"A HOSPITAL BASED ONE YEAR CROSS SECTIONAL STUDY TO KNOW THE PREVALENCE OF OSTEOPOROSIS IN MEN AGED MORE THAN 50 YEARS USING DUAL ENERGY X-RAY ABSORPTIOMETRY SCAN (DEXA)"

By

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DISSERTATION

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ENDORSEMENT

This is to certify that the dissertation entitled **"A HOSPITAL BASED ONE YEAR CROSS SECTIONAL STUDY TO KNOW THE PREVALENCE OF OSTEOPOROSIS IN MEN AGED MORE THAN 50 YEARS USING DUAL ENERGY X-RAY ABSORPTIOMETRY SCAN (DEXA)"** is a bonafide research work done by **CANDIDATE (REG NO. BL0110002)**

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ABSTRACT

Background and Objectives:

Osteoporosis is one of the most common non communicable disease in elderly men. It is also one of the most common under diagnosed condition in our Indian population. Aim of the study was to know the prevalence of osteoporosis in men aged more than 50 years in our region. To find out the various risk factors associated with osteoporosis.

Methodology :

Data was collected from all men with age more than 50 years attending outpatient and inpatient Orthopaedics department and also males attending osteoporosis check up camps who were willing to undergo DEXA Scan. DEXA scan of hip and spine was done, to assess BMD. Various other risk factors were evaluated through a questionnaire. T Scores and Z Scores were evaluated for the presence of osteoporosis based on WHO Criteria.

Results:

101 men aged more than 50 years were studied. Prevalence of osteoporosis at the spine was 37.62% while at the hip was 28.71%. The overall prevalence was 39.60%. Mean height of osteoporotic men was not significantly different from other men, however osteoporotic men had lower body weight and significantly lower body mass index. Predominantly osteoporotic men were those involved in indoor office work & Retired men staying in home (52.2%) with reduced duration of exposure of sunlight. Also most osteoporotic men were vegetarians (47.22%).The prevalence of osteoporosis was higher among the group with inadequate exposure to sunlight (45.45%). 3.96% men had positive family history for fracture of the hip and wrist after trivial fall and all the 3.96% men had osteoporosis in this study.

Conclusion and interpretation:

High prevalence in this semi urban group of men is a cause for concern. Measures such as adequate calcium and vitamin D intake, physical activity and exposure to sunlight will be useful in preventing occurrence of osteoporosis. As the diagnosis and long term treatment of osteoporosis and consequent fractures are expensive for the individual as well as the health system, there is a need for careful consideration in determining the risk factors as well as the future course of action on scientific evidence.

Key words: Prevalence, Osteoporosis, Men, DEXA

LIST OF ABBREVIATIONS USED

BMD	-	Bone Mineral Density
BMI	-	Body Mass Index
DEXA	-	Dual Energy X-ray Absorptiometry
SPA	-	Single Photon Absorptiometry
H/O	-	History of
Ht.	-	Height
IP No.	-	Inpatient Number
Lt	-	Left
OP.No.	-	Out Patient Number
qUS	-	Quantitative Ultrasound
pDEXA	-	Peripheral Dual Energy X-ray Absorptiometry
PTH	-	Parathyroid Hormone
QCT	-	Quantitative Computerized Tomography
RA	-	Radiographic Absorptiometry
ROM	-	Range of movement
BUA	-	Broadband ultrasound attenuation
Rt	-	Right
Sl No.	-	Serial Number
USG	-	Ultra Sonography
Wt.	-	Weight
SERMs	-	Selective estrogen receptor modulators
Dpd	-	Deoxypyridinoline
RA	-	Radiographic Absorptiometry

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INTRODUCTION

Osteoporosis is a disease in which the density and quality of bone are reduced, leading to weakness of the skeleton and increased risk of fracture, particularly of the spine, wrist and hip. Osteoporosis and associated fractures are an important cause of mortality and morbidity [1]

Osteoporosis is a global problem which is increasing in significance as the population of the world both grows and ages. Worldwide, lifetime risk for osteoporotic fractures in men is 15-30%. In women risk is 30-50%.[2] Three main types of osteoporosis fractures are wrist fracture, vertebral fracture and hip fracture. Osteoporosis is often called the "silent disease" because bone loss occurs without symptoms. In many cases, the first "symptom" is a broken bone. Patients with osteoporosis may not know that they have the disease until their bones become so weak that a sudden strain, bump, or fall causes a hip fracture or a vertebra to collapse. Collapsed vertebra may initially be felt or seen in the form of severe back pain, loss of height, or spinal deformities such as kyphosis, or severely stooped posture.[3]

Osteoporosis is defined as “a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture”.[4,5] This definition indicates that measurement of bone mineral density (BMD) is a central component to diagnosis of the disease.[5]

The diagnosis of osteoporosis is based on bone mineral density (BMD) measurements and is defined by the World Health Organisation (WHO) as:

1. Normal: a value of BMD or bone mineral content (BMC) ≤ 1 standard deviation (SD) below the young adult average value
2. Osteopenia: a value of BMD or BMC >1 SD below the young adult average value but >2.5 SD above
3. Osteoporosis: a value of BMD or BMC ≥ 2.5 SD below the young adult average value
4. Severe osteoporosis (established osteoporosis): a value of BMD or BMC ≥ 2.5 SD below the young adult average value and presence of one or more fragility fractures. [6,7]

Incidence and prevalence of osteoporosis

1 in 5 men over 50 will suffer a fracture due to osteoporosis; this increases to 1 in 3 over 60.[111] 1 in 3 women over 50 will suffer a fracture due to osteoporosis; this increases to 1 in 2 over 60.[111] Approximately 1.6 million hip fractures occur each year worldwide, the incidence is set to increase to 6.3 million by 2050.[8] The highest risk of hip fractures are seen in Norway, Sweden, Iceland, Denmark and the USA.[8] Currently, there is an increasing incidence of hip fractures in the developed cities in Asia. 1 out of 4 hip fractures occur in Asia and Latin America. This number of hip fractures will increase to 1 in 2 by 2050.[8] In the Middle East, the burden of osteoporosis in the general population is expected to increase and is becoming a heavy financial burden.[9]

Burden of osteoporosis

According to World Health Organization (WHO), osteoporosis is second only to cardiovascular disease as a global healthcare problem.[10] Since osteoporosis affects the elderly population which is growing, it will put a bigger burden to the healthcare system as treatment is expensive. Unless swift action is taken, it can escalate into an

economic threat.[11] International Osteoporosis Foundation (IOF) estimates that the annual direct cost of treating osteoporosis fractures of people in the workplace in the USA, Canada and Europe alone is approximately USD48 billion.[12] The worldwide cost burden of osteoporosis (for all ages) is forecast to increase to USD131.5 billion by 2050.[13] Osteoporosis also results in huge indirect costs that are rarely calculated and which are probably at least 20% of the direct costs.[13] Once a man suffers a first vertebral fracture, there is a five-fold increase in the risk of developing a new fracture within one year [13]

1 **Osteoporosis diagnosis:** 93% of men acknowledge seriousness of osteoporosis, but 8 out of 10 do not believe they are personally at risk; 80% of men with osteoporosis were not aware of their risk before diagnosis.[14] Find out if you have osteoporosis risk factors by taking the One-Minute Risk Test developed by the International Osteoporosis Foundation. If you answered 'yes' to any of the questions, you may be at risk of developing osteoporosis, and it is recommended that you consult your physician who will advise whether further tests or treatment may be necessary.[15] Loss of bone mass can be made by a physician through a bone mineral density test (BMD).[16] The test measures bone density in the spine, wrist, and/or hip (the most common sites of fractures due to osteoporosis), while others measure bone in the heel or hand. These tests are painless, noninvasive, and safe. Bone density tests can detect low bone density before a fracture occurs. Confirm a diagnosis of osteoporosis if you have already fractured. Predict your chances of fracturing in the future. Determine your rate of bone loss and/or monitor the effects of treatment if the test is conducted at intervals of a year or more. [17]

OBJECTIVES

1. To find out the prevalence of osteoporosis in men aged more than 50 years
2. To find out the risk factors affecting osteoporosis
    a. Smoking
    b. Alcohol
    c. Corticosteroids
    d. Proton pump inhibiting drug intake
    e. Body weight
    f. Weight loss
    g. Trauma
    h. Age
    i. Falls
    j. Genetic
    k. Lifestyle
    l. Weight in infancy
    m. Diet
    n. Socio economic status
    o. Sunlight exposure
    p. BMI
    q. Occupation

REVIEW OF LITERATURE

History:

1770s—John Hunter discovers that as new bone is formed, old bone is destroyed (resorbed).

1922—Elmer McCollum discovers vitamin D.

1923-1925—Parathyroid hormone is independently isolated by Adolph Hanson and James Collip and shown to boost levels of calcium in the blood.

1930s—Hans Selye shows that small doses of parathyroid hormone foster bone formation in rats.

1930s and 1940s—Fuller Albright defines postmenopausal osteoporosis and begins treating women with the condition with estrogen.

1960s—Herbert Fleisch discovers compounds known as bisphosphonates that inhibit bone resorption.

1960s—Researchers discover that compounds known as selective estrogen receptor modulators (SERMs) can simultaneously block breast tumors and trigger the growth of uterine cells.

1970s—Researchers discover that osteoclasts and white blood cells come from the same parent cells in the bone marrow.

1970s—Researchers discover compounds called cytokines, which are generated by cells in bone and marrow and influence bone cells' own development and activity.

1980s and 1990s—Researchers discover cytokines that influence the development and activity of osteoclasts.

1990s—The bisphosphonates alendronate and risedronate enter the market as anti-osteoporosis drugs.

1990s—Researchers discover some of the molecules that enable osteoclasts to break down bone.

1990s—Researchers uncover growth factors and other compounds that stimulate the production and activity of osteoblasts.

