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Assessment of Mandibular Bone Architecture in Patients with Endocrine Disorders Using Fractal Dimension and Histogram Analysis

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Abstract:

Objective: Endocrine disorders, including diabetes mellitus and thyroid dysfunctions, can significantly impact bone metabolism and structure. This study aimed to assess mandibular trabecular architecture in patients with type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), hyperthyroidism, and hypothyroidism using fractal dimension (FD) and histogram analysis (HA), comparing the findings with a healthy control group. **Methods:** This retrospective study analyzed panoramic radiographs from 200 individuals, comprising 40 patients in each of the four endocrine disorder groups and 40 healthy controls. Fractal analysis and pixel intensity histogram analysis were conducted using ImageJ™ software. Two standardized regions of interest (ROIs) were selected for FD and HA measurements, and statistical comparisons were performed using one-way ANOVA and chi-square analysis. **Results:** No statistically significant differences were observed in FD values between the study groups for both the right and left mandibular sides ($p>0.05$). Similarly, HA values did not show significant variations across the groups ($p>0.05$). Gender distribution and mean age comparisons among the groups did not reveal significant differences ($p>0.05$). **Conclusion:** Despite the known systemic effects of endocrine disorders on bone metabolism, this study found no significant alterations in mandibular trabecular architecture in affected patients compared to healthy controls. These findings suggest that while systemic bone changes occur in endocrine disorders, their impact on the mandibular trabecular structure may be limited or require more advanced imaging techniques for detection. Future studies with larger sample sizes, longer disease durations, and comprehensive biochemical analyses are recommended to further explore the relationship between endocrine diseases and jawbone architecture.

Keywords: Fractal dimension analysis; mandibular bone microarchitecture; endocrine disorders; panoramic radiography

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1. Introduction

Endocrine system diseases arise from hormonal imbalances and can impact multiple organ systems [1]. Among these, diabetes, hyperthyroidism, and hypothyroidism are key examples. Hormones play a crucial role in regulating various tissues and organs, including the cardiovascular, respiratory, gastrointestinal, neurological, and musculoskel-

etal systems, with a significant influence on bone health [1-2]. As a primary target of hormonal activity, bone undergoes remodeling processes that are directly affected by hormonal fluctuations [2].

Osteoporosis is a condition marked by reduced bone mass and microarchitectural deterioration, increasing susceptibility to fractures [3]. Endocrine disorders are a major cause of secondary osteoporosis [4]. Diabetes, in particular, negatively affects bone metabolism, raising fracture risk [5]. Type 1 diabetes mellitus (T1DM) results from insulin deficiency, while type 2 diabetes mellitus (T2DM) is characterized by insulin resistance [6]. Both conditions impair bone health by disrupting bone formation, resorption, collagen synthesis, inflammatory processes, and calcium metabolism [5]. Despite differing effects on bone mineral density (BMD), both T1DM and T2DM are associated with an increased risk of fractures [7-9].

Thyroid hormones are essential for skeletal development and bone homeostasis [10]. Hyperthyroidism, characterized by excessive thyroid hormone production, is commonly linked to decreased BMD and a higher risk of fractures [11-12]. Hypothyroidism can be either subclinical—where TSH levels are elevated but free T4 remains normal—or overt, with both high TSH and low free T4 levels [13]. In both cases, thyroid dysfunction can negatively impact bone health [14].

BMD, measured using dual-energy X-ray absorptiometry (DXA), is the gold standard for diagnosing osteoporosis [15]. However, BMD alone is insufficient to fully assess fracture risk, as bone fragility is influenced by factors such as bone turnover, trabecular microarchitecture, mineralization, and collagen quality [16-17]. Fractal analysis (FA) is a valuable technique for evaluating bone microarchitecture [18]. Since trabecular bone exhibits fractal properties, FA is widely used to analyze its structural complexity [19-20]. This method quantifies bone structure using fractal dimension (FD) values, where higher values indicate greater structural complexity [21]. The box-counting algorithm, a commonly applied FA technique, assesses the fractal dimension of the trabecular bone and bone marrow interface [22]. Studies have demonstrated the effectiveness of FA in detecting structural bone changes [23-24]. Pixel intensity (PI) analysis is another imaging technique used to evaluate bone tissue in digital images [25]. By measuring grayscale variations, PI analysis provides insight into bone density, often utilizing histogram analysis for interpretation [25-26].

Although extensive research has explored the impact of endocrine diseases on overall bone health, studies focusing on the maxillofacial region remain limited. In particular, the effects of thyroid disorders on jawbone structure are not well understood. This study aims to assess the impact of T1DM, T2DM, hypothyroidism, and hyperthyroidism on mandibular trabecular architecture using fractal dimension and histogram analysis, comparing findings with those from healthy individuals.The introduction should briefly place the study in a broad context and highlight why it is important. It should define the purpose of the work and its significance. The current state of the research field should be carefully reviewed and key publications cited. Please highlight controversial and diverging hypotheses when necessary. Finally, briefly mention the main aim of the work and highlight the principal conclusions. As far as possible, please keep the introduction comprehensible to scientists outside your particular field of research. References should be numbered in order of appearance and indicated by a numeral or numerals in square brackets—e.g., [1] or [2,3], or [4–6]. See the end of the document for further details on references.

2. Materials and Methods

Ethics Approval

This retrospective study was conducted using panoramic radiographs from the database of the Department of Oral, Dental, and Maxillofacial Radiology, Faculty of Dentistry, Ankara Yıldırım Beyazıt University, collected between 2022 and 2023. The study adhered to the ethical principles outlined in the Declaration of Helsinki. Ethical approval was granted by the Health Sciences Ethics Committee of Ankara Yıldırım Beyazıt University (Decision No: 339/07).

