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Research Article

### UNDERSTANDING OSTEOPOROSIS, IT'S RISK, PREVENTION AND TREATMENT

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<sup>1</sup>Assistant Professor, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune.,<sup>2</sup>Student Final year M.Pharm, Dr D. Y. Patil College of Pharmacy, Akurdi, Pune.,<sup>3</sup>Student Final year B.Pharm, Dr D. Y. Patil College of Pharmacy, Akurdi, Pune.**Article Received:** March 2022**Accepted:** April 2022**Published:** May 2022**Abstract:**

*Osteoporosis refers to porous bone which is an ailment wherein the bones become weak and delicate, brittle from loss of tissue, typically because of hormonal changes, or lack of calcium or vitamin D. Estrogen and Calcium deficiency, Poor nutrition, Malabsorption, Amenorrhea, Inactive lifestyle, Female gender, Smoking, Hyperthyroidism could be the main factors responsible for osteoporosis. Signs and symptoms of osteoporosis include tenderness or bone pain, loss of height overtime, neck or lower back pain due to fractures, etc More than 200 million individuals worldwide suffer from osteoporosis, and the prevalence of the disease increases as people age. Bone density is directly affected due to hormonal changes that happens at menopause due to which women are at high risk than men for developing osteoporosis. Inability to reach peak bone mass and the Imbalance of bone absorption and formation are some combination factors that can result into osteoporosis. Bone Mineral Density(BMD) Measurement, Clinical risk factors and fracture risk assessment, Fracture Risk Assessment Tool (FRAX) can be used to diagnose the disease. The various kinds of models of osteoporosis are also been described in this article of osteoporosis. The treatment for osteoporosis includes biphosphates, Menopausal Hormone Therapy (MHT), Selective oestrogen receptor modulators (SERM), Denosumab, Anabolics like Teriparatide, Abaloparatide and Romosozumab.*

**Key Words:** *Osteoporotic fracture, Osteoporosis, Epidemiology, Osteoporosis management, Bone mineral density, Fracture risk.*

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**INTRODUCTION:**

World Osteoporosis Day is celebrated on 20 October across the world for awareness of the disease. Old Individuals are the quickest growing population on the planet and, as individuals age, bone mass decays and the danger of fractures increases. Subsequently the social and economic burden of osteoporosis is expanding consistently due to the aging of the total populace. [1]Osteoporosis is a significant general medical condition mainly a skeletal disorder described by low bone mass, permeable bone and its structural deterioration, which are related with higher fracture risk. It develops when bone density and thickness decreases.[2] The body reabsorbs more bone tissue and creates less to replace it.

The most influenced portions of the body are the bones of the lower arm, the hip, and the vertebrae in the spine. In more terrible conditions, bones might lose solidarity so much that it may break even with little stress. [3][4]

**Etiology:**

Three main factors responsible for Osteoporosis:

1. Estrogen Deficiencies in Women. Women typically suffer estrogen deficiencies during perimenopause and menopause.
2. Calcium Deficiencies. Bones are constantly losing and replacing minerals.
3. Inactive Lifestyle.[5][6]

The risk of fracture is high in the following:

- Advanced age
- Prior history of a fracture
- Female gender
- Menopause
- Use of corticosteroids
- Low body mass index
- Smoker
- Secondary osteoporosis
- Intake of alcohol

Having certain medical conditions, such as inflammatory bowel disease, cancer, thyroid problems, rheumatoid arthritis, diabetes, eating disorders, or history of bariatric surgery etc.[7]

