Multidisciplinary

Studying of osteoporosis

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Abstract
The results of the study showed that there was a significant increase in the numbers of white blood cells, the concentration of cathepsin, parathyroid hormone, and mass index for the study groups compared to the control group, as well as a significant decrease in the concentration of phosphate and vitamin D for the study groups compared to the control group There is a significant increase in the estrogen hormone in the group of pregnant women and a significant decrease in women with osteoporosis who are in menopause compared to the control group, as well as the presence of a significant decrease in red blood cells, hemoglobin, and the volume of packed blood cells in the group of pregnant women compared to the control group.

Keywords: cathepsin, Osteoporosis, parathyroid hormone, vitamin D

Introduction

Osteoporosis is a global health problem and is among the ten most prevalent diseases in the world, according to the World Health Organization, as the number of infected people has increased to 400 million around the world. Osteoporosis can be defined according to the International Osteoporosis Foundation as one of the skeletal diseases that It causes a decrease in bone mineral density and deterioration of the fine geometry of bone tissue, which increases the risk of fractures.

Osteoporosis (OP) is a serious public health problem that currently causes global concern (John Cecily, Helen Shaji, 2020) [20]. The National health network, as a chronic skeletal condition, describes osteoporosis as low bone mass and structural loss of the bone tissue due to the increased risk of wrist, spine and hip fractures (Anwar, F., *et al*, 2019) [2]. Osteoporosis is also known as a silent disorder, since the condition is usually asymptomatic before a fracture occurs, which affects morbidity and mortality considerably (Chen, Hai-ling, Li-li Deng, and Ju-fen Li, 2015) [17].

Also, many people are not alert to it till complications happen. It is very common in women after the menopause. Osteoporosis is hard to treat and is still incurable, and thus prevention is critically important. The osteoporosis operational description is based on the T-score of bone mineral density (BMD). The T-score describes the number of SDs by which the BMD in an individual differs from the mean value expected in young people with a good health status (Kanis, J. A.,2019) [21].

Z-score is another result variable for the dual energy X-ray absorptiometry (DXA) survey, which is the number of SDs in which an individual's bone density decreases above or below the reference group of the same age and gender and is useful for studying secondary causes of osteoporosis (Sözen, Tümay, *et al*.2017) [22].

Bone structure

Bones are the most differentiated organ that arises from the tissues of the mesenchyme. it is alive and dynamic. In terms of function, the bone is essentially a structural organ that tolerate load (Rogers, A., Saleh, G.,2002) [23].

1. Bone cells

Four cell types in bone are found: osteocytes, osteoblasts, osteoclasts, and lining cells (Suskin, J., & Shapiro, C. L. 2018) [24], as shown in figure 1-1.

i) Osteocytes

Osteocytes are osteoblast-derived cells incorporated into the bone matrix. Between 5% and 20% of osteoblasts are converted into osteocytes.When osteoblasts entrapped in the newly formed bone matrix developed into osteocytes. Osteocytes account approximately 95% of the bone cells, they are not divided and long-lived (Dera, Ayed A., 2017) [19].

ii) Osteoblast

It is the cells responsible for bone formation and located along the outer surface of the bone (Pérez-Castrillón, José Luis, 2020) [25]. Osteoblasts are cubic cells located along the surface of the bone 4% of the total resident bone cells are known for their role in bone formation (Capulli, Mattia, 2014) [18]. These cells demonstrate the morphological properties of protein synthesizing, including prominent Golgi apparatus abundant, rough endoplasmic reticulum and various secretory vesicles.

iii) Osteoclasts

Osteoclasts are bone-lining cells responsible for bone resorption. By creating an acidic environment, osteoclasts dissolve the bone mineral content (BMC) and compromise the strength of the existing bone. To complete the process of resorption, osteoclasts release enzymes to remove the remaining collagen bone matrix (Rizzoli, René. 2018) [26].

iv) Bone lining cells

These cells are derived from a curved and flat type of osteoblast cells. Bone surface is separated from bone marrow by lining

cells which protect bone surfaces against excessive absorption. In addition to these functions. The response of these cells to any bone distortion caused by external impact is believed to respond to other signals initiate biological mechanisms to adjust the skeletal shape and size to meet the altered mechanical demand (Terndrup, Haley Frances, *et al*. 2016) [27].

