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THE SKELETAL SYSTEM DISEASE ON OSTEOPOROSIS

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ABSTRACT

Osteoporosis which is characterised by increased bone fragility and osteoporosis also known as silent disease osteoporosis is one of main basis of fracture and age associated disease, more common in women than men. And which weakens bones and commonly causes fragility fractures. Multifactorial factor is responsible for the pathogenesis of osteoporosis. Decrease of bone mineral density lead to risk factor of osteopenia. For the diagnosis of osteoporosis bone mineral density test is helpful to measure the bone strength. Radiography and dual energy X - ray help to identify the fracture assessment. There are no clinical signs and symptoms of osteoporosis until a fracture occur. The mini overview of article provides the introduction, classification, history, pathophysiology, aetiology, signs and symptoms, diagnosis, treatment and prevention of osteoporosis. Objective Osteoporosis means porous bones, causes bones to become weak and brittle associated with age. The aim of this review is to describe the overview regarding the identification and management of osteoporosis.

KEYSWORDS: Fragility fracture, Osteoporosis, Minor trauma, Estrogen, corticosteroids, Skeletal system.

Skeletal system osteoporosis

The skeletal system functions as the basic framework of a body and the entire body are built around the hard framework of Skeleton. It is the combination of all the bones and tissues associated with cartilages and joints. Almost all the rigid or solid parts of the body are the

main components of the skeletal system. Joints play an important role in the skeletal system as it helps in permitting the different types of movements at different locations. If the skeleton were without joints, then there would be no sign of the movements in the human body.

Skeletal system anatomy

Axial skeletal system

Appendicular skeletal

Skeletal system physiology

Support

Protection

Movement

Storage[1]

Osteoporosis

Osteoporosis is defined as low bone mineral density caused by altered bone microstructure, ultimately predisposing patients to low-impact, fragility fractures. Osteoporotic fractures lead to a significant decrease in quality of life, increasing morbidity, mortality, and disability.[2]

Osteoporosis is a silent disease until it is aggravated by fractures, which can develop after minor trauma or without trauma in rare circumstances. Fractures are prevalent and impose a significant medical and personal hardship on the elderly who suffer from them, as well as a significant economic burden on the country. Before a fracture occurs, osteoporosis can be prevented, diagnosed, and treated. Importantly, there are effective treatments to reduce the risk of additional fractures even after the first one has happened. Osteoporosis prevention, detection, and treatment should be a requirement for primary care physicians.[3]

Bone tissue is continuously lost and restored by resorption and production; bone loss occurs when the resorption rate exceeds the creation rate. From birth until maturity, bone mass is moulded (grows and gets its final shape): bone mass reaches its peak (referred to as peak bone mass (PBM) at puberty, after which bone mass begins to deteriorate. Genetics, health during growth, nutrition, endocrine state, gender, and physical activity all have a role in peak bone mass.[4]

The clinical consequences of osteoporosis can lead to osteopenia (decrease in bone density mineral). In normal young female bone mineral density ranges between 1 to 2.5 standard deviations of T score is considered as osteopenia. In Postmenopausal women, T-score <–1.0 are considered as osteoporosis and are also at increased risk of spine, lumbar vertebrae, hip, and wrist fracture. Fragility fractures of ribs are also common in men. Nonetheless, the above-mention diagnostic criteria is used for women as well as men.[5]

Two categories of osteoporosis have been identified primary and secondary. Primary osteoporosis is more common in females. In primary osteoporosis, postmenopausal osteoporosis generally develops after menopause because of drop in estrogen levels. Senile osteoporosis generally occurs at the age of 70 years in which thinning of bone occurred. Senile osteoporosis is degenerative osteoporosis because of wear and tear on the bones. Secondary osteoporosis is less common as it is caused by certain medical condition or treatment, which affect the bone mass and cause bone loss.[6]

Fragility fracture

Fragility fractures are the clinical outcome of osteoporosis. These fractures arise following an event which would otherwise not be expected to result in a fracture. Fractures occurring in a setting of low-level or low-energy trauma, defined as falling from standing height or less, are usually considered as osteoporotic.

