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Review article

Prevalence and risk factors of osteoporosis among post-menopausal women.

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Abstract

Background: Osteoporosis is a widespread disease affecting about 75 million people, mostly postmenopausal women and represents a major cause of fractures in elderly.

Aim and objectives: The aim of this review article is to give insight on this critical issue to increase the awareness toward this problem by the following objectives: to define the osteoporosis problems and its types in postmenopausal women; to demonstrate the prevalence of osteoporosis worldwide especially in

KSA; and to recognize the causes and risk factors of osteoporosis in post-menopausal women.

Literature of review: Osteoporosis may be primary or secondary with predominant primary type. The prevalence of osteoporosis was increased as women age increased as women lose around 2% to 3% of their bone for every year for the initial 5 years after menopause.

Conclusions: Several prevalence studies showed increased osteoporosis among postmenopausal women, ranged from 22.8% to 50.7%. The most common reported risk factors were family history, gender, age that can't be modified as well as there were some risk factors can be modifiable such as, physical inactivity and sedentary lifestyle, obesity, smoking, estrogen and vitamin D deficiency. As there are many complications of osteoporosis, so it is very important to detect osteopenia early to prevent the development of osteoporosis and associated bone fractures.

Keywords: *osteoporosis; postmenopausal women; epidemiology; risk factor; prevalence.*

ABBREVIATION:

Abbreviation	Meaning
(BMD)	Bone mass density
(WHO)	World Health Organization
(KSA)	Kingdom Saudi Arabia
(T1DM)	Type 1 diabetes ellitus
(T2DM)	Type 2 diabetes mellitus
(PHPT)	Primary hyperparathyroidism
(WHI-OS)	Women's Health Initiative Observational Study
(RANKL)	Receptor activator of nuclear factor kappa-B ligand
(TNF alpha)	Tumor Necrosis Factor alpha
(IL-1)	Interleukin-1

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INTRODUCTION:

Background:

Osteoporosis is a known health concern worldwide [(1),] it characterized by a reduction in Bone Mass Density (BMD), and this reduction leads to deterioration in structure of bone and damage of connectivity between bone tissue, causing a greater fragility and an augmented fracture risk. One year

before the start of menopause, there is a rise in the osteoclastic activity without similar rises in activity of osteoblastic, causing an enhanced bone loss as a result of estrogen deficiency [(2).] It has been estimated that around 75% of bone loss in the years after menopause is related to deficiency of estrogen rather than age.

Osteoporosis is a common disease disturbing about 75 million people, typically postmenopausal women. In the United States, an estimated 10 million adults aged 50 years or above had osteoporosis, with more than 5 million having osteoporosis in the neck of femoral bone, involving 4.5 million women and 800,000 men. Among Arab population, high prevalence of osteopenia and osteoporosis were stated among Kuwaiti women aged 50 years or above (26.8% and 9.9% correspondingly). While, higher prevalence was reported among Saudi women (58%) had low BMD (18% had osteoporosis and 40% had osteopenia) [(3).] These high rates indicated the significance of studying the underlying risk factors in order to design for preventive measures [(1).]

The osteoporosis risk increases alongside age and is higher in women than in men [4]. Although environmental factors, such as diet or physical exercise, have an important role in BMD, there are additional important risk factors for developing osteoporosis include age, genetics, gender, race and dietary calcium intake. Lifestyle issues, such as smoking, exercise, alcohol consumption and exposure of sunlight, also contribute to this risk. Body fat mass that is a weight component and a significant index of obesity is thought to apply unfavorable effect on bone [5]. Moreover, sequences of relationship studies have explored Interleukin- 6 gene polymorphisms in relation to osteoporosis risk. Another candidate gene for osteoporosis development is IL-16. It was found that it overwhelms osteoblastic differentiation in bone marrow cultures of mouse.

Among the numerous associated factors of bone mass changes, the role of physical activity is important because physical activity applies beneficial effect against losing of bone and bone fracture. However, the activity levels decrease by age and specifically due to osteoarthritis [6].

