



"Osteoporosis"- An Overview

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ABSTRACT

Osteoporosis becomes a serious health threat for aging postmenopausal women by predisposing them to an increased risk of fracture. It is characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture due to less calcium intake. In the present review article, the aetiology of osteoporosis, risk factors, various disease and drugs which are involved in development of osteoporosis are discussed. Recommended dose schedule for effective treatment of osteoporosis is elaborated.

Keywords: Bone fracture, Calcium, Osteoporosis, Preventive measures, Risk factors.

INTRODUCTION

Osteoporosis exerts a significant burden on both individuals and community. It becomes a serious health threat for aging postmenopausal women by predisposing them to an increased risk of fracture. According to WHO, 28.9 % of postmenopausal women and 36.8 % of population in world are suffering from osteoporosis.¹⁻³

In India, osteoporosis may afflict those 10-20 years younger, at age 50-60. 1 out of 8 males and 1 out of 3 females are suffering from osteoporosis. Incidence of hip fracture is 1 woman to 1 man in India.^{7,15} It has been projected that over half of hip fractures in world in year 2050 will occur in Asia.¹³ In most Western countries, while peak incidence of osteoporosis occurs at about 70-80 years of age. In osteoporotic fractures, common sites of fracture are the spine, wrist and hip. Hip fractures are associated with considerable morbidity and mortality in postmenopausal women, especially older women and increasingly high economic and social costs.⁵ Majority of those who survive are disabled and only 25% will resume normal activities.¹⁰

The word "ostro" comes from the greek word "ostan" means bone while "porosis" comes from the greek word "poros" means hole, passage. It is defined as a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.⁹ Osteoporosis occurs when body fails to form enough new bone, when too much old bone is reabsorbed by body, or both. Calcium and phosphate are two minerals that are essential for normal bone formation. Throughout youth, body uses these minerals to produce bones. If body did not get enough calcium or if body does not absorb enough calcium from diet, bone production and bone tissues may suffer. As age increases, calcium and phosphate may be reabsorbed back into body from the bones, which makes bone tissue weaker.

This can result in brittle, fragile bones that are more prone to fractures, even without injury.¹⁻³

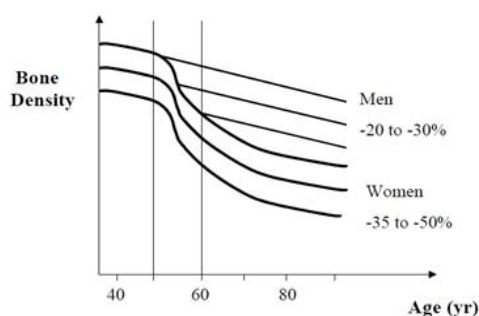


Figure 1: Bone Loss during Adult Life

Osteoporosis related fractures have been recognized as a major health problem, particularly in the elderly. The common sites of fracture are the spine, wrist and hip. The hip fractures are associated with high morbidity and a mortality rate of up to 20% in the first year. Majority of those who survive are disabled and only 25% will resume normal activities.³

Basic pathophysiology of osteoporosis¹²

Bone mass in older adults equals peak bone mass achieved by age 18-25 years minus amount of bone subsequently lost. Peak bone mass is determined largely by genetic factors, with contributions from nutrition, endocrine status, physical activity and health during growth. Process of bone remodeling that maintains a healthy skeleton may be considered a preventive maintenance program, continually removing older bone and replacing it with new bone. Bone loss occurs when this balance is altered, resulting in greater bone removal than replacement. Imbalance occurs with menopause and advancing age. With onset of menopause, rate of bone remodeling increases, magnifying impact of remodeling imbalance. Loss of bone tissue leads to disordered skeletal architecture and an increase in fracture risk. Pathogenesis of osteoporosis and related fractures is shown in figure 2.

