Sumer Journal for Pure Science (ISSN: 2790-7031)
2nd International Scientific Conference on Pure and Medical Sciences/University of Sumer 2024

The Effect of Total Thyroidectomy on Bone in Cancer Patients

Essam N. T[1*] , Dumooa .F. Joudah[2] , Wisam Jasim Abed Ali[3] , Zina Saleh Hassan[4]

[1, 2, 3]Pathological Analyses Department, College of Science, University of Sumer, Thi-Qar, Iraq.
[4]Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, Iraq.

Abstract

Background: Bone diseases are one of the most important problems that affect patients after thyroidectomy Objective: The aim of the study was to determine the extent to which bone properties are affected after the operation and the effect of the time after the operation. Materials and methods:. The study included 150 samples, distributed into 50 control groups and 100 patients, the first group of patients included 50 patients whose periods after the operation did not exceed one year, and the second group of patients included 50 patients who had undergone total thyroid operations for more than a year. The main reason for the operations was thyroid cancer. All patients had thyroid cancer and the patients' ages were 25-65 years were included in this study .Results of this study The study showed a decrease (Human Bone specific alkaline phosphatase, alkaline phosphatase, phosphate, PTH) in all groups compared with the control group. The results showed a clear significant decrease in the patient groups, and the first group had the greatest decrease. Conclusion :The study showed a clear change in bone function after total thyroidectomy, and the periods following the operation were effective.

Keywords: Thyroidectomy, Cancer, Bones, Nasiriyah Teaching Hospital

تأثير استئصال الغدة الدرقية الكامل على العظام لدى مرضى السرطان

عصام نغيمش تعيب[1*] , دموع فلاح جودة[2] , وسام جاسم عبدعلي[3] , زينة صالح حسن[4]

[1, 2, 3]قسم التحليلات المرضية , كلية العلوم ,جامعة سومر , محافظة ذي قار , العراق.
[4]قسم الكيمياء , كلية العلوم ,جامعة ذي قار , محافظة ذي قار , العراق.

الخلاصة

الخلفية: تعتبر أمراض العظام من أهم المشاكل التي تصيب المرضى بعد استئصال الغدة الدرقية. . الهدف: كان الهدف من الدراسة هو تحديد مدى تأثر خصائص العظام بعد العملية وتأثير الوقت بعد العملية. المواد وطرق العمل:. شملت الدراسة 150 عينة، تم توزيعها على 50 مجموعة مراقبة و100 مريض، ضمت المجموعة الأولى من المرضى 50 مريضاً لم تتجاوز الفترة بعد العملية سنة واحدة، والمجموعة الثانية من المرضى ضمت 50 مريضاً خضعوا لعمليات الغدة الدرقية الكلية والفترة بعد العملية اكثر من سنة. وكان السبب الرئيسي للعمليات هو سرطان الغدة الدرقية. جميع المرضى في هذه الدراسة كانت أعمارهم بين 25 الى 65 سنة. نتائج هذه الدراسة أظهرت الدراسة انخفاضا في إنزيم الفوسفاتيز القلوي النوعي لعظام الإنسان، الفوسفاتيز القلوي، والهرمون جار درقي في جميع المجاميع مقارنة مع مجموعة السيطرة. أظهرت النتائج انخفاضاً معنوياً واضحاً في مجموعات المرضى، وكانت المجموعة الأولى هي الأكثر انخفاضاً. الاستنتاج: أظهرت الدراسة تغيراً واضحاً في وظيفة العظام بعد استئصال الغدة الدرقية الكلي، وكانت الفترات التي تلي العملية مؤثرة في النتائج .

1. Introduction

The thyroid gland consists of the thyroid follicles, which are regarded as the functional components of the thyroid gland [1]. The synthesis of the thyroid hormones takes place within these follicles [1, 2]. The thyroid hormones, namely triiodothyronine (T3) and thyroxine (T4), exert their influence on metabolic processes throughout the entire body [1]. They play a crucial role in maintaining normal bone turnover [1, 3]. In recent times, it has been recognized that the thyroid gland significantly contributes to bone development and the preservation of bone mass. Disturbances in thyroid hormone levels can lead to growth abnormalities, bone loss, and an elevated susceptibility to fractures [2, 4].

