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# Evaluation of the Relationship Between Jaw Involvement and Systemic Involvement in Type 1 Gaucher Disease

## Tip I Gaucher Hastalığında Çene Tutulumu ve Sistemik Tutulum Arasındaki İlişkinin Değerlendirilmesi

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## Abstract

**Objective:** This study aimed to assess osteopenia and trabeculation loss in the jaws of patients diagnosed with Type 1 Gaucher disease (GD) using cone-beam computed tomography (CBCT) images, unlike the routine computed tomography, and evaluate the correlation of jaw involvement with systemic involvement of GD. **Material and Methods:** A total of 16 patients, five males and 11 females, who were followed up with the diagnosis of Type I GD were included in the study group. Moreover, 16 age-and sex-matched healthy individuals in the study group were included in the control group. The records of patients at the time of diagnosis were obtained, and the presence of generalized osteopenia of jaws was investigated in the CBCT images, which were taken for maxillofacial examinations. **Results:** In comparison, the incidence of generalized osteopenia of jaws was significantly higher in the study group than in the control group (p=0.001). In addition, six out of seven patients with hepatomegaly and seven of 11 splenomegaly/operated patients had generalized osteopenia. However, no statistically significant relationship was observed between the presence of hepatomegaly/splenomegaly and generalized osteopenia. In addition, no significant difference was observed among bone involvement, hematological parameters, and jaw involvement in patients with Type 1 GD (p>0.05). **Conclusion: T**rabecular bone loss and osteopenia increased in Type 1 GD; therefore, patients with Type 1 GD should be evaluated periodically in terms of jaw involvement along with other parameters.

**Keywords:** Gaucher disease; jaw involvement; cone-beam computed tomography; generalized osteopenia

## Özet

**Amaç:** Bu çalışmada, Tip I Gaucher hastalığı (GH) tanısı konmuş hastaların rutin bilgisayarlı tomografiden farklı olarak konik ışınlı bilgisayarlı tomografi (KIBT) görüntülerinde çenelerde osteopeni ve trabekülasyon kaybının incelenmesi ve çene tutulumunun GH'nin sistemik tutulumuyla korelasyonunun değerlendirilmesidir. **Gereç ve Yöntemler:** Tip I GH tanısı ile izlenen 5 erkek, 11 kadın toplam 16 hasta çalışma grubuna dâhil edildi. Çalışma grubundaki hastalara benzer yaş ve cinsiyette 16 sağlıklı birey kontrol grubuna dahil edildi. Tanı anındaki dosya kayıtları elde edildi ve maksillofasiyal incelemeler için alınan KIBT görüntülerinde çenelerde generalize osteopeni varlığı sorgulandı. **Bulgular:** Çalışma ve kontrol grupları çenelerin generalize osteopenisi açısından karşılaştırıldığında, Tip I GH hastalarından oluşan çalışma grubunda bu bulgu kontrol grubuna göre anlamlı düzeyde yüksek bulundu (p=0.001). Hepatomegalik toplam 7 hastanın 6'sında; splenomegalik/opere olan toplam 11 hastanın 7'sinde generalize osteopeni vardı. Ancak, çalışma grubunda hepatomegali/splenomegali ile generalize osteopeni arasında istatistiksel anlamlı bir ilişki bulunmadı. Ayrıca Tip I GH hastalarının kemik tutulumu ve hematolojik parametreleri ile çene tutulumu arasında anlamlı bir farklılık bulunmadı (p>0.05). **Sonuç:** Tip I GH'de trabeküler kemik kaybı ve osteopeni artmıştır. Bu nedenle, Tip I GH hastaları diğer parametrelerle birlikte çenelerin tutulumu açısından periyodik olarak değerlendirilmelidir.

**Anahtar kelimeler:** Gaucher hastalığı; çene tutulumu; konik ışınlı bilgisayarlı tomografi; generalize osteopeni

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## Introduction

Gaucher disease (GD) is an autosomal recessive inherited disease characterized by glucocerebroside accumulation in the reticuloendothelial system because of glucocerebrosidase (GBA) enzyme deficiency (1). The incidence of GD is approximately one in 40,000-50,000 live births. The most common form is Type 1, which is the non-neuronopathic type. It constitutes nearly 90% of the patients. It is common in Ashkenazi Jews, and the ratio of the disease carrier is 1:13 (2).