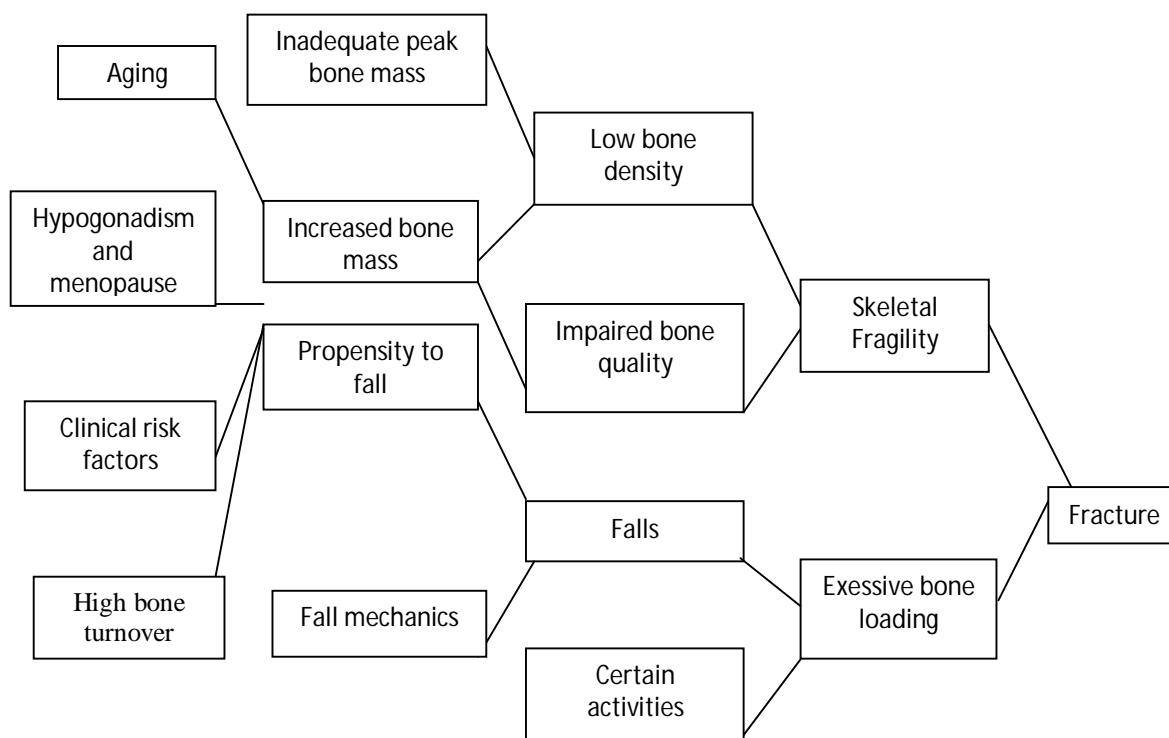


Figure 2: Pathogenesis of osteoporosis related fractures

Classification of Osteoporosis^{8,9}

There are mainly two classes of osteoporosis

Primary osteoporosis

This is primarily linked with natural changes in body. There are two types:

a. Post-menopausal osteoporosis

It usually occurs between ages of 50 to 70, largely because of estrogen loss at menopause. It mainly affects trabecular bone that is spongy looking bone inside of vertebrae.

b. Age-related osteoporosis

It is related directly to aging process. It usually occurs in people older than 70 years. It affects both trabecular and cortical bone. 20% of bone is trabecular bone and 80% is cortical bone. It has been observed that 80% of bone turnover occurs in smaller amount of trabecular bone.

Secondary osteoporosis

It is caused by factors which are not directly responsible but are likely to cause bone degeneration. They are also side effects of certain habits and diseases like alcoholism and liver disease. In secondary osteoporosis age is no criteria.

Risk factors of osteoporosis¹³

Osteoporosis is a silent disease without any symptoms in most patients until fractures have occurred. While screening is not cost effective, identification of risk factors will help in case finding. Various risk factors of osteoporosis are shown in table 1.