Thyroid hormones play a vital role in the maturation of the skeletal system and are crucial for maintaining the structure and strength of adult bones [5, 6]. Although it is well known that thyroid dysfunction increases the risk of bone disease, the significance of thyroid hormone in the development of osteoporosis and the risk factors for fractures has been underestimated, and the precise mechanisms involved remain uncertain [2, 3]. Hyperthyroidism is characterized by the suppression of Thyroid-Stimulating Hormone (TSH) and elevated levels of T3 and T4, primarily caused by conditions such as Graves' disease, toxic multinodular goiter, and toxic adenoma [3]. This condition has a detrimental impact on bone mass, as evidenced by an accelerated bone remodeling cycle, along with elevated levels of biochemical markers for both bone resorption and formation [7, 8].

An increase in the apposition and formation of minerals, accompanied by a decrease in the density of bone minerals, has been observed [7]. Delitala et al. [3] have concluded that subclinical hyperthyroidism may be associated with elevated biochemical markers of bone turnover and a slight reduction in bone mineral density. Hypothyroidism is characterized by an elevation in TSH levels and a decrease in T3 and T4 levels below the lower limit of the reference range. It is primarily caused by acquired hypothyroidism, Hashimoto's thyroiditis, post-ablative effects of surgery and neck irradiation, and drug-induced factors [2, 3, 8]. This condition hinders bone turnover by diminishing both osteoclastic bone resorption and osteoblastic activity [3].

Bone is a metabolically active tissue that undergoes continual osteoblastic bone production and osteoclastic bone resorption. The ability of bone tissue to accommodate damages like implant placement is connected to numerous processes and can be influenced by various factors, such as smoking, oral hygiene, and prosthetic rehabilitation. These factors have an impact on osseointegration and decrease the success rate of dental implants. Remarkably, in the long-term follow-up, outstanding results have been achieved in terms of the survival rate and success rate of dental implants, specifically in patients without general pathology. Furthermore, in patients without any oral or systemic diseases, the success rate of oral rehabilitation utilizing dental implants is 98.8% after 3 months, 97.9% after 6 months, 97.7% after 1 year, and 97.4% after 2 to 9 years. After accounting for all the variables, including age, sex, implant placement, diameter, length, type, bone quality, bone graft, status of periodontal disease, and insertion torque, these results show that patients without systemic disease had a successful rehabilitation [9]. If osteoclasts or their impact on bone resorption are directly impacted by people with thyroid problems [3]. It has been suggested that calcitonin gene-related peptide (CGRP) has a function in bone metabolism because transgenic mice with increased osteoblastic CGRP expression have higher bone density as a result of increased bone production [10, 11].

2. Patients and Methods

This study has been conducted at Nasiriyah Teaching Hospital in Thi-Qar, The Endocrine Glands Center in Thi Qar governorate, Biochemistry Laboratory, at the period between 1/4/2022 to 1/2/2024. It included (150) patients, control (50) and patients (100). Divided into two groups, each group containing 50 patients:

All patients had thyroid cancer and the patients' ages were 25-65 years were included in this study. They divided into three groups as the following: -

Group A (patients**,** after thyroidectomy**):** Includes patients who have not had gland lift operations for more than one year

Group B (patients**,** after thyroidectomy**):** Includes patients who have undergone gland lift operations for one year or more.

Group C (control): - included thirty (50) healthy subjects aged (25-65).

Medical tests were performed on the patients' blood, including (Human Bone specific alkaline phosphatase, alkaline phosphatase, PTH) from (Elabscience, China) and(SIGMA-ALDRICH, America) , using the ELISA device.

3. Results

The mean age of the patients who were involved in our study was 25-65 years, All patients were suffering from thyroid cancer and had total thyroidectomy. The results are shown in the table .1.