Patient Selection

Panoramic radiographs included in the study met the following criteria: Clear visualization of the anterior, premolar, molar, mandibular canal, and mental foramen regions. Absence of image artifacts, ghost images, or patient positioning errors. Radiographs with insufficient image quality were excluded. Patient medical history and demographic data, including age and gender, were obtained from anamnesis records and the hospital automation system.

The required sample size for this retrospective study was determined using the G*Power (ver. 3.1.9.7) statistical software. The study included five groups: four disease subgroups (hyperthyroidism, hypothyroidism, type 1 diabetes mellitus, and type 2 diabetes mellitus) and one control group. Using a one-way ANOVA design, the parameters were set as follows: Statistical power: 0.80, Effect size: 0.25 (based on the F-test effect size range), Type I error (α): 0.05. Based on these calculations, a total of 200 panoramic radiographs were analyzed, with at least 40 samples per group.

Panoramic Radiography Protocol

All panoramic radiographs were acquired using a digital dental panoramic device (Planmeca, Helsinki, Finland) under standardized conditions: Exposure time: 13.8–15.8 seconds, voltage: 64–68 kVp, current: 6.3–10 mA. To ensure consistency, patients were positioned according to the manufacturer's guidelines, maintaining the Frankfort plane parallel to the ground with light beam markers aligned appropriately.

Fractal Dimension and Pixel Intensity Analysis

Before analysis, panoramic radiographs were saved in high-resolution Tagged Image File Format (TIFF) and processed using ImageJ™ software (National Institutes of Health, Bethesda, Maryland) [27]. Fractal dimension and histogram analyses were performed using this software.

For each panoramic radiograph, two manually selected square-shaped regions of interest (ROIs) were placed anterior to the right and left mental foramen, avoiding the mandibular cortical borders, lamina dura, periodontal ligament, and root apices.

Fractal dimension (FD) was calculated using the box-counting method proposed by White and Rudolph [28]. The procedure included: Selection of 64 × 64-pixel ROIs., application of gaussian blur (sigma = 35) to minimize brightness variations due to overlying soft tissues and bone thickness differences. subtraction of the blurred image from the original image. enhancement of trabecular bone structures by adding 128 gray values to each pixel. application of binary, erode, dilate, invert, and skeletonization operations to segment trabecular and bone marrow spaces. calculation of the fractal dimension (FD) (Figures 1–3).

Mean pixel intensity (PI) values for each ROI were obtained using the histogram tool in ImageJ™ software (Figure 4). This analysis provided quantitative information on bone density based on grayscale variations.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). One-way ANOVA was used to compare normally distributed data across three or more groups. Chi-square analysis was applied to assess re-

lationships between categorical variables. Pearson correlation analysis was conducted to evaluate associations between continuous variables. A p-value < 0.05 was considered statistically significant.

3. Results

This retrospective study included panoramic radiographs of 200 individuals, including 40 patients with type 1 diabetes mellitus, 40 patients with type 2 diabetes mellitus, 40 patients with hyperthyroidism, 40 patients with hypothyroidism, and 40 individuals from the control group.

3.1. Comparisons of age and gender variables between the subgroups

Table 1 shows the age and gender comparisons of the patient groups and the control group. No statistically significant difference was found between the disease groups (hyperthyroidism: 50.83±8.1, hypothyroidism: 50.78±8.6, type 1 diabetes: 50.85±13.5, type 2 diabetes: 50.78±9.0) and the control group (50.73±9.9) in terms of mean age ($p>0.05$). The number of female individuals in the disease groups and the control group (hyperthyroidism n=31, hypothyroidism n=34, type 1 diabetes n=27, type 2 diabetes n=31, control group n=31) was higher than the number of male individuals (hyperthyroidism n=9, hypothyroidism n=6, type 1 diabetes n=13, type 2 diabetes n=9, control group n=9). No statistically significant difference was found between the groups in terms of gender distribution ($p>0.05$).

3.2. Correlations of Fractal Dimension (FD) and Histogram Analysis (HA) values between the study groups

The comparison of Fractal Dimension (FD) and Histogram Analysis (HA) values between the study groups is presented in Table 2.

In the fractal dimension (FD right) analyses performed on the right side of the mandible, no statistically significant difference was observed between the groups (hyperthyroidism: 1.55±0.06, hypothyroidism: 1.55±0.06, type 1 diabetes: 1.52±0.09, type 2 diabetes: 1.54±0.05, control group: 1.54±0.06) ($p>0.05$).

In the fractal dimension (FD left) analyses performed on the left side of the mandible, no statistically significant difference was found between the groups (hyperthyroidism: 1.53±0.06, hypothyroidism: 1.54±0.06, type 1 diabetes: 1.54±0.07, type 2 diabetes: 1.55±0.06, control group: 1.55±0.07) ($p>0.05$). In the histogram analyses performed on the right side of the mandible, no statistically significant difference was observed between the groups (hyperthyroidism: 116.1±21.5, hypothyroidism: 107.2±19.8, type 1 diabetes: 113.1±24.3, type 2 diabetes: 107.9±21.4, control group: 111.7±18.5) ($p>0.05$).

Similarly, in histogram analyses performed on the left side of the mandible, no statistically significant difference was found between the groups (hyperthyroidism: 110.2±18.8, hypothyroidism: 109.2±23.5, type 1 diabetes: 104.8±19.0, type 2 diabetes: 107.3±19.0, control group: 108.0±18.3) ($p>0.05$).

