EJMA

DOI: 10.14744/ejma.2023.26349
EJMA 2023;3(1):15–18

Research Article

Secondary Causes of Osteoporosis: Tertiary Endocrine Center Experience

Zafer Pekkolay,[1] Omer Faruk Ince,[2] Sadiye Altun Tuzcu,[3] Bekir Tasdemir,[3] Alpaslan Kemal Tuzcu[1]

[1]Deparment of Endocrinology, Dicle University Faculty of Medicine, Diyarbakır, Türkiye
[2]Deparment of Internal Medicine, Dicle University Faculty of Medicine, Diyarbakır, Türkiye
[3]Deparment of Nuclear Medicine, Dicle University Faculty of Medicine, Diyarbakır, Türkiye

Abstract

Objectives: The aim of this study was to investigate the causes of secondary osteoporosis in tertiary endocrine center.

Methods: This retrospective study consisted of patients applying to tertiary endocrine center between January 1, 2019 and December 31, 2021 whose bone mineral density has been examined for any reason, as well as patients aged 18-50 who are suspected of secondary osteoporosis with a Z score of-2.0 SD or below.

Results: There were 5688 DXA reports screening, and 1686 were between the ages of 18 and 50. The study included 184 patients with complete data. There was a mean age of 30.9 years. The majority of the patients were males (58.2%). Men's Z score was found to be lower (-3.4 vs-2.98) ($p<0.01$). Steroid use was the most common cause of drug-induced osteoporosis. Vitamin D level was <30 ng/ml in 73.9% of patients with secondary osteoporosis. When the study patients were evaluated in terms of secondary etiologies, hypogonadism 12%, thalassemia 10.9%, gluten enteropathy 9.8%, steroid use 8%, 7.6% connective tissue diseases, 7.1% hypercalciuria, 7.1% idiopathic, 4.9% vitamin D deficiency, 3.8% cachexia, 2.7% parathyroid adenoma were found as etiology in the patient.

Conclusion: Secondary osteoporosis is more common in men. Men's bone mineral density is worse than women's. Etiological causes were determined as hypogonadotropic hypogonadism, thalassemia, celiac disease, and steroid use, respectively. Steroid use was the most common cause of drug-induced osteoporosis. About three-quarters of patients with secondary osteoporosis do not have enough vitamin D.

Keywords: Adult, bone mineral density, secondary osteoporosis

Cite This Article: *Pekkolay Z, İnce OF, Altun Tuzcu S, Tasdemir B, Tuzcu AK. Secondary Causes of Osteoporosis: Tertiary Endocrine Center Experience. EJMA 2023;3(1):15–18.*

Secondary osteoporosis is characterized by loss of bone mass due to an underlying disease or drug use, as well as increased fracture risk.[1] Almost 50% of men suffer from secondary causes of osteoporosis, over 50% of premenopausal women, and 1/3 of postmenopausal women.[2] Secondary osteoporosis has many causes. Among these are endocrine disorders, hematological disorders, some drugs, malabsorption syndromes, and inflammatory conditions.[3] As a result of secondary osteoporosis, peak bone mass is insufficient. Fractures are most likely to occur in these situations. Determining and treating the etiological cause is critical to preventing fractures.[4]

The etiologies of secondary osteoporosis in Türkiye are unclear. The aim of this study was to investigate the causes of secondary osteoporosis in tertiary endocrine center.

Address for correspondence: Zafer Pekkolay, MD. Dicle Üniversitesi Tıp Fakültesi, Endokrinoloji Anabilim Dalı, Diyarbakır, Türkiye
Phone: +90 412 248 80 01 **E-mail:** drpekkolay@gmail.com

Submitted Date: January 21, 2023 **Accepted Date:** March 05, 2023 **Available Online Date:** June 23, 2023

Methods

Patient Selection and Evaluation

In this study, 2248 patients between the ages of 18–50 and 5688 DXA results who applied to tertiary endocrine center between January 2019 and December 2021 were selected and among these patients, DXA result Z score < –2, DXA result not secondary to chronic kidney failure, malignancy and diabetes. The total number of patients who underwent DXA was 5688. Of the 5688 patients who received DXA, 1686, ie 29% (29.5), were between the ages of 18–50. 245 of the patients who were examined were 14.5% of the patients who met the definition of secondary osteoporosis. Among these patients, the information available in the registry in terms of the etiology of secondary osteoporosis in 184 patients who were examined for secondary osteoporosis was retrospectively reviewed.

During diagnosis and before treatment, patients' clinical information, drugs used, routine tests (hemogram, urea, creatinine, glucose, albumin, ALT, AST, ALP, GGT, iron, iron binding capacity, calcium, phosphorus, 25-OH vitamin D, PTH) , TSH, freeT3, free T4, FSH, LH, estradiol, testosterone, prolactin, IGF-1, cortisol, ACTH, ferritin, cortisol level after dexamethasone suppression test, 24-hour urine calcium, tissue transglutaminase IgA, HLAB27, ANA, AntidsDNA, Anti ccp antibody and HbA1c levels were scanned from the files.