Table 1- Results of the parameters (PTH, Human Bone specific alkaline phosphatase, alkaline phosphatase)

Parameters	No	Age Mean±SD	PTH (pg/mL) Mean± SD	PAP(U/L) Mean± SD	ALP (UL/L) Mean± SD
Groups					
Group A (patients, after thyroidectomy): Includes patients who have not had gland lift operations for more than one year	50	45.13±6.42	10.73 ± 1.34[c]	63.19 ± 4.41[C]	60.27 ± 4.33[b]
Group B (patients, after thyroidectomy): Includes patients who have undergone gland lift operations for one year or more.	50	54.23±6.3	18.91 ± 3.47[b]	76.65 ± 6.08[b]	77.43 ± 3.30[c]
Group C (control): - included thirty (50) healthy subjects aged (25-65).	50	57.23±4.3	55.83 ± 4.45[a]	91.25 ± 5.29[a]	88.66 ± 3.96[a]
L.S.D			7.59	12.19	8.78

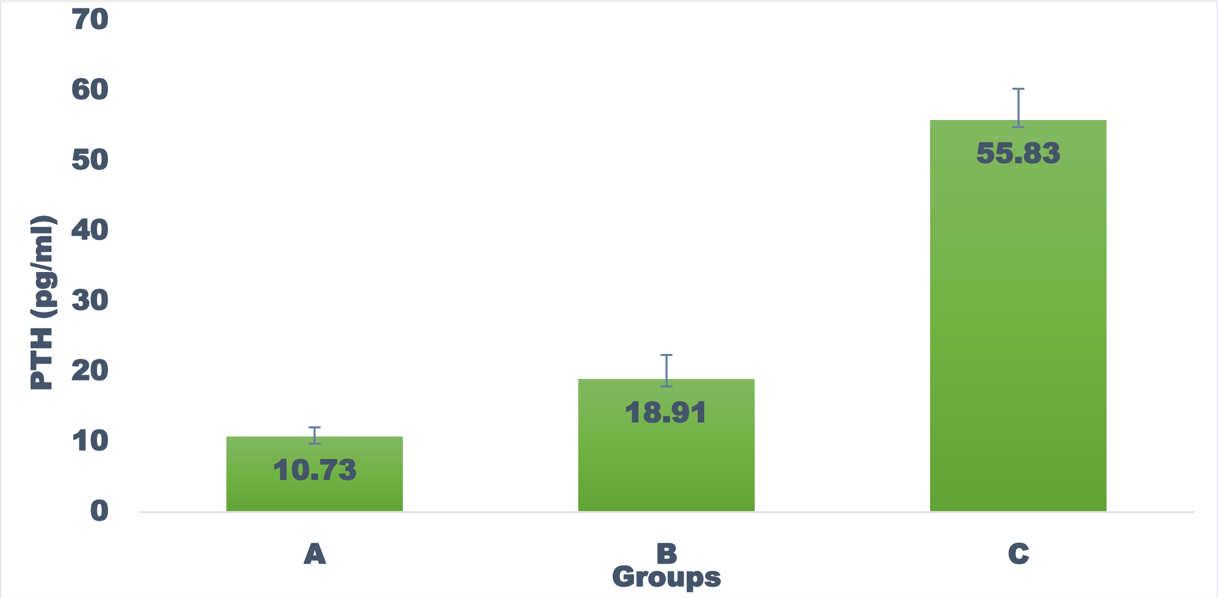

Figure -1 PTH serum level of the two patient groups and control group

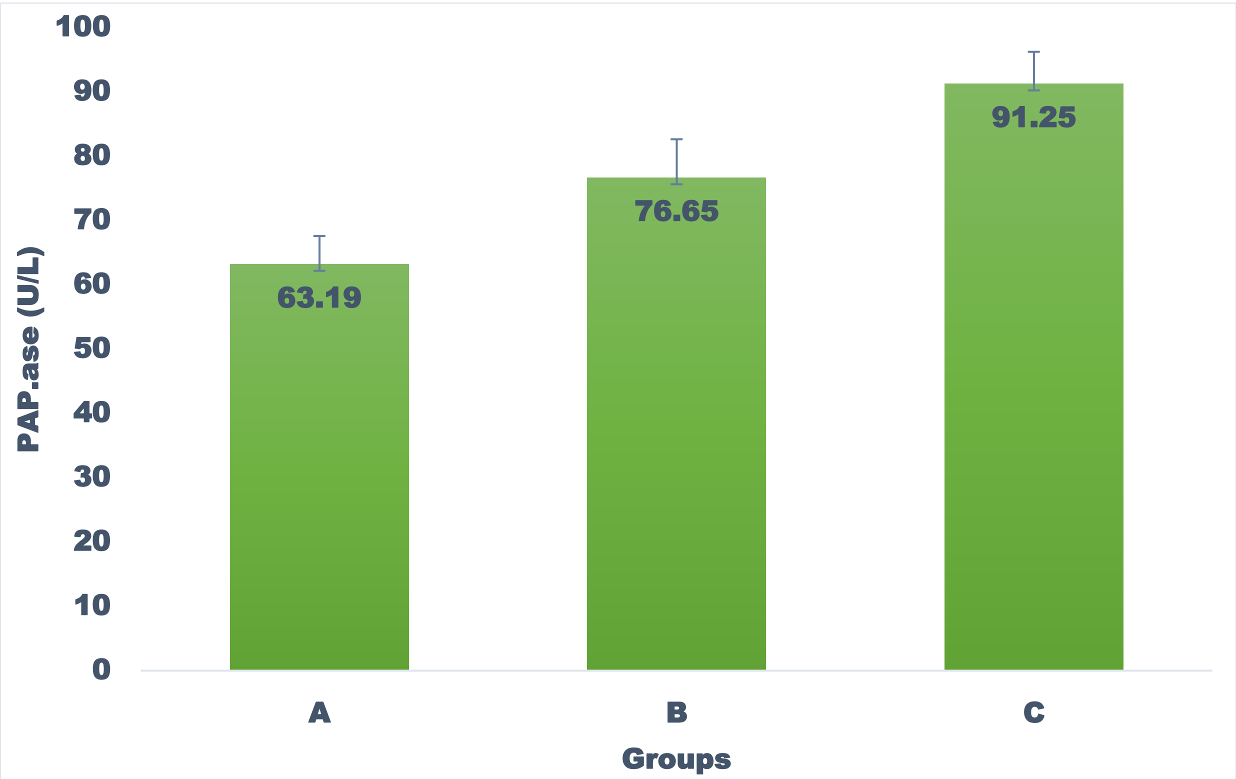

Figure -2 PAP.ase serum level of the two patient groups and control group

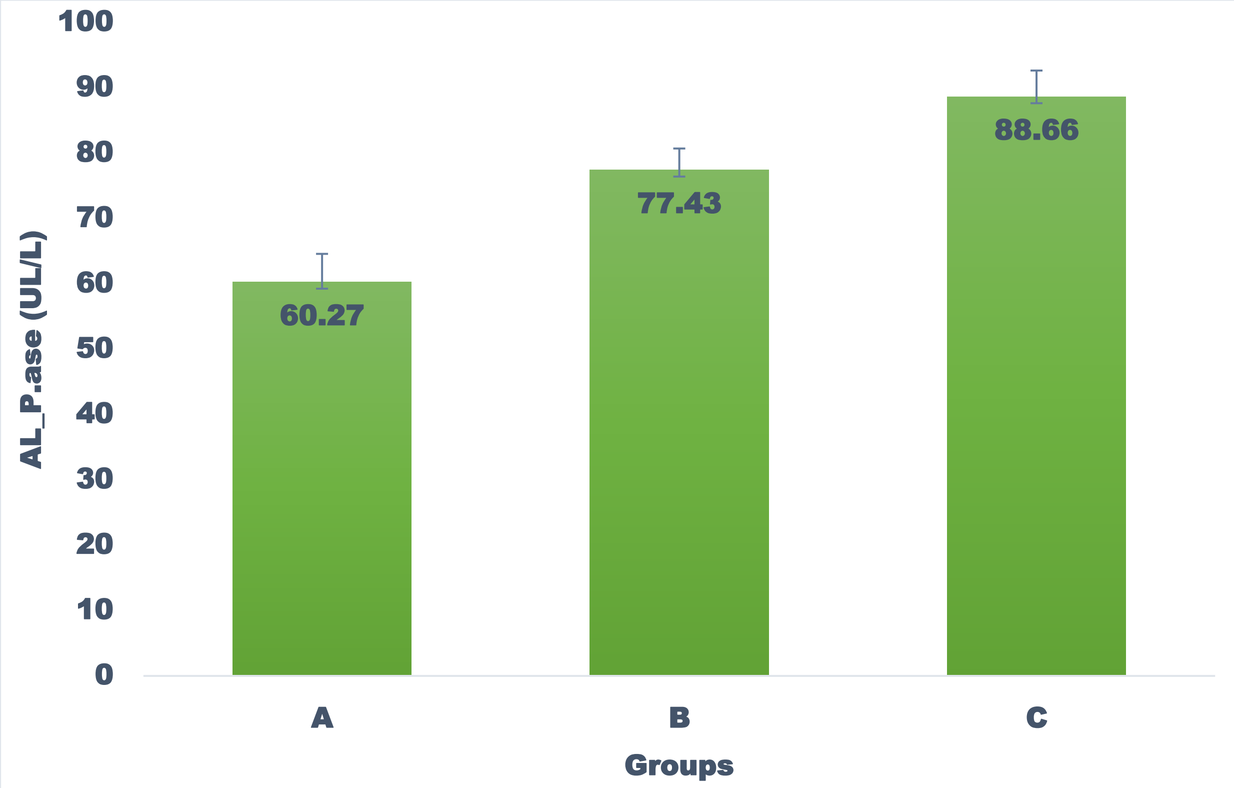

Figure -3 ALP.ase serum level of the two patient groups and control group

4. Discussion

The aim of this study was to ascertain the impact of a postoperative calcium and calcitriol supplementation program guided by postoperative serum parathyroid hormone (PTH) on the rate of hypocalcemia and hospital readmissions among patients after complete thyroidectomy. The most frequent side effect following a complete thyroidectomy is hypocalcemia. Bone pain and deformities are common symptoms in patients with thyroid hormone issues [12].