Rationale/ justification:

- Osteoporosis is a general cause of elderly fractures, resulting in disability, pain, costly rehabilitation, poor quality of life and early death [7].
- It is expected that every 3 seconds one osteoporotic fracture happens anywhere in the world [8].
- This problem is commonly spread particularly in our country (Saudi Arabia), as Vitamin D deficiency is a public problem in Saudi Arabia and contributes adversely to bone health [3]. Vitamin D deficiency should be supposed and cured in all subjects with osteopenia and osteoporosis.

AIM AND OBJECTIVES:

Therefore, the purpose of this review article is to give insight on this critical issue in order to increase the awareness toward this problem with the following objectives:

- *To define* the osteoporosis problems and its types in postmenopausal women.
- *To demonstrate* the prevalence of osteoporosis worldwide especially in KSA.

- *To recognize* causes and risk factors of osteoporosis in post-menopausal women.

LITERATURE OF REVIEW

I-Concept of osteoporosis, menopausal women:

I.a Definition of osteoporosis:

Osteoporosis word 'derives from 'osteo' meaning bone and the Greek word 'por' means passage i.e. simply it means porous bone'. Normal bone is consisting of a mixture of calcium and further minerals such as phosphate and magnesium. It is also composed of collagen (protein), which forms the framework of bone structure [(9).] Osteoporosis happens when the minerals are lost from bone mostly in the form of calcium as well as loss of architectural of normal bone structure. The loss of bone mineral content is mentioned as a loss of BMD in the bone [(9).] So, osteoporosis is described as a systemic skeletal disease characterized by low bone density and deterioration in

micro-architectural of the bone tissue with the following rise in fragility of the bone that significantly increases the fractures risk [10] *(Figure 1)*[11].

The World Health Organization (WHO) defines T-scores as its description for bone loss degrees. T-score indications to determine your bone density is higher or lower than the density of healthy bone 30-year old adult. A healthcare provider looks at the lowest T-score to diagnose osteoporosis [12] *(Table 1)*[13].

I. b Definition of Menopause:

Menopause is defined as cessation of permanent menses and ovulation; it is known to be occurred after 12 months of amenorrhea with no clear causes of pathology. It suggests a near-complete but decrease naturally of ovarian hormone secretion.

Menopausal women typically state range of symptoms, involving vasomotor symptoms (hot flushes and night sweats), vaginal symptoms, difficulty in sleeping, sexual dysfunction, depression, labile mood urinary

incontinence, loss of memory, anxiety, fatigue, headache, joint pains, and weight gain. Symptoms such as fatigue and loss of memory may be presented because of frequent hot flushes or difficulty in sleeping [14].

II-Types of osteoporosis

There are two types of osteoporosis, primary and secondary, the most common one is primary. Primary osteoporosis is related to the natural aging process. While, secondary osteoporosis progresses when another medical conditions and medications rise the remodeling of bone resulting in disrupted reformation of the bone [15].

Primary osteoporosis can be additionally divided into **"primary type I"** and "**primary type II"** osteoporosis [15].

- **Type I osteoporosis (postmenopausal osteoporosis**) after menopause, usually develops, when levels of estrogen fall quickly that's changes lead to bone loss, usually looked as the *trabecular* (spongy) bone with the hard-cortical bone.
- **Type II osteoporosis (senile osteoporosis)** usually happens after age 70 and involves a diminishing of both the trabecular (spongy) and cortical (hard) bone.

Postmenopausal osteoporosis:

Postmenopausal osteoporosis (Type 1) happens in 5% to 20% of women, including those with 15 to 20 years of menopause, with a peak occurrence in the 60s and mid-70s [16].

Women can lose of their bone about 2% to 3% for each year for the early 5 years after menopause. As a result of the drop-in estrogen formation, women can lose half of their trabecular bone and 35% of their cortical bone all within their lifetime. At least 75% of the bone trouble that happens in women during the initial two decades after menopause can be attributed to absence of estrogen instead of maturing. Losing of bone with menopause does not begin with the onset of amenorrhea but may occur 1 to 3 years before the real termination of menstrual periods [16].