The patients with GD commonly present with hepatosplenomegaly, osteopenia, bone pain, and cytopenia. These findings generally occur because of the local effects of the accumulated substances, organomegaly, and organ dysfunction (3). The diagnosis of GD should be confirmed through the measurement of GBA activity in peripheral blood leukocytes. Splenomegaly, which is seen in approximately 90%-95% of patients with GD, plays an essential role in the diagnosis (4). As the disease progresses, changes such as nodular lesions, infarct areas, necrosis, and fibrosis can be observed in the spleen (Figure 1) (5).

Bone findings can be frequently observed in Type 1 GD. However, Wenstrup et al. (6), in their study, examining the skeletal aspects of GD, divided GD-associated bone pathologies into three groups: a focal disease (irreversible lesions, for e.g., osteonecrosis and osteosclerosis); local disease (reversible abnormalities adjacent to the heavily involved bone marrow, for e.g., cortical thinning and bone deformities); and generalized osteopenia. However, this descriptive and morphology-focused classification of bone pathologies in GD does not explain different pathologies. Apart from this classification, GD can also be observed as a sequence of events (7). Glucosylceramide accumulation and progressive infiltration of Gaucher cells in the bone marrow may lead to thinning of the cortex, pathologic fractures, bone pain, bony infarcts, and osteopenia. Moreover, these bony features may be associated with macrophage-produced cytokines that disrupt the osteoblast and osteoclast balance. It is believed that the infiltration caused by Gaucher cells in the bone marrow increases the intra-bone pressure, thus causing ischemia and infarctions. The classic 'remodeling' disorder seen in GD is the Erlenmeyer flask deformity observed in the long bones, particularly in the distal femur in conventional radiological imaging (Figure 2). Erlenmeyer flask deformity is not a specific finding of GD; however, it is observed in approximately 80% of patients (8) and can help in diagnoses.

GD is a rare disease; hence, it is necessary to suspect the disease first for an accurate diagnosis. GD should be considered in pa-

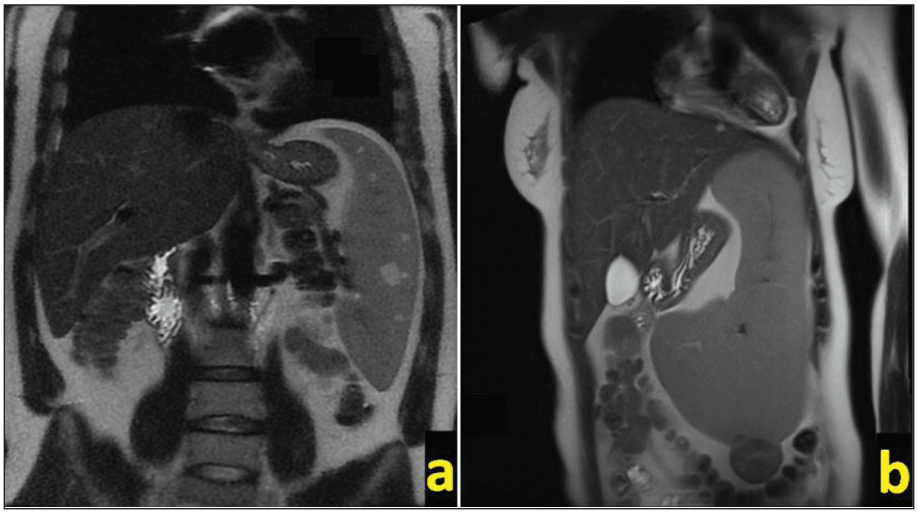


**FIGURE 1:** a) The multiple nodular appearance of the spleen on T2-weighted coronal magnetic resonance image of a 33-year-old male patient with Gaucher disease. b) The massive hepatosplenomegaly on T2-weighted coronal magnetic resonance image of a 39-year-old female patient with Gaucher disease.
*(Courtesy of Prof. Dr. Fahri Bayram)*

