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*Review Article*

# Risk Factors Associated With Osteoporosis

Suman VB[1*], Khalid P[2], Pratik K Chattergee[1]

[1]Department of Physiology, Manipal University, Kasturba Medical College, Mangalore, Karnataka, India.
[2]Department of Biotechnology, P A College of Engineering, VTU, Mangalore, Karnataka, India.

[*]Correspondence Email: suman.vb14@gmail.com

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## ABSTRACT

Osteoporosis is a global problem affecting 150 million men and women worldwide. Osteoporosis is a condition characterized by decreased bone strength. Women are four times likely to develop osteoporosis than men. It is prevalent in post-menopausal women but also occurs in men and women with underlying conditions or major risk factors associated with bone demineralization. Its chief clinical manifestations are vertebral and hip fractures, although fractures can occur at any skeletal site. Osteoporosis ranks as one of the 5 costliest diseases of aging after diabetes, hyperlipidemia, hypertension and heart diseases. As age advances, the incidence of osteopenia and osteoporosis increase and with the progressive aging of the world's population, there will be a resultant increase in the osteoporotic fractures. It is a matter of great concern that although the effects of osteoporosis are seen in the elderly population particularly women, the roots of osteoporosis are laid much earlier in life. Thus osteoporosis has been described as a condition dealt with by geriatrician but with roots in pediatrics. We are trying to elaborate on risk factors, measurement of BMD and management of osteoporosis.

***Key words:*** Osteoporosis, BMD (Bone mineral density), Menopause, Ageing.

## INTRODUCTION

***Osteoporosis:*** is defined as a reduction of bone mass (or density) or the presence of a fragility fracture. Based on recommendation of a WHO committee, osteoporosis is operationally defined as a bone density that falls 2.5 standard deviation (SD) below the mean for young healthy adults of the same race and gender also referred to as T-score of -2.5. Those who fall at the lower end of the young normal range (a T-score of >1SD below the mean) are defined as osteopenic having low bone density and are considered to be at increased risk of osteoporosis.

***Osteoporosis classification****:*

***Primary Osteoporosis***

1. *Postmenopausal osteoporosis (Type 1):*

In women main cause of bone loss after menopause is primarily estrogen deficiency hence estrogen treatment arrests the progress of the disease. Estrogen inhibits the secretion of cytokines such as IL-1 and IL-6 and TNF and these cytokines foster the development of osteoclasts. There are estrogen receptors on the osteoblasts and direct stimulatory effect on them is a possibility. Estrogen also stimulates the

production of TGF-B and this cytokine increases the apoptosis of osteoclasts. [1]This occurs typically between 55-75 years of age which affects mainly trabecular bone and is more common in women compared to men (ratio 6:1). Prior to menopause, bone loss occurs at the rate of 0.5 to 1.0% per year. At menopause, bone loss accelerates at the rate of 2.5to 5% per year mainly due to decline in estrogen levels and is greatest in the first 3-6 years post menopause. The rapid phase of bone loss in the early post menopause is due to loss of the direct action of estrogen on bone cells and that this phase is poorly responsive or nonresponsive to calcium supplementation. The subsequent slower phase of bone loss has been thought to be caused, at least in part by age-related changes in non-skeletal calcium homeostasis, including impaired calcium absorption and enhanced renal losses, leading to increases in serum PTH and increases in bone resorption. [2]

Four of the major discriminatory peaks in the diagnostic profile were identified as fragments of interalpha-trypsin-inhibitor heavy chain H4 precursor (ITIH4), a plasma kallikrein-sensitive glycoprotein that is a component of the host response system. These data suggest that these serum protein fragments are the serum-borne reflection of the increased osteoclast activity, leading to the increased bone turnover that is associated with decreasing BMD and presumably an increased risk of fracture in postmenopausal women. [3]

2. *Senile or age related osteoporosis (Type 2):*

The type 2 osteoporosis also known as involutional osteoporosis occurs after the age of 70 years, affects both cortical and trabecular bone associated with advancing age and menopause and hence affects women twice as frequently as men. Involutional osteoporosis is a common disease and has become a major public health problem in United States and Europe as the number of elderly people in population has increased. [2]

***Secondary osteoporosis:***

This can occur due to specific causes such as endocrine diseases like hyperthyroidism, hyperparathyroidism, glucocorticoid excess, drug induced such as glucocorticosteroids, barbiturates, heparin, ethanol and miscellaneous conditions like prolonged immobilization, rheumatoid arthritis or chronic liver failure.

***Risk factors associated with osteoporosis:***

Risk factors may help explain contributing causes of osteoporosis or help guide therapeutic recommendations, but they cannot be used to diagnose osteoporosis. Although many risk factors for osteoporosis and fractures have been identified, yet one cannot determine why some individuals show marked reduction in bone mass and are prone to multiple fractures, whereas others with similar risk factors do not exhibit these characteristics. [4]

The risk of developing osteoporosis is increased in women with slender built, inactive lifestyle, extensive bed rest, a life time diet low in calcium and vitamin D, history of excessive alcohol intake, cigarette smoking, tobacco use, premature or surgical menopause or with use of medications which affect bone turnover. EtOH consumption in the period immediately post weaning may significantly impair the mother´s skeletal health and lead to long-term osteopenia. [5]