Inclusion Criteria

Patients between the ages of 18–50 who were diagnosed with secondary osteoporosis and who were evaluated and examined in terms of secondary osteoporosis etiologies were selected.

Exclusion criteria

I. Patients younger than 18 years old and patients older than 50 years
II. Menopause
III. History of malignancy
IV. Diabetes mellitus
V. Patients whose causes of secondary osteoporosis were not examined.

Statistical Analyses

Data analysis was performed using the SPSS 26 (Statistical Package Social Science) statistical program. Categorical data were evaluated with the Mann Whitney U test and Kruskal Wallis tests, since the chi-square and continuous data did not fit the normal distribution. P<0.05 was considered statistically significant.

Results

A total of 5688 patients were screened. 184 patients with complete data were included in the study (Fig. 1). 52.8% of the patients were male. Steroid use was the most common in drug-related osteoporosis. The mean age was 31.4 years for males and 30.6 years for females, respectively. The mean Z score was found to be-3.4 for males and –2.98 for females, respectively. The percentage of patients with vitamin D levels >30 ng/ml and <20 ng/ml were 43% and 26.1%, respectively (Table 1).

The most common secondary cause of osteoporosis was found to be hypogonadism (12%).

Then the etiological causes, thalassemia, celiac disease, steroid use, idiopathic hypercalciuria, idiopathic causes and pituitary insufficiency respectively (Table 2).

The mean Z scores of the patients according to the etiology are summarized in Table 3.

Discussion

In this study, we detected secondary osteoporosis in one of seven patients who underwent DXA for any reason. Women are more likely to develop secondary osteoporosis than men, but men have a lower bone mineral density. We determined the etiological causes as hypogonadotropic hypogonadism, thalassemia, celiac disease, and steroid use, respectively. In about 10% of patients aged 18–50 years who underwent DXA, a secondary etiology was detected.

Secondary causes of osteoporosis are common. It found that secondary causes of osteoporosis were identified in more than half of men with osteoporosis, half of perimenopausal women, and twenty percent of postmenopausal women.[5]

If the initial biochemical tests for the etiology of patients with secondary osteoporosis include calcium, parathormone, 24-hour calcium level, thyroid functions, gonadal status, 25-hydroxyvitamin D level, ferritin, and antibodies to celiac disease, most secondary causes will be screened.

Glucocorticoid-induced osteoporosis is the most common cause of iatrogenic osteoporosis.[6]

In our study, the most common drug causing secondary osteoporosis was corticosteroids. Steroids cause severe bone loss, especially within a month of starting to use them. Therefore, adequate vitamin D and calcium replacement should be given to patients who will receive steroids.

DXA data cannot distinguish between osteomalacia and osteoporosis. Therefore, vitamin D level should be requested in all patients with osteoporosis. Osteoporosis is characterized by bone microarchitecture deterioration; osteomalacia is characterized by a disorder of mineralization. The two conditions can lead to fractures of the bones.[7] In our study, only one-fourth of the patients had adequate levels of vitamin D.

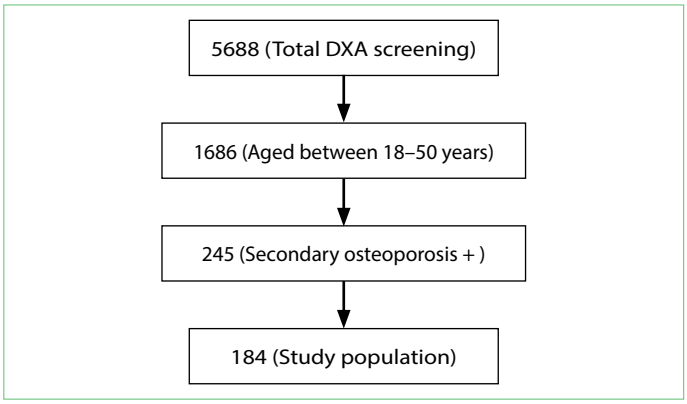

Figure 1. Patients' flow chart.

Thalassemia causes osteoporosis in many ways. These can be listed simply as deterioration of bone structure, cytokines, iron deposition in the bone and hypogonadism.[8] The high number of thalassemia patients in our study was interesting and showed that these patients were not examined in detail in terms of osteoporosis.

In male patients with secondary osteoporosis, hypogonadism, alcohol use, and steroid use are common causes.[9] In our study, the high number of patients diagnosed with osteoporosis due to pituitary involvement and the male gender predominance was interesting.

About 1% of the population suffers from celiac disease. The majority of patients go undiagnosed. Osteoporosis is also an extra-intestinal complication of celiac disease.[10] Celiac disease is characterized by deficiencies in bone mineralization and decreased peak bone mass due to insufficient intestinal absorption of calcium, phosphorus, and vitamin D. In our study, one of ten patients had celiac disease. Patients with celiac disease-related osteoporosis may be asymptomatic for celiac disease.

Idiopathic hypercalciuria associated with increased intestinal calcium absorption, decreased tubular calcium reabsorption and increased bone resorption may be the cause of secondary osteoporosis.[11] In patients with secondary osteoporosis, 24-hour urine calcium testing may be helpful for etiology; If >300 mg in men and >250 mg in women, hypercalciuria is present.