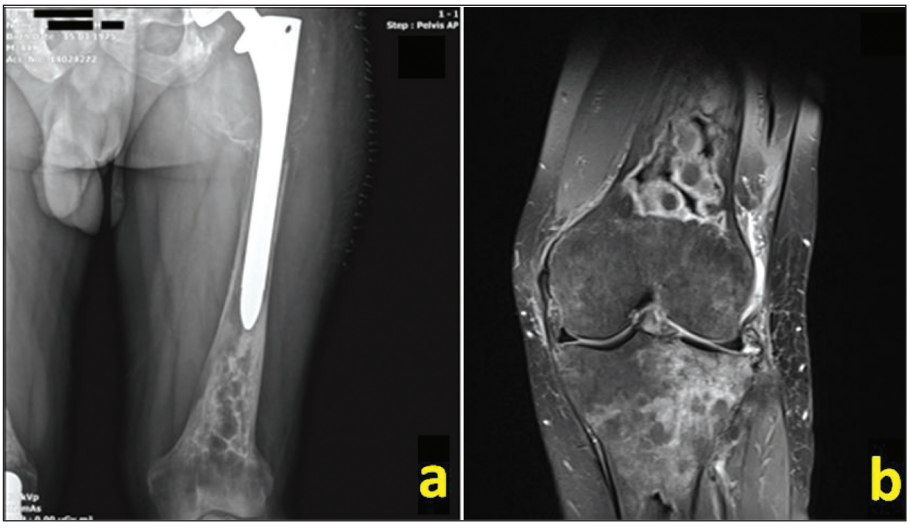


**FIGURE 2:** a) Erlenmeyer flask deformity caused by an enlargement of the distal femur on T1-weighted coronal magnetic resonance image of a 44-year-old male patient who was operated because of osteonecrosis and joint deformation; b) The osteonecrosis areas on the magnetic resonance image of the same patient *(Courtesy of Prof. Dr. Fahri Bayram)*

tients with bone pain, chronic fatigue, thrombocytopenia and/or hepatosplenomegaly, and low bone densitometry values for their age (secondary osteoporosis). For dentistry, early diagnosis of the disease is crucial to distinguish GD lesions from other bone diseases such as mandibular osteoporosis or ameloblastoma because of its similar radiographic features. This study aimed to examine the osteopenia and trabeculation loss of the jaws using cone-beam computed tomography (CBCT) images of patients with Type 1 GD who were referred to our department and evaluate the correlation of jaw involvement with systemic involvement of GD.

## Material and Methods

This study was evaluated by the Erciyes University Faculty of Medicine Clinical Research Ethics Committee and approved with decision number 2019/11 (12.06.2019). The study was conducted in accordance with the Helsinki Declaration principles.

### Study Group

A total of 16 patients (five males and 11 females) being followed up with the diagnosis of Type 1 GD in the Erciyes University, Faculty of Medicine, Department of Endocrinology and Metabolism, Gastroenterology, and Hematology were included in the study. Patients had basic examinations, including routine laboratory examinations, measurements of liver and spleen sizes, bone symptom findings, and dual-energy X-ray absorptiometry (DEXA) examinations at the time of diagnosis. The medical records obtained during the first evaluation phase of the patients with Type 1 GD were examined. The patients' age at the time of admission, complaints, parental consanguinity, family history of a similar disease or sibling history, physical examination findings at the time of diagnosis, GBA gene mutations, GBA enzyme activity, history of splenectomy, the age of initiation of enzyme replacement therapy, and the total treatment duration were recorded. Body mass index (BMI) was calculated using the weight and height values of the patients at the time of diagnosis (weight [kg]/height [$m^2$]). Underweight was defined as BMI of less than 18.5 kg/$m^2$, normal weight as 18.5 to <25 kg/$m^2$, overweight as 25.0 to <30 kg/$m^2$, and obese as 30.0 kg/$m^2$ or higher.

Complete blood count values and biochemical examination results of the patients were obtained at the time of diagnosis. Normal values for hemoglobin were 12-16 g/dL for women and 14-18 g/dL for men. Thrombocytopenia was considered if the platelet values were below 130×10/$mm^3$ and leukopenia if the leukocyte values were below 4500/mm (9).

Bone involvement assessment was performed by assessing bone marrow in magnetic resonance images of a limited number of patients and using DEXA (Hologic QDR 4500 Elite densitometer, Hologic Inc., Waltham, MA, USA) in all patients. Bone mineral density measurements were made using DEXA, including lumbar 1-4, vertebrae, and femur.

Symptom severity scores of patients were calculated using examinations performed at the time of diagnosis. Symptom Severity Score Index (SSI) was developed in 1989 to objectively evaluate the phenotypic expression of Type 1 GD (10). However, the scoring criteria were changed in 1992, and SSI became useable in all GD types. In this study, the modified symptom severity index (Zimran Severity Score Index) of Zimran was used (9).

