

Manifestations of Osteoporosis in Systemic Diseases

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Annotation: In recent years, EULAR, European Osteoporosis Society, British Society of Rheumatology have recommendations for Osteoporosis treatment. Due to the variety of clinical manifestations and the severity of the prognosis, it is always difficult to choose a treatment strategy for patients with Osteoporosis.

The need for timely diagnosis of PAG is determined by the need for early initiation of therapy.

Keywords: Systemic diseases, osteoporosis, vitamin D.

Systemic diseases are connective tissue diseases of unknown etiology with clinically heterogeneous manifestations and chronic progressive course. In this disease, there are 3 pathological processes: vasculopathy, cellular and humoral-autoimmune condition and the process of progressive visceral and vascular fibrosis in many organs. In the United States, 9 to 19 cases of this disease per 1 million inhabitants are registered annually. Osteoporosis in most cases develops as a complication of systemic scleroderma. In Spain, the incidence of osteoporosis in patients with systemic scleroderma is considered very high.

Purpose: assessment of the risk of a decrease in bone mineral density and the occurrence of osteoporosis caused by vitamin D deficiency in systemic scleroderma and, as a consequence, a violation of calcium metabolism in bones.

Materials and methods: the study involved 42 patients aged 24 to 68 years with a diagnosis of SSD (according to the ACR/eular classification) (other rheumatological patients were not diagnosed) who were hospitalized in cardiorheumatology and rheumatology departments and were registered in the arthrology clinic. IADK TMA Clinic for 2017-2019.

Research methods: Clinical and biochemical methods: assessment of skin damage and the amount of vitamin D in the blood using the mrSS scale. Instrumental studies: Assessment of bone mineral density using an ultrasound Densitometric apparatus. Statistical processing of the obtained results.

The selected patients in clinical or laboratory tests had no signs of vascular diseases, liver or kidney diseases, did not detect coagulopathy, did not take oral or transdermal estrogen, progesterone, androgens or other steroids, did not take bisphosphanates that affect bone metabolism. Of these, 4 (4.4%) are male and 38 (95.6%) are female, the duration of the disease is 6.5 (4.6) years. The number of those who are currently taking corticosteroid medications is 8 (19.1%), those who have taken them before - 4 (9.5%), those who have never taken them - 30 (71.4%), and patients did not take vitamin D preparations at all In 29 (69%) gastrointestinal tract damage was detected in 13 patients (31%), and no MIT damage was detected in 13 (31%). None of the study participants were diagnosed with bone fractures.

Bone mineral density depends not only on the metabolism of calcium, but also on the metabolism of vitamin D, which contributes to its absorption. Our gastrointestinal system and skin are especially important when we receive vitamin D from the outside. Consequently, with SSD, damage to these areas develops from the early stages of the disease. The bone mineral density of these patients was also

assessed. Thus, according to the results, it was found that in 18 (43%) patients the bone mineral density was normal, in 14 (33%) - a decrease in bone mineral density, i.e. the state of osteopenia, and in 10 (24%) patients the state of bone mineral density was at the level of osteoporosis.

Results: in most patients, the mucous membrane of the gastrointestinal tract is damaged as a result of the disease, in patients with SSD, due to skin damage, its ability to synthesize vitamin D decreases.

Systemic diseases are connective tissue diseases of unknown etiology with clinically heterogeneous manifestations and chronic progressive course. In this disease, there are 3 pathological processes: vasculopathy, cellular and humoral-autoimmune condition and the process of progressive visceral and vascular fibrosis in many organs. In the United States, 9 to 19 cases of this disease per 1 million inhabitants are registered annually.

According to the National Osteoporosis Foundation (IOF), in 2010, more than 10 million adults over the age of 50 in the United States had diagnosed osteoporosis, and more than 43 million had low bone mineral density. In 2015, 2.3 million cases of osteoporosis were reported in the United States out of nearly 2 million requests for medical care. About 15% of patients who had a new osteoporotic fracture suffered one or more subsequent fractures within 1 year and almost 20% died. Mortality was highest among patients with hip fractures: 30% died within 12 months.

In most studies assessing the prevalence and incidence of osteoporosis, the degree of bone fracture is used as a marker of the disease. But bone mineral density (BMD) is also associated with the risk of diseases and fractures. It is believed that women and men with metabolic disorders associated with secondary osteoporosis have a 2-3 times higher risk of hip sprain and spinal fractures. Worldwide, osteoporosis is the most common bone disease that affects more than 200 million people worldwide. About 75 million people in Europe, the USA and Japan suffer from osteoporosis.