Fragility fractures result from low-energy trauma (a mechanical force that would not ordinarily cause a fracture), such as a fall from standing height or less. These fractures are the main clinical consequence of osteoporosis, although they may occur in postmenopausal women even in the absence of osteoporosis.

The most common sites of fragility fractures are the

- Spine
- Hip
- Distal forearm (Wrist)
- Proximal humerus (Upper arm).[7]

Classification of osteoporosis

Primary osteoporosis

Primary osteoporosis is the most common type of osteoporosis. It is more common in women than men. A person reaches peak bone mass (Density) at about age 30. After that, the rate of bone loss slowly increases, while the rate of bone building decreases. Whether a person develops osteoporosis depends on the thickness of the bones in early life as well as health, diet, and physical activity at all ages.

Secondary osteoporosis

Secondary osteoporosis has the same symptoms as primary osteoporosis. But it occurs as a result of having certain medical conditions, such as hyperparathyroidism, hyperthyroidism, or leukaemia. It may also occur as a result of taking medicines known to cause bone breakdown, such as oral or high-dose inhaled corticosteroids (if used for more than 6 months), too high a dose of thyroid replacement, or aromatase inhibitors (used to treat breast cancer). Secondary osteoporosis can occur at any age.

Osteogenesis imperfecta

Osteogenesis imperfecta is a rare form of osteoporosis that is present at birth. Osteogenesis imperfecta causes bones to break for no apparent reason.

Idiopathic juvenile osteoporosis

Idiopathic juvenile osteoporosis is rare. It occurs in children between the ages of 8 and 14 or during times of rapid growth. There is no known cause for this type of osteoporosis, in which there is too little bone formation or excessive bone loss. This condition increases the risk of fractures.[8]

History

The early history of osteoporosis as a clinical syndrome

In 1822, Sir Astley Paston Cooper, a British surgeon and anatomist, commented on an observed association between abnormal bones and fractures. The French pathologist and surgeon Jean Lobstein was the first to use the term ‘osteoporosis’ in 1835, although in the context of describing a condition with blue-grey sclera, which was probably osteogenesis imperfecta type I. In 1941, Fuller Albright reported the cases of women with vertebral fractures after loss of ovarian function. Oestrogen treatment improved the calcium balance in these women and arrested their height loss 7. These findings were the basis for defining

postmenopausal osteoporosis and established the link between osteoporosis and vertebral fractures. Several subsequent studies have demonstrated that vertebral fractures represent impaired bone quality and structural decay of the bone. Vertebral fractures reflect the severity of osteoporosis and are strong predictors of future fractures, thus serving as the hallmark of the disease.[9]

Research on age-related reductions in bone density goes back to the early 1800s. French pathologist Jean Lobstein coined the term *osteoporosis*. The American endocrinologist Fuller Albright linked osteoporosis with the postmenopausal state.

Anthropologists have studied skeletal remains that showed loss of bone density and associated structural changes that were linked to a chronic malnutrition in the agricultural area in which these individuals lived. "It follows that the skeletal deformation may be attributed to their heavy labour in agriculture as well as to their chronic malnutrition", causing the osteoporosis seen when radiographs of the remains were made.[10]

Pathophysiology

Bone remodelling includes two steps

1) Bone resorption

Bones contain cells called osteoclast that breakdown the bone tissue.

2) Bone formation:

Other cells called osteoblast make new bone tissue using minerals such as calcium and phosphate from the blood.

Hormones such as oestrogen, growth hormone and testosterone help keep the number and activity of osteoblast higher than osteoclast so that more bone is made than removed.

Osteoporosis is caused by an imbalance of bone resorption and bone remodelling, leading to decreased skeletal mass. In most individuals, bone mass peaks in the third decade, after which bone resorption exceeds bone formation. Failure to reach a normal peak bone mass or acceleration of bone loss can lead to osteoporosis.[11]

Etiology

Primary osteoporosis is related to the aging process in conjunction with decreasing sex hormones. The bones demonstrate deterioration in microarchitecture, leading to loss of bone mineral density and increased risk of a fracture. Other diseases or their treatments cause

secondary osteoporosis. Men are much more likely than women to have secondary osteoporosis. Medications that can lead to secondary osteoporosis include glucocorticoids and anti-epileptics. Other medications such as chemotherapy agents, proton pump inhibitors, and thiazolidines are less well studied but suspected to also contribute to osteoporosis.