Subsequently, patients were directed to the Erciyes University, Faculty of Dentistry, Department of Oral and Maxillofacial Radiology for maxillofacial examinations. The changes in the maxillofacial regions of patients were evaluated, and the relationship between initial hematological parameters, visceral involvement, and bone involvement was examined.

### Control Group

A total of 16 healthy individuals were included in the study to compare the CBCT findings of GD patients. The control group was formed by retrospectively scanning the patient records, and those patients were selected who did not have any systemic disease or continuous drug usage. The exclusion criteria of the control group were as follows:

- Having a systemic disease that may affect the bone metabolism
- Using a medication that can affect the bone metabolism
- Images that do not have sufficient diagnostic quality in terms of making the necessary evaluations
- Being below the age of 18 years

Presence of lesions involving the maxillofacial area

- History of surgery and traumatic operations involving the maxillofacial area

### Cone-Beam Computed Tomography Protocol and Evaluation of Images

CBCT images of the patients included in the study were obtained using the New Tom 5G CBCT device (FP, Quantitative Radiology, Verona, Italy). All images had the following parameters: 110 kV and 3-5 mA, 0.25 mm voxel size, 18×16 cm FOV (field of view), 0.25 mm slice thickness, and 5.4 s exposure time. CBCT images were analyzed on a Dell Precision T5400 workstation (Dell, Round Rock, Texas, USA) using NNT software (NNT version 3.0; NewTom, Verona, Italy), with a 32-inch Dell liquid-crystal display with a resolution of 1280×1024 pixels in a dark room. A total of 16 CBCT images of patients with Type 1 GD were questioned in terms of loss of trabeculation and generalized osteopenia in jaws.

All radiological examinations were performed by two researchers working at the Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Erciyes University. Moreover, 20% of the evaluations were repeated one month after the first evaluation to determine the intra-observer reliability.

### Statistical Analysis

The IBM SPSS.23 (IBM Corp., Armonk, NY, USA) program was used for statistical analysis. Normality assumptions of continuous variables were examined using Skewness and Kurtosis coefficients, Shapiro-Wilk test, and histograms. Mean, standard deviation, median, and rank average were given in the descriptive statistics of continuous variables, and frequency (n) and percentage (%) values were given in the definition of categorical variables. The Mann-Whitney test was used for comparison of continuous variables that did not show normal distribution with two-level variables, and the Kruskal-Wallis test was used for comparison with three or more levels. Relationships between categorical variables were examined with chi-square/Fisher exact analysis, and that between continuous variables were examined with Spearman's (Spearman's rho) correlation analysis. Spearman's correlation coefficient was calculated to determine the consistency between the measurements obtained at different times and the internal consistency between the observers. The significance level was accepted as $p<0.05$ in all analyses.

## Results

A total of 32 patients (11 [68.75%] females, five [31.75%] males each in both study and control groups) were included in the study. No significant difference was observed in age and gender distribution between the control and study groups (p>0.05). The age of the patients included in the study group ranged between 19 and 60 years, and the mean age was 34.56 years. Table 1 shows the distribution of the initial characteristics of the patients with GD. The most common gene mutation was P.N409S homozygote. Of the 16 patients included in the study group, 56.3% had osteopenia in lumbal vertebrae and 81.3% in the femur (Table 2). Table 3 shows the results of the laboratory tests of patients in the study group. The distribution of the characteristics of visceral involvement and SSI of the patients in the study group is shown in Table 4. In the study group, 43.8% of patients had hepatomegaly, and 50% had splenomegaly.

In CBCT images of patients with GD, generalized osteopenia of jaws was observed in 10 (62.5%) patients and not in six (37.5%) patients. In the control group, only one (6.3%) patient had generalized osteopenia, whereas no findings were observed in the remaining 15 (93.8%) patients. In comparison, a statistically significant difference was found between the two groups (p=0.001). Table 5 shows the comparison of the DEXA results of patients with GD according to the hepatomegaly and splenomegaly groups; no significant difference was found between the groups in any of the parameters (p>0.05). In the study group, no significant relationship was found between the hepatomegaly and splenomegaly findings and generalized osteopenia of jaws (p=0.145, p=1.000, respectively). In addition, six (85.7%) out of seven patients with abnormal hepatomegaly parameters and seven (63.6%) out of 11 patients whose splenomegaly parameter was abnormal/who were operated had generalized osteopenia of jaws (Table 6).