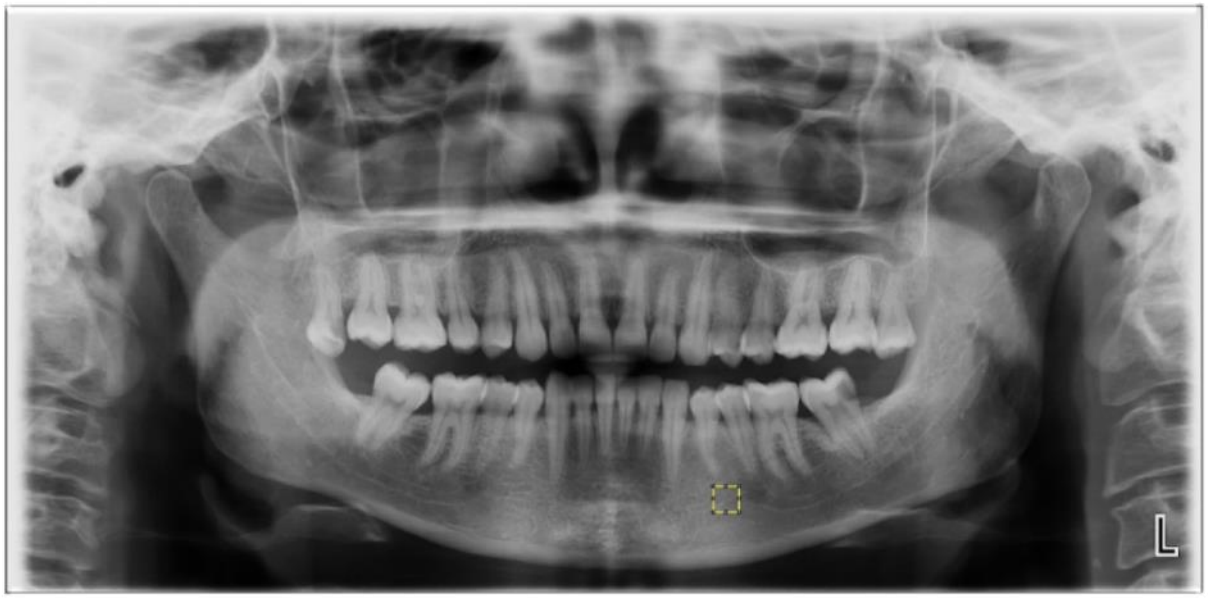


Figure 1. Selection of region of interest (ROI) for fractal dimension

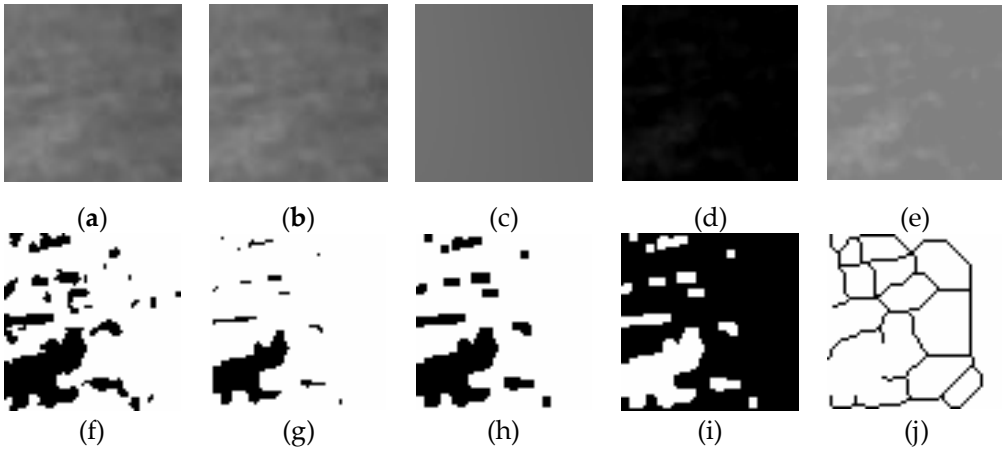


Figure 2. Steps of fractal dimension analysis.

(a), The selected ROI from panoramic radiographs was cropped and **(b)**, duplicated. **(c)**, Gaussian blur filter was applied on duplicated image. **(d)**, The blurred image was subtracted from the original image. **(e)**, Addition of a gray value of 128 to each pixel location. **(f)**, Binarization **(g)**, Erosion **(h)**, Dilation **(i),** Inversion **(j),** The skeletonized image was used for fractal dimension analysis.

Figure 3: Calculation of fractal dimension

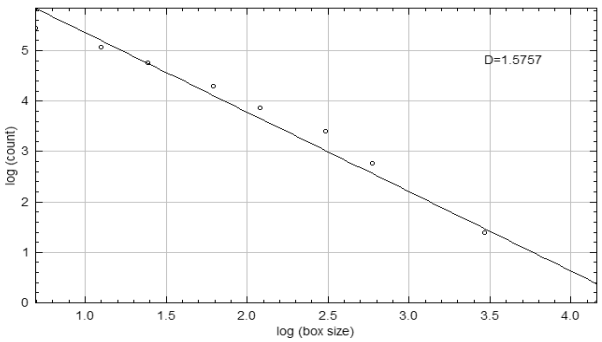
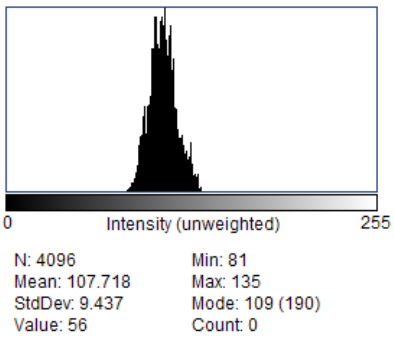


Figure 4: Histogram of selected ROI



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Similarly, in histogram analyses performed on the left side of the mandible, no statistically significant difference was found between the groups (hyperthyroidism: 110.2±18.8, hypothyroidism: 109.2±23.5, type 1 diabetes: 104.8±19.0, type 2 diabetes: 107.3±19.0, control group: 108.0±18.3) ($p>0.05$).