Osteoporosis is a polyetiological disease, the development of which depends on genetic predisposition, lifestyle, physical activity, endocrinological status, history of other diseases, medication use, and individual life expectancy. Bone mass gain occurs in childhood and adolescence, reaching a maximum by 20-30 years. After reaching a peak until the age of 35-40, bone mass remains almost unchanged, after which it begins to gradually decrease.

Bone tissue is in a constant state of change. Two opposing processes occur simultaneously: bone formation and bone resorption, the balance of which determines BMD, the quality and strength of bone. In conditions of estrogen deficiency, this balance shifts towards bone loss. However, estrogen deficiency is not the only cause of BMD loss, as previously thought. Bone tissue remodeling depends on the state of phosphorus-calcium metabolism, PTH, vitamin D, growth hormone, calcitonin, thyroid hormones, GC, etc. In general, all effects on the state of bone tissue metabolism are realized through the main regulatory systems of osteoblastogenesis and osteoclastogenesis. Changes in the expression of molecules that regulate osteoblastogenesis and osteoclastogenesis with age and due to the negative influence of other factors lead to a decrease in bone strength, which can be manifested by a decrease in bone mass, BMD and/or disruption of internal microarchitecture and, as a consequence, fractures with minimal trauma.

Primary osteoporosis develops as an independent disease without any other identified cause of decreased skeletal strength; it accounts for 95% of the structure of osteoporosis in postmenopausal women (postmenopausal osteoporosis) and 80% of the structure of osteoporosis in men over 50 years of age. Primary osteoporosis also includes idiopathic osteoporosis, which develops in women before menopause, men under 50 years of age, and juvenile osteoporosis, which is diagnosed in children (up to 18 years of age). Idiopathic and juvenile forms of primary osteoporosis are extremely rare.

Secondary osteoporosis develops as a result of various diseases or conditions, as well as taking medications, that is, there is a specific cause leading to osteoporosis. Factors in the development of secondary osteoporosis:

✓ Genetic diseases (cystic fibrosis, Gaucher disease, Marfan syndrome, hemochromatosis and others)

- ✓ Hypogonadal conditions (anorexia nervosa, athletes' amenorrhea, premature menopause, Turner and Klinefelter syndromes)
- ✓ Lifestyle factors (excess vitamin A, sudden weight loss, malnutrition)
- ✓ Gastrointestinal disorders
- ✓ Endocrine disorders
- ✓ Hematological disorders
- ✓ Rheumatological and autoimmune diseases
- ✓ Medicines

Physical examination of the patient includes:

- Measurement of the patient's height and weight with the calculation of body mass index. When recording height results, it is necessary to clarify the maximum height at a young age (25 years) and/or at the last previous height measurement. If height decreases by 2 cm or more over 1-3 years or by 4 cm or more over a lifetime, compression fracture(s) of the vertebral body should be suspected.
- The presence of folds of skin on the back and sides (symptom of "excess skin"), a decrease in the distance between the costal arches and the iliac crests less than the width of 2 fingers are physical signs of compression fractures of the vertebral bodies.
- When measuring height, you should pay attention to the inability to fully straighten up, the appearance of a distance from the wall to the back of the head, which is a symptom of compression fractures of the vertebral bodies.
- Characteristic kyphotic deformation of the chest, a relative increase in the abdomen in volume ("protrusion" of the anterior abdominal wall), relative elongation of the limbs and shortening of the chest are presented in picture and are symptoms of multiple compression deformities of the vertebral bodies

In addition, during a physical examination, attention should be paid to the presence of symptoms of diseases leading to secondary osteoporosis, which are quite specific for each pathology.

The risk of osteoporosis increases with age as the BMD decreases. Senile osteoporosis is more common in people over 70 years of age. Secondary osteoporosis can occur in people of any age. Although bone destruction in women begins slowly, it accelerates during menopause, usually it occurs around the age of 50 and later. The frequency of postmenopausal osteoporosis is highest in women aged 50-70 years. Half of postmenopausal women have fractures during their lifetime due to osteoporosis, while 25% of these women develop spinal deformity, and 15% have a clear fracture. The risk factors for an apparent fracture are similar in different ethnic groups.