III- Prevalence of osteoporosis:

III. a Prevalence of osteoporosis Worldwide:

Osteoporosis is one of worldwide musculoskeletal diseases that probably affect 200 million women worldwide and causes annually more than 8.9 million fractures [17]. The osteoporosis prevalence was 8% in women 45–54 aged range, 19.2% in women 55–64 aged range, and 32.7% in women 65 years.

A preceding study conducted in **Indonesia** showed osteopenia signs in 36% of the studied subjects, and 29% of them had osteoporosis [18]. Osteoporosis occurred in the under 50 age of Indonesians are around 14%, while 28% in the 50 to 60 age range and 47% in the 60 to 70 age range [18].

Also, additional study conducted among **Australian** women in 2004 showed increase of osteoporosis to 2.2 million in 2006 and assessed to be 3 million in 2021[19].

In **Europe**, in 2010 about 22 million women and 5.5 million men aged among 50 and 84 years are appraised to have osteoporosis [20].

In 2012, National Osteoporosis Foundation found 10 million Americans; including 8 million women had osteoporosis. *In 2014*, it described that a total of 54 million adults aged 50 and older in USA had osteoporosis and low bone density [21]. Many previous studies conducted in **Egypt** revealed that 53.9% of postmenopausal women had osteopenia and 28.4% had osteoporosis [22].

A current study in **Europe** by ***Svedbom A et al., 2013*** showed that 22 million women can be affected by osteoporosis [(23).] In addition, another study on the osteoporosis epidemiology in the **United States** found a prevalence of 15.4% between women older than 50 years and a prevalence of 34.9% between women older than 80 years [(24).]

Also, elevated osteoporosis prevalence was discovered among **Iraqi** postmenopausal women (22.8%) which were within the range of other studies and revealed prevalence of 5.0% up to 48 % [(25).] Furthermore, very recent study in 2016 in Iran revealed high osteoporosis prevalence (50.7%) among women above the age of 45 years [(26).] ***(Figure 2)***[(24).]

III. b Prevalence of osteoporosis in KSA

The study conducted by ***El-Desouki MI, 2003*** between post-menopausal Saudi women discovered that 24.3% in 50-59 age range, 62% in 60-69 age range, and 73.8% in 70-79 age range have been osteoporosis [(26).27] Another study conducted by ***Sadat-Ali M et al., 2012*** revealed that 34% of

healthy Saudi women, 50-79 years of age are osteoporotic [28]. Recent study conducted by *Oommen A, AlZahrani I, 2014* showed that result 58% of the Saudi women had low BMD (18% had osteoporosis and 40% had osteopenia) [3] *(Figure 3)*[29].

IV- Causes and risk factors of osteoporosis:

Osteoporosis is a common health problem currently threatening the health of millions of women. An old study measuring women's knowledge of osteoporosis in 2001 revealed that low calcium and vitamin D in diet, premature menopause, family history of osteoporosis, lack of activity and smoking are risk factors for osteoporosis. However, a one of them determine that underweight (29.3%) is a risk factor for osteoporosis. Similarly, the common risk factors for osteoporosis are genetics, race, advancing age, smoking, alcohol consumption, lack of exercise, bad nutrition habits, calcium balance disorders, and many other unknown factors as reported by several studies. However, some risk factors are better evidenced than others, with factors' influence varying among individuals [30].