Table 1: Risk factors for osteoporosis²

Non- modifiable factors	Modifiable factors
Advanced age	Low calcium intake
Ethnic group (Oriental & Caucasian)	Sedentary lifestyle
Female gender	Cigarette smoking
Premature menopause (< 45 years) including surgical menopause	Excessive alcohol intake
Slender build	Excessive caffeine intake
Family history of osteoporosis in first degree relative	

Diseases prone to osteoporosis^{9, 10}

a. Chronic medical and systemic diseases

- Amyloidosis
- Ankylosing spondylitis
- Chronic obstructive pulmonary disease
- Human immunodeficiency virus or acquired immunodeficiency syndrome
- Inflammatory bowel diseases
- Liver disease (severe)
- Multiple myeloma
- Renal insufficiency or renal failure
- Rheumatoid arthritis
- Systemic lupus erythematosus

- b. Endocrine and metabolic disorders
- Athletic amenorrhea
 - Cushing syndrome
 - Type 1 diabetes mellitus (Insulin dependent)
 - Hemochromatosis
 - Hyperadrenocorticism
 - Hyperparathyroidism (primary)
 - Hyperthyroidism
 - Hypogonadism (primary and secondary)
 - Hypophosphatasia
- c. Drugs prone to osteoporosis¹⁰
- Anticonvulsants (e.g., phenobarbital, phenytoin [Dilantin])
 - Drugs causing hypogonadism (e.g., parenteral progesterone, methotrexate, gonadotropin releasing hormone agonists)
 - Glucocorticoids
 - Heparin (long-term treatment)
 - Immunosuppressants (e.g., cyclosporine [Sandimmune], tacrolimus)
 - Lithium
 - Excess Thyroid hormone therapy
 - Selective serotonin reuptake inhibitors (e.g. trazodone, naphazodone)

Symptoms of osteoporosis⁹

There are no symptoms in early stages of osteoporosis. Symptoms occurring late in the disease include

- Bone pain or tenderness
- Fractures with little or no trauma
- Loss of height (as much as 6 inches) over time
- Low back pain due to fractures of spinal bones
- Neck pain due to fractures of spinal bones
- Stooped posture or kyphosis, also called a "dowager's hump"

Treatment of Osteoporosis¹⁰

Goals of osteoporosis treatment are given below;

- Control pain from disease
- Slow down or stop bone loss
- Prevent bone fractures with medicines that strengthen bone
- Minimize the risk of falls that might cause fractures

There are several different treatments for osteoporosis, including lifestyle changes and a variety of medications.

Bisphosphonates

Bisphosphonates are primary drugs used to both prevent and treat osteoporosis in postmenopausal women. Bisphosphonates taken by mouth include alendronate (Fosamax), ibandronate (Boniva), risendronate (Actonel). Most are taken by mouth, usually once a week or once a month. Reclast (Zoledronic acid) and aredia (pamidronate) are given through IV injection.

Calcitonin

Calcitonin is a medicine that slows rate of bone loss and relieves bone pain. It comes as a nasal spray or injection. Main side effects are nasal irritation from spray form and nausea from injectable form. It appears to be less effective than bisphosphonates.

Hormone replacement therapy

Estrogens or hormone replacement therapy (HRT) is rarely used anymore to prevent osteoporosis and are not approved to treat a woman who has already been diagnosed with condition. Sometimes, if estrogen has helped a woman, and she cannot take other options for preventing or treating osteoporosis, doctor may recommend that she continue using hormone therapy.

Testosterone treatment

When a man has osteoporosis because of low testosterone production, testosterone treatment may be recommended. However, as with breast cancer, testosterone may accelerate growth of prostate cancer as well as increasing risk of prostate cancer recurrence.