1998—The selective estrogen receptor modulator drug raloxifene enters the market as a drug to treat and prevent postmenopausal osteoporosis.[18-21]

ANATOMY

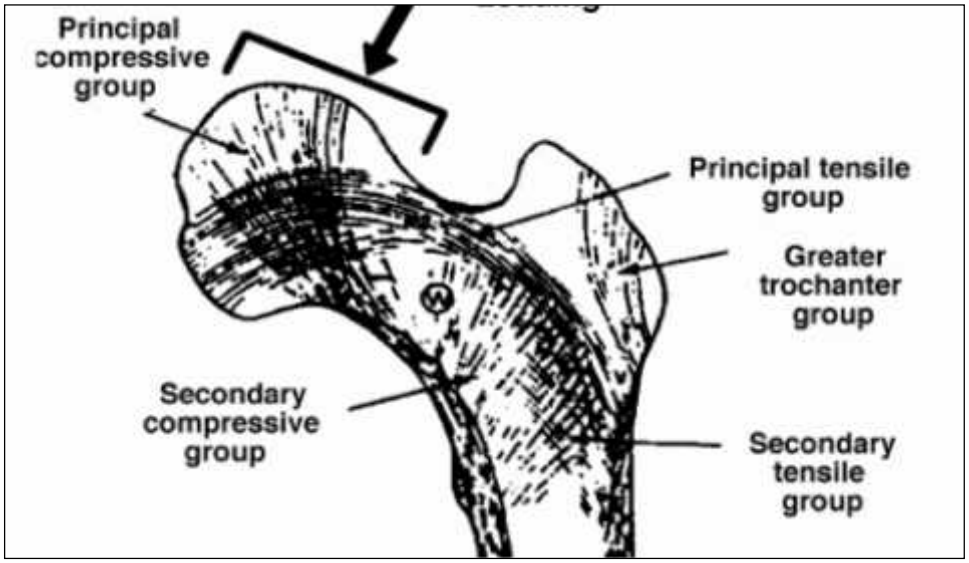


Fig 1: Trabecular pattern of the femur

Hall examined thirty cadaveric femora chosen at random. By comparing the principal tensile compressive trabeculae, he divided the femora into three categories representing normal, osteoporotic, and severely osteoporotic bones. In the absence of

correlation with changes in the rest of the skeleton. This division was purely arbitrary, but like Urist, Hall noted that in osteoporosis the compressive trabeculae became more prominent as the tensile trabeculae became roentgenographically inconspicuous.

The present study deals with the progressive changes that occur in the trabecular pattern of the upper end of femur as normal bone deteriorates to severe osteoporosis. The changes in the upper end of the femur have been related to histological and clinical data in the same patients.

The Normal Trabecular Pattern

Before describing our study in detail, we should first comment on the normal internal architecture of the upper end of the femur and explain the terminology used in this paper. The cancellous bone of the upper end of the femur is composed of two distinct systems of trabeculae. In a frontal section, these trabeculae are seen to form two arches: one arising from the medial (or inner) cortex of the shaft of femur and the other taking origin from the lateral (or outer) cortex. The trabeculae forming these arches are compressive and tensile trabeculae, respectively, because they are disposed along the lines of maximum compression and tension stresses produced in the bone during weight-bearing. These trabeculae (Fig. 1) have been divided into the following five groups [22]:

1. **Principal compressive group**: The uppermost compression trabeculae which extend from the medial cortex of the shaft to the upper portion of the head of femur, in slightly curved radial lines. These are some of the thickest and most closely packed trabeculae in the upper end of the femur.

2. **Secondary compressive group**: The rest of the compression trabeculae which arise from the medial cortex of the shaft. These arise below the principal compressive group and curve upwards and laterally towards the greater trochanter and the upper portion of the neck. The trabeculae of this group are thin and widely spaced.

3. Greater trochanter group: Some slender and poorly defined tensile trabeculae which arise from the lateral cortex just below the greater trochanter and sweep upward to end near its superior surface.

4. **Principal tensile group**: Trabeculae which spring from the lateral cortex immediately below the greater trochanter group. These trabeculae, which are the thickest amongst the tensile group, curve upward and inward across the neck of the femur, to end in the inferior portion of the femoral head.

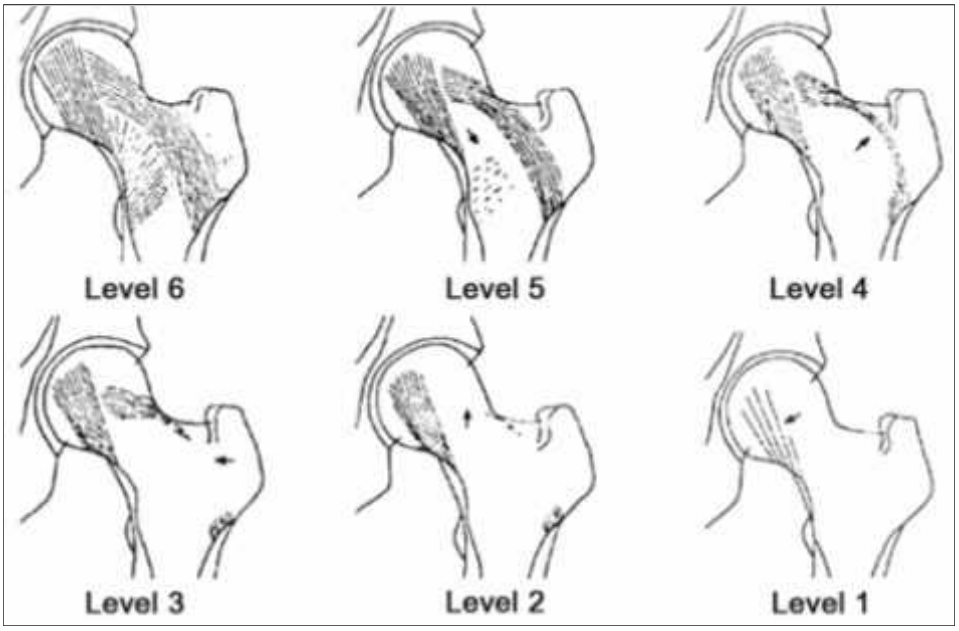
5. **Secondary tensile group**: Trabeculae which arise from the lateral cortex below the principal tensile trabeculae. The trabeculae of this group arch upward and medially across the upper end of the femur and end more or less irregularly after crossing the mid-line.

In the neck of the femur, the principal compressive, the secondary compressive, and the tensile trabeculae enclose an area containing some thin and loosely arranged trabeculae. This is called Ward's triangle.

The trabeculae of the upper end of the femur can be studied in living subjects by making roentgenograms of the hip region, using an exposure sufficient to delineate the macroscopic details of the internal architecture of bones. In such roentgenograms, which are two dimensional photographic images of a complex three-dimensional structure, the thick trabeculae appear as dense continuous lines while the delicate ones

are not visible. Thus, in normal hip roentgenograms all the trabecular group described above are clearly demarcated, but areas like Ward's triangle, where the trabeculae are thin and roentgenographically inconspicuous, appear empty.[23]

Fig 2 : Singh's Index



Level 6 – All trabecular groups are present.

Level 5 – The main tension and compressive groups are emphasized

Level 4 – The main tension trabeculas have been reduced

Level 3 – The main tension trabeculas have been broken opposite the great trochanter. This level marks the definite osteoporosis.[24,25]

Level 2 – The presence of only main compressive trabeculas.

Level 1 – The main compressive trabeculas have been reduced.[26,27]

RISK FACTORS

What Causes Osteoporosis?

Bone is constantly changing—that is, old bone is removed and replaced by new bone. During childhood, more bone is produced than removed, so the skeleton grows in both size and strength. For most people, bone mass peaks during the third decade of life. By this age, men typically have accumulated more bone mass than women. After this point, the amount of bone in the skeleton typically begins to decline slowly as removal of old bone exceeds formation of new bone. Men in their fifties do not experience the rapid loss of bone mass that women do in the years following menopause. By age 65 or 70, however, men and women are losing bone mass at the same rate, and the absorption of calcium, an essential nutrient for bone health throughout life, decreases in both sexes. Excessive bone loss causes bone to become fragile and more likely to fracture. Fractures resulting from osteoporosis most commonly occur in the hip, spine, and wrist, and can be permanently disabling. Hip fractures are especially dangerous. Perhaps because such fractures tend to occur at older ages in men than in women, men who sustain hip fractures are more likely than women to die from complications.[28]

Primary and Secondary Osteoporosis

There are two main types of osteoporosis: primary and secondary. In cases of primary osteoporosis, either the condition is caused by age-related bone loss (sometimes called *senile osteoporosis*) or the cause is unknown (*idiopathic osteoporosis*). The term idiopathic osteoporosis is used only for men younger than 70 years old; in older men, age-related bone loss is assumed to be the cause. The majority of men with osteoporosis have at least one (sometimes more than one)

secondary cause. In cases of secondary osteoporosis, the loss of bone mass is caused by certain lifestyle behaviors, diseases, or medications. The most common causes of secondary osteoporosis in men include exposure to glucocorticoid medications, hypogonadism (low levels of testosterone), alcohol abuse, smoking, gastrointestinal disease, hypercalciuria, and immobilization.[28]

Causes of Secondary Osteoporosis in Men

• Glucocorticoid medications

• Other immunosuppressive drugs

• Hypogonadism (low testosterone levels)

• Excessive alcohol consumption

• Smoking

• Chronic obstructive pulmonary disease and asthma

• Cystic fibrosis

• Gastrointestinal disease

• Hypercalciuria

• Anticonvulsant medications

• Thyrotoxicosis

• Hyperparathyroidism

• Immobilization

• Osteogenesis imperfecta

• Homocystinuria

• Neoplastic disease

• Ankylosing spondylitis and rheumatoid arthritis

• Systemic mastocytosis[28]

