

## Correlation of vitamin D with osteoporosis

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### Abstract

**Introduction:** Osteoporosis is a disease of bone metabolism, which is characterized by the silent and progressive reduction of bone density and is followed by a risk for fractures that can be fatal to the patient. The causes leading to this disease are endogenous and exogenous, but it is mainly related to the decrease in vitamin D level.

**Aim:** Our study is the review and presentation of a more complete picture regarding osteoporosis and the effect of vitamin D on osteoporosis.

**Material and Method:** Is a literary review of studies published in PubMed, Medline, WebMD, on the topic of vitamin D and its correlation with osteoporosis, an essential indicator with a wide range of applications in diagnosis and analysis of this illness. The scientific studies referenced, highlight the effectiveness of diagnosing osteoporosis through a bone density scan with a dual energy X-ray (DEXA), which provides the most accurate assessment to date on bone density. According to 'International Osteoporosis Foundation' statistics conducted for EU countries, Switzerland, UK the estimated number of individuals with osteoporosis above 50 years old in 2019 was 32 million, from which 25.5 million were of the gender female and 6.5 million male, deriving the conclusion that females are more prone to osteoporosis. Apart from diagnosis of osteoporosis, in the studies referenced, of great importance is the role of vitamin D levels and its correspondence with osteoporosis. In a study by Michael Holick Vitamin D deficiency. *N Engl J Med.* a vitamin D deficiency is defined by concentration of 25(OH)D less than 10ng/mL and an insufficiency of 20-30 ng/mL. At last, treatments and recommendations for osteoporosis regarding vitamin D deficiency have elaborated to supplementary diets, bisphosphonates treatments and even hormone replacement therapy.

**Conclusion:** 25-OH-Vitamin D is essential for vitamin D status. To prevent the rapid progress of osteoporosis, factors that need immediate attention such as diet, lifestyle and an early diagnosis through DEXA are to be a priority, especially in risk patients.

**Keywords:** Vitamin D, Osteoporosis, Patient, Diet, Vitamin D deficiency

### Introduction

Osteoporosis is a disease of bone metabolism, which is characterized by the silent and progressive reduction of bone density and is followed by a risk for fractures that can be fatal to the patient. Osteoporosis is defined as a silent disease, because individuals may not realize that they have osteoporosis until a fracture of the bone occurs [1]. As the most common areas for fractures include the wrist, spine, shoulder, and hip, symptoms can include: stooped posture overtime, bone pain or tenderness, rounding of the back called kyphosis, height loss overtime [2]. It is known also as a metabolic disease: bone is an active tissue in the sense of biochemical reactions. Thanks to this activity,

the bone is continuously regenerated, absorbed, increased in quantity and improves its qualities. All this activity, the bone tissue realizes thanks to its metabolic abilities[3]. There are signs common to rheumatic diseases with anxiety, joint deformation and weight loss, so osteoporosis is a rheumatic disease known as a non-inflammatory rheumatic disease. The causes leading to this disease are endogenous and exogenous, but it is mainly related to the decrease in vitamin D level explaining a connection between osteoporosis and vitamin D in the study of the factors of each of them, where we encounter many commonalities, such as lifestyle, nutrition, culture, hormones. If these factors are not used for the benefit of health, but are abused, then we see that we have an impact

on both vitamin D and osteoporosis. Osteoporosis is classified into primary osteoporosis of the first type which is post-menopausal, occurs 10-15 years after menopause and is a result of hormonal disorders in women during this period, primary osteoporosis of the second type which is age-related, secondary osteoporosis where sex and age are encountered without distinction and is installed without obvious external causes. Various stresses, poor food, vitamin D deficiency, hyperthyroidism can be some of the reasons for the pathological situation. Also, in this classification are imperfect and idiopathic juvenile osteoporosis [4].

Many studies have been done regarding osteoporosis impact on the population and the main causes, ways of identification and treatments. In these studies, vitamin D has been a key that shows the importance of its status in this delicate disease. The question arises how?

Bones are composed of tissue, proteins, minerals and vitamins. The formation, modelling and breakdown of bone is regulated by bone cells such as osteoblasts, and osteoclasts (International Osteoporosis Foundation, 2017). Osteoblasts are the cells responsible for producing and secreting bone matrix proteins for bone synthesis and remodelling, while osteoclasts are responsible for bone breakdown through the reabsorption. When the activity of osteoclasts surpasses the bone formation by osteoblasts, the bones become brittle and porous leaving them susceptible to fractures (International Osteoporosis Foundation, 2017). All this is related to the effects of vitamin D. Vitamin D exerts its effects on bone and mineral metabolism mainly by altering the expressions of several genes in the small intestine, kidneys, parathyroid glands, and bone. Activation of VDR by 1,25(OH)<sub>2</sub>D promotes intestinal calcium and phosphate absorption and renal tubular calcium reabsorption, which help maintain an adequate calcium-phosphate product that crystallizes in the collagen matrix in the bone [5].