Secondary osteoporosis is common in men, and 45 to 60% of them are the result of hypogonadism, alcoholism or an overdose of glucocorticoids. And 35-40 percent of them are primary osteoporosis. In general, the ratio of women to men with osteoporosis is 4: 1. It follows from this that osteoporosis is not only a medical problem, but also has great socio-economic importance. There is a lot of data on a variety of causes leading to the disease of osteoporosis, according to modern ideas. These include genetic, microtrauma, metabolic changes, endocrine disorders, inflammatory diseases of the joints, long-term use of medications. Including systemic scleroderma as a complication of the disease develops in most cases. In Spain, the incidence of osteoporosis in patients with systemic scleroderma is considered very high.

Research results

The study involved 42 patients aged 24 to 68 years with a diagnosis of SSD (according to the ACR/eular classification) (other rheumatological patients were not diagnosed) who were hospitalized

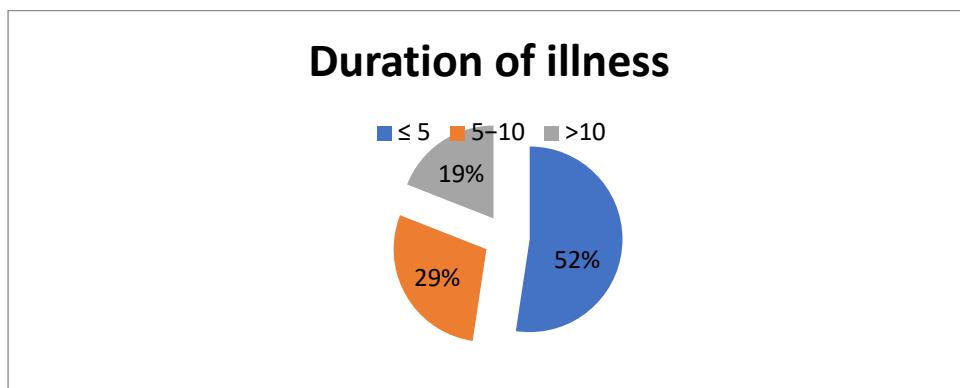
in cardiorheumatology and rheumatology departments and were registered in the arthrology clinic. IADK TMA Clinic for 2017-2019. The selected patients in clinical or laboratory tests had no signs of vascular diseases, liver or kidney diseases, did not detect coagulopathy, did not take oral or transdermal estrogen, progesterone, androgens or other steroids, did not take bisphosphanates that affect bone metabolism. Of these, 4 (4.4%) are male and 38 (95.6%) are female, the duration of the disease is 6.5(4.6) years, the number of people who are currently taking corticosteroids is 8 (19.1%), 4 (9.5%) have previously taken them, 30 (71.4%) have never taken them), patients With vitamin D, 29 (69%) patients were found to have gastrointestinal tract damage, and 13 (31%) had no GIT damage. None of the study participants were diagnosed with bone fractures.

The average duration of the disease in patients selected for the study is 6.5 (4.6) years (Table 1):

Table 1

Duration of illness (year)	≤ 5	5–10	>10
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Figure 1

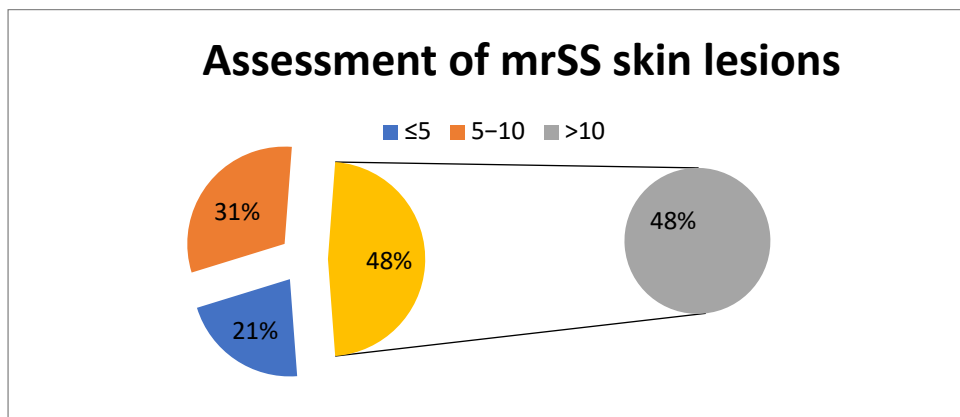


The number of patients who had the disease for less than 5 years was 22 (52%). While the number of patients who last from 5 to 10 years is 12 (29%), and 8 (19%) patients suffer from SSD for more than 10 years. When assessing skin lesions by mRSS according to the obtained clinical analyses:

Table 2

Evaluation (Score)	≤5	5 –10	>10
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Figure 2



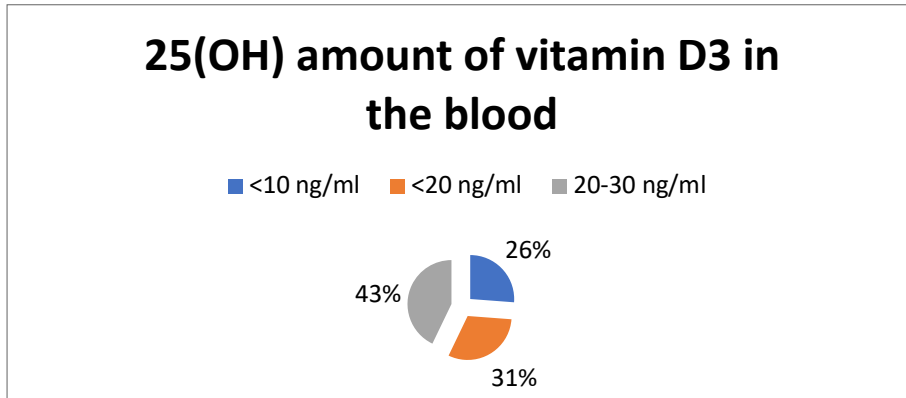
In the method of determining skin compaction with a finger (mrss), when patients were evaluated for skin damage: 20 (48%) of study participants received a score higher than 10 points, 13 (31%) received a score from 5 to 10 points, and the remaining 9 (21%) received a score less than 5 points.

A blood sample was taken from all patients participating in the study and the level of vitamin D3 in the blood was assessed 25(OH) (Table 3):

Table 3

25(OH)Vitamin D3	<10 ng/ml	<20 ng/ml	20-30 ng/ml
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Figure 3



At the same time, the lowest value (<10 ng/ml) was found in 11 (26%) patients. On the other hand, normal quantitative indicators (20-30 ng/ml) were found in 18 (43%). Deficiency status (<20 ng/ml) was found in 13 (31%) of the remaining patients.

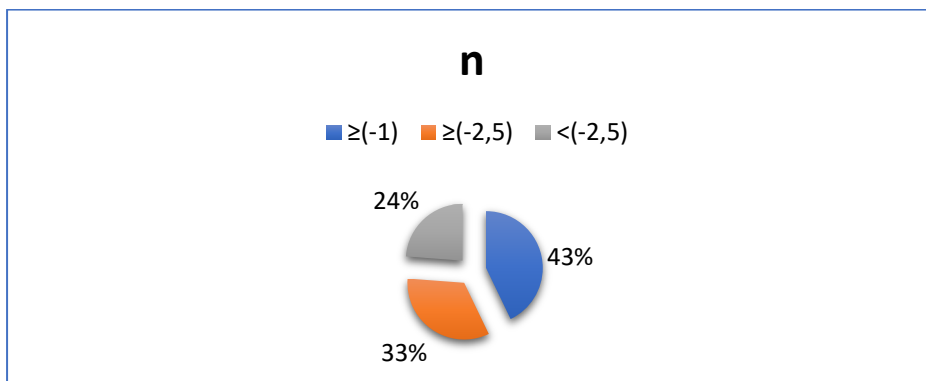
A portable ultrasound densitometer device called "SONOST 3000" was used to assess the bone tissue of the study participants.

Results of the T score of the study participants 24%(10) =<-2,5 33% aida (14) ≤ -2.5 it was found that 43% of IDA (18) ≤ -1 (Table 4).