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231 **Table 1.** Distribution of gender and age among study groups

		Study Groups												Chi-square test	
		Hyperthyroidism		Hypothyroidism		T1DM		T 2DM		Controls		Total			
		n	%	n	%	n	%	n	%	n	%	n	%	X^2	p
Gender	Male	9	22.5	6	15.0	13	32.5	9	22.5	9	22.5	46	23	3.5	0.478
	Female	31	77.5	34	85.0	27	67.5	31	77.5	31	77.5	154	77		
	Total	40	100	40	100	40	100	40	100	40	100	200	100		
Age														ANOVA	
														F	p
	Mean	50.83		50.78		50.85		50.78		50.73		50.79		0.001	1
	Median	52		49		52.5		51.5		49.5		51			
	Minimum	37.0		32.0		21.0		35.0		35.0		21			
	Maximum	66.0		72.0		75.0		74.0		74.0		75			
	Standard Deviation	8.1		8.6		13.5		9.0		9.9		9.9			

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234 **Table 2**. comparison of fractal dimension and histogram analysis values between study groups

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							ANOVA	
		n	Mean	Median	Minimum	Maximum	SD	F	p
FD Right	Hyperthyroidism	40	1.5467	1.5543	1.4001	1.6431	.0566	1.45	0.219
	Hypothyroidism	40	1.5542	1.5555	1.3958	1.6719	.0596		
	Type 1 Diabetes Mellitus	40	1.5212	1.5234	1.2835	1.6732	.0872		
	Type 2 Diabetes Mellitus	40	1.5433	1.5470	1.3560	1.6617	.0524		
	Control Group	40	1.5406	1.5427	1.3825	1.6724	.0612		
	Total	200	1.5412	1.5471	1.2835	1.6732	.0649		
FD Left	Hyperthyroidism	40	1.5320	1.5320	1.4102	1.6344	.0588	0.58	0.680
	Hypothyroidism	40	1.5386	1.5390	1.3893	1.6287	.0596		
	Type 1 Diabetes Mellitus	40	1.5445	1.5696	1.3291	1.6391	.0721		
	Type 2 Diabetes Mellitus	40	1.5466	1.5503	1.4120	1.6642	.0567		
	Control Group	40	1.5520	1.5680	1.3016	1.6486	.0717		
	Total	200	1.5428	1.5515	1.3016	1.6642	.0639		
HA Right	Hyperthyroidism	40	116.103	116.077	56.744	154.831	21.520	1.22	0.302

	Hypothyroidism	40	107.222	106.209	70.752	148.564	19.790		
	Type 1 Diabetes Mellitus	40	113.142	112.879	65.934	158.440	24.282		
	Type 2 Diabetes Mellitus	40	107.877	110.096	54.440	156.143	21.399		
	Control Group	40	111.702	109.510	64.414	150.381	18.459		
	Total	200	111.209	110.998	54.440	158.440	21.228		
HA Left	Hyperthyroidism	40	110.289	108.479	80.444	165.643	18.793	0.44	0.776
	Hypothyroidism	40	109.231	108.878	64.359	159.208	23.545		
	Type 1 Diabetes Mellitus	40	104.804	105.715	52.605	142.247	18.996		
	Type 2 Diabetes Mellitus	40	107.272	105.732	71.001	161.941	18.995		
	Control Group	40	108.004	103.626	82.968	155.508	18.302		
	Total	200	107.920	106.081	52.605	165.643	19.709		

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4. Discussion

This study is among the few that have investigated mandibular bone structure in patients with hyperthyroidism, hypothyroidism, type 1 diabetes mellitus (T1DM), and type 2 diabetes mellitus (T2DM) using fractal dimension (FD) and histogram analysis (HA). Our findings indicate no statistically significant differences in FD and HA values between these patient groups and the control group. Given that endocrine disorders, such as thyroid diseases and diabetes, can influence bone metabolism and structure [2], assessing these changes is crucial for understanding their impact on bone health.

Radiologic imaging techniques play a key role in evaluating disease-related changes in bone structure. Panoramic radiographs are widely used due to their broad anatomical coverage and low radiation exposure. Non-invasive techniques like fractal analysis allow for the quantification of trabecular bone structure and have been employed to evaluate bone alterations in systemic conditions such as diabetes [31], thalassemia [32], familial Mediterranean fever [33], sickle cell disease [34], osteogenesis imperfecta [35], chronic renal failure [36], hyperparathyroidism [37], and celiac disease [38]. Fractal dimension values provide numerical assessments of trabecular complexity, with higher values indicating a more intricate structure [21,22]. Consequently, fractal analysis was deemed a suitable method for examining changes in jawbone architecture in our study.

Yavuz et al. [39] compared periapical, panoramic, and CBCT imaging techniques in assessing trabecular bone structure using fractal analysis. Their study concluded that periapical and panoramic radiographs yielded comparable and reliable results, while CBCT images showed inconsistencies with other methods. Accordingly, our study relied on panoramic radiographs for bone structure assessment.

Digital images are composed of pixels, each containing brightness and color data [26]. Pixel intensity (PI) represents the grayscale value of a pixel, reflecting its degree of brightness or darkness [25]. Histogram analysis (HA) allows for the numerical evaluation of pixel brightness variations within an image [26]. Güngör et al. [26] examined osteoporotic changes in jawbones using CBCT imaging and compared radiomorphometric indices, CT values, HA, and FD measurements across osteoporosis, osteopenia, and healthy control groups. Their findings demonstrated that osteoporotic patients exhibited

significantly lower mandibular indices, CT values, and HA measurements than osteopenic and control subjects. Additionally, a positive correlation was found between spinal bone mineral density (BMD) and mandibular CT and HA measurements. These results highlight the effectiveness of FD and HA in assessing bone structural changes.

