialoprotein is all down-regulated by TSH, which also inhibits osteoblasts [38].

In conclusion, in both the hyperthyroidism and hypothyroidism study groups, there was a statistically significant increase in CTX-1 relative to the control group. This rise could be interpreted as a predictive marker of osteoporosis in thyroid disease. Osteoporosis is the most significant problem that coexists with bone diseases; variations in thyroid hormone levels and thyroid disease treatment are factors that impact bone health.

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Author contribution

Ghadban: did the laboratory works. Dr. Tahir and Dr. Jawad supervised the work and prepare the manuscript.

Conflict of interest

A conflict of interest does not exist.

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References

1. Deng T, Zhang W, Zhang Y, et al. Thyroid-stimulating hormone decreases the risk of osteoporosis by regulating osteoblast proliferation and differentiation. BMC Endocr Disord. 2021; 21(1): 49. doi: 10.1186/s12902-021-00715-8.
2. Azmy Abd El-Motelp B, Tarek Ebrahim M, Khairy Mohamed H. Salvia officinalis extract and 17β-estradiol suppresses ovariectomy induced osteoporosis in female rats. Pak J Biol Sci. 2021; 24(3): 434-44. doi: 10.3923/pjbs.2021.434.444.
3. Lee K, Lim S, Park Het al. Subclinical thyroid dysfunction, bone mineral density, and osteoporosis in a middle-aged Korean population. Osteoporos Int. 2020; 31(3): 547-55. doi: 10.1007/s00198-019-05205-1.
4. Singh R, Garg S, Aggarwal S, et al. Markers of bone mineral metabolism in thyroid disorders. Ind J Med Special. 2024. doi: 10.4103/injms.injms_47_24.
5. Delitala AP, Scuteri A, Doria C. Thyroid hormone diseases and osteoporosis. J Clin Med. 2020; 9(4): 1034. doi: 10.3390/jcm9041034.
6. Yildirim HS, Ates M, Gun IO, et al. Osteocalcin and cross-linked C-terminal telopeptide of type I collagen in gingival crevicular fluid during piezocision accelerated orthodontic tooth movement: A randomized split-mouth study. Niger J Clin Pract. 2023; 26(4): 470-7. doi: 10.4103/njcp.njcp_539_22.
7. Siddiqui JA, Partridge NC. Physiological bone remodeling: Systemic regulation and growth factor involvement. Physiology (Bethesda). 2016; 31(3): 233-45. doi: 10.1152/physiol.00061.2014.
8. Hasan FF, Mohammed HL. Comparison between benign and malignant primary bone tumors-A histopathological study of 119 cases. Al-Mustansiriyah J Sci. 2018; 29(2): 74-82. doi: 10.23851/mjs.v29i2.182.
9. Jouda J, Alsamawi AI, Ali LQ, Effect of hyper-and hypothyroidism on many physiological parameters and the rate of some diseases. Karbala J Pharm Sci. 2017, 8(13): 70-8.