1. **Glucocorticoid medications:** Glucocorticoids are steroid medications used to treat diseases such as asthma and rheumatoid arthritis. Bone loss is a very common side effect of these medications. The bone loss these medications cause may be due to their direct effect on bone, muscle weakness or immobility, reduced intestinal absorption of calcium, a decrease in testosterone levels, or, most likely, a combination of these factors. When glucocorticoid medications are used on an ongoing basis, bone mass often decreases quickly and continuously, with most of the bone loss in the ribs and vertebrae. Therefore, people taking these medications should talk to their doctor about having a bone mineral density (BMD) test. Men should also be tested to monitor testosterone levels, as glucocorticoids often reduce testosterone in the blood. A treatment plan to minimize loss of bone during long-term glucocorticoid therapy may include using the minimal effective dose, and discontinuing the drug or administering it through the skin, if possible. Adequate calcium and vitamin D intake is important, as these nutrients help reduce the impact of glucocorticoids on the bones. Other possible treatments include testosterone replacement and osteoporosis medication.[28]
2. **Hypogonadism:** Hypogonadism refers to abnormally low levels of sex hormones. It is well known that loss of estrogen causes osteoporosis in women. In men, reduced levels of sex hormones may also cause osteoporosis. Although it is natural for testosterone levels to decrease with age, there should not be a sudden

drop in this hormone that is comparable to the drop in estrogen experienced by women at menopause. However, medications such as glucocorticoids (discussed above), cancer treatments (especially for prostate cancer), and many other factors can affect testosterone levels. Testosterone replacement therapy may be helpful in preventing or slowing bone loss. Its success depends on factors such as age and how long testosterone levels have been reduced. Also, it is not yet clear how long any beneficial effect of testosterone replacement will last. Therefore, doctors usually treat the osteoporosis directly, using medications approved for this purpose. Recent research suggests that estrogen deficiency may also be a cause of osteoporosis in men. For example, estrogen levels are low in men with hypogonadism and may play a part in bone loss. Osteoporosis has been found in some men who have rare disorders involving estrogen. Therefore, the role of estrogen in men is under active investigation.[28]

3. **Alcohol abuse:** There is a wealth of evidence that alcohol abuse may decrease bone density and lead to an increase in fractures. Low bone mass is common in men who seek medical help for alcohol abuse. In cases where bone loss is linked to alcohol abuse, the first goal of treatment is to help the patient stop, or at least reduce, his consumption of alcohol. More research is needed to determine whether bone lost to alcohol abuse will rebuild once drinking stops, or even whether further damage will be prevented. It is clear, though, that alcohol abuse causes many other health and social problems, so quitting is ideal. A treatment plan may also include a balanced diet with lots of calcium- and vitamin D-rich foods, a program of physical exercise, and smoking cessation.[28]
4. **Smoking:** Bone loss is more rapid, and rates of hip and vertebral fracture are higher, among men who smoke, although more research is needed to determine

exactly how smoking damages bone. Tobacco, nicotine, and other chemicals found in cigarettes may be directly toxic to bone, or they may inhibit absorption of calcium and other nutrients needed for bone health. Quitting is the ideal approach, as smoking is harmful in so many ways. As with alcohol, it is not known whether quitting smoking leads to reduced rates of bone loss or to a gain in bone mass.[28]

5. **Gastrointestinal disorders:** Several nutrients, including amino acids, calcium, magnesium, phosphorous, and vitamins D and K, are important for bone health. Diseases of the stomach and intestines can lead to bone disease when they impair absorption of these nutrients. In such cases, treatment for bone loss may include taking supplements to replenish these nutrients.[28]
6. **Hypercalciuria:** Hypercalciuria is a disorder that causes too much calcium to be lost through the urine, which makes the calcium unavailable for building bone. Patients with hypercalciuria should talk to their doctor about having a BMD test and, if bone density is low, discuss treatment options.[28]
7. **Immobilization:** Weight-bearing exercise is essential for maintaining healthy bones. Without it, bone density may decline rapidly. Prolonged bed rest (following fractures, surgery, spinal cord injuries, or illness) or immobilization of some part of the body often results in significant bone loss. It is crucial to resume weight bearing exercise (such as walking, jogging, dancing, and lifting weights) as soon as possible after a period of prolonged bed rest. If this is not possible, you should work with your doctor to minimize other risk factors for osteoporosis.[28]
8. **Genetic causes:** The genes predisposing men to Osteoporosis have not yet been identified. Several case reports, however, have implicated estrogens as key Players in the regulation of peak Bmd in men. In these case reports, In which each patient was osteoporotic, Estrogen was not available To bone, either because of a

mutation In the estrogen receptor gene Or an inability to convert androgens To estrogen. several genetic disorders, Including homocystinuria, Marfan syndrome, and osteogenesis Imperfecta, are known to cause osteoporosis And osteopenia.[29,30]

9. **Lifestyle factors:** Lifestyle choices can have a profound Impact on bone health. Chronic alcohol use (>7 oz/wk) directly Suppresses osteoblast activity. Smoking lowers BMD and increases The risk of hip and vertebral fracture.[31,32] Smoking also increases the Risk of hip fracture by 40%. Low calcium And vitamin d levels, as well As insufficient sun exposure, also contribute to the development of osteoporosis. Although the literature Shows mixed results, in general, inactivity Is thought to contribute to loss of BMD.
10. **Idiopathic Osteoporosis:** Primary, or idiopathic, osteoporosis is generally attributed to aging, although in actuality the exact cause is unknown. Idiopathic loss of BMD is credited to a variety of metabolic alterations, such as diminished androgen levels, decreased bioavailable estrogen levels, and reduction in insulin-like growth factor-I levels.[33] Although testosterone often is implicated as the key sex hormone for male growth, the level of bioavailable estrogen is the major factor in maintaining bone density in men.[34-36] Fracture status also is predicted by levels of bioavailable estrogen but not levels of testosterone.[37] Absolute levels of estrogen remain relatively stable over time; however, the amount available to interact on behalf of bones is dependent on the level of steroid hormone–binding globulin.[38] As levels of this molecule increase with age, the level of free estrogen available to interact with tissues decreases. By age 80 years, levels decline progressively to 30% to 50% of young adult values.[38] Estrogen prevents bone resorption; without adequate levels, the rate of bone turnover is greater than that of bone formation. This is evidenced by higher levels of urinary markers of bone

turnover in the absence of bioavailable estrogen.[39] Deficiencies in estrogen receptor-α also have been implicated in idiopathic osteoporosis.[40]

11. **Role of sex steroids***:* Because most men do not develop overt hypogonadism with aging, the prevailing opinion had been that sex steroid deficiency was not a major cause of age related bone loss in men. It is now clear, however, that the failure of earlier studies to find major decreases in serum levels of total sex steroids was caused by the fact that they did not account for the confounding effect of a greater than 2-fold age-related rise in levels of serum SHBG.[41] It is generally believed that circulating sex steroids that are bound to SHBG have restricted access to target tissues, whereas the 1 to 3% fraction that is free and the 35 to 55% fraction that is bound loosely to albumin are readily accessible[42,43]. Although there are various methods to assess the bioavailable, or non-SHBG-bound, sex steroids, several groups have reported substantial decreases in serum levels of free or bioavailable sex steroid levels with aging.[41,44] Data from a population of 346 men from Rochester, Minnesota.[41] Similar findings were reported by Orwoll *et al*.[45] From the MrOs study, where in a sample of 2623 men over the age of 65 yr, serum free testosterone and free estradiol declined significantly with age, and this was associated with increases in serum SHBG levels. The precise cause of the age-related increase in serum SHBG levels and the failure of the hypothalamic-pituitary testicular axis to compensate for this and maintain free or bioavailable sex steroids at young normal levels is unclear and is the focus of ongoing studies. Although both serum free or bioavailable testosterone and estradiol levels decline with age in men, the traditional notion had been that because testosterone is the major sex steroid in men, it was the decrease in bioavailable testosterone levels that would be associated most closely with bone loss in men. The initial attempts

to address this issue came from cross-sectional observational studies in which sex steroid levels were related to a real BMD by DEXA at various sites in cohorts of adult men. Slemenda *et al*. (124) found that BMD at various sites in 93 healthy men over age 55 yr correlated with serum estradiol levels (correlation coefficients, depending on the site, of_0.21 to_0.35; *P*_0.01 to 0.05) and, in fact, inversely with serum testosterone levels (correlation coefficients of _0.20 to _0.28; *P* _ 0.03 to 0.10). Subsequent to this report, other similar cross-sectional studies have demonstrated significant positive associations between BMD by DEXA and estrogen levels in men [41,44,47-51] , particularly circulating bioavailable estradiol levels. Although these findings are compatible with the hypothesis that estrogen plays an important role in maintaining bone mass in men, they suffer from two potential weaknesses. First, cross-sectional data cannot clearly dissociate the effects of estrogen to maintain or prevent bone loss from the effects of estrogen to achieve peak bone mass. For example, a particular individual with a relatively low bone mass at age 50 yr and low estradiol levels (relative to his age-matched peers) could have had lifelong low estradiol levels going back to childhood. In this case, the low estradiol levels would reflect a deficiency in achieving peak bone mass, not necessarily an effect of estrogen to maintain or prevent bone loss. A second weakness of cross-sectional observational data is that correlation does not prove causality. To circumvent the first of these problems, Khosla *et al*.[52] studied, in a longitudinal manner, elderly (60 to 90 yr) men in whom rates of change in BMD using DXA at various sites over 4 yr were related to sex steroid levels. Forearm sites (distal radius and ulna) provided the clearest data, perhaps because of the greater precision of peripheral site measurements as compared with central sites such as the spine or hip. BMD at the forearm sites declined by 0.49 to 0.66% per