Both Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM) are linked to impaired bone health. Chronic hyperglycemia disrupts osteoblast function and promotes the formation of advanced glycation end-products (AGEs), which weaken bone strength. Prolonged disease duration and poor glycemic control further increase fracture risk. Moreover, lower levels of glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide-1 (GLP-1) inhibit bone formation, while inflammatory states accelerate bone resorption. Given these metabolic effects, it is crucial to perform quantitative assessments of bone structure in diabetic patients. However, in our study, no significant differences in FD or HA values were observed between diabetic patients and control groups. This lack of significant findings may be attributed to several factors, including sample size, disease duration, glycemic control, fasting blood glucose levels, and HbA1c values.

Kurşun-Çakmak et al. [31] examined mandibular cortical width, panoramic mandibular index (PMI), mandibular cortical index, and FD in panoramic radiographs of T1DM and T2DM patients, reporting no significant differences in FD values between the diabetic and control groups, which is consistent with our findings. Similarly, Dedeoğlu et al. [40] performed FD analysis on panoramic radiographs taken five years apart in T2DM patients and controls, finding no significant differences between the groups, although a time-dependent decline in FD values was noted. Ay et al. [41] used DXA-calibrated copper stepwedge phantoms on panoramic radiographs to measure bone mineral density (BMD) in T2DM patients and found no significant differences between diabetic and control groups. Jolly et al. [42] compared trabecular and cortical bone densities in the maxillary and mandibular regions using spiral CT, finding no significant differences between controlled diabetic and non-diabetic individuals with HbA1c levels ranging from 6.1% to 8%. Kayıpmaz et al. [43] analyzed cone beam computed tomography (CBCT) images in T2DM patients, reporting no significant differences in FD values, but observed thinner mandibular cortical bone in diabetic individuals. In a meta-analysis, Pan et al. [44] examined the relationship between T1DM and BMD, demonstrating a significant reduction in total body BMD in T1DM patients and suggesting that age and gender may influence the impact of T1DM on BMD. Although our study did not evaluate age subgroups, the similar mean age between the study groups likely minimized the confounding effects related to age.

Rodic et al. [45] conducted a post-mortem study comparing jawbone quality in T2DM patients and healthy individuals using micro-CT, qBEI, Raman spectroscopy, and bone histomorphometry. They found increased trabecular thickness, reduced cortical porosity, and higher mineralization in T2DM patients, particularly in those using insulin. These findings highlight the complexity of diabetes-related bone changes. However, our study focused exclusively on trabecular bone using FD and HA, which may not fully capture the complete spectrum of bone alterations associated with diabetes.

In hypothyroidism, both osteoid formation and bone mineralization are impaired, leading to a decrease in bone turnover. This condition is characterized by reduced osteoclastic resorption and an accumulation of bone, despite a reduction in osteoblastic activity [46,47]. In contrast, hyperthyroidism accelerates bone turnover, increasing both resorption and formation rates, which in turn heightens the risk of osteoporosis and fractures [48].

Öztürk et al. [49] assessed FD in hyperthyroid and hypothyroid patients using panoramic radiographs. They found significant differences between the patient and control groups in Region of Interest 1 (ROI1) (located at the midpoint of the mandibular notch and foramen) and ROI2 (the mandibular angle center), whereas no significant differences were observed in ROI3 (anterior to the mental foramen), ROI4 (the basal cortical area), or ROI5 (mandibular ramus center). These findings suggest that thyroid disorders influence mandibular bone structure in a region-specific manner.

However, this study has several limitations. It did not account for variations in disease duration, severity, or glycemic control (e.g., HbA1c levels) in diabetic patients, which could influence bone metabolism and FD/HA values. Additionally, the potential effects of medications, including insulin, thyroid hormone replacement, and anti-diabetic drugs, on bone structure were not evaluated, which may have impacted the results.

That said, the absence of these variables does not necessarily diminish the relevance of our findings. The focus of this study was to assess the overall bone metabolism and structure in diabetic patients, providing valuable insights into the general impact of diabetes on bone health. While the unaccounted variables could influence the outcomes, they represent areas for future research to further refine and clarify the relationship between diabetes, thyroid disorders, and bone structure. Furthermore, the study's design aimed to minimize confounding factors by using a homogenous sample group, which likely reduced the potential impact of unmeasured variables on the overall findings. Future studies incorporating these additional variables will be essential for understanding the full spectrum of metabolic effects on bone health.

5. Conclusions

This study found no significant differences in FD and HA values between patients with T1DM, T2DM, hyperthyroidism, hypothyroidism, and healthy controls. Given the intricate interactions between systemic diseases and bone metabolism, future research should involve larger sample sizes and more comprehensive evaluations of disease duration, medication use, and biochemical markers of bone metabolism.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Figure S1: title; Table S1: title; Video S1: title.

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Written informed consent for publication must be obtained from participating patients who can be identified (including by the patients themselves). Please state "Written informed consent has been obtained from the patient(s) to publish this paper" if applicable.

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Abbreviations

The following abbreviations are used in this manuscript:

T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
BMD	Bone mineral density
DXA	Dual-energy X-ray absorptiometry
FA	Fractal analysis
FD	Fractal dimension
PI	Pixel intensity
TIFF	Tagged Image File Format
ROI	Region of interest
HA	Histogram analysis
CBCT	Cone beam computed tomography
AGE	Advanced glycation end-products
GIP	Glucose-dependent insulinotropic peptide
GLP-1	Glucagon-like peptide-1

References

References must be numbered in order of appearance in the text (including citations in tables and legends) and listed individually at the end of the manuscript. We recommend preparing the references with a bibliography software package, such as EndNote, ReferenceManager or Zotero to avoid typing mistakes and duplicated references. Include the digital object identifier (DOI) for all references where available.