Table 4

T- score	≥ (-1)	≥ (-2,5)	< (-2,5)
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Figure 4

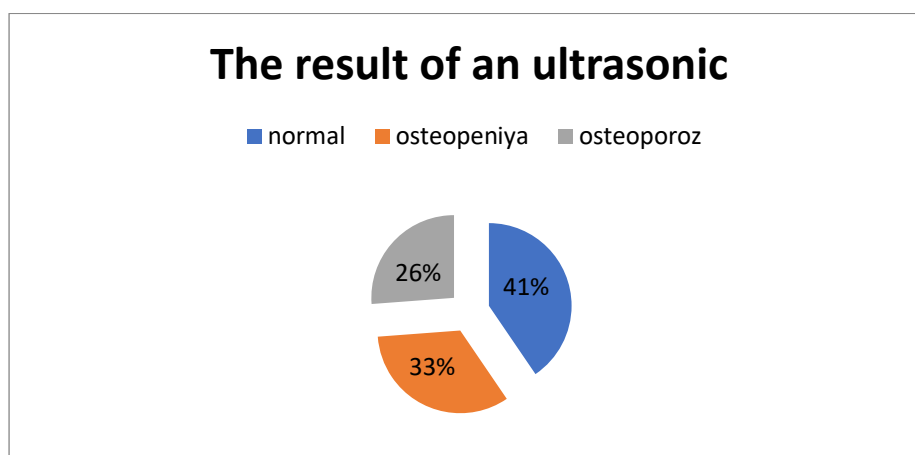


So, according to the results obtained, it was found that in 18 (43%) patients the bone mineral density is normal, in 14 (33%) -a decrease in bone mineral density, i.e. the state of osteopenia, in 10 (24%) patients the state of bone mineral density is at the level of osteoporosis (Table 5).

Table 5

Bone mineral density condition	Normal	Osteopeniya	Osteoporoz
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Figure 5



Discussion of the results obtained

Our study included patients with well-formed SSD disease, which allowed us to analyze in detail the most important factors of bone mineral density.

In most of the selected patients, the gastrointestinal tract and skin lesions are in the first place. The selected patients had no lesions of other organs. This condition is important in order to exclude the influence of other affected organs on the decrease in bone mineral density. The gastrointestinal system and the skin are of particular importance for our intake of vitamin D from the outside. Consequently, SSD develops from the early stages of the disease due to damage to these areas.

But not all patients had a damaged gastrointestinal system, and this condition allowed us to learn about the effect of this system on reducing the amount of vitamin D in the body.

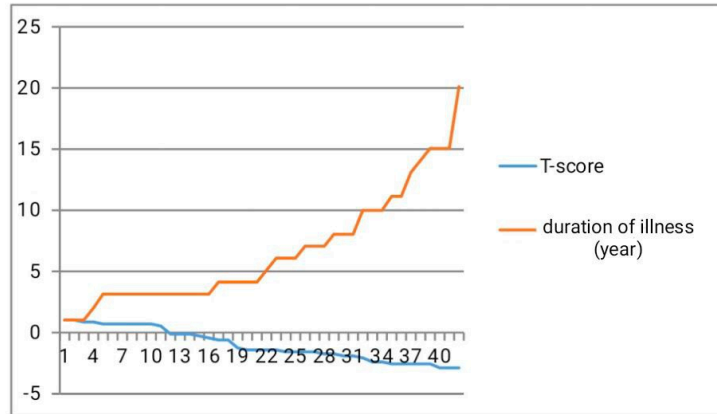
So far, studies have shown that glucocorticosteroids, widely used as anti-inflammatory agents in autoimmune diseases, are the main cause of a decrease in bone mineral density. But we know that bone mineral density depends not only on the metabolism of calcium, but also on the metabolism of vitamin D, which ensures its absorption. SSD as the main sign of skin damage, as well as gastrointestinal tract, mucosal damage occurs.

We assessed the amount of vitamin D in the blood of selected patients to see how these conditions affect vitamin D metabolism, and also assessed the bone mineral density of these patients. In that way, according to the results, it was found that in 18 (43%) patients the bone mineral density was normal, in 14 (33%) - a decrease in bone mineral density, i.e. the state of osteopenia, and in 10 (24%) patients the state of bone mineral density was at the level of osteoporosis.

This means that the amount of vitamin D 25(OH) in the blood obtained from SSD patients was distributed at 3 different levels: insufficient, insufficient and insufficient. Analyzing the results obtained accordingly, we see that 57% of patients have a vitamin D level of 25 (oh) below normal. But if we look at these figures separately, the condition of vitamin D deficiency in the blood of 25(OH) was found in 21% of patients. However, we have different SSD diagnosis times for individual patients, so it was also necessary to determine the duration of the disease. The average duration was 6.5 years. But patients who developed the disease in less than 5 years accounted for 52%.