year in these men, and these decreases were associated more closely with serum bioavailable estradiol levels than with bioavailable testosterone levels. Moreover, further analysis of the data suggested that there may be a threshold bioavailable estradiol level of approximately 40 pmol/liter (11 pg/ ml), below which the rate of bone loss in these men clearly was associated with bioavailable estradiol levels. Above this level, there did not appear to be any relationship between the rate of bone loss and bioavailable estradiol levels. In these older men, the bioavailable estradiol level of 40 pmol/liter (11 pg/ml) represented the median bioavailable estradiol level and corresponded to a total estradiol level of approximately 114 pmol/liter (31 pg/ml), which is close to the middle of the reported normal range for estradiol levels in men (10 to 50 pg/ml). Similar findings were reported by Gennari *et al*.[53] where, in a cohort of elderly Italian men, those subjects with serum free estradiol levels below the median value lost bone over 4 yr at the lumbar spine and femur neck, whereas the men with free estradiol levels above the median did not lose bone. In further studies using QCT at various sites, Khosla *et al.*[54]found that in elderly men, bioavailable estradiol was the most consistent predictor of vBMD and some of the geometric variables related to bone size, and that the possible "threshold" for skeletal estrogen deficiency was most evident at cortical sites. Moreover, at least in men, serum estradiol levels measured by either a sensitive RIA or by tandem mass spectroscopy provided virtually identical correlations with BMD.[55] Because 85% or more of circulating estrogen levels in men are derived not from direct testicular secretion but rather from peripheral aromatization of testosterone.[56] several studies have examined possible relationships between variations in the enzyme aromatase (CYP19) that is responsible for the conversion of androgens to estrogens in the testis and in

peripheral tissues and BMD in men.[57,58] Thus, Gennari *et al.*[58] found that males with a high number of TTAA repeat sequences in intron 4 of the CYP19 gene had higher serum estradiol levels and decreased rates of bone loss compared with those with a lower number of repeats, irrespective of serum SHBG or androgen levels. Interestingly, the association between the CYP19 polymorphisms and serum estradiol levels was attenuated with increases in fat mass, consistent with a role for peripheral adipose tissue in contributing to circulating estrogen levels in men and in reducing the impact of genetic variation in the CYP19 enzyme by simply increasing the amount of enzyme present peripherally. Although these studies helped to establish that estrogen levels are associated with skeletal maintenance in males, they could not definitively establish causal relationships. To address this issue, Falahati-Nini *et al.*[59] performed a direct interventional study to distinguish between the relative contributions of estrogen *vs.* testosterone in regulating bone resorption and formation in normal elderly men. Endogenous estrogen and testosterone production were suppressed in 59 elderly men using a combination of a long-acting GnRH agonist and an aromatase inhibitor. Physiological estrogen and testosterone levels were maintained by simultaneously placing the men on estrogen and testosterone patches delivering doses of sex steroids that mimicked circulating estradiol and testosterone levels in this age group. After baseline measurements of bone resorption [urinary deoxypyridinoline (Dpd) and N-telopeptide of type I collagen (NTx)] and bone formation [serum osteocalcin and aminoterminal propeptide of type I collagen (PINP)] markers, the subjects were randomized to one of four groups: group A (_T, _E), discontinued both the testosterone and estrogen patches; group B (_T, _E), discontinued the testosterone patch but continued the estrogen patch; group C (_T, _E), continued

the testosterone patch but discontinued the estrogen patch; and group D (_T, _E) continued both patches. Because gonadal and aromatase blockade was continued throughout the 3-wk period, separate effects of estrogen *vs.* testosterone (in the absence of aromatization to estrogen) on bone metabolism could be delineated. As shown in Fig. 9A, significant increases in both urinary Dpd and NTx excretion, group A (_T, _E), were prevented completely by continuing testosterone and estrogen replacement [group D (_T, _E)]. Estrogen alone (group B) was almost completely able to prevent the increase in bone resorption, whereas testosterone alone (group C) was much less effective. Using a two-factor ANOVA model, the effects of estrogen on urinary Dpd and NTx excretion were highly significant (*P* _ 0.005 and 0.0002, respectively). Estrogen accounted for 70% or more of the total effect of sex steroids on bone resorption in these older men, whereas testosterone could account for no more than 30% of the effect. Using a somewhat different design, Leder *et al.*[60] have confirmed an independent effect of testosterone on bone resorption, although the data in the aggregate clearly favor a more prominent effect of estrogen on the control of bone resorption in men. The reductions in both osteocalcin and PINP levels with the induction of sex steroid deficiency (group A) were prevented with continued estrogen and testosterone replacement (group D). Interestingly, serum osteocalcin, which is a marker of function of the mature osteoblast and osteocyte.[61] was maintained by either estrogen or testosterone (ANOVA *P* values of 0.002 and 0.013, respectively). By contrast, serum PINP, which represents type I collagen synthesis throughout the various stages of osteoblast differentiation,[62] was maintained by estrogen (ANOVA *P* value 0.0001), but not testosterone. Collectively, these findings provided conclusive proof of an important (and indeed, dominant) role for estrogen in bone

metabolism in the mature skeleton of adult men. Similar findings were subsequently reported by Taxel *et al.*[63] in a study of 15 elderly men treated with an aromatase inhibitor for 9 wk, where suppression of estrogen production resulted in significant increases in bone resorption markers and a suppression of bone formation markers. Despite the increasing evidence of a more dominant role of estrogens than testosterone on bone metabolism in men, the relative role of estrogens and androgens on fracture risk in men remains understudied. Although some studies have shown an association in men between hypogonadism, or low serum testosterone levels, and fractures [64,65], estradiol levels were not measured in these studies, so it remains possible that low estradiol levels may have accounted for these effects because testosterone is aromatized to estradiol. In a large, population-based study of elderly men from the Rancho-Bernardo Study, low estradiol levels have been associated with vertebral fractures.[66] Men in the lowest quintile of total estradiol levels had significantly higher risk for fracture than those in the highest quintile (odds ratio, 4.16; 95% CI, 1.22 to 14.19), whereas men with low testosterone levels compatible with hypogonadism had no significant increased odds for fracture (odds ratio, 1.24; 95% CI, 0.54 to 2.83).[66] In addition, among 793 men from the Framingham Study followed for up to 18 yr, those with low total estradiol levels (_18 pg/ml) at the beginning of the follow- up period had an increased risk for incident hip fracture (hazard ratio, 3.1; 95% CI, 1.4 to 6.9) when compared with men with high estradiol levels (_34.1 pg/ml), whereas men with estradiol levels in the midrange had no apparent increased risk for incident hip fracture (hazard ratio, 0.9; 95% CI, 0.2–2.0).[67] This increased risk for hip fracture increased exponentially below serum estradiol levels of approximately 20 pg/ml (74 pmol/liter),[67] further supporting the theory of a threshold effect of low

estradiol on bone metabolism.[52,68] Although no association was observed between low testosterone levels and hip fracture risk, men with both low estradiol and low testosterone levels had the greatest risk for hip fracture (hazard ratio, 6.5; 95% CI, 2.9 to 14.3)[67] when compared with men with both estradiol and testosterone levels in the mid- to high range. Data from a Swedish cohort of elderly men indicate that free testosterone also independently predicted prevalent fractures in these men; interestingly, the effect of free testosterone was independent of BMD, suggesting that free testosterone may also be a marker for variables other than BMD that may impact on fracture risk, such as propensity to fall or overall general health[69]. Similar findings have recently been reported by Meier *et al.*[70] using data from the Dubbo Osteoporosis Epidemiology study. In this analysis, serum testosterone levels predicted fracture risk in elderly men independent of BMD, again suggesting an important role for testosterone in modulating nonskeletal factors, such as muscle strength, predisposing to fracture risk. It appears, therefore, that similar to women, declining bioavailable estrogen levels may play a significant role in mediating age-related bone loss and fracture risk in men. However, declining bioavailable testosterone levels may also contribute, because as demonstrated above, testosterone does have some antiresorptive effects and is important for the maintenance of bone formation. Moreover, it provides the substrate for aromatization to estradiol. In addition, at least in rodents, testosterone has been shown to enhance periosteal apposition,[71] and studies in young Swedish men indicate that whereas serum free estradiol was a negative predictor, serum free testosterone was a positive predictor of cortical bone size.[72] Because larger bones are more resistant to fracture, effects of testosterone on increasing bone size in men may also provide important protection against fracture risk. These findings

in adult men are consistent with reports of a male with homozygous deletion of the ER_ gene[73] and aromatase-deficient males,[74-77] all of whom had unfused epiphyses, elevated markers of bone remodeling, and low bone mass, despite normal or elevated testosterone levels. Moreover, the aromatase-deficient males responded to estrogen therapy with marked increases in bone mass by DEXA,[75,77-79] consistent with an "anabolic" effect of estrogen in this setting, in contrast to its predominantly antiresorptive action in postmenopausal women. A more recent study of the response to estrogen therapy in one of the aromatase-deficient males using pQCT found that the increase in bone mass by DXA was largely due to an increase in bone size, rather than changes in trabecular or cortical v BMD, suggesting a potentially important effect of estrogen on bone growth during puberty.[76] However, whether this was a direct effect of estrogen on periosteal growth or an indirect effect mediated, for example, by changes in circulating GH or IGF-I levels remains unclear at this point.

12. **Role of other factors, including nutrition and changes in muscle mass:** As noted above, vitamin D deficiency, with or without adequate calcium intake, likely contributes to the age-related increase in serum PTH levels and to bone loss, at least in a subset of aging men.[80] In several population-based studies, 25-hydroxyvitamin D, an indicator of vitamin D nutrition, decreased by 30–60% .[81] This may be a particularly important problem in housebound individuals with poor nutrition and inadequate exposure to UV radiation, especially populations who reside in countries with higher latitudes, such as Great Britain and France, and where dairy products are not fortified with vitamin D. Other nutritional factors, such as inadequate calcium[82] or protein[83] intake may also play a role in accelerating age-related bone loss in men. In addition to these nutritional factors,

Frost has suggested in a number of publications[84-86] that the loss of muscle mass with aging is perhaps the principal cause of involutional osteoporosis in both sexes. Indeed, a number of studies have shown high correlations between lean body mass and total body bone mineral.[86] Moreover, in a population sample, Proctor *et al.*[87] found that physical activity declined by 34 and 38% and lean body mass declined by 18 and 17% with aging in women and men, respectively, and decreases in muscle strength have been associated with the risk of osteoporosis in women as well as men.[82] Thus, it appears likely that with aging, a number of nutritional and lifestyle factors, particularly declining levels of physical activity and muscle mass, contribute to bone loss as well as risk of falls, ultimately increasing the overall risk of fractures.