What happens if the person is deficient in vitamin D? 25-hydroxyvitamin D (25(OH)D). This is the main circulating form of vitamin D used by doctors to determine vitamin D status. A low level of serum 25-hydroxyvitamin D causes a significant decrease in the intestinal absorption of calcium and phosphate. This leads to a transient decrease in the serum concentration of ionized calcium and subsequent secondary hyperparathyroidism. Elevated parathyroid hormone induces the differentiation of preosteoclast into mature osteoclast, thereby leading to an increased osteoclast number and activity. This causes increased bone resorption, loss of bone mineral and matrix, and subsequent low bone mass and osteoporosis. Furthermore, parathyroid hormone exhibits a phosphaturic effect, resulting in an increase in urinary phosphate excretion. Urinary phosphate loss along with decreased intestinal phosphate absorption due to vitamin D deficiency contributes to an inadequate calcium-phosphate product, thereby leading to bone mineralization defects and the development of rickets and osteomalacia [6].

Precisely the level of 25OH vitamin D is essential because it determines the need for this vitamin and the possibility of

developing osteoporosis as discussed above, so is important to know vitamin D deficiency, insufficiency and the adequate vitamin D threshold concentration. In Michael Holick's studies on vitamin D deficiency. Vitamin D deficiency is defined as a 25(OH)D concentration lower than 10 ng/mL and insufficiency 20-30 ng/mL [7].

One way to know if you're getting enough vitamin D is a blood test that measures the amount of vitamin D in your blood. In the blood 25-hydroxyvitamin D is measured in either nanomoles per liter (nmol/L) or nanograms per milliliter (ng/mL). One nmol/L is the same as 0.4 ng/mL. So: levels of 50 nmol/L (20 ng/mL) or above are adequate for most people for bone and overall health, levels below 30 nmol/L (12 ng/mL) are too low and might weaken your bones and affect your health, levels above 125 nmol/L (50 ng/mL) are too high and might cause health problems [8].

Vitamin D status is determined by factors such as lifestyle, cultural which affect dietary supplemental source of vitamin D. Physical factor including skin melanisation, 7DHC level and Solar Zenith Angle involving latitude, season, time of day have a great significance as they constitute the cutaneous source of vitamin D [9].

The geographical location is a determining element for the efficiency of the synthesis of vitamin D because, being an interconnected process and dependent on solar radiation, the angle of the sunlight plays an essential role. As the latitude increases, the amount of solar radiation that can reach the earth's surface decreases. For this reason, in countries with latitude of 35°, the synthesis of vitamin D is a seasonal process when it reaches the value of the maximum amount during the summer season and with little or almost non-existent quantitative values during the winter season. In a 1988 study, it was found that a person exposed to sunlight during days of calm weather in Boston (42.2 degrees N) from November to February did not produce previtamin D<sub>3</sub>. In Edmonton (52 degree N) this ineffective period continued from October until March. A few degrees further south (34 degrees N and 18 degrees N), solar radiation was effective in converting 7-dehydrocholesterol to previtamin D<sub>3</sub> in the winter season. These results determine the dramatic influence that differences according to geographical location have in solar ultraviolet radiation, more precisely UVB radiation, in the synthesis of vitamin D in the skin. The increase in geographical latitude will have a proportional impact on the duration of the "winter vitamin D" during which oral supplements are recommended [10].

In countries that do not get enough vitamin D due to the geographical location, there are more cases of hip fractures. This is shown by statistics on Age standardized hip fracture rates (per 100,000) across different continents. From this study In Europe, Scandinavia has the highest reported incidence of hip fracture worldwide. There are a large number of studies looking at the incidence as well as secular trends in this geographically northern region. The incidence rates vary from North to South Europe, the highest being in Sweden and Norway and the lowest in France and

Switzerland. From Norway the reported age standardised annual incidence rates of hip fracture are 920 per 100,000 in women and 399.3 per 100,000 in men and those in Switzerland are 346 per 100,000 and 137.8 per 100,000 in women and men, respectively [11].

Vitamin D synthesis is also influenced by lifestyle, environmental and physiological factors. By lifestyle are meant factors such as the use of sun cream, the time spent in environments with natural solar radiation and also have a significant impact on everyday clothing that can block UVB rays. Environmental factors that influence have to do with the level of pollution, the coverage of the geographical area by clouds and the effect of ozone. A 2002 study focusing on the vitamin D status of 34 children (9-24 months) who lived in a polluted area in Delhi, India, found serum vitamin D concentration levels up to 50% lower [12].