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1. Boswell SB, Patel DB, White EA, Gottsegen CJ, Forrester DM, Masih S, Matcuk GR Jr. Musculoskeletal manifestations of endocrine disorders. Clin Imaging. 2014 Jul-Aug;38(4):384-396. doi: 10.1016/j.clinimag.2014.02.014. Epub 2014 Mar 6. PMID: 24642251.
2. Cianferotti L, Cipriani C, Corbetta S, Corona G, Defeudis G, Lania AG, Messina C, Napoli N, Mazziotti G. Bone quality in endocrine diseases: determinants and clinical relevance. J Endocrinol Invest. 2023 Jul;46(7):1283-1304. doi: 10.1007/s40618-023-02056-w. Epub 2023 Mar 14. PMID: 36918505.
3. Mirza F, Canalis E. Management of endocrine disease: Secondary osteoporosis: pathophysiology and management. Eur J Endocrinol. 2015 Sep;173(3):R131-51. doi: 10.1530/EJE-15-0118. Epub 2015 May 13. PMID: 25971649; PMCID: PMC4534332.
4. Stein E, Shane E. Secondary osteoporosis. Endocrinol Metab Clin North Am. 2003 Mar;32(1):115-34, vii. doi: 10.1016/s0889-8529(02)00062-2. PMID: 12699295.
5. Palermo A, D'Onofrio L, Buzzetti R, Manfrini S, Napoli N. Pathophysiology of Bone Fragility in Patients with Diabetes. Calcif Tissue Int. 2017 Feb;100(2):122-132. doi: 10.1007/s00223-016-0226-3. Epub 2017 Feb 8. PMID: 28180919.
6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014 Jan;37 Suppl 1:S81-90. doi: 10.2337/dc14-S081. PMID: 24357215.
7. Pan H, Wu N, Yang T, He W. Association between bone mineral density and type 1 diabetes mellitus: a meta-analysis of cross-sectional studies. Diabetes Metab Res Rev. 2014 Oct;30(7):531-42. doi: 10.1002/dmrr.2508. PMID: 24376190.
8. Ma L, Oei L, Jiang L, Estrada K, Chen H, Wang Z, Yu Q, Zillikens MC, Gao X, Rivadeneira F. Association between bone mineral density and type 2 diabetes mellitus: a meta-analysis of observational studies. Eur J Epidemiol. 2012 May;27(5):319-32. doi: 10.1007/s10654-012-9674-x. Epub 2012 Mar 27. PMID: 22451239; PMCID: PMC3374119.
9. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes--a meta-analysis. Osteoporos Int. 2007 Apr;18(4):427-44. doi: 10.1007/s00198-006-0253-4. Epub 2006 Oct 27. PMID: 17068657.
10. Tsourdi E, Rijntjes E, Köhrle J, Hofbauer LC, Rauner M. Hyperthyroidism and Hypothyroidism in Male Mice and Their Effects on Bone Mass, Bone Turnover, and the Wnt Inhibitors Sclerostin and Dickkopf-1. Endocrinology. 2015 Oct;156(10):3517-27. doi: 10.1210/en.2015-1073. Epub 2015 Jul 28. PMID: 26218891.
11. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016 Oct;26(10):1343-1421. doi: 10.1089/thy.2016.0229. Erratum in: Thyroid. 2017 Nov;27(11):1462. doi: 10.1089/thy.2016.0229.correx. PMID: 27521067.1421.
12. Vestergaard P, Mosekilde L. Hyperthyroidism, bone mineral, and fracture risk--a meta-analysis. Thyroid. 2003 Jun;13(6):585-93. doi: 10.1089/105072503322238854. PMID: 12930603.
13. .Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber KA; American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012 Nov-Dec;18(6):988-1028. doi: 10.4158/EP12280.GL. Erratum in: Endocr Pract. 2013 Jan-Feb;19(1):175. PMID: 23246686.
14. Vestergaard P, Mosekilde L. Fractures in patients with hyperthyroidism and hypothyroidism: a nationwide follow-up study in 16,249 patients. Thyroid. 2002 May;12(5):411-9. doi: 10.1089/105072502760043503. PMID: 12097203.
15. Jiang N, Xia W. Assessment of bone quality in patients with diabetes mellitus. Osteoporos Int. 2018 Aug;29(8):1721-1736. doi: 10.1007/s00198-018-4532-7. Epub 2018 May 7. PMID: 29736760.

16. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996;312:1254–9.
17. McCreadie BR, Goldstein SA. Biomechanics of fracture: is bone mineral density sufficient to assess risk? J Bone Miner Res. 2000 Dec;15(12):2305-8. doi: 10.1359/jbmr.2000.15.12.2305. PMID: 11127195.
18. Lespessailles E, Chappard C, Bonnet N, Benhamou CL. Imaging techniques for evaluating bone microarchitecture. Joint Bone Spine. 2006 May;73(3):254-61. doi: 10.1016/j.jbspin.2005.12.002. Epub 2006 Jan 13. PMID: 16497531.
19. Updike SX, Nowzari H. Fractal analysis of dental radiographs to detect periodontitis-induced trabecular changes. J Periodontal Res. 2008 Dec;43(6):658-64. doi: 10.1111/j.1600-0765.2007.01056.x. Epub 2008 Jun 24. PMID: 18624949
20. Haire TJ, Hodgskinson R, Ganney PS, Langton CM. A comparison of porosity, fabric and fractal dimension as predictors of the Young's modulus of equine cancellous bone. Med Eng Phys. 1998 Nov;20(8):588-93. doi: 10.1016/s1350-4533(98)00063-0. PMID: 9888237.
21. Tosoni GM, Lurie AG, Cowan AE, Burleson JA. Pixel intensity and fractal analyses: detecting osteoporosis in perimenopausal and postmenopausal women by using digital panoramic images. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Aug;102(2):235-41. doi: 10.1016/j.tripleo.2005.08.020. Epub 2006 Jun 16. PMID: 16876068.
22. Chen SK, Oviir T, Lin CH, Leu LJ, Cho BH, Hollender L. Digital imaging analysis with mathematical morphology and fractal dimension for evaluation of periapical lesions following endodontic treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005 Oct;100(4):467-72. doi: 10.1016/j.tripleo.2005.05.075. PMID: 16182168.
23. Fazzalari NL, Parkinson IH. Fractal dimension and architecture of trabecular bone. J Pathol. 1996 Jan;178(1):100-5. doi: 10.1002/(SICI)1096-9896(199601)178:1<100::AID-PATH429>3.0.CO;2-K. PMID: 8778308.
24. Benhamou CL, Poupon S, Lespessailles E, Loiseau S, Jennane R, Siroux V, Ohley W, Pothuaud L. Fractal analysis of radiographic trabecular bone texture and bone mineral density: two complementary parameters related to osteoporotic fractures. J Bone Miner Res. 2001 Apr;16(4):697-704. doi: 10.1359/jbmr.2001.16.4.697. PMID: 11315997.
25. Law AN, Bollen AM, Chen SK. Detecting osteoporosis using dental radiographs: a comparison of four methods. J Am Dent Assoc. 1996 Dec;127(12):1734-42. doi: 10.14219/jada.archive.1996.0134. PMID: 8990743.
26. Güngör E, Yildirim D, Çevik R. Evaluation of osteoporosis in jaw bones using cone beam CT and dual-energy X-ray absorptiometry. J Oral Sci. 2016;58(2):185-94. doi: 10.2334/josnusd.15-0609. PMID: 27349539.
27. Available at: https://imagej.net/ij/download.html (Accessed: 12 February 2025).
28. White SC, Rudolph DJ. Alterations of the trabecular pattern of the jaws in patients with osteoporosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999 Nov;88(5):628-35. doi: 10.1016/s1079-2104(99)70097-1. PMID: 10556761.
29. Kato CN, Barra SG, Tavares NP, Amaral TM, Brasileiro CB, Mesquita RA, Abreu LG. Use of fractal analysis in dental images: a systematic review. Dentomaxillofac Radiol. 2020 Feb;49(2):20180457. doi: 10.1259/dmfr.20180457. Epub 2019 Aug 20. PMID: 31429597; PMCID: PMC7026934.
30. Sener E, Cinarcik S, Baksi BG. Use of Fractal Analysis for the Discrimination of Trabecular Changes Between Individuals With Healthy Gingiva or Moderate Periodontitis. J Periodontol. 2015 Dec;86(12):1364-9. doi: 10.1902/jop.2015.150004. Epub 2015 Aug 20. PMID: 26291294.
31. Kurşun-Çakmak EŞ, Bayrak S. Comparison of fractal dimension analysis and panoramic-based radiomorphometric indices in the assessment of mandibular bone changes in patients with type 1 and type 2 diabetes mellitus. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018 Aug;126(2):184-191. doi: 10.1016/j.oooo.2018.04.010. Epub 2018 May 3. PMID: 29805101.
32. Bayrak S, Göller Bulut D, Orhan K, Sinanoğlu EA, Kurşun Çakmak EŞ, Mısırlı M, Ankaralı H. Evaluation of osseous changes in dental panoramic radiography of thalassemia patients using mandibular indexes and fractal size analysis. Oral Radiol. 2020 Jan;36(1):18-24. doi: 10.1007/s11282-019-00372-7. Epub 2019 Jan 24. PMID: 30680524.
33. Altunok Ünlü N, Coşgun A, Altan H. Evaluation of bone changes on dental panoramic radiography using mandibular indexes and fractal dimension analysis in children with familial Mediterranean fever. Oral Radiol. 2023 Apr;39(2):312-320. doi: 10.1007/s11282-022-00639-6. Epub 2022 Jul 20. PMID: 35854189.
34. Temur KT, Magat G, Yılmaz M, Ozcan S. Evaluation of the effect of sickle cell disease on the mandibular bone of children and adolescents by image texture and radiomorphometric analysis. Oral Radiol. 2023 Oct;39(4):792-801. doi: 10.1007/s11282-023-00704-8. Epub 2023 Aug 3. PMID: 37535233.
35. Apolinário AC, Sindeaux R, de Souza Figueiredo PT, Guimarães AT, Acevedo AC, Castro LC, de Paula AP, de Paula LM, de Melo NS, Leite AF. Dental panoramic indices and fractal dimension measurements in osteogenesis imperfecta children under pamidronate treatment. Dentomaxillofac Radiol. 2016;45(4):20150400. doi: 10.1259/dmfr.20150400. Epub 2016 Mar 24. PMID: 26954289; PMCID: PMC4846176.