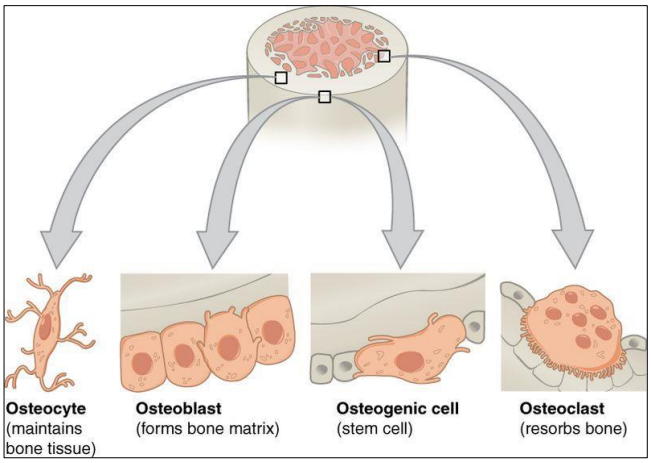

Fig 1: Bone cell types (Lakna, (2017)

2. Bone matrix

Bones are a dynamic mineralized tissue consisting of an extracellular organic matrix (ECM) and inorganic minerals, support the body structure and provide fluid balance of minerals in the body. Collagen type 1 which is approximately 9 percent of total protein, is the most abundant ECM compound in bone Collagen gives bone its flexibility whereas the addition of mineral to the collagen network provides bone its stiffness (Ida, T., Kaku, M., 2018) [29]. The procollagen molecule is excreted from osteoblasts, after which individual collagen molecules converge together to formed collagen fibrils.

Individual collagen fibrils are grouped together to create a collagen fibre spontaneously. ECM also comprises 90% of the total bone volume, which consists of mineralized matrix, organic matrix, lipids and water. Hydroxyapatite is the main component of the mineralized matrix and provides the majority of bone strength and stiffness. The mineralized matrix accounts for 85% of the phosphorous storage and 99% of storage of calcium. The organic matrix is secreted by osteoblasts and is mineralized within 10-15 days (Seeman, Ego, and Pierre D. Delmas, 2006) [30].

Bone remodeling and pathophysiology of osteoporosis

Osteoporosis pathophysiology describes an imbalance between bone formation and bone resorption. Bone resorption occurs more than bone formation in the case of osteoporosis, Therefore, a negative balance occurs with a net loss of bone and the associated risk of fractures Resulting in chronic deformation and pain. An imbalance between bone formation and bone absorption may occur as a result of one or a combination of the following factors: increased bone resorption and reduced bone formation within a remodeling unit. Bone re-modelling a complex process by which old bone is continuously replaced by new tissue (Fuchs, Robyn K., 2019) [31]. This process consists of five phases:

a) Activation phase

The recruitment of osteoblasts precursors into the surface of the bones followed by their differentiation and fusion into fully functional builder cells (Buck, Donald W.,2012) [32].

b) Step of resorption

Osteoclasts digest mineralized bone, causing scalloped erosions in the region of the bone (Francis, R. M., 2008) [33].

c) Reflection stage

Forming the conjugation to resorption. This requires bone proliferation of cells, their differentiation and the aggregation of modern bone cells in the resorption cavity.

d) Formation phase

The osteoblast's bone formation lasts the longest The osteoblast's bone formation lasts the longested slower than bone resorption include the formation of new bones and mineralization (Hadjidakis, Dimitrios J., 2006) [34].

e) Termination

When mineralization is complete, osteoblasts undergo apoptosis, are converted into cells that cover the bone or are trapped within the osteopathic matrix. Osteoporosis is caused by a defect in bone remodeling, which results in a decrease in bone strength. Bones become brittle due to a defect of the structure resulting in an excess risk of fracture. Bone loss generally develops over a long period and the pathogenesis can occur asymptomatic. Bone remodeling is a process where osteoclasts and osteoblasts work sequentially in the same bone remodeling unit. After the attainment of peak bone mass (Allen, Matthew R., 2019) [35]. When osteoclastic cells are more than osteoblastic cells, they possess a stronger force and accelerate the degradation and resorption of bone tissue. As a result, the inhibition of osteoblasts over time leads to an imbalance known as osteoporosis. Osteoporosis is diagnosed by the incidence of osteoporotic fractures or by the BMD criteria. An osteoporotic fracture is a low-level trauma injury that occurs due to a fall experienced from a lower height.

These fractures usually take place after a sustained reduction in BMD with a decrease in the quality of the bone tissue. In women the common fracture sites include the wrist, spine, ribs, humours and femur. However, the hip fractures are considered the most common and fatal osteoporotic injury. It has been reported that 10% of patients with osteoporotic hip injury die within 30 days of surgery, and the other 30% die within one year. Patients with osteoporosis at some level of increased risk have fracture fragility (Nguyen, 2012) [36]. Such as bending over or coughing can cause such fracture, as shown in figure 1-2.