Calcium and vitamin D supplements

Calcium makes bones strong. In fact, bones and teeth contain 99% of body's total calcium, with remaining 1% in intracellular and extracellular fluids. Bones act as a storehouse for calcium, which is used by body and replaced by diet throughout a person's life. Since the body's calcium needs change with age, calcium intake should be adjusted as necessary. Getting too much calcium is difficult. Body can absorb 2 grams (2,000 mg) of calcium a day, and anything more can be excreted in urine, although too much calcium excretion through kidneys can result in kidney stones.

Sunlight is a brilliant source of vitamin D. Vitamin D is needed for calcium absorption. National osteoporosis foundation says people under 50 require 400-800 IU of vitamin D daily, while those over 50 require 800-1,000 IU of vitamin D daily. Two types of vitamin D supplements are available i.e vitamin D₂ and D₃. Suggested daily calcium and vitamin D intake is shown in table 2.

Table 2: Suggested daily calcium and vitamin D intake⁸

Life stage group	Daily intake of Calcium (mg)	Daily intake of vitamin D (IU)
Infants 0-6 months	200	400
Infants 6-12 months	260	400
1-3 years old	700	600
4-8 years old	1000	600
9-18 years old	1300	600
19-50 years old	1000	600
51-70 years old males	1000	600
51-70 years old females	1200	600
> 70 years old	1200	800
14-18 years old (Pregnant and lactating)	1300	600
19-50 years old (Pregnant/Lactating)	1000	600
Premenopausal women and postmenopausal women taking estrogen	1000	600
Premenopausal women and postmenopausal women taking estrogen	1500	600

From all calcium supplements present in market, calcium carbonate provides 40% elemental calcium. This means that a product which is 1,250 milligrams (mg) of calcium carbonate yields 500 mg of elemental calcium. Advantages of calcium carbonate are that it is probably the most cost-effective supplement. It has highest percentage of elemental calcium and it has a track record of effectiveness whereas calcium citrate and calcium phosphate are highly expensive and gives less elemental calcium than calcium carbonate. Caltrate and OsCal are common formulations of calcium carbonate present in market. Calcium citrate and calcium phosphate also contain elemental calcium. Generally four tablets of calcium carbonate contain 600 mg of elemental calcium which was found to be more than other calcium supplements like calcium citrate, calcium gluconate, calcium lactate and calcium phosphate (dibasic and tribasic). These supplements contain 45-500 mg of elemental calcium.^{7,11,17}

There are some other supplements of calcium which are given parenterally include calcitonin, calcitriol, α -calcidol. Calcitonin is mainly given as nasal sprays. Nowadays elemental calcium is available in tablet, capsule, syrup, suspension and injectable form. There are some other supplements of calcium are available in market include calcium folinate, calcium leucovorin, calcium pantothenate, calcium polystyrene sulfonate, calcium gluconate, calcium dobesilate, calcium polycarbophil, calcium orotate, calcium gluconolactobionate etc.

Parathyroid hormone

Teriparatide (Forsteo) is approved for the treatment of postmenopausal women who have severe osteoporosis and are considered at high risk for fractures. It is given through daily shots underneath skin.

SERMs (Selective Estrogen Receptor Modulators)

These drugs help prevent bone density loss. They mimic the beneficial effects of estrogen on bone density in postmenopausal women without the risk of triggering cancers. Raloxifene and lasofoxifene are example of this type of drug. Patients who have a history of blood clots should not take this medication. A common side effect is hot flashes. This drug is only approved for women with osteoporosis, not men.

Stem cell therapy

Scientists report that stem cells could halt osteoporosis, promote bone growth and new pathways that controls bone remodeling.

Food and nutrients

Postmenopausal women must eat healthy diet rich in carbohydrates, proteins, fats, vitamins etc. In addition to this every woman must eat soy and soy products. They contain plant estrogens which help maintain bone density. Intake of food and nutrients per day is given in table 3. Recommended dose schedule for osteoporosis is shown in table 4.

