

Osteoporosis - Designer Disease of Modern Era

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Just like Hypertension, Osteoporosis, or porous bone, is a silent killer disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased risk of fractures of the hip, spine, and wrist. As the longevity of life has increased, the prevalence of Osteoporosis has increased. With Vitamin D deficiency being identified as an important risk factor, Osteoporosis has become a disease of modern air conditioned lifestyle. Men as well as women are affected by osteoporosis, a disease that can be prevented and treated.

Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporotic fracture every 3 seconds. Worldwide, 1 in 3 women over 50 will experience osteoporotic fractures, as will 1 in 5 men. About 20-25% of hip fractures occur in men. The overall mortality is about 20% in the first 12 months after hip fracture and is higher in men than women. A prior fracture is associated with an 86% increased risk of any fracture¹.

Osteoporosis is greatly underdiagnosed and undertreated in Asia, even in the most high risk patients who have already fractured. The problem is particularly acute in rural areas where hip fractures are often treated conservatively at home instead of by surgical treatment in hospitals. It is projected that more than about 50% of all osteoporotic hip fractures will occur in Asia by the year 2050².

This silently progressing metabolic bone disease is widely prevalent in India and osteoporotic fractures are a common cause of morbidity and mortality in adult Indian men and women. Expert groups peg the

number of osteoporosis patients in India at approximately 26 million (2003 figures), with the numbers projected to increase to 36 million by 2013³. Recent modernization of India resulting in working indoor, and reduced physical activity have resulted in limited sun exposure, Vit D deficiency and Osteoporosis.

The known risk factors for Osteoporosis are older age, female gender, especially small thin boned women of Caucasian and Asian ethnicity. Family history of fractures is an important risk factor implicating hereditary factors.

The modifiable risk factors include deficiency of estrogen in females and testosterone deficiency in males, diet low in Calcium, Vit D deficiency and Long term use of medications like steroids, antiepileptics, antacids etc³. I consider Osteoporosis as a designer disease of Modern era because modern lifestyle which consists of obesity, lack of exercise, less sunlight exposure due to air conditioned cars and interiors, food fads causing anorexia nervosa and nutritional deficiencies and social trends of smoking and alcoholism significantly contributes to early development of Osteoporosis & consequences like fractures.

An emergent well defined risk factor is Body Mass Index (BMI). Study by Emaus N. et al examined the effect of combined profiles of smoking, physical activity and body mass index (BMI) on lifetime bone loss. BMI had the strongest effect on BMD, especially in the oldest age groups, but a BMI above 30?kg/m² did not exert any additional effect compared to the population average BMI of 27?kg/m². At the age of 80 years, a lifestyle of moderate BMI to light overweight, smoking avoidance and physical activity of 4 hours vigorous activity per week through adult life may result in 1-2 standard deviations higher BMD levels compared to a lifestyle marked by heavy smoking, inactivity and low weight⁵.

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Neelam Agrawal et al. found that out of 200 women studied, 106 were found to have low BMD (osteopenia and osteoporosis). The mean age was 52.50 ± 5.94 years in group with low BMD, and average age at menopause was 51.23 ± 4.82 years. There was a significant positive correlation between increasing age, low BMI, low calcium intake, lack of exercise, and low BMD⁵.

I would mainly like to highlight on Calcium and Vit D deficiency and its role in Osteoporosis. More than 99 percent of the body's calcium is contained in the bones and teeth. The remaining 1 percent is found in the blood. Many published studies show that low calcium intake appears to be associated with low bone mass, rapid bone loss, and high fracture rates. National nutrition surveys show that many people consume less than half the amount of calcium recommended to build and maintain healthy bones. Daily calcium requirement in 51-70 year old males is 1000 mg and 1200 mg in females.

Calcium and vitamin D in combination are more beneficial in reducing fracture rates than either treatment alone. This combination has minimal adverse effects but compliance remains a limitation. Combined calcium and vitamin D should be used in all patients diagnosed with osteoporosis unless other non-pharmacological measures are deemed adequate. Although concerns have been raised for the increased risk of cardiovascular events with excessive doses of calcium, there is no suggestion of any increase in risk with calcium and vitamin D in combination with or without antiresorptive drugs in patients with osteoporosis. Inadequate calcium intake was proposed as an additional factor contributing to the low BMD. This was shown in a study by Shatrugna et al on Indian women from low income groups who consume diets that have inadequate calcium coupled with too few calories, proteins and micronutrients. BMD and T scores at all the skeletal sites were much lower than the values reported from the developed countries and were indicative of a high prevalence of osteopenia and osteoporosis. Body weight, age, menopause and calcium intake were found to be important determinants of BMD⁶.