IV. a Types of risk factors: *Table (2)*[31].

1. Non-Modifiable risk factors
2. Modifiable risk factors

1- Non-modifiable risk factor:

a) Family history:

Osteoporosis may have a genetic background, the study conducted by ***Raisz LG, 2005*** demonstrated that a higher risk of osteoporosis was among individuals with a family history of osteoporosis, the heritability of BMD decrease was found to vary widely from 25 to 80 %, and to be related with more than 30 genes [(32).]

b) Age:

The probability to prone fracture in osteoporosis women rises with age. The risk of fracture may be double in age of 50. So, one of the most risk factors in females for osteoporosis is ageing, which is a non-modifiable factor [(32),] and it has been documented that BMD reduces with age after reaching its peak value [(33).]

c) Gender

Sex is an additional non-modifiable risk factor. The prevalence rates of osteoporosis were found to be strangely higher among females than males in all groups of age [(33).] The probable reason for the gender difference is the deficiency of estrogen hormone related with menopause which may be cause of reducing BMD in women [(33).]

d) Race/ethnicity

In some population based studies, it was found that BMD is always higher in African American women than in white women at every level of body weight and could contribute to their lower fracture rates. These findings may be attributed to differences in bone geometry. For example, hip axis lengths are

apparently smaller among African Americans and Asians, even after adjusting for height [34].

Moreover, two small cross-sectional studies among Chinese women in comparison to white women showed that Chinese women have higher trabecular number and lower trabecular spacing, also have higher cortical thickness and density than white women [35].

2- Modifiable risk factor:

a) Physical inactivity and sedentary lifestyle

According to WHO report in 2000 on prevention and management of osteoporosis, a significant reported cause of decreasing BMD was immobility, and has a detrimental effect on bony mass Also, it was found that enforced immobility in healthy volunteer decreases bone mineral mass, the same as motor deficits do which results from neurological disorders such as hemiplegia or paraplegia [36].

In contrast, BMD was found to rise in response to physical loading and mechanical stress and many cross-sectional studies, showed a favorable effect of weight-bearing exercise on increasing BMD [36].

b) Deficiency vitamin D and Low level of calcium:

In vitamin D deficiency states, reduced the absorption of calcium occurs in the intestines, producing increased stimulation of osteoclast, which increases the mobilization of calcium in the bone. Therefore, if the deficiency of vitamin D is not improved, calcium remains to be declining in the bone that may be cause rickets in children, and osteoporosis may be occur in adults [(37).]

In a clinical trial with randomly allocated of 36,000 healthy postmenopausal women to take doses of 1000 mg calcium carbonate daily and vitamin D doses of 400 units with follow up during a seven-year with respect to fractures and BMD showed that women with highest risk of fracture at age 60 or more had a significant 21% decrease in the fracture risk of hip bone [(37).]

Based on evidence, the supplementation of vitamin D and calcium is vital to ensuring peak fracture risk reduction. It seems that the supplementation of vitamin D may show more favorable effect in reducing fracture and rising BMD in old women who have fracture in hip bone when given with calcium [(37).]

Therefore, osteoporosis should start with a good education about a healthy lifestyle, including vitamin D, optimal calcium and exercise in adolescence to prevent losing of the bone. A low calcium intake can cause

increasing bone matrix resorption with demineralization and raise the risk of fracture [37].

c) Estrogen hormone deficiency:

Recent study by *Pollycove et al., 2012* demonstrated that osteoporosis in postmenopausal may be caused by enhanced bone resorption and systemic calcium disturbance which result from the deficiency of estrogen induced by menopause [37].38 Therefore, Low estrogen levels are a major factor for 20% of BMD lost within 5 to 7 years of menopause [39].

d) Smoking:

Smoking reduces BMD and enhanced metabolic breakdown of exogenous estrogen in women, as documented before. Despite of the large number of studies documenting the adverse effects of smoking on peak bone mass, but there are few studies of the relationship between smoking and bone loss have been carried out [36].

A recent meta-analysis of 48 distributed reviews showed significant difference in thickness of the bone at age 50 years among smokers and non-smokers. The results revealed reduction in bone thickness in women who smoked by around 2% for every 10-year increase in age, reaching 6% reduction at age 80 years in compared to non- smokers [(36)].

e) Obesity

long-standing observations revealed that the adipose tissue doesn't insulates the skeleton only, but may increase load that could enhance mechanical signaling to the osteocyte and hence the cortical bone. On the other hand, several lines of evidence suggest that high body weight may be detrimental to the skeleton. For example, during aging, menopause and steroids therapy, fat mass is redistributed or increased at a time when BMD is declining. Low body weight has long been founded as an important risk factor for hip fracture. In contrast obesity is often related with high cortical bone mass [(40)].