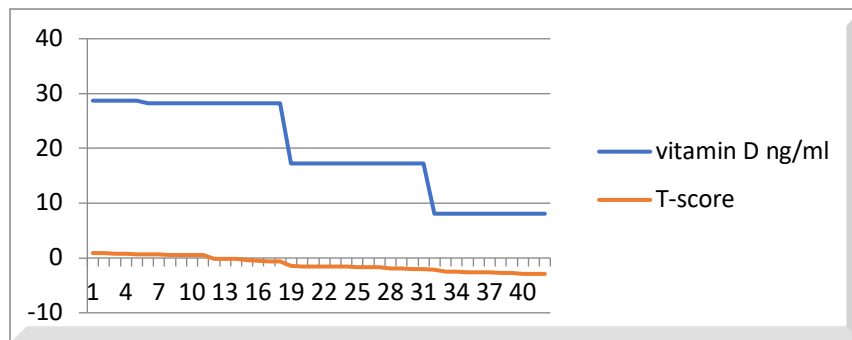
In this case, we see that the amount of vitamin D in the blood depends on the duration of the disease. (Fig.6) more specifically, it was found that there is an inverse correlation with the duration of the disease with a change in the amount of vitamin D 25 (OH) in patients. $R = -0.88$ (strong feedback)

Figure 6



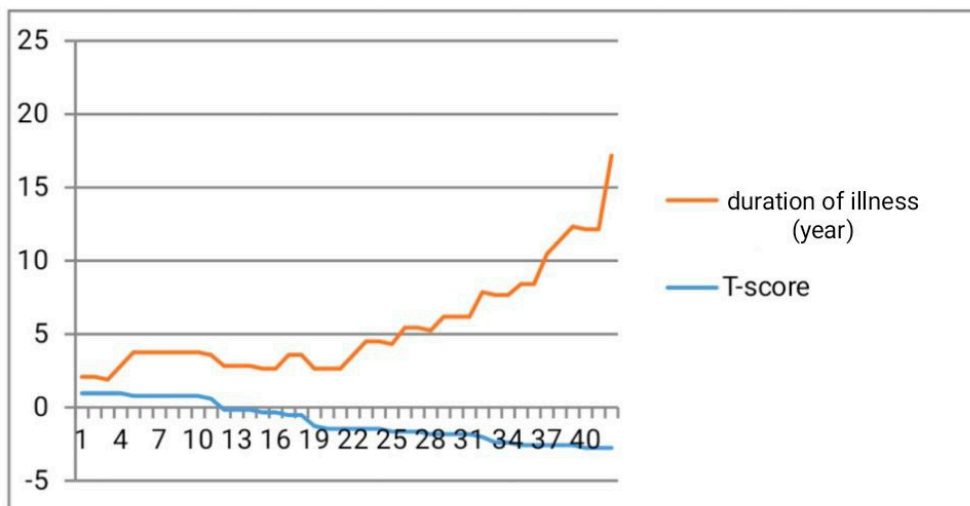
Ultrasound densitometric analysis was performed in selected patients. The results were as follows: the average t-score was -1.09. This corresponds to the state of osteopenia in general. But if you look more specifically, 43% of patients had normal bone mineral density, and 57% of patients had reduced bone mineral density. (Figure 7) This circumstance suggests that we can see that there is a correlation between the number of patients whose vitamin D levels in the blood 25 (OH) decreased compared to normal, and the t-score obtained by analyzing an ultrasound densitometer. $r=0.9$ (strong direct relationship)

Figure 7



Also, the correlation between the decrease in bone mineral density and the duration of the disease is strongly inverted ($R=-0.8$) manifestation is reflected. (Fig. 8)