Disease states that can cause osteoporosis include hyperparathyroidism, anorexia, malabsorption, hyperthyroidism, or overtreatment of hypothyroidism, chronic renal failure, Cushing, and any disease that can lead to long-term immobilization. Secondary amenorrhea for more than one year from various causes, including non-estrogen hormonal therapy, low body weight, and excessive exercise, can also lead to rapid loss of bone mass.[12]

Risk factors for osteoporosis include increasing age, bodyweight of under 128 pounds, smoking, family history of osteoporosis, white or Asian race, early menopause, low levels of physical activity, and a personal history of a fracture from a ground-level fall or minor trauma after the age of forty. Patients afflicted with conditions affecting overall mobility level, such as spinal cord injuries (SCI), can experience rapid deterioration of bone mineral density levels within the first 2 weeks following these debilitating injuries.

The risk of fracture is high in the following

- Advanced age
- Prior history of a fracture
- Female gender
- Use of corticosteroids
- Low body mass index
- Smoker
- Secondary osteoporosis
- Intake of alcohol.[13]

Signs and Symptoms

- Osteoporosis has been called "silent disease" because bone mass is lost over many years with no signs or symptoms.

1. Loss of height.
2. Back pain.
3. Vertebrae collapse.

Risk factors

- Anyone can develop osteoporosis. Some groups of people are more likely to experience it, including:
- Anyone over 50.
- Women, especially if you're postmenopausal.
- People with a family history (If someone in your biological family has osteoporosis).
- People who smoke or use tobacco products.
- Some health conditions can make you more likely to develop osteoporosis, including:
- Endocrine disorders — any condition that affects your parathyroid glands, thyroid gland and hormones (Like thyroid disease and diabetes).
- Gastrointestinal diseases (Like celiac disease and inflammatory bowel disease [IBD]).
- Autoimmune disorders that affect your bones (Like rheumatoid arthritis or ankylosing spondylitis — arthritis that affects your spine).
- Blood disorders (Or cancers that affect your blood like multiple myeloma).
- Some medications or surgical procedures can increase your risk of osteoporosis:
- Diuretics (Medications that lower your blood pressure and clear extra fluid from your body.
- Corticosteroids (Medications that treat inflammation).
- Medications used to treat seizures.
- Bariatric (Weight loss) surgery.
- Hormone therapy for cancer (Including to treat breast cancer or prostate cancer).
- Anticoagulants.
- Proton pump inhibitors (Like those that treat acid reflux, which can affect your calcium absorption).
- Certain aspects of your diet and exercise routine can make you more likely to develop osteoporosis, including:
- Not getting enough calcium or vitamin D in your diet.
- Not getting enough physical exercise.
- Regularly drinking alcohol (More than two drinks per day).[14]

Diagnosis

Fractures are typically the first indicator of osteoporosis, as age-related loss of bone density is otherwise difficult to perceive. Estimates of bone mineral density (BMD) can be made using non-invasive dual-energy X-ray absorptiometry (DEXA). The National Osteoporosis

Foundation (NOF) recommends BMD testing via DEXA based on age, sex, and risk factors.[15]

After diagnosis and initiation of therapy, BMD testing should be repeated every two years, and more often in the case of recurring fractures.[16]

The time between scans can also be increased to 15 years in patients with normal BMD or mild osteopenia or five years in patients with moderate osteopenia.[17]

Osteopenia can be distinguished from osteoporosis by the T-score of BMD testing, with a T-score between −1.01 and −2.49 indicating osteopenia and −2.50 or lower being osteoporosis. While it is important to note that BMD test results do not always correlate with fracture probability, early identification of low BMD can inform preventative clinical decision-making.[18]

National Osteoporosis foundation DEXA scan recommendation	
Women Men	
Age 65 and other Age below 65 and post-menopausal Age 50 and older with history of fracture in adulthood	Age 70 and older Age 50-69 with risk factors
DEXA, dual-energy X-ray absorptiometry.	