Review of Literature:

Asia Pacific Update

- With socio-economic development in many Asian countries and rapid ageing of the Asian population, osteoporosis has become one of the most prevalent and costly health problems in the region.[88] Unsurprisingly, Asia is the region expecting the most dramatic increase in hip fractures during coming decades; by 2050 one out of every two hip fractures worldwide will occur in Asia.[112]

China

- Osteoporosis has reached epidemic proportion, 300% increase in the last 30 years.[89]
- Total prevalence rate of osteoporosis in the middle- aged and elderly in China was 16. 1% in 2002. The prevalence rate among males was 11. 5% and among females was 19. 9%.[90]

- With the advances in quality of life and health conditions in China, the population has been experiencing aging, and osteoporosis has therefore become an important public health problem.[114]

Hong Kong

- The incidence of hip fracture has increased by 200% in Hong Kong over the past 20 years: about 10 elders fracture their hip everyday. The mortality rate for hip fracture patients is 20% while 70% remain permanently disabled.[91]
- 50% of men and women aged 60 years and over could be diagnosed as "osteoporotic"[89]
- Osteoporosis is currently among the top five conditions causing disability and prolonged hospital stay for elders in Hong Kong.[88]
- The cost of treating hip fractures in Hong Kong exceeds 1% of the total hospital budget.[113]
- The total healthcare cost for treating the disease is projected to reach USD128 million by the year 2010.[89]
- For women aged 65 and over: 45% is osteoporosis, 42% is osteopenia (low bone mass). For men aged 65 and over: 13% is osteoporosis, 47% is osteopenia.[92]

Singapore

- It is estimated that 800 to 900 hip fractures occur in Singapore every year due to osteoporosis.93
- Over the past 3 decades, hip fractures in women aged 50 and above have increased 5 folds from 75 cases to 402 cases per 100,000 populations. Among

men aged 50 and above, the increase was 1.5 times over the same period; from 103 cases to 152 cases per 100,000 populations.94

- About 1 in 5 persons died within a year of sustaining an osteoporotic hip fracture and 1 in 3 became wheelchair bound or bedridden.115
- Treatment cost for fracture is USD4706 on average and is expected to increase.91
- More than 100,000 women suffer from osteoporosis, with fracture treatment adding up to USD3.4 million a year.[91]

Malaysia

- The number of hip fracture cases for men and women in Malaysia is 88 and 218 per 100,000 populations[95]
- 51.8% urban Malaysian women in her menopause age group had mild osteoporosis[96]

Japan

- In Japan, the number of total prevalent cases of osteoporosis is estimated to increase from 9.716 million to 12271 100 from 2001 to 2010.[97]
- At present, the total number of osteoporotic patients in Japan is estimated to be ten million.[98]
- The incidence of hip fracture was approximately 50,000 in 1987 and 80,000 in 1992.[94]

India

- 1 out of 8 males and 1 out of 3 females in India suffers from osteoporosis, making India one of the largest affected countries in the world.[99]
- Expert groups peg the number of osteoporosis patients at approximately 26 million (2003 figures) with the numbers projected to increase to 36 million by 2013.[100]
- Two points worth noting about osteoporosis in India - the high incidence among men and the lower age of peak incidence compared to Western countries. The incidence of hip fracture is 1 woman to 1 man in India[96]
- In most Western countries, while the peak incidence of osteoporosis occurs at about 70-80 years of age, in India it may afflict those 10-20 years younger, at age 50-60.[96]

Australia

- 2 million Australians are affected by osteoporosis.[101]
- Every 8.1 minutes in Australia someone is admitted to hospital with a fracture.[111]
- The numbers of fractures are increasing at a rate of 4% per annum.[102]
- Prevalence increase to 2.2 million in 2006 and 3 million in 2021.[111]
- Total costs relating to osteoporosis in Australia are USD7.4billion per year of which USD1.9 billion are direct costs.[102]

New Zealand

- In New Zealand, osteoporosis causes 15,000 fractures each year, of which around 3,000 are hip fractures.[102]
- Affects more than half of women, and nearly a third of men over age 60.[96]
- Osteoporosis is estimated to cost New Zealand over $135 million per annum.[96]
- Up to 20% of aged osteoporosis patients die after a hip fracture, and 40% can no longer live independently within a year of their injury.[103]

Korea

- It is estimated that as many as 2 million people are suffering from osteoporosis in Korea.[104]
- The prevalence of hip fractures has increased about 4 folds during past 10 years.[105]

Indonesia

- The prevalence of osteoporosis in Indonesia is relatively unknown.
- In order to provide a preliminary overview of osteoporosis in Indonesia, ultrasound bone density screenings were held in 2002 in five major cities across the country.[106]
- The results showed that out of the total number of people screened, some 35% were normal, 36% showed signs of osteopenia, while 29% suffered from osteoporosis.[101]
- Osteoporosis occurred in only 14% in the below 50 age range of Indonesians, while that figure rose to 28% in the 50 to 60 age range and 47% in the 60 to 70 age range.[101]

Sri Lanka

- The prevalence of osteoporosis in Sri Lanka is unknown due to lack of investigation facilities.[107]
- A large epidemiological studies done in Sri Lanka, Galle Prospective Osteoporosis Survey, found 42.4% of women in the entire sample of 350 women and 61.5% in women over 50 years to have osteoporosis.[108]

Thailand

- The number of hip fracture cases for men and women in Thailand is 114 and 289 per 100,000 populations.96
- The prevalence of Khon Kaen (Thai rural area) women has osteporosis in femoral neck and lumbar spine is 19.3% and 24.7% respectively109
- The age-specific prevalence of osteoporosis among Thai women rose progressively with increasing age to more than 50% after the age of 70[110]

BMD Assessment

BMD- measurement site In general, densitometry techniques can be performed in either the axial or the appendicular skeleton, depending On the modality employed. Peripheral measurements, performed in the appendicular Skeleton, help to predict the risk of fracture, however, they are less sensitive for the monitoring of therapy than are measurements in the axial skeleton because changes due to age, therapeutic intervention, and estrogen deficiencies occur less rapidly in appendicular bone than they do in the axial skeleton for single energy measurements it is often necessary to surround the anatomical site by a constant thickness of tissue equivalent material to

correct for overlying soft tissue – this restricts measurement to peripheral sites[116] For these modalities

Single Photon Absorptiometry (SPA)

- The SPA technique uses a single gamma ray source (125I) and a scintillation detector to measure photons transmitted through a particular anatomical site in the appendicular skeleton.
- The gamma source and detector were coupled and scanned in a rectilinear fashion across the region of interest.
- To correct for overlying soft tissue the anatomical site has to be surrounded by tissue equivalent material. Water is normally used because its attenuation closely matches that of soft tissue.
- This technique was applied to peripheral skeletal sites, most commonly the non-dominant forearm, wrist or heel.
- For application to sites in the axial skeleton, dual absorptiometry (DPA) was developed.[117]

DPA

- DPA allows for simultaneous measurement of the transmission of gamma radiation of two different energies which compensates for the variation in overlying tissue and removes the need for the tissue equivalent material.
- 153Gd is a common radionuclide used which provided dual energy peaks at 44 & 100keV photons which were counted separately by scintillation detectors.

Factors which affect the accuracy of photon absorptiometry include:

- In homogeneity of soft tissue
- Uncertainty in values of density and attenuation coefficients for both bone mineral and soft tissue components. The accuracy error of photon absorptiometry has been estimated at 4-8% [Blake et al, 1999].[118]

Limitations of SPA & DPA include:

- Radionuclide decays and has to be replaced regularly
- Long scanning times due to low photon flux (~40 minutes)
- Poor spatial resolution.
- The introduction of SXA & DXA systems which employ the use of an X-ray tube as a source of radiation overcame these limitations.

SXA

- A collimated photon beam is directed from an x-ray source through the measurement site.
- The photon attenuation of the beam by bone is then measured and converted to bone mineral content.
- The bone mineral content is computed from the increased absorption of the beam as it passes from a constant thickness of soft tissue or water bath into the bone.
- SXA is commonly used because it is relatively quick & simple to perform and results in a low radiation dose.
- SXA scan time approx 4 minutes and delivered a radiation exposure of 1.68 mrem (16.8μSv) [Kelly et al, 1993].

- However, the necessity of surrounding the body part with a soft tissue equivalent material restricts the SXA measurement to sites on the forearm or other parts of the appendicular skeleton. [Mirsky et al, 1998].

SXA- Performance

- Studies suggest SXA measurements correspond well with the status of the peripheral long bones but poorly with that of the axial skeleton [Schlenker et al, 1976]
- Blake estimates the accuracy of SXA as similar to PA methods [Blake, 1999].
- In a 1993 study Kelly et al, evaluated the performance of a SXA device with respect to precision in vivo and in vitro, scan time, image quality, and correlation with an existing dual energy X-ray absorptiometry (DXA) device.
- SXA precision in vivo, expressed as a coefficient of variation (CV), was 0.66% for bone mineral content (BMC) and 1.05% for bone mineral density (BMD).
- Precision in vitro, based on 78 BMC measurements of a forearm phantom over 195 days, was 0.53%.
- Correlation with DXA at the 8 mm distal forearm site was high (r=0.97 for BMC and r=0.96 for BMD).
- SXA image quality and spatial resolution were superior to SPA and comparable to DXA [Kelly et al, 1993][118,119]