No significant difference was found between jaw and hematological involvement in patients with Type 1 GD (Table 7).

Table 1. Distribution of the initial characteristics of the patients with Gaucher disease.

| | n (%) |
|---|---|
| Parental consanguinity | |
| Absent | 8 (50.0) |
| Present | 8 (50.0) |
| Sibling history | |
| Absent | 3 (18.8) |
| Present | 13 (81.3) |
| Complaints at the time of admission | |
| Fatigue, weakness, and bone pain | 1 (6.3) |
| Presence of hepatosplenomegaly in the patient presenting with excessive sweating | 1 (6.3) |
| DEXA scans | 7 (43.8) |
| Osteoporosis | 1 (6.3) |
| Abdominal and bone pain | 1 (6.3) |
| Abdominal pain and weakness | 2 (12.5) |
| Abdominal pain | 1 (6.3) |
| Splenomegaly | 2 (12.5) |
| Body mass index | |
| Underweight | 2 (12.5) |
| Normal weight | 9 (56.3) |
| Overweight | 5 (31.3) |
| GBA gene activity | |
| Abnormal | 16 (100) |
| Normal | 0 (0) |

DEXA: Dual-energy X-ray absorptiometry; GBA: Glucocerebrosidase.

Table 2. Distribution of the findings regarding bone involvement.

| | n (%) |
|---|---|
| Lumbal vertebrae | |
| Normal | 2 (12.5) |
| Osteopenia | 9 (56.3) |
| Osteoporosis | 5 (31.3) |
| Femur | |
| Normal | 1 (6.3) |
| Osteopenia | 13 (81.3) |
| Osteoporosis | 1 (6.3) |
| - | 1 (6.3) |
| Subjective skeletal findings | |
| Absent | 1 (6.3) |
| Mild/intermittent pain | 10 (62.5) |
| Chronic pain | 5 (31.3) |
| Fractures | |
| Absent | 15 (93.8) |
| Post-traumatic fracture | 1 (6.3) |

-; DEXA scan could not be performed because of leg prosthesis in a patient.

Table 3. Laboratory findings of the patients with Gaucher disease.

| | n (%) |
|---|---|
| Leukocyte | |
| Lower than normal | 6 (37.5) |
| Normal | 7 (43.8) |
| Higher than normal | 3 (18.8) |
| Hemoglobin | |
| Lower than normal | 6 (37.5) |
| Normal | 10 (62.5) |
| Platelet | |
| Lower than normal | 6 (37.5) |
| Normal | 8 (50.0) |
| Higher than normal | 2 (12.5) |
| AST, ALT, GGT | |
| Normal | 16 (100) |
| ALP | |
| Normal | 15 (93.8) |
| Higher than normal | 1 (6.3) |
| TSH | |
| Normal | 14 (87.5) |
| Higher than normal | 2 (12.5) |
| Ferritin | |
| Normal | 12 (75.0) |
| Higher than normal | 4 (25.0) |
| Vitamin B12 | |
| Lower than normal | 2 (12.5) |
| Normal | 12 (75.0) |
| Higher than normal | 2 (12.5) |
| Cholesterol | |
| Normal | 15 (93.8) |
| Higher than normal | 1 (6.3) |
| LDL | |
| Lower than normal | 13 (81.3) |
| Normal | 3 (18.8) |
| HDL | |
| Lower than normal | 7 (43.8) |
| Normal | 5 (31.3) |
| Higher than normal | 4 (25.0) |
| Triglyceride | |
| Normal | 9 (56.3) |
| Higher than normal | 7 (43.8) |
| Total protein | |
| Lower than normal | 1 (6.3) |
| Normal | 15 (93.8) |
| Albumin | |
| Lower than normal | 1 (6.3) |
| Normal | 15 (93.8) |
| Lyso level | |
| Higher than normal | 7 (43.8) |
| Not examined | 9 (56.3) |
| Normal | 15 (93.8) |
| Higher than normal | 1 (6.3) |

AST: Aspartate transaminase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; TSH: Thyroid-stimulating hormone; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

When SSI scores were compared according to jaw involvement, patients with and without generalized osteopenia of jaws were not different in terms of SSI score (p=0.267). Patients who were underweight, normal, and overweight in BMI were not different in terms of SSI score (p=0.820). When examining the relationship between generalized osteopenia of the jaws and bone involvement in patients with GD, patients with signs of jaw involvement in their CBCT images did not show a statistically significant difference in terms of values (p>0.05) (Table 8).