Furthermore, the study conducted by ***Colaianni et al., 2014*** demonstrated that obesity is probably increase the BMD through mechanical loading applied by body mass on bone formation, while ageing and weight loss result in reduction of bone mass. During postmenopausal period, there is a simultaneous rise of adiposity and reduction of bone mass [(41)].

f) Alcohol intake

Dependent on WHO studies result, elevated levels of alcohol intake showed harmful effect to bone, protein and calcium metabolism, gonadal function, mobility and has also a direct noxious influence on the osteoblast. However, moderate intake of alcohol has not dependably been related with decrease bone density or increased fracture risk. The consumption of Alcohol in postmenopausal women seems to decrease equally the risk of vertebral fracture and bone loss at the hip [(36).]

IV. b Other factors may be associated with osteoporosis in postmenopausal women:

a) **Diabetes:**

Osteoporosis is a metabolic bone disease in diabetic patients as detected by *Inzerillo and Epstein 2004 study* [(42).] In addition, a cohort study of 32,089 postmenopausal women in women's health study revealed that women with type 1 diabetes mellitus (T1DM) were 12 times more probable to report fractures bone than women without T1DM [(43).] However, women with type 2 diabetes mellitus (T2DM) also had a 1.7-fold higher risk for reporting hip fractures compared with women without T2DM [(43).]

The causes behind these findings are indistinct; it could be specifically identified with an absence of insulin or it could be the consequence of glucose

levels. In fact, fractures of diabetics occur with less bone misfortune than in non-diabetics especially in Type 2 diabetics which have an expanded danger of fracture because of lower bone thickness [(44)].

b) Thyroid dysfunction:

Hyperthyroidism is a condition which results in overproduction of thyroid hormone by the thyroid gland. Thyroid hormone is vital for functioning of many substantial organs including the heart, gastrointestinal tract, eyes and bones. It was found that excess thyroid hormone production can cause later bone diminishing which prompts to osteoporosis and possible fractures [(44)].

The precise mechanism of bone loss in primary hyperparathyroidism (PHPT) is not totally known but it was revealed that hoisted levels of parathyroid hormone (PTH) stimulate a condition of high bone turnover and have been related with a low BMD as well as with modifications in the mineralization thickness and bone stiffness and quality [(45)].

Also, increase taking of oral thyroid hormone as a treatment for cases of hypothyroidism can cause hyperthyroidism. Thus, people taking thyroid treatment should undergo annual blood trial of T4 and Thyroid-stimulating hormone to keep them balanced in blood [(44).]

c) Cancer and cancer treatments:

In a study concerning rate of changes in bone density between postmenopausal women with cancer breast and postmenopausal women without any cancers in the Women's Health Initiative Observational Study (WHI-OS), showed that women with breast cancer would have low BMD and high risk for osteoporosis in comparison to women of a similar age without any history of cancer [(46).]

d) Inflammatory diseases and chronic immune response

Although, many inflammatory and immune diseases as multiple sclerosis, systemic lupus, emphysema, asthma, and rheumatoid arthritis showed no relationship to the development of osteoporosis, but they repeatedly require

corticosteroids use in large doses within the course of treatment, which may cause secondary osteoporosis [44].

e) **Medications as steroids (corticosteroids)**

Strong evidence regarding corticosteroid induced osteoporosis is significantly reported. It was found that steroid impaired the body's ability to maintain and absorb calcium, affect on vitamin D metabolism, and decrease estrogen production. However, this effect is reversible after its stoppage [44].

CONCLUSIONS:

Osteoporosis is a major public health concern worldwide that is affecting about 75 million people, mostly postmenopausal women. According to WHO, osteoporosis is the cause of over 8.9 million fractures globally each year. Many prevalence studies show increased postmenopausal women's osteoporosis, ranged from (22.8% to 50.7%).