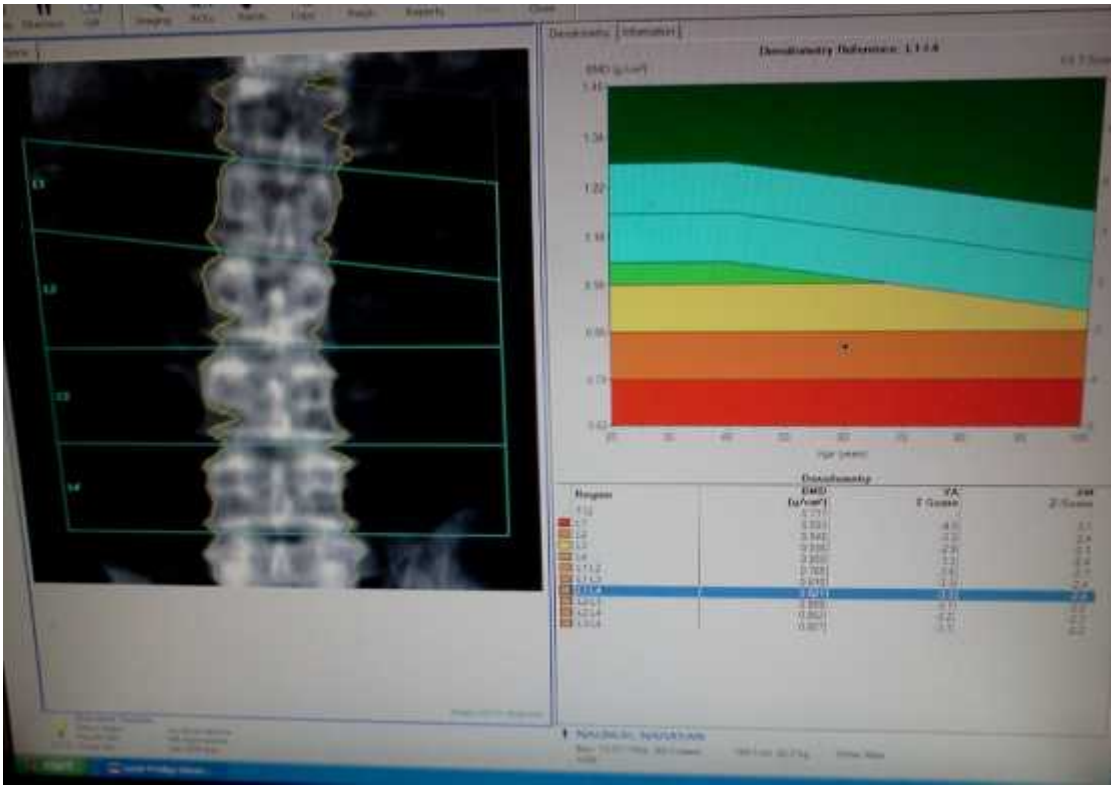
DEXA

- Most widely used modality for the clinical measurement of bone mineral content [Compston et al, 1995]
- DEXA was introduced in 1987 and its measurement principle is based on the method of X-ray Spectrophotometry.
- Digital imaging to locate the skeletal regions of interest followed by estimation of X-ray attenuation in these regions
- Comparison of attenuation at high and low energy regions of the X-ray spectra yields an estimate of the BMD (g/cm2).
- DEXA provides bone mineral density measurements both axially and peripherally, as well as total body scans, but is most commonly applied to scanning of the lumbar spine (L1-L4) and the proximal femur.

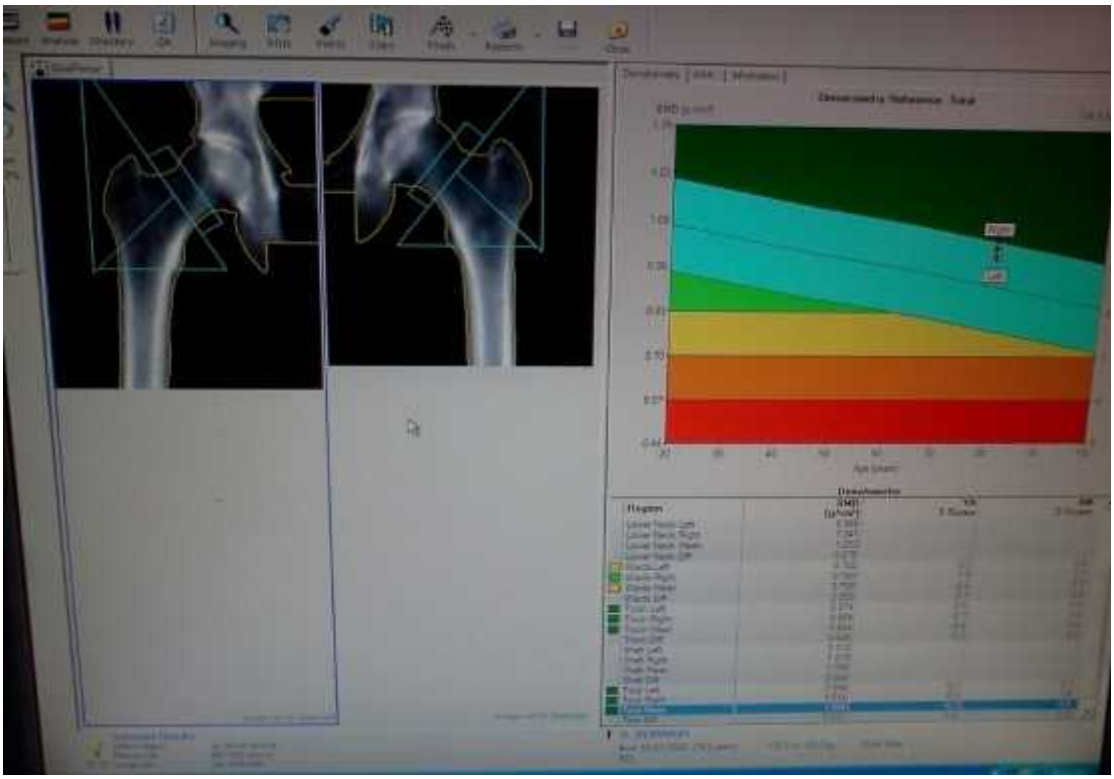
DEXA SCAN MACHINE

Factors affecting the accuracy of DEXA measurements:

- Variations in soft tissue composition within the X-ray beam
- Correct patient positioning and scan analysis
- Artifacts due to metal or clothing
- Scanner calibration
- Beam hardening
- Interference from Isotopes (Nuclear Medicine facility in close proximity)



DEXA SCAN OF LUMBAR SPINE



DEXA SCAN OF HIP

Factors affecting the precision of DEXA measurements:

- Random errors due to photon & electronic noise
- Drifts in scanner calibration
- Changes in soft tissue composition (patient weight gain or loss)
- Consistent patient positioning and scan analysis.
- Literature suggests that DEXA can be used to detect small changes in bone mineral content at multiple anatomical sites, with little exposure to radiation, short examinations time, high resolution images [Mazess et al, 1993], and excellent precision (0.5 -> 2%) and accuracy (3->5%) [Sorenson et al, 1998]
- Other studies report accuracy as 5% and precision as 2-6% [ereadiography.net]
- Compared with DPA, DEXA requires less time per examination, is more reproducible, and involves less exposure to radiation [Mirsky et al, 1998]
- Compared with qCT, DEXA has superior precision is less expensive, and is associated with lower absorbed doses of radiation [Mirsky et al, 1998].
- Main disadvantage of DEXA is that it does not enable the examiner to differentiate between cortical and trabaceular bone.
- Some literature suggests that DEXA is of limited use in people with a spinal deformity or those who have had previous spinal surgery.
- The presence of vertebral compression fractures or osteoarthritis may interfere with the accuracy of the test; in such instances, CT scans may be more useful.[120,121]

Quantitative Ultrasound (qUS)

- The use of US for the measurement of bone density has received widespread attention because:
- Does not involve the use of radiation
- Inexpensive (lower cost than DEXA)
- Relatively simple to implement and process
- Portable
- US can provide information about the density and elasticity of bone by measuring the velocity of sound through bone, and about the structure of bone by measuring the attenuation of the signal.
- Bone tissue can be characterized in terms of speed of sound and broadband ultrasound attenuation (BUA).
- Speed of sound and attenuation of a sound wave are affected by the density, compressibility, viscosity, elasticity, and structure of the material it is travelling through.
- This technology assumes that bones with different biomechanical properties have different ultrasound-determined values for attenuation and velocity.
- The propagation of the US wave through bone is affected by bone mass, bone architecture, and the directionality of loading.
- Pulse-echo (reflection) technique: uses a single transducer to transmit and receive the signal. The generated US pulse travels through the sample and is reflected at an interface to be detected by the same transducer.
- Transmission technique: uses two transducers, positioned either side of the heel, one to transmit and a second to receive. (preferred method with dealing with bone due to the bones highly attenuating nature).

- Transducers can be either fixed or mobile
- Fixed transducers are not in direct contact with the heel and a set heel width is assumed when calculating the speed of sound and broadband ultrasound attenuation.
- Mobile transducers can be brought into direct contact with the heel and the correct width can be measured.[123]
- Difficult to use US to measure common fracture sites (hip & vertebrae) because the depth of soft tissue surrounding these bones attenuates too much of the US signal so a reading cannot be obtained.
- Most popular US measurement site is the calcaneus
- There is very little soft tissue which makes it easy to measure bone
- It has a relatively flat surface which ensures good contact between the heel and the transducers
- It is similar in composition to the main fracture sites (approx 90% trabecular bone)
- It is easily accessible and requires very little patient preparation. [Evans, 2006]
- Newer US imaging devices offer a parametric image of broadband US attenuation (BUA) at the calcaneus.
- For a given material the attenuation of the US wave will be constant, known as its BUA index.
- This is a measure of the increase in attenuation of the ultrasound wave as a function of increasing frequency.
- An US wave covering a range of frequencies is passed through a known thickness of sample.

- The amplitude spectrum of the received signal is then compared to the spectrum of a reference material.
- The difference between the two spectra is plotted against frequency and the slope is the BUA index (dB/MHz).
- If it is then divided by the thickness of the measured sample, it gives a volumetric parameter in (dB/MHz)/cm.
- The precision of this technique was found to be 1.4 to 3.3 percent [Roux, 1996], the authors also noted that parametric imaging enhanced the reproducibility of US measurements of the calcaneus.
- Factors which affect accuracy & precision in qUS:
- Operator dependant: Incorrect placement of the measurement region
- Device dependant: Diffraction affects both attenuation & velocity measurements.
- Patient dependant: Variability of bone width, soft tissue thickness or composition, marrow composition and temperature. [Evans, 2006].
- In some studies the values obtained with use of qUS have been shown to correlate well with those obtained with the use of standard bone densitometery techniques such as DEXA [Mirsky, 1998].
- At the calcaneus qUS and DEXA measurements have to have a correlation of approx. 0.8 to 0.85 [Gluer, 1997].
- However other studies found that the precision of QUS is generally poor and changes in qUS of the heel may not reflect changes in BMD at the spine or hip.
- Studies suggest that qUS is a useful tool in determining fracture risk [Hernandez, 2004].