Studies show that vitamin D production decreases in the elderly, in people who are housebound, and for people in general during the winter. Adults should have vitamin D intakes of 600 IU (International Units) daily up to age 70. Men and women over age 70 should increase their uptake to 800 IU daily. Arya et al¹⁸ used a serum 25 (OH) vitamin D level of 15 ng/ml as a cut-off, and found 66.3 per cent of subjects to be vitamin D deficient. Of these, 20.6 per cent had severe vitamin D deficiency (<5 ng/ml), 27.2 per cent had moderate (5- 9.9 ng/ml) while 18.5 per cent had mild vitamin D deficiency (10-14.9 ng/ml). When a serum 25 (OH) vitamin D level of 20 ng/ml was used as a cut-off, 78.3 per cent subjects were diagnosed to be vitamin D deficient / insufficient. The serum 25 (OH) vitamin D level correlated with sunlight exposure and femoral neck BMD⁷.

Osteoporosis may be asymptomatic or may cause mild symptoms like bony and joint pains and fatigability. Usually it is detected when patients present with fractures. The diagnosis can be achieved by determination of Bone mineral density by Ultrasound or DEXA Scan which is more specific. Serum markers of bone formation include bone-specific alkaline phosphatase and osteocalcin. Markers of bone resorption are the collagen cross-links : deoxypyridinoline, N-telopeptide (NTx), and C-telopeptide (Ctx). Although the resorption markers are measured in the urine, blood measurements have recently become available⁸.

Osteoporosis may not be totally preventable but its onset can be delayed. Prevention programs include a comprehensive approach with control of risk factors. In the prevention of osteoporosis and fracture risk, the effect of combined lifestyles through adult life should be highlighted. We have drugs which increase bone formation and prevent bone loss. They can be used along with lifestyle modification. The pharmacotherapy of Osteoporosis includes **1) Bisphosphonates** - They are the most commonly used medications. Alendronate, clodronate and risedronate are taken orally in a fasting state due to low bioavailability and with precautions to avoid gastrointestinal adverse

effects. The intravenous bisphosphonate, zoledronic acid, has been approved for treatment of osteoporosis and has the advantage of once yearly dosing and a reduction in gastrointestinal adverse effects. The HORIZON - Recurrent Fracture showed a reduction of 35% in the risk of any new clinical fracture and a 28% (RR=0.72, CI: 0.56-0.93) risk reduction in death from any cause in the zoledronic acid group [Lyles et al. 2007].

2) Parathormone : Two PTH-related analogues are currently in use : teriparatide (PTH 1, 34) and recombinant human PTH 1, 84. For teriparatide, the pivotal trial was the Fracture Prevention Trial (FPT), which showed that after daily subcutaneous injection of teriparatide 20 µg for a median duration of 21 months, new vertebral fractures were reduced by 65%.

3) Denosumab is a recently launched human monoclonal antibody that targets and binds with high affinity and specificity to the receptor activator of nuclear factor-kappa B ligand (RANKL). The FREEDOM Trial investigated the efficacy of denosumab and found that it significantly reduced the risk of fractures, especially in elderly women.

4) Dual-action Bone Agents : Strontium ranelate is an antiosteoporotic agent thought to have a dual action (antiresorptive and bone forming). The SOTI study showed a significant 49% reduction in new vertebral fractures at 1 year in the treatment group. Alongwith these drugs Calcium and Vit D supplementation is important in reducing osteoporosis and consequent fractures^{9,10}.

In the end I would like to specifically stress the magnitude of osteoporosis in elderly. The number of people over the age of 60 years is projected to more than triple globally in the next half century, from 593 million to 1.97 billion. It is estimated that 30% of all fragility fractures in women occur over the age of 80 years and this figure increases to 60% when hip fracture is considered separately. Even Elderly men are more prone to fractures especially hip and vertebral. In this issue Dr. M. A. Thakare has discussed about Osteoporosis in elderly in details and has provided valuable guidelines for management of Osteoporosis in elderly. I would like to add that medications can be given to elderly but with due caution and monitoring. Calcium and Vit D

supplementation is a must. Many trials have shown the efficacy of medications in treatment of osteoporosis in elderly¹¹.

Thus Osteoporosis, a disease of the modern Era will continue to be a major health concern in men and women, especially the elderly population. A comprehensive preventive strategy incorporating non pharmacological as well as pharmacological therapy needs to be formulated. The evidence highlights that a number of drugs can safely reduce osteoporosis risk in older patients and appropriate management will reduce the morbidity, mortality and economic costs associated with this disease. Public awareness about the problem and enthusiastic implementation of preventive programs is required.

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