Figure 8

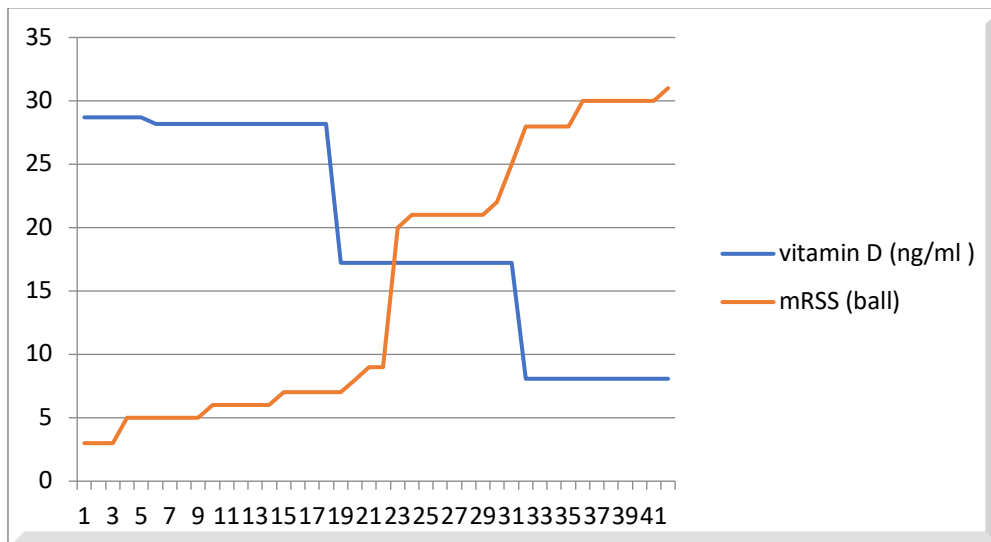


According to the analysis of the ultrasound densitometer conducted in patients, the level of bone mineral density in 24% of patients was assessed as a condition of osteoporosis.

The average result was 15.4 when assessing the degree of skin damage in patients selected using the mmse scale. But in 48% of patients, the mrss score is higher than 20, which means that the degree of skin damage is higher. (Figure 9)

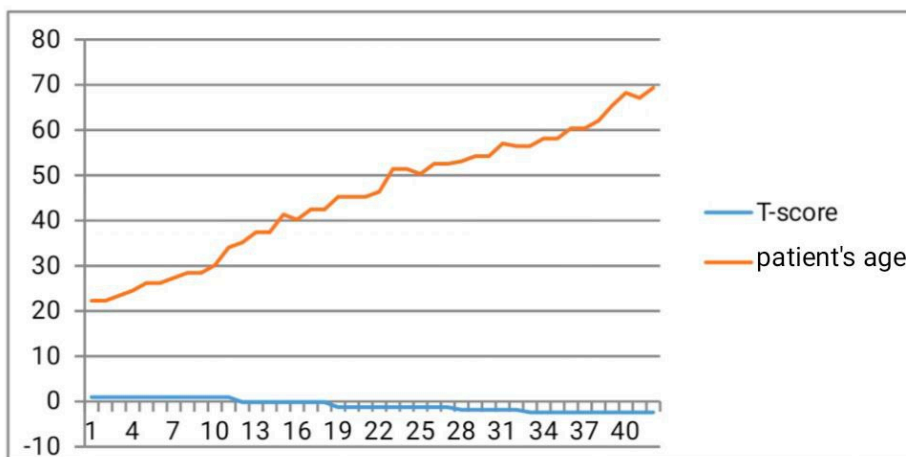
Given the special place of the skin in vitamin D metabolism, there should have been a correlation between the amount of vitamin D in the blood of 25(OH) patients. The result was: $R=-0.69$ (inverse average)

Figure 9



Considering that bone growth begins to lag behind its resorption after 30-35 years, it is also necessary to note age-related changes in our patients. (Fig.10) the selected patients are patients on average aged 45 years. The correlation between the age of the patients and the result of their ultrasound densitometer had a weak feedback. ($r=-0,21$)

Figure 10



Conclusion

1. It was found that patients with SSD have a serum vitamin D level of 25(OH) below normal, and it was found that this condition is associated with organ damage affecting vitamin D metabolism. It was confirmed that the extent of skin and gastrointestinal tract damage directly affects the amount of vitamin D in the body.

2. SSD was performed in patients, taking into account the influence of many factors on bone mineral density. The analysis of the ultrasound densitometer showed that the bone mineral density was low, and the levels of vitamin D in the blood of 25(OH) with this disease also had a correlation difference between the duration of SSD disease. We can interpret this state as:

- ✓ In patients with SSD, due to skin damage, its ability to synthesize vitamin D decreases.
- ✓ in most patients, the mucous membrane of the gastrointestinal tract is damaged as a result of the disease, both conditions worsen depending on the duration of the SSD.

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