- There is some evidence that qUS of the heel can predict fracture risk of hip and spine independently of BMD measurements.
- There is also some evidence that qUS in addition to BMD evaluation by DEXA may give a better estimate of fracture risk than DEXA scanning alone
- But qUS has limited usefulness (compared to DEXA) for monitoring and comparing the effect of medications used to treat osteoporosis.
- Some studies suggest that qUS may reliably screen out patients unlikely to have a BMD in the osteporotic range, however subjects classified as osteporotic using this method require further investigation such as DEXA to confirm the diagnosis [Taal et al, 1999].[123]
- qUS is generally used as an initial screening test. If results from an ultrasound test indicate that bone density is low, DEXA is recommended to confirm the results.
- PA, SXA and DEXA techniques are projection techniques and as a result can only measure BMD as an area density (2D), and they include mineral from both cortical and trabecular bone in the beam path.
- qCT provides a cross-sectional or 3- dimensional image from which the bone is measured directly, independent of the surrounding soft tissue
- A form of qCT called peripheral qCT (pQCT) measures the density of bones in peripheral limbs, wrist etc.
- Advantages of qCT include
- Can measure trabecular and cortical bone separately, which offers an advantage in terms of the choice of treatment because cortical and trabecular bone do not change in parallel.

- it is the only modality which allows direct measurement of a volume of bone, which can be expressed directly as density.
- Can be performed on a standard hospital CT.
- Disadvantages are the relatively high radiation dose involved (~29μSv) [Kalender, 1992] and the high cost of scans, limited access to scanners due to their high clinical demand.[123,124]

Clinical indications for QCT, defined by the

National Osteoporosis Foundation

- To establish a diagnosis of osteoporosis or assess its severity in the context of general clinical care.
- To monitor bone density in patients receiving glucocorticoid therapy.
- To diagnose low bone density in patients with metabolic disorders such as mild primary hyper-parathyroidism
- qCT involves the use of a mineral calibration phantom and a CT scanner.
- The phantom usually consists of hydroxyapatite in plastic and is scanned simultaneously with the vertebrae.
- A lateral CT scan localizes the mid-plane of two, three or four lumbar vertebral bodies.
- Quantitative readings are then obtained from a region of trabecular bone in the anterior portion of the vertebrae.
- The CT determinations of vertebral bone density are compared with known readings of solutions in the phantom.
- The measurements of the vertebrae are then averaged, and a commercially available software package is used to convert Hounsfield units into Bone mineral equivalents

qCT - Principles

- qCT is available in both single energy and dual energy modalities.
- The single energy technique offers better reproducibility and it is more commonly recommended [Mirsky, 1999].
- However, standard single energy CT analysis of the lumbar spine fails to account for increases in bone marrow fat concentration that occur with increasing age.
- As a result, measurements in elderly, osteoporotic patients may be falsely decreased by 20-25% [Cann, 1980].
- The accuracy is reportedly reduced with the use of Dual Energy CT but the dose of radiation is higher [Cann, 1980].
- Peripheral qCT systems with a small circular gantry are now available.
- Principle advantage of this technique is the reduced radiation exposure (typically 0.4μSv to the skin) [Hosie et al, 1986].

qCT Accuracy

- Soft tissue inhomegenity affects the accuracy of qCT.
- The content of yellow marrow in the vertebrae may have a significant effect on the accuracy of BMD measurements.
- Machine related artifacts such as beam hardening, detected scatter and system drift can introduce errors.
- Accuracy and precision of qCT are reported as 5-8%.[124]

Radiographic Absorptiometry (RA)

Radiographic absorpitometry (RA) is a technique for bone mass measurement from radiographs of peripheral sites, most commonly the hand or heel. Its advantages include that it is less expensive and more widely available than other bone densitometry techniques, there is no need for specialized equipment, and it has been shown to be both precise and accurate, for obtaining bone-mineral content measurements of the phalanges of the hand [Yang, 1994]. The major disadvantage of RA is that, because measurements are sensitive to changes in overlying soft tissues, the technique is limited to the appendicular skeleton [Mirsky, 1999].

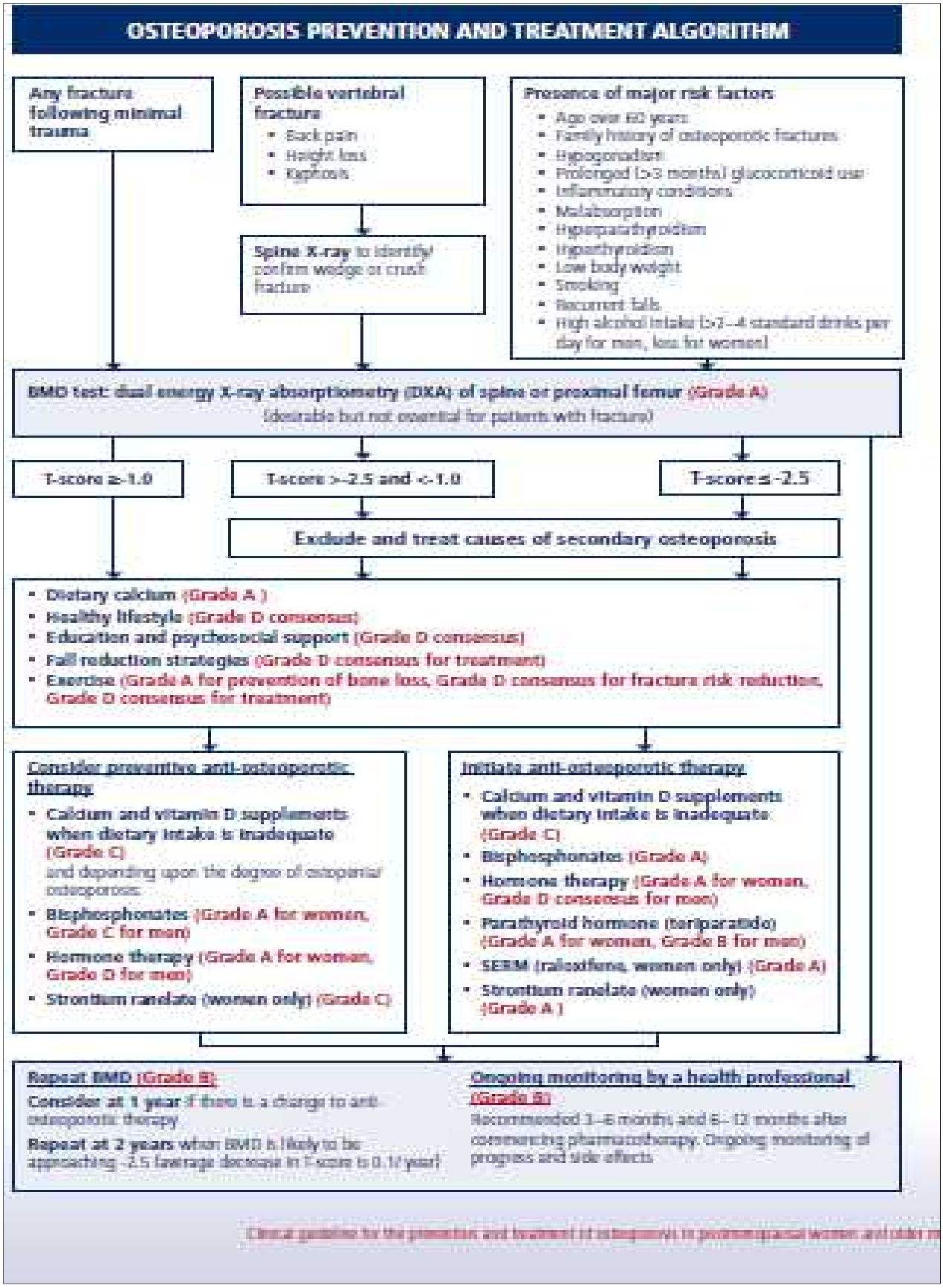
- The principle was first described in 1939, and RA became relatively widely used as a research technique in the 1960s, although interest in RA subsequently dwindled as more precise nonradiographic densitometry techniques became available.
- In traditional RA measurements, an aluminium wedge is included in the radiograph in order to correct for variables, such as voltage setting, exposure time, and film variables.
- However, it has recently gained renewed interest as a simpler, readily available screening tool.
- Initially, two radiographs of the hand and an aluminium reference wedge are taken at different energies.
- The radiograph was then sent to a central reading facility where the image was captured electronically and was analyzed to determine the mean density of the middle phalanges of the second, third and fourth fingers is calculated and the results are reported in aluminium equivalents.