Table 3 Daily intakes of food and nutrients^{7,9}

Food group	Daily Intake(g)	Nutrients	Daily Intake (g)
Millets	7±27.7	Proteins (g)	37.3±16.16
Pulses and cereals	322.3±28.37	Fats (g)	26.0±14.2
Oils	23±14.8	Calcium (mg)	270±54
Milk and milk products	62±63.2	Phosphorus (mg)	842±204
Green leafy vegetables	11±28.7	Vitamin A (retinol) (IU)	208±304
Fruits	31±56.4	Thiamin (mg)	0.5±0.21
Fresh foods	7±17.9	Riboflavin (mg)	0.5±0.16
Fish	0.3±1.39	Niacin (mg)	9.2±2.36
Sugar	26±14.6	Iron (mg)	6.8±2.57
Other vegetables	57±60.3	Folate (µg)	35±19.9

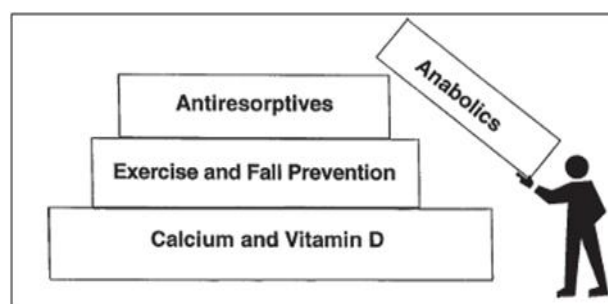
**Figure 2:** Prevention and treatment of osteoporosis

Table 4: Recommended dose schedule for treatment of osteoporosis^{10,13,14}

Medication	Initial dose	Therapeutic/goal dose/duration of treatment
i. Alendronate ii. Risendronate [PA]for intolerance to alendronate	70 mg once weekly or 10 mg daily 35 mg once weekly or 5 mg daily	5 years
Zoledronic acid [PA] for GI intolerance oral bisphosphonates	5 mg IV infused over at least 15 minutes every 12 months	No studies have evaluated the optimal duration of treatment
i. Denosumab ii. Raloxifene [PA] (Selective estrogen receptor modularors) iii. Calcitonin[PA]	60 mg as single dose, once every 6 months	No studies have evaluated the optimal duration of treatment
	60 mg once daily	No studies have evaluated the optimal duration of treatment
	One spray (200 IU) daily in alternating nostrils	No studies have evaluated the optimal duration of treatment The maximum duration of therapy evaluated was 3 years.
Teriparatide (Parathyroid hormone)	20 µg SC once daily	Not more than 2 years
Estradiol (Hormone replacement therapy)	0.5 mg daily	No studies have evaluated the optimal duration of treatment

Osteoporosis develops very slowly over a period of many years. The condition may creep upon the patients without any obvious symptoms. Initially, it can take several months and even several years to become noticeable. It is predicted that a genetic algorithm will be developed to identify at-risk patients before they develop osteoporosis, so that preventive measures can be instituted.⁵ One area of focus for future therapeutics in osteoporosis will be on osteogenic agents, which should have a high likelihood of success because the skeleton has the innate capacity to regenerate itself.

CONCLUSION

Osteoporosis is common disease occurred in postmenopausal women. Osteoporosis risks can be reduced with lifestyle changes and sometimes medication; in people with osteoporosis, treatment may involve both. Lifestyle change includes diet and exercise, and preventing falls. With respect to prevention and management, the general public health approach of improving calcium and vitamin D nutrition, exercise and fall prevention is clearly critical to avoid a major epidemic of osteoporotic fractures in the future. Exercise with its anabolic effect, may at the same time stop or reverse osteoporosis. Osteoporosis is a component of the frailty syndrome. It is predicted that a genetic algorithm will be developed to identify at-risk patients before they develop osteoporosis, so that preventive measures can be instituted. One area of focus for future therapeutics in osteoporosis will be on osteogenic agents, which should have a high likelihood of success because the skeleton has the innate capacity to regenerate itself.

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