There are many risk factors affecting BMD whether modifiable or non-modifiable such as age, race, family history, physical in activities. Estrogen

hormone deficiency and vitamin D deficiency were the most reported risk of osteoporosis in postmenopausal women. There were many complications of osteoporosis especially in elderly people So, it is very important to detect osteopenia early to prevent the development of osteoporosis and associated bone fractures.

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ANNEXES:

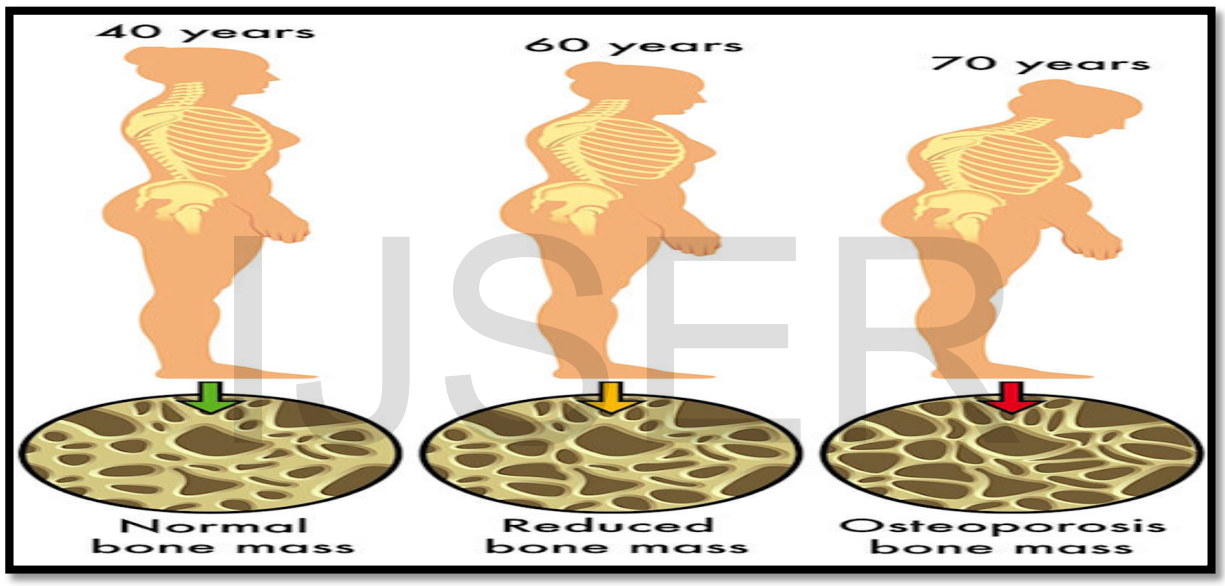


Figure (1): Healthy bone and osteoporosis (Coggan, 2017)[11].