It has been recognized in recent years that the thyroid is primarily responsible for the formation and preservation of bone mass, and that changes in thyroid hormone levels can cause malformations, bone loss, and an elevated risk of fracture. Thyroid hormones play a critical physiological role in maintaining adult bone strength and shape and are necessary for skeletal maturity. Thyroid hormone has been underappreciated in the pathophysiology of osteoporosis and fracture risk factors, despite the fact that thyroid dysfunction has been established as a risk factor for bone disease. The underlying processes are also unknown. The definition of hyperthyroidism is defined as elevated T3 and T4 combined with suppression of thyroid-stimulating hormone (TSH), primarily due to Graves' illness [12, 13].

According to the British Association of Endocrine and Thyroid Surgeons (BAETS), postoperatively. Post-surgical hypocalcaemia may arise from various causes, including: (a) disruption of the parathyroid blood supply and inadvertent gland excision; (b) acute calcium transfer into bones leading to hungry bone syndrome; (c) release of calcitonin following surgery; and (d) delusional hypocalcaemia. Paresthesia and neuromuscular instability, including cramps, tetany, and convulsions, can result from acute hypocalcaemia. Bone metabolism is reflected by serum alkaline phosphatase (ALP) and its isoenzymes: ALP inhibits the synthesis of minerals by lowering the concentration of extracellular pyrophosphate and by increasing the ratio of inorganic phosphate to pyrophosphate. It also promotes mineralization. Low ALP activity, on the other hand, is linked to a decrease in bone turnover. Depending on the tissue expression site, ALP comprises four isoenzymes: intestinal ALP, placental ALP, placental ALP, germ cell ALP and tissue nonspecific ALP or liver/bone/kidney ALP [14, 15].

