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The Relationship of Osteoporosis with Menopause: Review of  
Article

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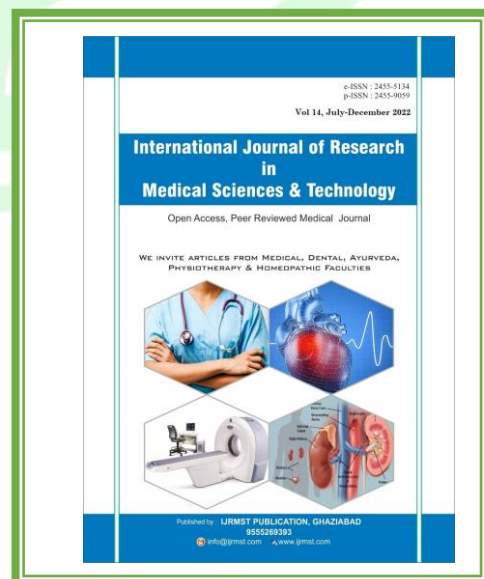
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**ABSTRACT**

Osteoporosis is the most problem of women's bone disease, it has a multitude of causes, including menopause. It affects about one in three women. Before a fracture, osteoporosis does not exhibit any clinical symptoms. Important pathology is brought on by fractures. Postmenopausal osteoporosis can be avoided with early diagnosis of this condition before fractures happen; Menopausal hormone therapy (MHT) significantly reduces the fracture risk in all body bones by halting bone loss and degeneration of bone microstructure. The fast bone loss brought on by declining estrogen peaks in the first two to three years following menopause. Even in women with modest fracture risk, MHT is the only anti-osteoporosis medication that has been shown to be effective regardless of baseline risk. There is no rationale for using specific, efficient drugs to treat osteoporosis, making MHT the first option for maintaining bone health in women. It is also advisable to evaluate the advantages and risks of MHT. MHT has become the leading therapeutic choice for preserving bone health in early postmenopausal women.

**Keywords:** *Menopause, Women, Osteoporosis, Estrogen.*

**INTRODUCTION**

Osteoporosis causes weak bones and increased fracture risk. Its symptoms include low bone mass, bone tissue deterioration, and disturbances in bone microstructure [1]. Especially for postmenopausal women, Osteoporosis concedes as a silent illness that poses serious subsequent health risks [2]. In Europe, it is anticipated 30% of female patients will suffer an osteoporotic hip fracture and that 40% of postmenopausal women will develop osteoporosis over the course of their lifetimes [3, 4]. Due to the quantitative and qualitative alterations in bone brought on by estrogen decline during the early stages of the menopausal

transition, postmenopausal osteoporosis can develop. Estrogen plays a critical function in gaining and maintaining bone mineral content in bone throughout life. As estrogen insufficiency causes osteoporosis by increasing osteoclast production and reducing apoptosis, hormonal variables control the rate of bone resorption by controlling the release of cytokines including interleukin-6, TNF, and prostaglandin E<sub>2</sub>, which causes a rise in osteoclast formation in the bone marrow [5, 6].

Estrogen's function in bone health affects osteoblasts directly through a particular receptor and indirectly through the progenitors of osteoclasts and T

lymphocytes to suppress osteoclast development and activity. Preserving the activity of bone production, particularly by lowering osteoblastic cell death [5]. The main effects of menopause include an irreversible relative deficit in bone development, estrogen insufficiency, and enhanced cellular activity of bone resorption and reformation. As a result, the bone microstructure changes, loss of bone accelerates, and the trabecular bone becomes disorganized, thins, and ruptures, all of which increase the risk of fractures in the entire skeleton, while early signs of increased bone remodeling happen up to three years before the last period [8, 9]. The spine often experiences the biggest loss the one year before finishing the last period and the beginning of the first two to three years following menopause [10,11]. Following that, the decline stabilizes over a protracted, aging-related period. Furthermore, an early rise in bone remodeling results in alterations in bone microstructure [12]

### **Which bones are more affected by osteoporosis?**

That Osteoporosis occurs in the trabecular bones (ribs, wrists, and vertebrae), which are the most metabolically active bones and they are more susceptible to hormonal

changes that occur at menopause beginning [9,13]. This contributes to the explanation of the variation in the incidence of fracture by sites, such as (wrist and rib) fractures, and by age. Vertebral fractures happen after about 10 to 15 years, whereas hummer destruction is more noticeable during menopause and the early postmenopausal years. Although each postmenopausal woman's bone mineral content varies significantly from the other women's, this is mostly due to the fact that bone mass peaked towards the end of puberty, also thinness, and early menopause have a role in this state [14, 15], even menopausal circumstances (surgical versus natural), and active smoking may be the primary causes of these disparities [16].