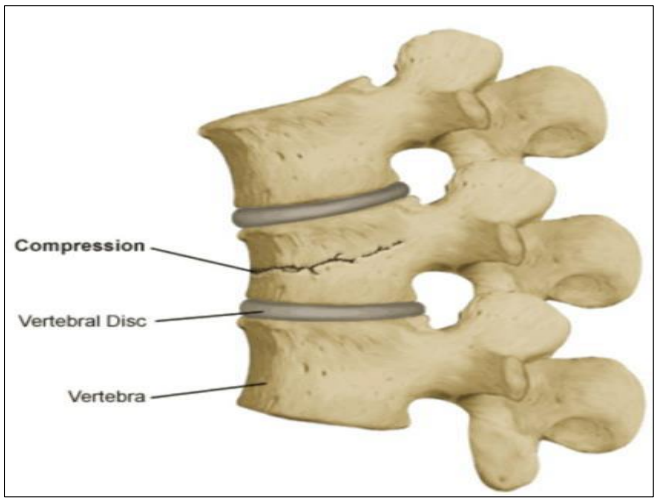

Fig 2: The natural bone has the appearance of a honeycomb matrix (top)

Classification of osteoporosis

Osteoporosis can be classified as idiopathic or primary and secondary (Buck, Donald W., 2012) [32].

Idiopathic or primary osteoporosis: which includes senile osteoporosis and juvenile postmenopausal. It is the most common type of osteoporosis (Francis, R. M., 2008) [33].

Secondary osteoporosis can be followed by several diseases: such as-

- Blood diseases: (multiple myeloma and thalassemia).
- Endocrine (thyrotoxicosis, primary hyperparathyroidism, cushing's syndrome, hypogonadism, anorexia nervosa, and diabetes type 1).
- Gastrointestinal (celiac disease and mala-bsorption).
- Rheumatisms (systemic lupus erythematous, rheumatoid arthritis and scleroderma).
- Kidney disorders (kidney failure, chronic tubular acidosis).
- Drugs such as, anticoagulants, diuretics, glucocorticoids and others (Allen, Matthew R., 2019) [35].

Epidemiology of osteoporosis

The aging population is increasing at exceptional rate. This burst in population will cause large number of individuals with OP. It has been assessed that the prevalence of OP will increase from 1/3 in people 50-60 to over 50% of people over 80 years of age. By 2050, the global osteoporosis sufferers will reach 6 million (including both males and females), 3/4 of who will reside in developing countries (Nguyen, 2012) [36].

Knowing of the global diffusion of OP is relevant towards understanding its complex etiology within the associated gene pools of different races and ethnicities. It also highlights the serious impact of this silent killer on families and societies around the world (Parra-Torres, *et al*, 2013) [37]. Postmenopausal women were found more likely to diagnose osteoporosis, with 41% being found to have OP, compared to 23.7% of women who did not have menopause. This is to be expected because oestrogen is known to be a protective factor against OP because it helps maintain bone density and this is lost in postmenopausal women.

Prevalence of OP in postmenopausal Iraqi women had been reported to be 22.8 percent. The prevalence of OP among postmenopausal women (PMW) is increasing across the globe. One study showed that 28.4% of Malaysian women are osteoporotic. The prevalence recorded of osteoporosis was15% in Germany and France, 9% in UK, 38% in Japan and 16% in USA, whereas in men the prevalence was 3% in Canada, 4% in Japan, 1% in the UK and 8% in France. Prior studies reported that the prevalence of OP in Caucasian women older than 50 years ranged between 7.9 and 22.6 percent Meanwhile, in Taiwan Nutrition and Health Survey found that prevalence of OP in men 11.6% and in the forearm, women is 25.0% (Vijayakumar., 2016) [38] OP affects the population of about 1.4 million Canadians mostly PMW and the elderly. OP fractures in India are common in both sexes and may occur at a younger age than in the west. Data shows that deficiency of vitamin D is widespread in India, poor sunlight exposure, skin pigmentation and a vitamin D deficient diet are some apparent causes for this finding. About Arab countries, the prevalence of OP and osteopenia among Jordanian PMW was 37.5 and 44.6 percent respectively (Langdahl, Bente, 2016) [39].