The bone isoenzyme (B-ALP) is involved in bone calcification and is a marker of bone turnover because of osteoblastic activity. ALP and its isoenzymes are crucial in the diagnostic process of all the forms of rickets. The most common cause of rickets is vitamin D nutritional deficiency. The aim of this review is to update on the role played by ALP serum concentrations as a relevant marker in thediagnosis and treatment of rickets. Indeed, the diagnosis of rickets is based on its clinical, radiological and laboratory characteristics. An elevated ALP level is one of the markers for the diagnosis of rickets in children, though it is also associated with bone formation process [15, 16].

ALP is also useful for the differentiation between rickets and other disorders that can mimic rickets because of their clinical and laboratory characteristics, and, together with other biochemical markers, is crucial for the differential diagnosis of the different forms of rickets. Age, severity and duration of rickets may also modulate ALP elevation. Finally, ALP measurements are useful in clinical and therapeutic follow-up, it decreases when hypothyroidism and. The study was conducted at Al-Sadr Medical City in Al-Najaf city, in Iraq, from October 2020 to March 2021. Thyroid-stimulating hormone (TSH) was very high in patients at a hypothyroid stage after hypothyroidism. The study also revealed a significant increase in the liver enzymes aspartate aminotransferase (AST) and alanine transaminase (ALT) and a significant decrease in alkaline phosphatase (ALP) in patients with thyroidectomy compared to the control group and. Elevated serum alkaline phosphatase as well as bone specific alkaline phosphatase is found associated with osteomalacia which is caused due to vitamin D deficiency but this is not considered as confirmatory test as some patient have normal or borderline elevated ALP levels .Metabolic pathways directly or indirectly regulated by thyroid hormones[14, 17].