Rapid bone loss is caused by certain factors, weight gain and obesity [17, 18], delayed menopause, and postmenopausal bone loss are typically linked to affect by 17 beta-hydroxysteroid genes and estrogen receptors [19,20].

When the resorption rate outpaces the formation rate, loss of bone happens. Continuous resorption and creation result in the loss and replacement of bone tissue. Mass of sculpted (growing and developing the shape) starts from infancy to reach

adulthood: Peak peak mass of bone (PBM), then the mass of bone starts to decrease. PBM is influenced by genetics, health development, diet, the status of endocrine, physical activity, and gender. Remodeling bone involves removing damaged bone and replacing it with new bone formation to microfractures to treat and prevent them from developing into bigger fractures, preserving the structural integrity of the bone [21].

Bone Resorption increases higher than absorption due to an imbalance between the rates of resorption and production brought on by menopause and advancing age, which raises the risk of fractures. Bone loss results from several causes that stimulate resorption more than production, exposing the intricate structure. Loss of plates in a single trabecular bone result in an architecturally frail structure with a large loss of mass, which increases the likelihood of fractures. Osteoporosis and fracture risk is increased by rapid bone growth [22].

Fractures brought on by osteoporosis are more frequently the outcome of multiple factors. Some of these include more specialist risk factors, such as glucocorticoid use, which has an impact on both bone quality and bone development

and loss, as well as more general risk factors like aging and sex steroid deficiency [23].

### **Classification of osteoporosis**

The two main kinds of osteoporosis—primary osteoporosis and secondary osteoporosis—can be distinguished by taking into account the factors that influence bone metabolism [2].

Autonomic osteoporosis type I, A variant of primary osteoporosis that largely affects the trabecular bone is known as postmenopausal osteoporosis. Women are therefore more vulnerable to osteoporosis than men [2].

Age-related loss of mass of bone is a feature of type II autonomic osteoporosis [24].

The clinical effects of osteoporosis that are relevant include fractures and squeals. Whether there was trauma or not, the location of the structural fracture in the body, It should be stated as the spine or vertebrae, the hip of the proximal femur, the distal wrist forearm, or the area shoulder [25, 26].

### **Osteoporosis Diagnosis**

The density of bone mineral is measured using absorptiometry of dual X-ray



(DXA), which is usually stated in terms of grams of bone scanned as Ca\square centimeter. Osteoporosis is detected or confirmed by BMD measures of the hip and spine, which are also used to monitor patients and forecast future fracture risk[27].

With the absence of bone biochemical markers, the degree of bone deterioration cannot be evaluated in clinical settings; nevertheless, BMD may detect bone density quantified [28].

Applied T-score criteria to measure BMD by DXA at the hip femoral and spine lumbar for women postmenopausal 50 years of age and older [29]. Numerous conditions, drugs, and way of life modifications might result in secondary osteoporosis.

### **Combating osteoporosis**

All calcium supplements work best when consumed with meals, especially when there isn't any stomach acid-secreting. Calcium dosages should not exceed 500–600 mg per dose for best absorption. The benefit of calcium carbonate for patients is the cheap price and the least amount of dosage but its side effects can cause problems in the gastrointestinal tract. Despite the fact that calcium citrate is very

expensive and more doses require to take, it does not affect digestion and does not require stomach acid for absorption. Some dietary items include too much oxalate, which binds to calcium and inhibits it from being absorbed. If you take more than 1200-1500 mg per day, you could develop kidney stones. For patients under the age of 70, doctors recommend 600 IU/day of calcium and 800 IU/day of vitamin D, as these nutrients are both essential for calcium absorption, bone health, and muscle function[30,17].

Fortified milk, juices, cereals, saltwater seafood, and liver as food sources of V-D. You can use V-D2 (ergocalciferol) or V-D3 as supplements (cholecalciferol). Vit-D<sub>3</sub> 25(OH)D levels in serum who are at risk of deficit V-D should be evaluated. With the usage of V-D supplements, the level of blood of V-D should be raised to around (75 nmol/L) [31].