Risk factor for osteoporosis

There are two type of OP risk factors:

A. Non modifiable risk factors

a) Age

The most significant risk factor for OP is advance age. With rising age, BMD decreases in both sex and this is due to the effect of hormonal changes on the bone remodeling operation. Both estrogen and testosterone impact the intestinal absorption of calcium from the blood stream. When the intestinal absorption of calcium is reduced, storage of calcium in both cancellous and compact bone are retrieved to keep levels of serum calcium. Calcium is absorbed from the bones in greater amounts than it can be replaced, and a decrease in bone mass occurs (Qaseem, A. (2008) [40].

b) Gender

Women experience bone loss at a younger age and at a faster rate compared to men. Women aged 50 or more have four times

the OP rate and two times the osteopenia rate compared to men (Giannoudis, P. V., 2016) [41].

c) Family history of fragility fracture

Fragility fracture causes extreme complications and even death for all menopause women. About 61% of fragility fractures occur in women, with the female-male ratio reaching 1.6 (Zang, J., 2017) [42].

d) Race

Conventionally, Caucasian race is a risk factor for osteoporosis, but Asian people appear to be at risk of osteoporosis itself (Soen, S., 2014) [43]. The prevalence of fragility fractures is maximum in elderly white women, with one in every two women having a fragility fracture in their life. Anyhow, osteoporotic fractures are 2.6 times more usual in older white women than in African-American women of a same age, still the prevalence is significantly high in both populations (Tarantino, U., Iolascon, G., 2017) [44].

B. Modifiable Risk Factors

a) Medication

The use of a prednisolone in a dose ≥ 5.0 mg/day for more than 3 months, and other medications such as glucocorticoids, anticoagulants, anticonvulsants, aromatase inhibitors, cancer chemotherapeutic drugs, and gonadotropin-releasing hormone agonists are risk factor of OP (Adami, G., and Saag, K. G. (2019) [1].

b) Short time of sun exposure

Short time of sun exposure have been supposed to afford to low BMD, since enough time of sun exposure to ultraviolet light is essential for vitamin D synthesis, which is essential for calcium homeostasis in human body (Alanli, R., Kucukay, M. B., and Yalcin, K. S. (2020) [3].

c) Smoking

Smoking is harmful to bone, reduce body weight, calcium absorption reproductive hormones, and bone mineral density, induces early menopause, and elevates bone-turnover markers and fracture risk.Smokers tend to have spinal deformities more than nonsmokers (Al-Daghri, N. M., Yakout, S., Ghaleb, A., Hussain, S. D., and Sabico, S. (2022) [4].

d) Consumption of Alcohol

Consumption of alcohol is increasing the risk of OP by inhibiting function of osteoblast and reducing bone formation, therefore resulting in more hip fractures (Allison, H., and McNamara, L. M. (2019) [5].

e) Nutrietion

The abundant nutrients used in our daily diet can affect bone health. Bones can be affected by different mechanisms including Adjusting bone structure, the Process of endocrine and Metabolism of bones (Alyassin, F. F., and Taher, M. A. (2015) [45].

Osteoporosis genetic predisposition

There are both genetic and non-genetic factors that play a role in the development of osteoporosis and the emergence of a fragile fracture. The non heritable factors include advantage of the general environmental such as nutrition, other illness, smoking and those factors more immediately linked to falls such as soft tissue padding, visual acuity, neuromuscular function. The heritable factors related to OP are those genes that determine bone mass, architecture, microarchitecture, bone size and intrinsic properties (Aspray, T. J., and Hill, T. R. (2019) [6]. Osteoporotic fractures have also an inheritable aspect, but with age, this will reduce environmental factors like the risk of falling. The inheritance of some features like body mass index, age at menarche, age at menopause, the heritability of serum parathyroid hormone (PTH) and 1,25 dihydroxyl cholecalciferol (Vitamin D3) levels and biochemical markers of bone turnover such as bone specific alkaline phosphatase, osteocalcin, have all been presented to be significantly influenced by genetic factors in twin studies (Awasthi, H., Mani, D., Singh, D., and Gupta, A. (2018) [7].

Bone Minerals Density (BMD)

The bone mineral density is measured with double x-ray Absorption. It the actual expression of bone in absolute terms from mineral grams (mainly g / cm2). Bone mineral density is a way for measuring bone strength and how many grams of calcium and other bone minerals are packed into a segment of bone. It is believed to the standard measure for the diagnosis of osteoporosis and osteopenia. In a number of locations, which is subdivided into and peripheral sites (wrist, finger and heel) central sites (spin or hip), BMD is possible for calculation by different techniques. Although BMD measurements are predictive of fragility in all locations, central measurement (hip and spine) is the most predictive (Bala, S., Prabha, M., and Krishna, T. P. (2016) [8].

Bone mineral density measurement indications

- Females of 65 years and older.
- Women with clinical causes of risk of fractures during menopause changes, such as prior fractures, high risk medication and low body weight.
- Fragility fracture after the age of 40 years.
- Prolonged use of glucocorticoid.
- Vertebral fracture or osteopenia identified on radiography (Balasubramanian, S., and Ganesh, R. (2008) [9].

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