Treatment of osteoporosis

There are various pharmacological options for osteoporosis treatment that aim to reduce the risk of fractures. These include:

1. Calcium and vitamin D
2. Antiresorptive therapy—Bisphosphonates, Denosumab.
3. Hormonal treatment—Selective oestrogen receptor modulators, Testosterone, PTH analogues.
4. Novel therapies—Romosozumab, Dickkopf-1 (Dkk1) inhibitors.[19]

Materials

Apart from the rapid development of materials for treatment of osteoporosis, novel adjunctive techniques have been developed for assisting the fabrication of biomaterials with superior mechanical property, improved scaffold microstructure and better biological activity. The present section provides an overview of the three most promising adjunctive techniques: 3D printing, electric-fields-assisted techniques and artificial intelligence.

Methods

The National Institute of Clinical Excellence in the UK recommends fracture risk stratification as part of falls assessment for anyone over the age of 65 years in women, or 75 years in men, or anyone under these ages who displays risk factors (e.g. alcohol use, smoking, and previous fragility fracture). However, there remains debate as to how fracture risk should be measured, as some osteoporotic fractures (e.g. vertebral fractures) are not closely correlated to reduced bone mineral density (BMD) in isolation. At present, DXA is the current consensus gold standard. By emitting two low-energy x-ray radiation beams, it can estimate BMD by subtracting the attenuation effect from the surrounding soft-tissues. DXA scanning has proved to be cost-effective and is a standardized method of assessment. There is also evidence to suggest that DXA scanning is an effective predictor of major fragility fractures (e.g. hip fractures).

While BMD is an essential component of screening, DXA scanning does not take into account other significant material properties, such as the increase in cross-sectional area and changes in organic composition. Organic component evaluation, which DXA does not account for, is therefore vital in measuring 'bone quality'. Hence, measurement of bone quality has been proposed as this encompasses parameters such as BMD, microarchitecture of trabecular bone, microcrack prevalence, bone geometry, and bone matrix material properties. This has led to the development of 3D imaging techniques. One such method is quantitative peripheral CT (qpCT), which is calibrated using solid phantoms (representing various BMDs) and is a measure of true volumetric bone density without the superimposition of cortical bone or an enlarged soft-tissue envelope. Quantitative peripheral CT has been shown to be more sensitive than DXA in the detection of osteoporosis. There are, however, significant limitations to qpCT, including lack of standardization, increased radiation exposure, and increased cost.

As a result of the limitations of qpCT, a further method of peripheral assessment of bone quality, which encompasses bone density and microarchitectural morphology (both cortical and cancellous) and its effect on the mechanical integrity of bone, was designed; high-resolution quantitative peripheral CT (HR-qpCT). The radiation dose is significantly reduced, maintaining a reduced scanning time and high precision of BMD assessment. More recently, this has been combined with finite element analysis testing, whereby the HR-qpCT images are converted into finite element blocks within a cubic structure, which models the material

properties of bone, followed by simulation of load in order to predict mechanical behaviour. Both of these techniques have been validated. However, qpCT and HR-qpCT remain in their early development stage and are currently used only for research purposes. Additionally, their ability to monitor longitudinal changes has been questioned as changes in quantitative CT have yet to be correlated with clinical outcomes.

The role of MRI in the evaluation of osteoporosis has also evolved, largely due to the assumption that there is progressive adipose involution of bone marrow with osteoporosis. Varying methods have been proposed to evaluate the subsequent fat fraction, such as T1-weighted imaging, diffusion weighted imaging, and proton magnetic resonance spectroscopy. These methods are still under evaluation and not yet available for universal screening.

As a result of concerns regarding radiation exposure and the problem of lack of portability, quantitative ultrasound scanning of the calcaneus has been studied. While this is non-ionizing and portable, it has not yet been validated and its accuracy is reduced in patients with inflammatory disease. Currently there is no agreed diagnostic criteria for this technique and it is not yet recommended for screening of osteoporosis.