10. Hong AR, Kang HC. Evaluation and management of bone health in patients with thyroid diseases: A position statement of the korean thyroid association. Endocrinol Metab (Seoul). 2023; 38(2): 175-89. doi: 10.3803/EnM.2023.1701.
11. Wu X, Zhai F, Chang A, et al. Association between sensitivity to thyroid hormone indices and osteoporosis in euthyroid patients with type 2 diabetes mellitus. Ther Adv Chronic Dis. 2023; 14:20406223231189230. doi: 10.1177/20406223231189230.
12. Cikim AS, Oflaz H, Ozbey N, et al. Evaluation of endothelial function in subclinical hypothyroidism and subclinical hyperthyroidism. Thyroid. 2004; 14(8): 605-9. doi: 10.1089/1050725041692891.
13. Korevaar TIM, Mínguez-Alarcón L, Messerlian C, et al. Association of thyroid function and autoimmunity with ovarian reserve in women seeking infertility care. thyroid. 2018; 28(10): 1349-58. doi: 10.1089/thy.2017.0582.
14. Sanyal D, Raychaudhuri M. Hypothyroidism and obesity: An intriguing link. Indian J Endocrinol Metab. 2016; 20(4):554-7. doi: 10.4103/2230-8210.183454.
15. Biondi B. Subclinical hypothyroidism in patients with obesity and metabolic syndrome: A narrative review. Nutrients. 2023; 16(1): 87. doi: 10.3390/nu16010087.
16. Santini F, Marzullo P, Rotondi M, et al. Mechanisms in endocrinology: the crosstalk between thyroid gland and adipose tissue: signal integration in health and disease. Eur J Endocrinol. 2014;171(4):R137-52. doi: 10.1530/EJE-14-0067. PMID: 25214234.
17. Vandevijvere S, Jaacks LM, Monteiro CA, et al, Swinburn B. global trends in ultraprocessed food and drink product sales and their association with adult body mass index trajectories. Obes Rev. 2019; 20 Suppl 2: 10-19. doi: 10.1111/obr.12860.
18. Helmy MY. Correlation between uric acid and thyroid hormones in patients with thyroid disorders. a case control study. Egypt J Hospital Med. 2020; 81(2): 1499-505.
19. Juma'a YH, Allami RH. The Association of TSHR gene rs2268458 polymorphism with thyroid disorders (hyperthyroidism and hypothyroidism) in a sample of iraqi patients. Ind J Forensic Med Toxicol. 2021; 15(3). 1450-6. doi: 10.37506/ijfmt.v15i3.15509
20. Mackawy AM, Al-Ayed BM, Al-Rashidi BM. Vitamin d deficiency and its association with thyroid disease. Int J Health Sci (Qassim). 2013; 7(3):267-75. doi: 10.12816/0006054.
21. Talaei A, Ghorbani F, Asemi Z. The Effects of vitamin D supplementation on thyroid function in hypothyroid patients: A randomized, double-blind, placebo-controlled trial. Indian J Endocrinol Metab. 2018; 22(5): 584-8. doi: 10.4103/ijem.IJEM_603_17.
22. Al-Sarray ZA, Hussein RH, Al-Hafidh AH, et al. Vitamin D deficiency associates with disease severity in rheumatoid arthritis patients. Al-Mustansiriyah Journal of Science. 2023; 33(5): 33-8.
23. M R, Prabha AG, K S. Study of calcium, magnesium and Phosphorus Levels among Hypothyroid Patients in Trichy, Tamil Nadu. Journal of Evidence Based Medicine and Healthcare. 2021; 8: 2797-803.
24. Ale AO, Ogbera AO, Ebili HO, et al. Prevalence, Predictive factors, and characteristics of osteoporosis in hyperthyroid patients. Int J Endocrinol. 2018; 2018:3540256. doi: 10.1155/2018/3540256.
25. Jat RK, Panwar AK, Agarwal P, et al. Assessment of serum minerals in subclinical hypothyroid and overt hypothyroid patients. Cureus. 2021; 13(8): e16944. doi: 10.7759/cureus.16944.
26. Babu BS, Shaik A, Khan SA, et al. Study of serum calcium, magnesium and phosphorous levels in hypothyroidism. Eur J Mol Clin Med. 2022; 9(3): 1286-92.
27. Priya BD, Prathyusha U. Association of acid and alkaline phosphatase among thyroid patients: A brief study. Highlights on Medicine and Medical Science. Vol. 8. BP International; 2021. p. 70-6. doi: https://doi.org/10.9734/bpi/hmms/v8/9711D.
28. Cheng X, Zhao C. The correlation between serum levels of alkaline phosphatase and bone mineral density in adults aged 20 to 59 years. Medicine (Baltimore). 2023; 102(32): e34755. doi: 10.1097/MD.0000000000034755.
29. Mohamed AH, Naji NS, Al-Saadi AH. Study of the relationship between FT3, FT4, and TSH with bone resorption indices in men with hypothyroidism. J Popul Ther Clin Pharmacol. 2022; 29(2): e33-9. doi: 10.47750/jptcp.2022.929.
30. Garin MC, Arnold AM, Lee JS, et al. Subclinical thyroid dysfunction and hip fracture and bone mineral density in older adults: the cardiovascular health study. J Clin Endocrinol Metab. 2014; 99(8): 2657-64. doi: 10.1210/jc.2014-1051.
31. Huang M, Yang S, Ge G, et al. Effects of thyroid dysfunction and the thyroid-stimulating hormone levels on the risk of atrial fibrillation: A systematic review and dose-response meta-analysis from cohort studies. Endocr Pract. 2022; 28(8): 822-31. doi: 10.1016/j.eprac.2022.05.008.
32. Mudri D, Bilić Ćurčić I, Meštrović L, et al. Hyperthyroidism and wnt signaling pathway: influence on bone remodeling. Metabolites. 2023; 13(2): 241. doi: 10.3390/metabo13020241.
33. Gonzalez Rodriguez E, Stuber M, Del Giovane C, et al. skeletal effects of levothyroxine for subclinical hypothyroidism in older adults: A trust randomized trial nested study. J Clin Endocrinol Metab. 2020; 105(1): dgz058. doi: 10.1210/clinem/dgz058.
34. Li Z, Yu X, Ren L, et al. Influence of low total triiodothyronine levels on bone turnover markers in type 2 diabetes mellitus. Diabetes Metab Syndr Obes. 2021; 14: 2727-33. doi: 10.2147/DMSO.S309079.
35. Heemstra KA, van der Deure WM, Peeters RP, et al. Thyroid hormone independent associations between serum TSH levels and indicators of bone turnover in cured patients with differentiated thyroid carcinoma. Eur J Endocrinol. 2008; 159(1): 69-76. doi: 10.1530/EJE-08-0038.

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36. Sendak RA, Sampath TK, McPherson JM. Newly reported roles of thyroid-stimulating hormone and follicle-stimulating hormone in bone remodelling. Int Orthop. 2007; 31(6): 753-7. doi: 10.1007/s00264-007-0417-7.
37. Tsai JA, Janson A, Bucht E. Weak evidence of thyrotropin receptors in primary cultures of human osteoblast-like cells. Calcif Tissue Int. 2004; 74(5): 486-91. doi: 10.1007/s00223-003-0108-3.
38. Blum MR, Bauer DC, Collet TH, et al. Thyroid studies collaboration. subclinical thyroid dysfunction and fracture risk: a meta-analysis. JAMA. 2015; 313(20): 2055-65. doi: 10.1001/jama.2015.5161.

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