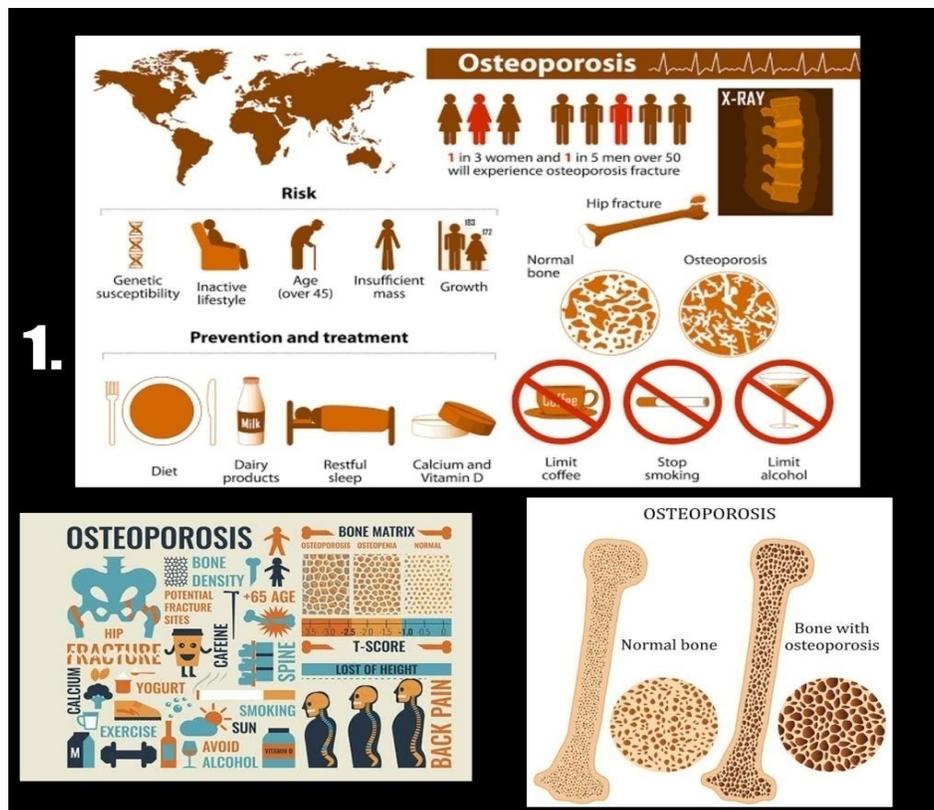


Fig:

1) and 2) Explains risk factors, prevention to be taken and Treatment. 3) Compare pores of normal bone vs bone with Osteoporosis.

**Epidemiology :**

Osteoporosis affects more than 200 million people worldwide, and its prevalence rises as people get older. Over 70% of persons over the age of 80 suffer from the condition. Females are more likely than males to suffer from this condition. Approximately 2% to 8% of males and 9% to 38% of females in the developed world are afflicted. Osteoporosis causes over 9 million fractures each year worldwide.

An osteoporotic fracture affects one in every three females and one in every five males over 50. In comparison to persons living at lower latitudes, people living in areas of the world with less vitamin D from sunlight had higher fracture rates.

**Pathogenesis:**

Osteoporosis can result from a combination of factors, including-

- 1) Inability to reach peak bone mass and
- 2) Increased bone resorption and/or insufficient bone production during remodelling.

1) Peak Bone Mass- Achieving peak bone mass is critical for avoiding osteoporosis and consequent fractures in age. With a 10% increase in peak bone mass, the risk of hip fracture can be lowered by 30%. According to twin studies, genetic variables play a significant role in peak bone mass and bone loss, accounting for up to 80% of peak bone mass variability. Environmental factors like nutrition, activity, and smoking all play a part in reaching optimal bone mass. It is now known that peak bone mass can be modulated.[8]

2) Imbalance of bone absorption and formation- The bone remodelling process, which heals areas of microdamage, is critical for bone health maintenance in adulthood. This is a biological mechanism in which osteoclasts (bone resorbing cells) and osteoblasts (bone making cells), which make up the multicellular unit of the bone, coordinate their functions. The most prominent mediators of osteoclast activity are OPG/RANK and its ligand (RANKL). Hormones, growth factors (TGF-, IGF-1, BMP2), cytokines (IL-1, IL-6, TNF-, prostaglandins E2), and medications all have an impact on OPG/RANKL expression and, as a result, bone turnover. Oestrogen insufficiency causes an imbalance in bone remodelling during the menopause.[9]

**Diagnosis:**

1. BMD measurement- The gold standard for diagnosing osteoporosis is dual X-ray absorptiometry (DXA). The findings of BMD testing are stated in

standard deviations and are compared to a sex-matched young healthy adult (T-score) or a sex-matched and age-matched healthy population (Z-score). A T-score of less than or equal to 2.5 indicates osteoporosis, while a T-score of 1.0 to 2.5 indicates osteopenia.[10]

2.Clinical risk factors and fracture risk assessment- Several clinical risk factors, such as age, falls, and a history of fragility fractures, should be considered. A complete medical history, physical examination, and a variety of investigative procedures, depending on the case, are all part of differential diagnosis.[11][12]

The WHO task force created and introduced a country-specific Fracture Risk Assessment Tool (FRAX) to aid doctors in their clinical management process, based on data collected from large international cohorts in which clinical risk factors, BMD, and fractures were examined. The technology calculates a 10-year likelihood based on BMD measurements and clinical risk factors.[13][14]

**Different models used in osteoporosis:**

Various kinds of animals used in Osteoporosis are Zebra fish, Medaka, OVX rodents, Sheeps, Rabbits, Dogs and Primates, Etc.