Novel techniques

Bone is a composite material, however DXA only quantifies the mineral content, neglecting the organic component. Impairment of the organic component of bone decreases its toughness, resulting in brittleness. Early work has been undertaken to evaluate the ability of spectroscopy to detect osteoporosis. One such method is Fourier Transform Infrared Spectroscopy, whereby the metabolic changes associated with osteoporosis can be detected, namely by estimating the relative abundance of trace metabolites of both the organic and inorganic constituents of bone using infrared radiation. More recently, X-ray dark-field vector radiography (XVR) has emerged as a new alternative approach in the assessment of bone strength. An XVR image is formed through the mechanism of small angle scattering and is compatible with conventional X-ray tube sources, efficiently yielding high-quality dark-field scatter images. Not only is this able to provide imaging of bone microstructure, but it is also able to yield information on associated bone strength by estimating the anisotropic properties of bone.

At present, none of the above techniques are routinely available in the acute trauma setting. As a consequence, measurements of bone material properties are not available pre-fracture

fixation and cannot be used to guide surgical management. One technique that is readily available is estimation of cortical bone thickness. Cortical bone carries a considerable part of the physiological load, and previous studies have shown that structural behaviour of whole bones is determined by the contribution of cortical bone. Therefore, correlation of cortical bone with bone properties could provide an accurate, rapid, and inexpensive method for predicting those at risk of osteoporotic fracture. It would also have the advantage of being available preoperatively and therefore could help guide choice of surgical fixation.

In this month's edition of *Bone & Joint Research*, two studies have evaluated the accuracy of cortical bone thickness for the estimation of BMD. Firstly, Schmidutz et al estimated the correlation between cortical bone thickness of the distal radius on plain radiographs and predicted BMD from DXA and HR-qpCT. Using measurements from cadavers of human forearms, Schmidutz et al found that cortical bone thickness of the distal radius had a good correlation with local DXA ($r = 0.78$, $p < 0.001$) and moderate correlation with local HR-qpCT ($r = 0.63$, $p < 0.001$). Estimation of cortical bone thickness of the distal radius was modified from the techniques previously described by Ting art et al and Mather et al. Interobserver (0.83 to 0.92, $p < 0.001$) and interobserver (0.79 to 0.86, $p < 0.001$) variation for this modified technique was found to be excellent. In the second study, 54 consecutive patients with distal radius fractures underwent standard posteroanterior and lateral plain radiographs with an aluminium step wedge and DXA. Cortical bone thickness of the distal radius had a low correlation coefficient ($r = 0.34$ to 0.52) with DXA. Inclusion of an aluminium step wedge alongside the wrist for calibration allowed an estimate of density to be obtained, which was found to have a better correlation ($r = 0.65$) with forearm DXA values. However, it should be noted that only 27/54 underwent DXA of the hip and lumbar spine, of which only 13 underwent DXA of the contralateral forearm. Once again, interobserver reliability for estimation of cortical bone thickness was found to be excellent (0.82 to 0.96).[20]

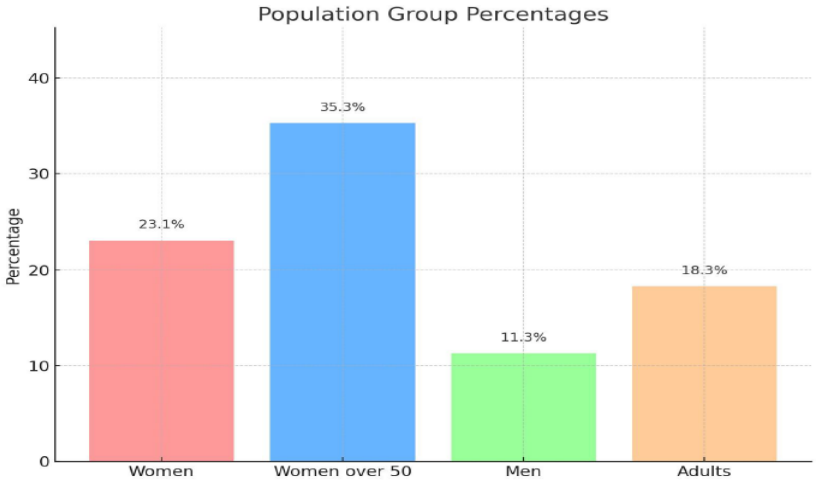
CONCLUSION

Osteoporosis weakens bones and hence usually causes fragility fractures, despite the fact that it is not dangerous in and of itself. These can be the beginning of a succession of fractures, leading to degeneration and loss of independence. Those at risk of osteoporosis should be given lifestyle guidance for optimal bone health. Secondary causes of osteoporosis should be treated/managed if they are present. The most appropriate osteoporosis treatment for each

patient should be selected. It's important to look at strategies that try to lessen the chance of falling.