The strengths of our study are the large number of adult patients referred to a reference endocrine center for the etiology of secondary osteoporosis, and the detailed analysis of secondary etiologies.

Another feature of our study was that patients with hyperparathyroidism, thalassemia, idiopathic hypercalciuria, osteogenesis imperfecta and hypogonadism had worse bone mineral density than other diseases.

This study has limitations in that, as a retrospective study, most patients who fit the definition of secondary osteoporosis were excluded from the study because the etiological causes were not adequately explored.

In conclusion, secondary osteoporosis is more common in men, and men have worse bone mineral density. The vast majority of patients with secondary osteoporosis do not have enough vitamin D. Etiological causes, in order of frequency, are hypogonadotropic hypogonadism, thalassemia, celiac disease and steroid use. Steroid use in drug-induced osteoporosis is still in the foreground.

Table 1. Baseline characteristics of patients

Characteristics	Female	Male
n: 184	47.2%	52.8%
Age (mean, years)	30.6	31.4
Z score (mean)	–2.98	–3.4
Drug: Steroid use (%)	25.9	18.6
Most common disease	hypogonadism	
Vitamin D level >30 ng/ml	26.1%	
Vitamin D level <20 ng/ml	43%	

Table 2. Etiological distribution and percentage of secondary osteoporosis patients

Disease	n	%
Hypogonadism	22	12
Thalassemia	20	10.9
Celiac disease	18	9.8
Steroid use	15	8
Idiopathic hypercalciuria	13	7.1
Idiopathic	13	7.1
Pituitary insufficiency	12	6.5
Osteogenesis imperfecta	9	4.9
Vitamin D deficiency	9	4.9
Parathyroid adenoma	5	2.7
Miscellaneous	48	26.1

Table 3. Relationship between common causes of secondary osteoporosis and Z score

Disease	n	%	Mean Z score
Thalassemia	20	10.9	–3.4±1.16
Osteogenesis imperfecta	9	4.9	–3.84±1.64
Gluten enteropathy	18	9.8	–3.0±0.77
Hypogonadism	22	12	–3.4±0.92
Steroid use	15	8	–3.0±0.72
Pituitary insufficiency	12	6.5	–2.85±0.57
Idiopathic osteoporosis	13	7.1	–2.82±0.44
Idiopathic Hypercalciuria	13	7.1	–3.3±1.77
Cachexia	7	3.8	–2.9±0.84
Vitamin D deficiency	9	4.9	–2.8±0.42
Parathyroid adenoma	5	2.7	–4.0±1.2

Disclosures

Ethics Committee Approval: The Ethics Committee of Dicle University provided the ethics committee approval for this study (120/12.05.2022).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – Z.P.; Design – Z.P., O.F.I.; Supervision – B.T., A.K.T.; Materials – O.F.I., Z.P.; Data collection and/or processing – B.T., S.A.T., Z.P.; Analysis and/or interpretation – Z.P., O.F.I., A.K.T.; Literature search – S.A.T., Z.P.; Writing – Z.P.

References

1. Painter SE, Kleerekoper M, Camacho PM. Secondary osteoporosis: a review of the recent evidence. Endocr Pract 2006;12:436–45.
2. Hudec SM, Camacho PM. Secondary causes of osteoporosis. Endocr Pract 2013;19:120–8.
3. Ebeling PR, Nguyen HH, Aleksova J, Vincent AJ, Wong P, Milat F. Secondary Osteoporosis. Endocr Rev 2022;43:240–313.
4. Hofbauer LC, Hamann C, Ebeling PR. Approach to the patient with secondary osteoporosis. Eur J Endocrinol 2010;162:1009–20.
5. Lewiecki EM. Evaluating patients for secondary causes of osteoporosis. curr osteoporos rep 2022;20:1–12.
6. Ilias I, Milionis C, Zoumakis E. An overview of glucocorticoid-induced osteoporosis. 2022 Mar 19. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000.
7. Cianferotti L. Osteomalacia is not a single disease. Int J Mol Sci 2022;23:14896.
8. Gaudio A, Xourafa A, Rapisarda R, Zanoli L, Signorelli SS, Castellino P. Hematological diseases and osteoporosis. Int J Mol Sci 2020;21:3538.
9. Bandeira L, Silva BC, Bilezikian JP. Male osteoporosis. Arch Endocrinol Metab 2022;66:739–47.
10. Tovoli F, Negrini G, Sansone V, Faggiano C, Catenaro T, Bolondi L, et al. Celiac disease diagnosed through screening programs in at-risk adults ıs not associated with worse adherence to the gluten-free diet and might protect from osteopenia/osteoporosis. Nutrients 2018;10:1940.
11. García Nieto VM, Luis Yanes MI, Tejera Carreño P, Perez Suarez G, Moraleda Mesa T. The idiopathic hypercalciuria reviewed. Metabolic abnormality or disease? Nefrologia (Engl Ed) 2019;39:592–602.