Need to maintain a regular exercise schedule throughout your life, concentrating on weight-bearing exercises (such as 30 to 40 minutes per session walking) and including exercises for back on the majority of your workout days. Physically active kids and teens had more peak bone mass than others[32].

These exercises benefit elderly people by slowing the bone loss brought on by inactivity, enhancing balance, and building muscle strength, all of which lower the risk of falls [33].

Bending, lifting, pushing, and dragging impose tension on the spine and can cause fractures, so patients should refrain from forward bending exercises, lateral bending exercises, and heavy lifting.

preventing falls The majority of osteoporotic fractures are caused by falls. Disabled patients who take specific medications that impair mental awareness and increase the risk of stroke [34].

#### **DRUGS AND THERAPY**

Prior to beginning treatment, all patients with osteoporosis should have their secondary causes of the condition assessed. They should also have their BMD measured using central DXA if necessary adding spine imaging investigations. Obtaining BTM levels is necessary if therapy monitoring is intended for the use of pharmaceuticals to treat osteoporosis following are the primary objectives of treatment for those with osteoporosis. In order to preserve normal bodily function, the majority of modern pharmaceuticals are made for the

prevention of osteoporosis and fractures to reduce resorption of bone and are known as drugs of anti-abortion. Include the drugs that lower the fracture risk like estrogen and raloxifene, a selective estrogen receptor modulator (SERM), bisphosphonates (BPs) including (strontium ranelate, alendronate, risedronate, ibandronate, and finally zoledronic acid (SR)) [8].

The fractures incidence is decreased by hormone therapy, but the risks of cardiovascular disease, cerebrovascular accidents, and breast cancer are all raised [35].

Estrogen is a potent inhibitor of the rise in bone activity that takes place in early menopause and prevents postmenopausal bone loss. Due to the coupling of these two biological activities, As a result, after three to six months of treatment, there is a rapid decline in resorption bone, which is followed by a bone formation decline. A bone mass new steady state of is attained about 6.0 to 12 months after the therapy is started.

Collagen type C- and N-telopeptides, which are biochemical of bone markers uptake and e a considerable drop after the sixth month of treatment before plateauing, provide evidence of the effect. Bone

mineral density treatment is different during the first year and begins to increase, with minimal increments in the 2ed year, and then stabilizes, as MHT is continued [36].

One study found that in a sample chosen without taking into account the ratio of low BMD, five joint fractures for 10,000 women for one year and a total of 47 fractures fragility for 10,000 women for a year occurred [37].

It is now the only anti-osteoporosis medication that has been demonstrated to lower the fracture risk in women postmenopausal. The Age, index of body mass, smoking, fracture history in oneself or in one's family, or total calcium consumption were all unaffected by this impact. Early with a poor fracture risk[38]. The only warning is that modest dosages of estrogen may not be effective at preventing fractures[39]

There is a limited indication that total fracture treatment continues to benefit former MHT patients, the preventive effect may decrease significantly after 5 years of treatment cessation (bone loss following MHT cessation often reverts to normal levels after menopause) [40].

For several years after ending therapy, the BMD of MHT-previously treated women was higher than that of placebo-treated women [41]. Other meta-analyses in WHI have discovered some indication that former MHT users continue to benefit longer than former placebo for more than 5 years after ceasing therapy [42,43].

The original conclusions of WHI have already been disputed by other trials, and it is evident that the balance between the advantages and hazards of MHT greatly depends on the dose, MHT, and an indicator of the risks unique to each woman [39, 40]. Within ten years of menopause and MHT use, a cardiovascular risk emerges [44]. Whereas in the WHI, MHT use elevated breast cancer risk [45-47] Evidence suggests that estrogen and also progesterone combined enhance the breast cancer risk compared to estrogen-only [48,49]. Additionally, it appears that the risk varies depending on the progesterone type utilized [50].

The number of studies demonstrating MHT's efficacy within the first 10 years in early postmenopausal women following menopause is actually expanding. Transdermal estradiol combined with natural progesterone or dydrogesterone can help to improve this equilibrium. The

osteoporosis induced by the management of glucocorticoids- involves the use of polyestrogen regimens, medications that reduce the fracture risk, etc. The reduction of spine and hip fractures has only been shown to occur with alendronate, risedronate, zoledronic acid, and SR [51, 52].