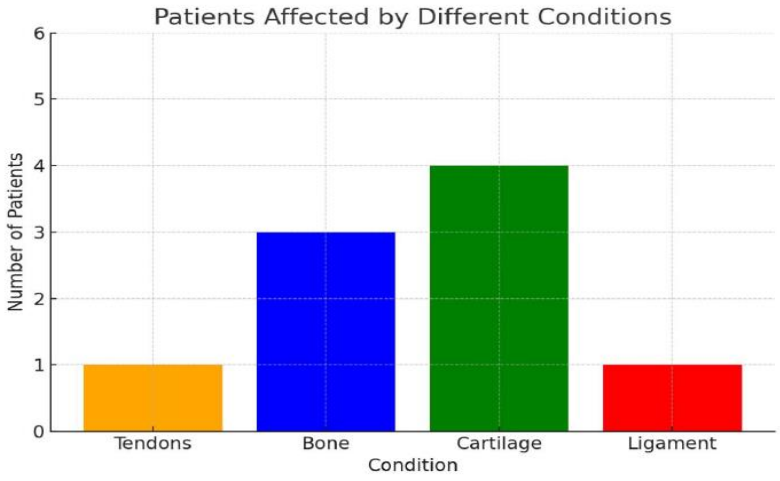
Report's: The table shows the categories of various that are suffering with osteoporosis disease Globally and Their prevalence

Category	Prevalence
Women	23.1%
Women over 50	35.3%
Men	11.7%
Adult	18.3%



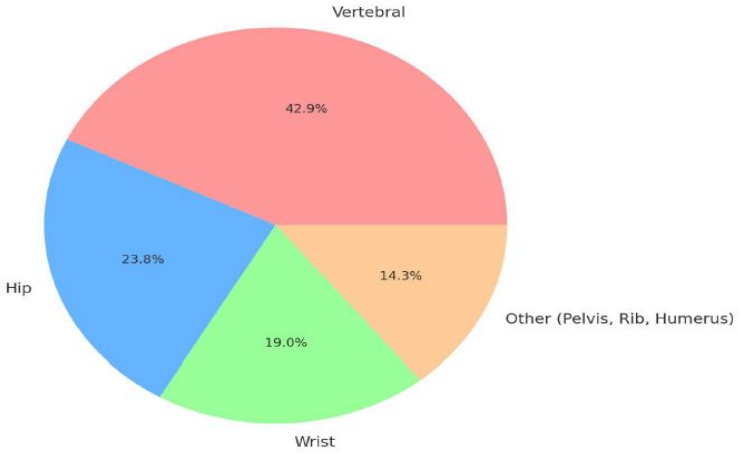
Graph based on parts of skeleton system effecting cartilage bones, Tendons, Ligaments

Patients	Tendons	Bones	Cartilage	Ligaments
1	✓	✓	✓	✓
2	_	✓	✓	_
3	_	✓	✓	_
4	_	_	✓	_



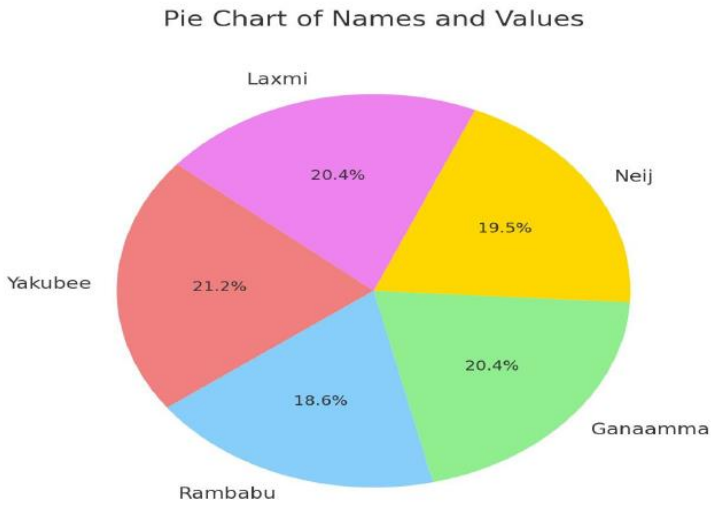
The table shows the different fractures that are takes place in the osteoporosis patients and their prevalence