Osteosarcopenia biomarkers needed for early detection and preventing deterioration. Elevated TSH and BAP increase the likelihood of osteosarcopenia. In contrast, elevated 25OHD decrease the likelihood of osteosarcopenia, osteosarcopenia is a new definitional approach that can increase the risk of falls and fractures in elderly compared with that of osteoporosis and sarcopenia alone. However, biomarkers for osteosarcopenia have not been well identified. [14, 17].

Alkaline phosphatase (ALP) is a nonspecific enzyme that hydrolyzes phosphate in alkaline medium and its total level reflects the combined activity of several isozymes found in the bone, liver, kidney, and intestinal lining. Its bone-specific isoforms (bone-specific alkaline phosphatase, BAP) originates in osteoblasts that release large amounts of the enzyme when bone repair activity occurs, for example bone metastases. Serum alkaline phosphatase (ALP) and its isoenzymes reflect bone metabolism: ALP increases the ratio of inorganic phosphate to pyrophosphate systemically and facilitates mineralization as well as reduces extracellular pyrophosphate concentration, an inhibitor of mineral formation. On the contrary, low ALP activity is associated with reduction of bone turnover. ALP includes four isoenzymes depending on the site of tissue expression: intestinal ALP, placental ALP, germ cell ALP and tissue nonspecific ALP or liver/bone/kidney ALP [14, 18].

The bone isoenzyme (B-ALP) is involved in bone calcification and is a marker of bone turnover because of osteoblastic activity. ALP and its isoenzymes are crucial in the diagnostic process of all the forms of rickets. The most common cause of rickets is vitamin D nutritional deficiency. Increased bone turnover in hyperthyroidism and low bone turnover in hypothyroidism and decreased B-ALP. Bone alkaline phosphatase has been considered as another marker of TH status in bone. Bone alkaline phosphatase concentrations in blood are increased in hyperthyroid patients compared to euthyroid controls and a positive correlation was observed between bone alkaline phosphatase and fT3 and fT4 in both hypothyroid and hyperthyroid and euthyroid patients. Bone alkaline phosphatase concentrations eventually decreased after adequate treatment for hyperthyroidism, although normalization could take a few months. In contrast, hypothyroid patients did not show aberrant bone alkaline phosphatase concentrations when compared to euthyroid controls. Therefore, this biomarker is not feasible to evaluate bone TH status [18, 19].

5. Conclusion

The process of removing the total thyroid gland affects some bone characteristics, as the first group(A) showed a significant decline more than the second group(B) of patients, and when comparing the patient groups with healthy people(C), it was found that there was a clear decrease in the patient groups. ($P \leq 0.05$).

References

[1] A. Torrejon-Moya, K. Izquierdo-Gomez, M. Perez-Sayans, E. Jane-Salas, A. Mari Roig, and J. Lopez-Lopez, "Patients with thyroid disorder, a contraindication for dental implants? A systematic review," *Journal of Clinical Medicine,* vol. 11, p. 2399, 2022.

[2] W. Samara, O. Moztarzadeh, L. Hauer, and V. Babuska, "Dental Implant Placement in Medically Compromised Patients: A Literature Review," *Cureus,* vol. 16, 2024.

[3] A. Mohammadi, N. R. Dehkordi, S. Mahmoudi, N. Rafeie, H. Sabri, M. Valizadeh, *et al.*, "Effects of Drugs and Chemotherapeutic Agents on Dental Implant Osseointegration: A Narrative Review," *Current reviews in clinical and experimental pharmacology,* vol. 19, pp. 42-60, 2024.

[4] A. Yari, P. Fasih, S. Alborzi, H. Nikzad, and E. Romoozi, "Risk factors associated with early implant failure: A retrospective review," *Journal of Stomatology, Oral and Maxillofacial Surgery,* vol. 125, p. 101749, 2024.