36. Gumussoy I, Miloglu O, Cankaya E, Bayrakdar IS. Fractal properties of the trabecular pattern of the mandible in chronic renal failure. Dentomaxillofac Radiol. 2016;45(5):20150389. doi: 10.1259/dmfr.20150389. PMID: 27091088; PMCID: PMC5084698.
37. Ergün S, Saraçoglu A, Güneri P, Ozpinar B. Application of fractal analysis in hyperparathyroidism. Dentomaxillofac Radiol. 2009 Jul;38(5):281-8. doi: 10.1259/dmfr/24986192. PMID: 19474255.
38. Neves FS, Barros AS, Cerqueira GA, Cruz GA, Reis AA, Alves LB, Crusoé-Rebello I. Assessment of fractal dimension and panoramic radiomorphometric indices in women with celiac disease. Oral Radiol. 2020 Apr;36(2):141-147. doi: 10.1007/s11282-019-00388-z. Epub 2019 Apr 30. PMID: 31041668.
39. Yavuz E, Yardimci S. Comparison of periapical radiography, panoramic radiography, and CBCT in the evaluation of trabecular bone structure using fractal analysis. Oral Radiol. 2024 Jul;40(3):394-400. doi: 10.1007/s11282-024-00743-9. Epub 2024 Feb 26. Erratum in: Oral Radiol. 2024 Jul;40(3):401. doi: 10.1007/s11282-024-00752-8. PMID: 38407759.
40. Dedeoğlu N, Eşer G, Çelik Özen D, Altun O. Five-year change of panoramic radiomorphometric indices and fractal dimension values in type 2 diabetes patients. Oral Radiol. 2024 Jan;40(1):49-57. doi: 10.1007/s11282-023-00707-5. Epub 2023 Aug 23. PMID: 37610653.
41. Ay S, Gursoy UK, Erselcan T, Marakoglu I. Assessment of mandibular bone mineral density in patients with type 2 diabetes mellitus. Dentomaxillofac Radiol. 2005 Nov;34(6):327-31. doi: 10.1259/dmfr/52540810. PMID: 16227473.
42. Jolly SJ, Hegde C, Shetty NS. Assessment of Maxillary and Mandibular Bone Density in Controlled Type II Diabetes: A Computed Tomography Study. J Oral Implantol. 2015 Aug;41(4):400-5. doi: 10.1563/AAID-JOI-D-12-00248. Epub 2013 Jul 8. PMID: 23834616.
43. Kayipmaz S, Akçay S, Sezgin ÖS, Çandirli C. Trabecular structural changes in the mandibular condyle caused by degenerative osteoarthritis: a comparative study by cone-beam computed tomography imaging. Oral Radiol. 2019 Jan;35(1):51-58. doi: 10.1007/s11282-018-0324-1. Epub 2018 Mar 26. PMID: 30484185.
44. Pan H, Wu N, Yang T, He W. Association between bone mineral density and type 1 diabetes mellitus: a meta-analysis of cross-sectional studies. Diabetes Metab Res Rev. 2014 Oct;30(7):531-42. doi: 10.1002/dmrr.2508. PMID: 24376190.
45. Rodic T, Wölfel EM, Milovanovic P, Fiedler IAK, Cvetkovic D, Jähn K, Amling M, Sopta J, Nikolic S, Zivkovic V, Busse B, Djuric M. Bone quality analysis of jaw bones in individuals with type 2 diabetes mellitus-post mortem anatomical and microstructural evaluation. Clin Oral Investig. 2021 Jul;25(7):4377-4400. doi: 10.1007/s00784-020-03751-1. Epub 2021 Mar 11. PMID: 33694028.
46. Mosekilde L, Melsen F. Morphometric and dynamic studies of bone changes in hypothyroidism. Acta Pathol Microbiol Scand A. 1978 Jan;86(1):56-62. doi: 10.1111/j.1699-0463.1978.tb02012.x. PMID: 636889.
47. Eriksen EF, Mosekilde L, Melsen F. Kinetics of trabecular bone resorption and formation in hypothyroidism: evidence for a positive balance per remodeling cycle. Bone. 1986;7(2):101-8. doi: 10.1016/8756-3282(86)90681-2. PMID: 3718785.
48. Williams GR, Bassett JHD. Thyroid diseases and bone health. J Endocrinol Invest. 2018 Jan;41(1):99-109. doi: 10.1007/s40618-017-0753-4. Epub 2017 Aug 29. PMID: 28853052; PMCID: PMC5754375.
49. Ozturk EMA, Artas A. Evaluation of Bone Mineral Changes in Panoramic Radiographs of Hypothyroid and Hyperthyroid Patients Using Fractal Dimension Analysis. J Clin Densitom. 2024 Jan-Mar;27(1):101443. doi: 10.1016/j.jocd.2023.101443. Epub 2023 Nov 16. PMID: 38070428.
50. Nair A, Patil V, Bhardwaj I, Singhal DK, Smriti K, Chhaparwal Y, Chhaparwal S, Prabhu D. Radiomorphometric Parameters in Mandibular Panoramic Radiographs of Hypothyroid Patients: A Cross-Sectional Study. Clin Cosmet Investig Dent. 2025 Jan 14;17:31-37. doi: 10.2147/CCIDE.S502528. PMID: 39830592; PMCID: PMC11742241.
51. Yilmaz SG, Bayrak S. DETERMINATION OF MANDIBULAR BONE CHANGES IN PATIENTS WITH PRIMARY HYPOTHYROIDISM TREATED WITH LEVOTHYROXINE SODIUM. Acta Endocrinol (Buchar). 2023 Apr-Jun;19(2):201-207. doi: 10.4183/aeb.2023.201. Epub 2023 Oct 27. PMID: 37908892; PMCID: PMC10614580.
52. Grimnes G, Emaus N, Joakimsen RM, Figenschau Y, Jorde R. The relationship between serum TSH and bone mineral density in men and postmenopausal women: the Tromsø study. Thyroid. 2008 Nov;18(11):1147-55. doi: 10.1089/thy.2008.0158. PMID: 18925834.