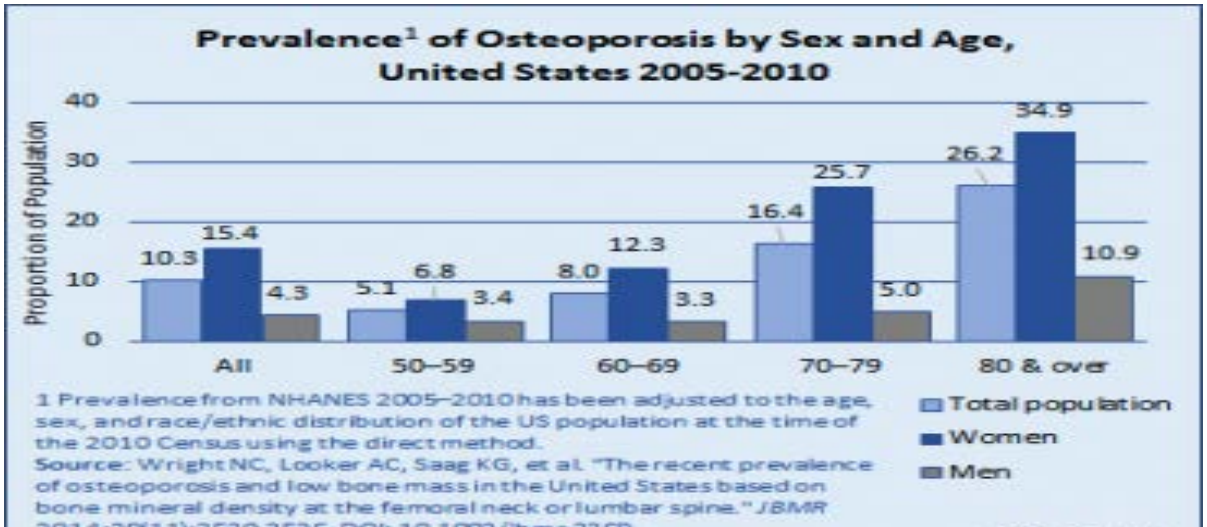
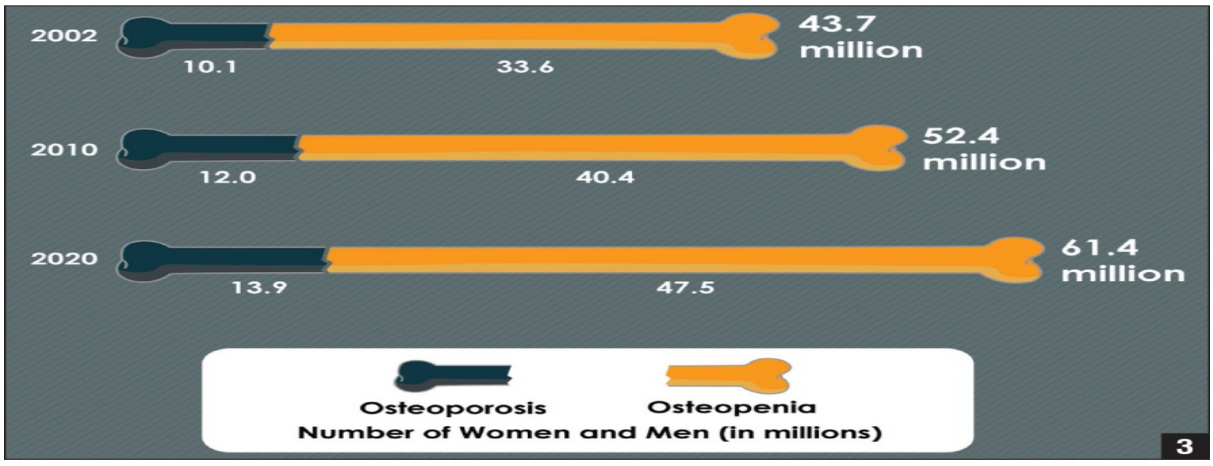


Figure (2)

Figure (2): Prevalence of osteoporosis by sex and age, United States 2005-2010 (Wright et al., 2014)[24].



Figure

Figure (3): prevalence of osteopenia and osteoporosis (Data from the National Osteoporosis Foundation, 2002)[29].

Table (1): Diagnostic criteria based on T-score (National Osteoporosis Foundation, 2010)[13].

Table1 Diagnostic Criteria Based on T-score

Diagnosis	T-score
Normal	-1.0 or above
Osteopenia	Between -1.0 and -2.5
Osteoporosis	At or below -2.5

Source: Reference 2.

Table (2): Classification of risk factors of osteoporosis according to National Osteoporosis Foundation, 2011 [31].

Table 2 Common Risk Factors for Osteoporosis

Nonmodifiable	Modifiable
Older age	Low levels of calcium and vitamin D
Female gender	Reduced intake of vegetables and fruits
Menopause	Increased intake of caffeine, sodium, or protein
Family history	Sedentary lifestyle
Small frame or low body weight	Smoking
History of broken bones or height loss	Increased use of alcohol

Source: Reference 4.