[5] J. Ji, Z. Li, L. Xue, H. Xue, T. Wen, T. Yang, *et al.*, "The impact of thyroid function on total spine bone mineral density in postmenopausal women," *Endocrine,* pp. 1-8, 2024.

[6] W. Qi, D. Wang, Y. Hong, J. Yao, H. Wang, L. Zhu, *et al.*, "Investigating the causal relationship between thyroid dysfunction diseases and osteoporosis: a two-sample Mendelian randomization analysis," *Scientific Reports,* vol. 14, p. 12784, 2024.

[7] S. Askari and M. Porgholi, "Narrative Review Hyperthyroidism, Thyroid cancers, and Osteoprosis."

[8] H. Sato, Y. Sugiyama, T. Hashimoto, T. Segawa, H. Bukawa, H. Sato, *et al.*, "Endocrine Diseases," in *Internal Medicine for Dental Treatments: Patients with Medical Diseases*, ed: Springer, 2024, pp. 99-116.

[9] R. Wang, S. Qin, T. Qiao, W. Jiang, J. Tong, G. Lu, *et al.*, "Body composition changes in patients with differentiated thyroid cancer after iodine-131 treatment and short-term levothyroxine replacement and suppression therapy," *Hormones,* pp. 1-9, 2024.

[10] P. Khairallah and T. L. Nickolas, "Managing osteoporosis in dialysis—a medical catch-22," *JAMA*, 2024.

[11] E. M. A. Ozturk and A. Artas, "Evaluation of Bone Mineral Changes in Panoramic Radiographs of Hypothyroid and Hyperthyroid Patients Using Fractal Dimension Analysis," *Journal of Clinical Densitometry,* vol. 27, p. 101443, 2024.

[12] A.-M. Chindris, K. Desai, S. K. Ozgursoy, M. G. Heckman, and J. D. Casler, "A Parathyroid Hormone–Guided Calcium and Calcitriol Supplementation Protocol Reduces Hypocalcemia-Related Readmissions Following Total Thyroidectomy," *Endocrine Practice,* vol. 29, pp. 260-265, 2023.

[13] C. Cipriani, J. Pepe, L. Colangelo, M. Cilli, L. Nieddu, and S. Minisola, "Presentation of hypoparathyroidism in Italy: a nationwide register-based study," *Journal of Endocrinological Investigation,* pp. 1-7, 2024.

[14] X. Jin, J. Shen, T. Liu, R. Zhou, X. Huang, T. Wang*, et al.*, "The significance of short-term preoperative calcium and activated vitamin D3 supplementation in thyroidectomy: a randomized trial and prospective study," *Endocrine Connections,* vol. 13, 2024.

[15] K. Rao and I. Upadhya, "A Study of Incidence and Management of Postoperative Hypocalcemia in Patients Undergoing Near-Total and Total Thyroidectomy," *Indian Journal of Otolaryngology and Head & Neck Surgery,* vol. 76, pp. 1903-1909, 2024.

[16] G. Cannalire, S. Pilloni, S. Esposito, G. Biasucci, A. Di Franco, and M. E. Street, "Alkaline phosphatase in clinical practice in childhood: Focus on rickets," *Frontiers in Endocrinology,* vol. 14, p. 1111445, 2023.

[17] E. Rush, M. L. Brandi, A. Khan, D. S. Ali, H. Al-Alwani, K. Almonaei*, et al.*, "Proposed diagnostic criteria for the diagnosis of hypophosphatasia in children and adolescents: results from the HPP International Working Group," *Osteoporosis International,* vol. 35, pp. 1-10, 2024.

[18] M. Rios-Leyvraz, T. D. Thacher, A. Dabas, H. H. Elsedfy, G. I. Baroncelli, and K. D. Cashman, "Serum 25-hydroxyvitamin D threshold and risk of rickets in young children: a systematic review and individual participant data meta-analysis to inform the development of dietary requirements for vitamin D," *European Journal of Nutrition,* vol. 63, pp. 673-695, 2024.

[19] P. S. Adamidis, M. Florentin, E. Liberopoulos, A. D. Koutsogianni, G. Anastasiou, G. Liamis*, et al.*, "Association of Alkaline Phosphatase with Cardiovascular Disease in Patients with Dyslipidemia: A 6-Year Retrospective Study," *Journal of Cardiovascular Development and Disease,* vol. 11, p. 60, 2024.