## Discussion

In this study, we examined the CBCT images of 16 patients and found that the jaw involvement was 62.5% in patients with Type 1 GD. Long bone involvement is common in GD, whereas maxillofacial bone involvement is less common. Jaw bone involvement is typically asymptomatic (11,12) and can be detected as incidental findings in routine dental radiographs (13). These radiographic findings may include generalized rarefaction of the jaw bone, loss of trabecular structure, enlarged bone marrow cavities, and pseudocystic radiolucent lesions. However, jaw involvement associated with GD varies from asymptomatic radiographic findings to painful lesions.

Only a few studies with a small number of patients exist in the literature regarding the jaw involvement of GD. In addition, no study comprehensively investigated the correlation between the systemic involvement of

Table 4. Distribution of the visceral involvement and SSI of the patients with Gaucher disease.

| | **n (%)** |
|---|---|
| Hepatomegaly | |
| Normal | 9 (56.3) |
| Abnormal | 7 (43.8) |
| Splenomegaly | |
| Normal | 5 (31.3) |
| Abnormal | 8 (50.0) |
| Operated | 3 (18.8) |
| SSI | |
| Mild | 15 (93.8) |
| Moderate | 1 (6.3) |

SSI: Symptom Severity Score Index.

Table 5. Comparison of DEXA scores according to hepatomegaly and splenomegaly.*

| | Groups | n | Mean rank | Median | p value |
|---|---|---|---|---|---|
| Hepatomegaly | | | | | |
| DEXA L Total Z score | Normal | 9 | 8.78 | -2.00 | .791 |
| | Hepatomegaly | 7 | 8.14 | -2.20 | |
| DEXA L Total BMD | Normal | 9 | 8.56 | .83 | .958 |
| | Hepatomegaly | 7 | 8.43 | .84 | |
| DEXA Total Z score | Normal | 9 | 8.67 | -1.40 | .478 |
| | Hepatomegaly | 6 | 7.00 | -1.70 | |
| DEXA Total BMD | Normal | 9 | 8.11 | .78 | .906 |
| | Hepatomegaly | 6 | 7.83 | .77 | |
| Splenomegaly | | | | | |
| DEXA L Total Z score | Normal | 5 | 6.60 | -2.40 | .280 |
| | Splenomegaly/operated | 11 | 9.36 | -1.70 | |
| DEXA L Total BMD | Normal | 5 | 6.60 | .79 | .282 |
| | Splenomegaly/operated | 11 | 9.36 | .86 | |
| DEXA Total Z score | Normal | 5 | 8.70 | -1.40 | .667 |
| | Splenomegaly/operated | 10 | 7.65 | -1.50 | |
| DEXA Total BMD | Normal | 5 | 8.00 | .78 | 1.000 |
| | Splenomegaly/operated | 10 | 8.00 | .78 | |

*Mann Whitney test. DEXA: Dual-energy X-ray absorptiometry; L: Lumbal vertebrae; BMD: Bone mineral density.

Table 6. Relationship between generalized osteopenia of jaws and hepatomegaly and splenomegaly in the study group.

| | | Normal n (%) | Hepatomegaly n (%) | p value |
|---|---|---|---|---|
| Generalized osteopenia of jaws | Absent | 5 (55.6) | 1 (14.3) | .145 |
| | Present | 4 (44.4) | 6 (85.7) | |
| | | **Normal n (%)** | **Splenomegaly/operated n (%)** | **p value** |
| Generalized osteopenia of jaws | Absent | 2 (40.0) | 4 (36.4) | 1.000 |
| | Present | 3 (60.0) | 7 (63.6) | |

GD, characterized by triple involvement: bone involvement, visceral involvement, and hematological involvement, and jaw involvement in these abovementioned studies. Several case reports have also stated that the mandible is a nidus of Gaucher cell infiltration and/or bone crisis (14-18).

In previous studies, loss of the trabecular structure of the jaws and an increase in osteopenia were frequently observed in patients with GD. Bender et al. (14) reported a loss of trabecular structure in the premolar-molar region and generalized osteoporosis in the mandibular region in their case report of a 13-year-old female patient, and they stated that there was an increased loss of trabecular structure, endosteal bone degeneration, and decreased bone thickness in the follow-up report of the same patient (19).