Fractures	Prevalence
Verteral fracture	40-50%
Hip frature	20-30%
Wrist fracture	15-25%
Other fractures E.g. - pelvis, rib, humerus.	10-20%



The table shows the information about the osteoporosis patients and their bone density levels

S. no	Osteoporosis patients	Bone density
1	Yakubee	-2.4
2	Rambabu	-2.5
3	Ganamma	-2.3
4	Neji	-2.2
5	Laxmi	-2.3



The table shows the medications and prevalence of osteoporosis patients

Medications	Prevalence
Biphosphates	50-60%
Selective estrogen receptor modulators	10-20%
Parathyroid hormone	5-15%
Rank ligand inhibitors	5-15%
Calcitonin	1-5%

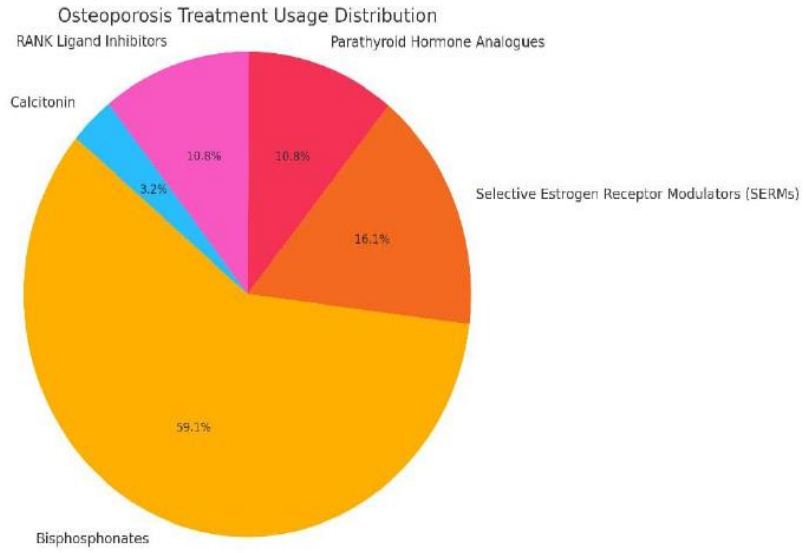
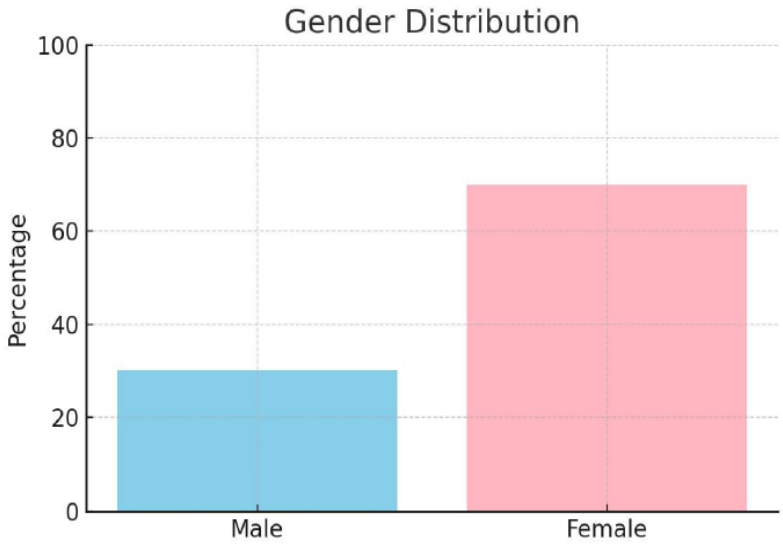


Table shows the prevalence study of patients suffering with osteoporosis in males and females

Sex	Prevalence
Male	30%
Female	70%



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