Another study in 2017 in Tehran, Iran, organized with 324 high school teenagers during the winter season, also came to the conclusion that air pollution is an essential factor in determining the UVB rays that reach the earth's surface [13].

There is a Swedish population-based prospective study on BMD, falls, fractures where N=987 and the final available report of this study is for 640 women (>75 years). In this population sample of elderly women, 25OHD insufficiency sustained over 5-years was associated with increased 10-year risk of osteoporotic fracture. This study shows that with the decrease of vitamin D status from high >75 nmol/l to medium 50-75 nmol/l to low <50 nmol, the 10-year fracture incidence rate is respectively 6.9%; 9.9%; 20.6%. It has been seen that as vitamin D status decreases, there is an increase in the incidence rate of fractures [14].

A study with graphic presentation for the incidence of osteoporotic fractures in men and women shows that the prevalence of vertebral and hip fractures tends to increase with age in men and women, with a steeper gradient in women [15].

According to 'International Osteoporosis Foundation' statistics conducted for EU countries, Switzerland, UK the estimated number of individuals with osteoporosis above 50 years old in 2019 was 32 million, from which 25.5 million were of the gender female and 6.5 million male, deriving the conclusion that females are more prone to osteoporosis. Based on the fracture numbers calculated from age- and sex- specific incidence and population sizes in 5-year age intervals for 2019 and 2034, the annual number of osteoporotic fractures in the EU27+2 is estimated to increase by 1.06 million from 4.28 million in 2019 to 5.34 million in 2034. The percentage increase over the 15-year interval will vary considerably by country, ranging from a modest 8% increase (Latvia) to 58% (Ireland). The number of deaths for EU countries due to fractures in 2019 is 248,487 [16].

Therefore, the diagnosis is of great importance in the detection and prevention of further complications, encouraging research into the

causes that influence the causation of this disease. The diagnosis of osteoporosis is made through X-ray examinations, computerised tomography, bone biopsy, bone scans, DEXA and blood tests. In blood or urine tests, references for a more accurate diagnosis of osteoporosis are also known as "markers". These are the elements that are affected in the case of osteoporosis. Alkaline phosphatases in patients with osteoporosis are at levels up to three times higher than in people under normal conditions. This marker is an indicator of the degree of bone formation in the entire skeleton. Osteocalcin is another marker for bone formation. Urinary N-telopeptide of type I collagen, or uNTX is a marker that indicates bone resorption, or their loss. Vitamin D levels are essential in the development of osteoporosis because vitamin D plays a key role in the absorption of calcium to develop bones. Low levels of vitamin D indicate a possible diagnosis of osteoporosis [17].

Bone density tests, also known as osteodensitometry, measure the level of minerals in the bones (BMD for bone mineral density measurements). This procedure uses a specialized x-ray technique called dual energy x-ray absorptiometry, DXA or DEXA. Basically, in these scans, x-rays are used, which provide information on their permeability in the bones. The more porous and weak the bones, the more rays pass between them. The amount of rays that pass, compared to the standard mass of the healthy bone of an adult, is given through the T-score. A T-score greater than -1 is considered normal and a score between -1 and -2.5 is considered low [18].

More exactly, T-score of -1.0 or above is normal bone density, T-score between -1.0 and -2.5 is low bone density, or osteopenia, T-score of -2.5 or lower is osteoporosis [19].

The analysis through this procedure gives the diagnosis if the bones are resistant to fractures or not, a criterion to determine the patient's osteoporosis. This medical approach is also used in the monitoring during the patient's treatment [20].

When the patient has been diagnosed with osteoporosis the first step is to talk with the doctor about a treatment plan that's tailored for him. This treatment has two goals: slow or stop bone loss, prevent fractures. The treatment plan includes medication, healthy diet, calcium, vitamin, exercising and preventing falls. There are medications that build new bone such as parathyroid hormone analogs: abaloparatide, teriparatide. Medications that slow bone loss and build new bone are monoclonal antibodies. Bisphosphonates are usually the first choice for osteoporosis treatment. These include: Alendronate (Fosamax), a weekly pill. Risedronate (Actonel), a weekly or monthly pill.

## Conclusion

25-OH-Vitamin D is essential for vitamin D status. To prevent the rapid progress of osteoporosis, factors that need immediate attention such as diet, lifestyle and an early diagnosis through DEXA are to be a priority, especially in risk patients.

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