It was previously believed that obesity and osteoporosis were two unrelated diseases, but recent studies have shown that both diseases share several common genetic and environmental factors. Body fat mass, a component of body weight, is one of the most important indices of obesity, and a substantial body of evidence indicates that fat mass may have beneficial effects on

bone. The common precursor stem cell that leads to the differentiation of both adipocytes and osteoblasts, as well the secretion of adipocyte - derived hormones that affect bone development, may partially explain these associations. [6]

It was shown over 50 years ago that menopause is associated with a period of rapid bone loss that is preventable by estrogen replacement therapy. [7] More recently, it became evident that this rapid phase of bone loss, which can last for up to 8-10 years, is followed by a slower phase of age-related bone loss that continues indefinitely. [8] Convincing evidence has now emerged that this continuing slow phase of bone loss is caused in large part by estrogen deficiency, through effects on the gut and kidney that impair intestinal calcium absorption and renal calcium conservation. Because testosterone and androstenedione produced by the ovary can serve as substrate for extragonadal endogenous estrogen production after menopause. [9]There could be effects on the skeleton of bilateral oophorectomy later in life, even after the rapid phase of bone loss has ceased. Little attention has been given to this potential problem, and there is controversy of whether the postmenopausal ovary is or is not an important source of these androgens. [10-15] However, population-based studies have shown that even slightly lower levels of circulating estrogens are associated with increased bone loss and fracture risk in postmenopausal women. [16-20] To the extent that ovarian androgens make a contribution to endogenous estrogen production after menopause, there may be unexpected adverse consequences of oophorectomy in elderly women.

Women who had a bilateral oophorectomy on average 14 years after natural menopause experienced a 32% increase in subsequent overall fracture risk and a 54% increase in the fractures traditionally associated with osteoporosis. This finding is consistent with the notion that postmenopausal women experience reductions in circulating testosterone and androstenedione levels after the removal of their ovaries. [10-14] The androgen reductions themselves could have an independent adverse effect on bone, but more importantly, they are aromatized to estrogens systemically in fat and locally in bone tissue, [21,22] to the extent that endogenous estrogen production is reduced even slightly, [23] postmenopausal bone turnover might be exacerbated and fracture risk increased. [24,25] Although most authors have concluded that circulating estrogen levels are not lowered after oophorectomy, in fact, small reductions are typically observed, though the differences may not be statistically significant. [26]

In addition to the well-known effects of age, the other risk factoridentified is the earlier incidence of fracture. Thus, a prior history of fractures has been shown to be a strong predictor of future osteoporotic fracture risk, while anticonvulsant use has been associated with an increased risk of fractures generally, [27-29] probably through a relationship with seizure disorders and falling. Anticoagulants also had an effect on overall fracture risk in this study, but other investigators have not found associations except with vertebral and rib fractures. Alcoholism has been linked to an increase in all sorts of fractures as we also observed. [30-32] The use of thiazide diuretics was linked with a 40% reduction in osteoporotic fractures, but we saw no independent protective effect of thiazides on specific fractures or on overall fracture risk in accordance with most other work on the subject. [33]

Osteoporosis is associated with many joint disorders. Osteoporosis is not an attendant feature of degenerative joint disease particularly around the knee but may

be present because of the age of the patient. It is obvious that since primary degenerative joint disease occurs in individuals of late middle age and in elderly, osteoporosis may be a common finding although not related to degenerative joint process unless disuse atrophy occurs. [34] Osteoporosis is also said to be associated with Vitamin C deficiency in which there is diminished production and maintenance of intercellular ground substance (osteoid) formation. [35]

***Osteoporosis in thyroid disorders:***

Considerable controversy surrounds the role that thyroid disorders play in exacerbating bone loss and the risk of osteoporotic fractures. Bone mass is generally said to be reduced with hyperthyroidism and in many but not all studies of thyroid replacement therapy, whereas bone mass is unchanged or increase in patients with hypothyroidism. [36-38] The secretion of calcitonin is dramatically reduced by total or subtotal thyroidectomy and/or radioiodine therapy, [39-41] and calcitonin deficiency has also been postulated to cause osteopenia. Thus, thyroidectomy could be associated with bone loss because of an endogenous excess of thyroxine, overenthusiastic thyroid replacement therapy following surgery, deregulation of bone resorption as a consequence of calcitonin deficiency, or some combination of these factors. Most studies, however, have included relatively few men, and the effects on bone density have not been large even in women. The practical result in terms of fractures has been uncertain, although fracture risk is reportedly increased in women with hyperthyroidismor on excessive thyroid replacement therapy**.** Interpretation of these results is hampered by the background of involutional osteoporosis in postmenopausal women. Since most biologically active calcitonin is produced by C-cells, which are centrally located in each lobe of the thyroid, even partial thyroidectomy renders a person relatively calcitonin deficient and there is evidence of reduced serum calcitonin levels following surgery. [42,43]

***Osteoporosis in men****:*

Particularly serum testosterone and estrogen levels are known to be associated with bone mass and with rates of bone loss in men. Associations between these bone mass / structural parameters and sex steroid levels are progressively stronger with age in men. DEXA has been an extremely useful clinical tool for defining osteoporosis and identifying individuals at increased risk of fracture and has been used extensively to relate bone mass or rates of bone loss to circulating sex steroid levels in men. [44]

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