Nobre et al. (20) found generalized osteopenia of jaws in the CBCT images in all of the ten patients in their study. Similarly, Zeevi et al. (12) found trabecular reduction/osteopenia/generalized rarefaction in 31 (83.8%) patients out of 37 cases compiled. Carter et al. (21) examined the panoramic images of 28 patients and found generalized osteopenia of jaws in only five patients. Several radiographic findings can only be confirmed by three-dimensional imaging, and two-dimensional conventional techniques may be insufficient in imaging

Table 7. Relationship between generalized osteopenia of jaws and triglyceride, hemoglobin, leukocyte, and platelets in the study group.

| | Triglyceride | Normal n (%) | Higher than normal n (%) | p value |
|---|---|---|---|---|
| Generalized osteopenia of jaws | Absent | 4 (44.4) | 2 (28.6) | .633 |
| | Present | 5 (55.6) | 5 (71.4) | |
| | **Hemoglobin** | **Lower than normal n (%)** | **Normal n (%)** | **p value** |
| Generalized osteopenia of jaws | Absent | 3 (50.0) | 3 (30.0) | .607 |
| | Present | 3 (50.0) | 7 (70.0) | |
| | **Leukocyte** | **Lower than normal n (%)** | **Normal/higher than normal n (%)** | **p value** |
| Generalized osteopenia of jaws | Absent | 3 (50.0) | 3 (30.0) | .607 |
| | Present | 3 (50.0) | 7 (70.0) | |
| | **Platelet** | **Lower than normal n (%)** | **Normal/higher than normal n (%)** | **p value** |
| Generalized osteopenia of jaws | Absent | 2 (33.3) | 4 (40.0) | 1.000 |
| | Present | 4 (66.7) | 6 (60.0) | |

Table 8. Comparison of DEXA scores according to the presence of generalized osteopenia of jaws.

| | Mean | Median | Mean rank | p value |
|---|---|---|---|---|
| DEXA L Total Z score | | | | |
| Generalized osteopenia of jaws | | | | .277 |
| Absent | -1.70 | -1.75 | 10.17 | |
| Present | -1.91 | -2.30 | 7.50 | |
| DEXA L Total BMD | | | | |
| Generalized osteopenia of jaws | | | | .278 |
| Absent | .87 | .88 | 10.17 | |
| Present | .85 | .81 | 7.50 | |
| DEXA Total Z score | | | | |
| Generalized osteopenia of jaws | | | | .953 |
| Absent | -1.45 | -1.40 | 7.92 | |
| Present | -1.44 | -1.60 | 8.06 | |
| DEXA Total BMD | | | | |
| Generalized osteopenia of jaws | | | | .814 |
| Absent | .76 | .78 | 7.67 | |
| Present | .77 | .78 | 8.22 | |

DEXA: Dual-energy X-ray absorptiometry; L: Lumbal vertebrae; BMD: Bone mineral density.

the bone architecture. Therefore, the results obtained by Carter et al. (21) may be lower than the real rates. Our findings were consistent with the literature.

There is considerable heterogeneity in the clinical presentation of skeletal manifestations among patients with GD. Zimran et al. (9) developed the SSI to facilitate communication regarding visceral and bone symptoms of GD. Painful bone crises, pathological fractures, and restrictive bone deformities are all associated with severe disease and impaired life quality in some patients with GD (21). According to our findings, the disease severity scores showed that the average SSI value was 6±2.56. In terms of SSI

values, 15 out of 16 patients (93.8%) had mild disease, and one (6.3%) had moderate disease. SSI values of our patients varied between 3 and 13. Carter et al. (21), in their study with 28 patients with GD, found the scores of patients in the range of 2 to 19, excluding two patients whose SSI data were not available. Nobre et al. (20) found that clinical and radiographic findings showed great differences in their patient group, and some clinical data were not correlated with radiographic images. This clinical heterogeneity, which determines all forms of GD, was probably because of more than 200 mutations such as point mutations, insertions, and deletions in the *GBA* gene (20,22,23). In our study, no significant relationship was found between SSI scores and the presence of generalized osteopenia of jaws in CBCT images and BMI.