1)Glucocorticoid-Induced Osteoporosis (GIOP)- Osteoblasts in glucocorticoid-induced osteoporosis (GIOP) undergo increased apoptosis and have decreased activity and number. In the early stages of GIOP, osteoclast proliferation, longevity, and activity all rise. Longer treatments, on the other hand, reduce the development and function of osteoclasts. The causes underlying osteoporosis are still being studied, and there is currently no effective treatment for GIOP.[15]

2)High glucose and high fat Induced Osteoporosis- Adult zebrafish exposed to glucose showed a decrease in scale matrix mineralization, the presence of bone resorption lacunae associated with intense osteoclast activity, and altered expression of bone regulatory genes 2019b), which is similar to what has recently been reported in diabetic rodents and humans' bones. [16]

3) Iron Overload Induced Osteoporosis- Iron overload hindered bone development and lowered expression of osteoblast marker genes in zebrafish larvae, presumably due to increased ROS generation and oxidative stress.

4) RANKL Overexpression Induced Osteoporosis- Active osteoclasts were produced ectopically in rankl transgenic fish and increased bone resorption in mineralized arches and vertebral bodies, similar to what is seen in human osteoporosis.

5) Microgravity Induced Osteoporosis- Adult medaka and transgenic larvae flown to the International Space Station showed decreased osteoblastic activity, increased osteoclastic activity, and a lower BMD as a result of microgravity. Several osteoclast marker genes (e.g., trap, ctsk, and mmp9) had their promoter activity and expression increased during spaceflight, indicating increased osteoclastic activity. [17]

#### Treatment:

1. Bisphosphonates- Bisphosphonates are the most commonly investigated and given BPs for postmenopausal osteoporosis therapy. Alendronate, ibandronate, risedronate, and zoledronic acid are among them, and they are accessible in oral and injectable forms. Blood pressure should be taken 30 to 60 minutes before any food or other fluids after an overnight fast with only water. These synthetic substances help to improve Bone Mineral Density and reduce the risk of vertebral fractures.[18]
2. MHT and SERM-
  - i) Menopausal Hormone Therapy (MHT), commonly known as Hormone Replacement Therapy (HRT), is a type of hormone replacement therapy that uses oestrogens alone or in combination with progestin. In early and late postmenopausal women, MHT has been found to reduce bone turnover and improve bone mineral density (BMD) at all skeletal locations.[19]
  - ii) Selective oestrogen receptor modulators (SERM) or oestrogen agonist/antagonists are nonsteroidal synthetic compounds that have the ability to weakly bind to oestrogen receptors throughout the body. Depending on the organ they target, they operate as oestrogen agonists or antagonists. The idea behind SERM is that tamoxifen, which is used to treat breast cancer, acts as a partial oestrogen agonist on bone in postmenopausal women. [20]
3. Denosumab- Denosumab is a completely human monoclonal antibody that binds with high affinity and specificity to the receptor activator of nuclear factor- $\kappa$ B ligand (RANKL). It inhibits the proliferation, activation, and survival of osteoclasts by blocking the interaction of RANKL with the receptor activator of nuclear factor- $\kappa$ B (RANK) on the cells of the osteoclastic lineage,

leading to a strong and rapid reduction of bone resorption.[21]

4. Anabolics-
  - i) Teriparatide-Teriparatide has been found to stimulate bone formation by increasing the number of osteoblasts and their activity on quiescent bone surfaces, largely through bone remodelling and to a lesser extent through bone modelling on quiescent bone surfaces.
  - ii) Abaloparatide- Abaloparatide is a synthetic peptide with 34 amino acids. It's a parathyroid hormone-related protein (PTHrP) analogue that's been chosen as a parathyroid hormone receptor selective activator (PTH1R).[22]
  - iii) Romosozumab- Romosozumab is a sclerostin-specific humanised monoclonal antibody. Sclerostin is a secreted protein by the osteocyte that inhibits bone growth and is expressed by the SOST gene.[23]

#### Complications:

The most significant effects of osteoporosis are pathological fractures, notably in the hip or spinal column. Hip fractures are commonly caused by falls and can result in disability and even an increased risk of death in the days after the injury. In the absence of patient falls, there are also spinal fractures, with compression fractures causing back pain and a kyphotic posture.[24]

#### Conclusion:

Osteoporosis prevention should begin early in life and continue throughout one's life with measures that improve or maintain bone health, such as regular physical activity and a well-balanced diet that includes not only an adequate intake of calcium but also other minerals, proteins, and antioxidant-rich foods.

Smoking and binge drinking should be avoided. The avoidance of falls and the maintenance of an appropriate vitamin D status are particularly important in older people who are at risk of fragility fractures. Fracture risk assessment should always be followed by proven non-pharmacological and pharmacological therapy techniques.

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