Osteoporosis in postmenopausal women is treated with ibandronate. With the exception of high-risk subgroup instances, it has been to reduce the vertebral risk fractures in women postmenopausal with osteoporosis but not the risk of vertebral or hip fractures. Ibandronate's effectiveness and safety have been studied in cases that lasted up to three years, and are still unclear after that point [53].

Zoledronic acid can be used to treat and prevent osteoporosis brought on by glucocorticoids, osteoporosis in men, and postmenopausal osteoporosis. Once a year, a 5 mg infusion lasting at least 15 minutes is administered intravenously [54].

#### **Warnings, contraindications, and complications of Ibandronate treatment**

If taken with any food or drink besides water or the drug and within two hours after taking the medication, oral absorption of ibandronate is less than 1%. In patients

with upper gastrointestinal disease, those who cannot stand upright for 30 to 60 minutes, those who have anatomical or functional abnormalities of the esophagus, V-D deficiency, calcium deficiency blood, drug hypersensitivity, and renal failure, oral administration should be used with caution. When BPs, such as ibandronate and zoledronate, is administered intravenously, some patients experience acute phase effects (such as fever, muscle pains, etc.) that begin with the first dosage and linger for several days; To prevent this from occurring, take acetaminophen. The condition known as osteonecrosis of the jaw (ONJ) is one of the issues that BPs have been linked to in the muscles, joints, and bones[55]. Osteoporosis in postmenopausal women with, raloxifene is used to lessen the incidence of fractures of vertebral, but not the risk hip fractures. These medications shouldn't be taken by women who are pregnant or who have the venous thromboembolic disease [56]. When non-estrogenic drugs are ineffective for treating high-risk patients for osteoporosis after menopause, estrogen replacement therapy (ERT) is employed. Regardless of age or the severity of the underlying condition, in women in postmenopausal with osteoporosis, strontium ranelate reduces the frequency



of both fractures of vertebral and nonvertebral [57, 58].

SR increases BMD and reduces the fracture risk in postmenopausal osteoporosis women. While SR has not gotten approval from the US Food and Drug Administration, the European Medicines Agency (EMA) has approved it for the treatment of osteoporosis in males who are at an increased fracture risk.

Postmenopausal women are at high fracture risk, as well as those who have tried and failed to react to various osteoporosis medications are all treated with denosumab or (human monoclonal antibody against RANKL). It has reduced the spine, hip, and non-vertebral regions' fracture risk, before starting therapy hypocalcemia must be corrected [59, 60].

Teriparatide is used to treat postmenopausal osteoporosis with a high risk of fracture in individuals who have failed or are unable to tolerate earlier osteoporosis treatments. It increases bone mass in men with osteoporosis of uncertain cause or hypogonadism. Teriparatide is also authorized for osteoporosis treatment caused by glucocorticoids in both males and females Serum Ca, PTH, and V-D levels should be

assessed prior to beginning treatment [61,62].

### **Sequential or combination therapy**

There is no proof that the use of therapeutic agents or combination therapy with two or more osteoporosis drugs improves the course of osteoporosis or lowers the danger of fracture.

### **CONCLUSION**

Osteoporosis is a common and silent condition. According to estimates, 50% of women over 50 will experience osteoporosis-related fractures during the course of their remaining lifetimes. These fractures result in lifelong impairment and an increase in mortality, placing a tremendous burden on nursing staff and the economy of the patient as well as the entire country. Before fractures happen, osteoporosis can be identified and treated effectively. Therefore, primary healthcare practitioners should have the authority to prevent, detect, and treat osteoporosis.

According to recommendations, the MHT use for the prevention of osteoporosis should be taken into account while balancing the total benefits and dangers for each patient, especially when troublesome symptoms are present. Keeping in mind the demands of certain newly

postmenopausal women to maintain skeletal health.

Finally, early women in postmenopausal with a low or moderate danger of fractures should have MHT reevaluated as a first-line preventative therapy option. It should be taken into account as a true first-line prevention strategy treatment to maintain the density of bone as well as minimize the fracture. at a time when there ought to be no such risk. It is crucial to take into account the body's estrogen resistance as well as the usage of various estrogens and progestogens, dosages, and delivery methods. It is obvious that the strategy picked needs to be adapted to strike a balance between benefits and risks.

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