Carter et al. (21) reported that the delay in tooth eruption was associated with mild to moderate general bone involvement rather than severe bone involvement. Nevertheless, among the dental findings and systemic parameters of GD, no correlation was reported between the presence of generalized osteopenia of jaws and general bone involvement and between the history of splenectomy and tooth eruption. However, in this study, the delay in tooth eruption could not be evaluated because of the time of diagnosis of adult patients. In addition, no statistically significant difference was found between the presence of generalized osteopenia of jaws in the CBCT images and DEXA scores.

The DEXA scores of patients with GD did not differ according to hepatomegaly and splenomegaly groups. On evaluating the relationship between the CBCT findings and hepatomegaly and splenomegaly, no significant relationship was found between hepatomegaly and splenomegaly and generalized osteopenia of the jaws. However, in six (85.7%) of the seven patients with hepatomegaly, trabeculation loss in the jaws was observed, and it was observed in seven (63.6%) of 11 patients with spleno-megaly. No significant relationship was found between the abnormalities of laboratory tests such as triglyceride, hemoglobin, leukocyte, and platelet levels and generalized osteopenia of the jaws in patients with GD. In detail, generalized osteopenia of jaws was observed in five (71.4%) of seven patients with higher triglyceride levels, three (50%) of six patients with lower hemoglobin values, three (50%) of six patients with lower leukocyte values, and four (66.7%) of six patients with a lower platelet value. Our findings were consistent with that of Carter et al.'s study (21), wherein no statistically significant relationship was reported between the dental findings of GD and its systemic parameters. However, although GD is a common disease among lysosomal storage diseases, it is a rare disease in the general population. Therefore, the limited number of patients included in the study group can be considered a limitation of the study. Studies with larger sample sizes should be conducted to verify the results we have obtained.

Decreased bone density and cortical thinning are observed in almost all patients with GD (8). The trabecular and cortical bone may be affected locally or widely. Osteopenia is associated with an increased risk of bone fractures in both adult and pediatric patients (24). In the literature, several case reports and studies have confirmed that an intense increase in osteopenia and losses in the trabecular structure were observed in the presence of jaw involvement of GD (12,16,17,23,25). CBCT provides a three-dimensional analysis of maxillofacial structures in the jaw involvement of GD. In addition, it allows qualitative and quantitative evaluation of bone structures (26). Serious problems such as osteomyelitis may occur because of trabecular bone loss in the mandible. Because of the decreased blood flow, the sensitivity of the bone to infection may increase with GD (27,28). In addition, a risk of pathological fracture exists in areas where trabeculae are weakened. Therefore, the importance of oral hygiene should be emphasized to prevent odontogenic infections and secondary osteomyelitis in the relevant bone if there is any finding related to GD. A soft diet should be recommended to avoid pathological fractures of the jaw.

## Conclusion

In conclusion, this study showed that the losses in the trabecular structure of the jaws were significantly higher in patients with GD,

whereas a difference between the jaw involvement and systemic involvement of GD was not found. Patients with Type I GD should be evaluated periodically because of the risk of jaw involvement. Several of these patients receive dental treatment without knowing about the disease, and their symptoms are not considered in the planning of the treatment because physicians have limited knowledge about disease symptoms. However, while evaluating patients with lysosomal storage disorders, taking a medical history with a comprehensive examination and careful analysis of the signs and symptoms of the disease are extremely crucial. When GD is suspected in undiagnosed patients, patients should be referred to the appropriate departments.

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## Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

## Authorship Contributions

Idea/Concept: Firdevs Aşantoğrol, Fahri Bayram, Emin Murat Canger; Design: Firdevs Aşantoğrol; Control/Supervision: Firdevs Aşantoğrol, Fahri Bayram, Emin Murat Canger; Data Collection and/or Processing: Firdevs Aşantoğrol, Fahri Bayram, Hüseyin Dursun; Analysis and/or Interpretation: Firdevs Aşantoğrol, Fahri Bayram, Emin Murat Canger, Hüseyin Dursun; Literature Review: Firdevs Aşantoğrol; Writing the Article: Firdevs Aşantoğrol; Critical Review: Firdevs Aşantoğrol, Fahri Bayram, Emin Murat Canger; References and Fundings: Fahri Bayram, Emin Murat Canger; Materials: Firdevs Aşantoğrol, Fahri Bayram, Hüseyin Dursun, Emin Murat Canger.

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