- Also, standardized hand radiographs are taken with an aluminium step-wedge placed on the film and the imaged is analyzed with an optical densitometer. The BMD is determined by comparison with the defined density of the aluminium step-wedge.
- This is a low-cost and potentially widely available technique but is it restricted to the appendicular bones such as the metacarpals and phalanges, which are surrounded by a relatively small amount of soft tissue.
- Recently, computerized image processing has been applied to radiography, with the result that current RA techniques applicable to a routine clinical setting are seemingly as precise and accurate as dual energy or single-energy x ray absorptiometry (DXA or SXA) [Yates et al, 1995].
- In addition, recent studies demonstrate that the strength of association between low bone mass measured by RA and fracture risk is comparable to that for other forms of bone mass measurement [Yates et al, 1995].[125]

RA Performance

- Cosman [1991] reported correlations between RA and the standard BMC techniques as r=0.58–0.9.
- Cosman also reported that RA measurements were found to predict low bone mass of the lumbar spine and femoral neck with 90% and 82% sensitivity respectively.
- Yang et al (1994) in a study of cadaver, found that the correlation between RA determination of BMC in the hand and DEXA determination of BMC in the forearm was good, at r=0.887, and that the short term precision error was small, CoV at 1% for BMC measurements.
- Problems include non-uniformity of film sensitivity and processing [Njeh, 2000].[125]

TREATMENTS FOR OSTEOPOROSIS (TABLE 1)



Pharmacologic Therapy for Osteoporosis Treatment and Prevention

AGENT	DOSE	COST/30 DAYS* Generic	Trade	OTHER CONSIDERATIONS
Prevention				
Calcium (typically as carbonate or citrate)	Total daily intake 1000-1500 mg of elemental calcium	$4-10		• Constipation is more common with calcium carbonate • Calcium citrate is more expensive, but probably better absorbed in patients with low stomach acidity (e.g., PPI use) • Nephrolithiasis is not a contraindication
Vitamin D	Total daily intake 800-1000 IU	$4		• 10-30 min sun exposure to arms & face 2-3x/week during summer months • For high doses or calcitriol consider specialist consultation
Treatment, listed in decreasing order of approximate quality and quantity of data supporting efficacy				
Bisphosphonates, oral				• Take 30-60 min before 1st food of day with 8 oz water; stand/sit upright for 30-60 min
Alendronate (Fosamax®)	70 mg po weekly	$11	$88	• Mild GI effects excess 0-5% cf. placebo; severe GI effects are rare
Ibandronate (Boniva®)	150 mg po monthly	NA	$112	• Reflux w/o esophagitis is relative but not absolute contraindication
Risedronate (Actonel®)	35 mg po weekly,	NA	$104	• Renally excreted, avoid if creatinine clearance <30-35.
	150 mg po monthly		$112	• Effects on fetal development are not known. Prolonged presence in bone of treated patients: discuss potential fetal risks if considering for women of child-bearing age
Bisphosphonates, parenteral				
Ibandronate (Boniva®)	3 mg IV Q 3 mo		$454	• Risk of osteonecrosis of jaw is less than 1 in 100,000 for oral bisphosphonates.
Zoledronic acid (Reclast®)	5 mg IV yearly		$1159	• For zoledronic acid – monitor for increased creatinine and hypocalcemia
Raloxifene (Evista®)	60 mg po daily	NA	$117	• Increased deep venous thrombosis and pulmonary embolism risk - approximately same as estrogen therapy *[4]* • Hot flash incidence 3-6% greater than placebo • Not recommended for men or for premenopausal women
Hormone therapy, Postmenopause				
Estrogens:				
Estradiol (Estrace®)	1 mg po daily	$6	$61	
Esterified estrogens (Estratab®)	0.625 mg po daily	NA	NA	
Estropipate (Ogen®)	0.625 mg po daily	NA	NA	• The relative risks and benefits of postmenopausal estrogen therapy should be reviewed with patients before starting treatment.
Conjugated estrogens (Premarin®)	0.625 mg po daily	NA	$52	• Women with uterus in place will need both estrogen and progestin therapy
Transdermal estradiol (various)	0.05 mg/d 1-2x/wk	$31	$58	• Level A evidence is only with conjugated estrogens, but this is likely a class effect *[2]*
Progestins:				
Medroxyprogesterone (Provera®)	02.5-5 mg daily	$7-9	$27-40	
Micronized progesterone (Prometrium®)	100-200 mg daily	NA	$53-102	
Combinations (various)				
Prempro™	0.625/2.5 mg daily	NA	$62	
Calcitonin Nasal Spray (Miacalcin®, Fortical®)	200 IU daily, alternate nostrils	$75	$93-121	• Rhinitis 5% excess compared to placebo *[4]* • Caution in renal failure • Reduces pain of acute fracture *[4]*
Teriparatide (rDNA origin) (FORTEO®)	20 mcg SQ daily	NA	$938	• Consider specialist consultation

* Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + $3 for generics on 30-day supply, Amerisource Bergen item catalog, 7/10, and Michigan Department of Community Health M.A.C. Manager, 7/10.

TABLE 2

A. **Lifestyle**

We should recommend the following important lifestyle choices for all men:

- adequate but safe exposure to sunlight as a source of vitamin D
- maintenance of a healthy weight and BMI
- cessation of smoking
- avoidance of excessive alcohol consumption.[126-128]

B. Education and psychosocial support

- education and awareness about the disease process
- promotion of a healthy lifestyle
- prevention of further fractures
- management and rehabilitation techniques
- pain management
- falls prevention techniques
- psychosocial welfare (dealing with depression, social isolation and fear of falling).[129]

C. Reducing the risk of falls

- education on the risk of falling and prevention strategies
- medication review and modification
- exercise programs tailored to the individual's specific needs and abilities
- use of appropriate assistive devices
- treatment of postural hypotension and cardiovascular (CV) disorders
- reduction of environmental hazards.[130-132]

D. Exercise

- Exercise programs should be individualized to the patient's needs, abilities and interests
- Particularly when the individual has not undertaken recent physical activity, exercise programs should commence at a low level and be progressive in intensity
- Two short intense exercise sessions separated by 8 hours are more effective than one long training session
- Most people should aim to exercise for 30–40 minutes per session, 4–6 times per week
- A physiotherapist or exercise physiologist can assist in developing the most appropriate program, providing education on safe and effective training techniques, increasing motivation, and ongoing monitoring
- Individuals with OP should receive education about back care to reduce the chance of back injury.[133-135]

E. Major pharmacological interventions

Details of the major pharmacological treatments are summarized below:

Bisphosphonates

The bisphosphonates are analogues of inorganic pyrophosphate and inhibit bone resorption.

1. **Alendronate:** is approved for the treatment of postmenopausal osteoporosis (10 mg daily or 70 mg once weekly by mouth) and osteoporosis in men (10 mg daily). It is also approved for prevention and treatment of glucocorticoid-induced osteoporosis (5 mg daily). It has been shown to reduce vertebral, non-vertebral and hip fractures. Approval for the 70 mg once weekly formulation

was granted on the basis of a bone mineral density bridging study. Alendronate is contraindicated in the presence of abnormalities of the oesophagus which delay emptying, inability to stand or sit upright for at least 30 minutes and hypocalcaemia. It should be used with caution in patients with other upper gastrointestinal disorders and is not recommended in patients with renal impairment (creatinine clearance <35 ml/min). Side-effects include upper gastrointestinal symptoms, bowel disturbance, headaches and musculoskeletal pain. Alendronate should be taken after an overnight fast and at least 30 minutes before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium). Tablets should be swallowed whole with a glass of plain water (~ 200 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 30 minutes after taking the tablet.[136,139,141]

2. **Ibandronate** 150 mg once monthly by mouth or 3 mg as an intravenous injection every 3 months is approved for the treatment of osteoporosis in increased risk of fracture. In a dose of 2.5 mg daily by mouth a significant reduction in vertebral fractures was demonstrated. No data are available for hip fracture. Approval for the oral 150 mg once monthly and 3 mg intravenously every 3 months formulations was granted on the basis of BMD bridging studies. Ibandronate is contra-indicated in patients with hypocalcaemia. Oral ibandronate should be used with caution with patients with upper gastrointestinal disease. Both oral and intravenous formulations should be used with caution in patients with renal impairment (serum creatinine above 200 μmol/l or a creatinine clearance below 30 ml/min). Side-effects with the oral preparation include upper gastrointestinal side-effects and

bowel disturbance. Intravenous administration may be associated with an acute phase reaction, characterized by an influenza-like illness; this generally is short-lived and typically occurs only after the first injection. Oral ibandronate should be taken after an overnight fast and 1 hour before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium). Tablets should be swallowed whole with a glass of plain water (180 to 240 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 1 hour after taking the tablet.[137,138]

3. **Risedronate** 5 mg daily or 35 mg once weekly by mouth is approved for the treatment of osteoporosis, to reduce the risk of vertebral fracture, to reduce the risk of hip fractures. It is also indicated for the treatment of osteoporosis in men at high risk of fractures. Risedronate 5 mg daily is approved for the prevention of glucocorticoid-induced osteoporosis. In osteoporosis risedronate 5 mg daily has been shown to reduce vertebral and non-vertebral fractures. In a large population, risedronate significantly decreased the risk of hip fractures. Approval for the 35 mg once weekly formulation was granted on the basis of a BMD bridging study. Risedronate is contraindicated in the presence of hypocalcaemia, pregnancy and lactation, and severe renal impairment (creatinine clearance <30ml.min). It should be used with caution in patients with upper gastrointestinal disease. Side-effects include upper gastrointestinal symptoms, bowel disturbance, headache and musculoskeletal pain. Risedronate should be taken after an overnight fast and at least 30 minutes before the first food or drink (other than water) of the day or any other oral medicinal products or supplementation (including calcium). Tablets should be

swallowed whole with a glass of plain water (~120 ml) while the patient is sitting or standing in an upright position. Patients should not lie down for 30 minutes after taking the tablet.[136,139]

4. **Zoledronate:** 5 mg intravenously once yearly is approved for the treatment of osteoporosis in men at increased risk of fracture, including those with a recent low trauma fracture, and in the treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in men. It has been shown to reduce the incidence of vertebral, nonvertebral and hip fractures in men with osteoporosis and to reduce the risk of clinical fracture and attendant mortality when given to patients shortly after their first hip fracture. Zoledronate is contraindicated in the presence of hypocalcaemia, pregnancy and lactation. It should be used with caution in patients with severe renal impairment (eGFR < 35 ml/min). Side-effects include an acute phase reaction (see above), usually only after the first infusion, and gastrointestinal symptoms. An increase in atrial fibrillation, reported as a serious adverse event, was also seen in the main phase III trial although this finding has not been replicated in other trials involving zoledronate. Zoledronate is given as an intravenous infusion over a minimum period of 15 minutes.8 Osteonecrosis of the jaw (ONJ) has been reported rarely in patients receiving oral bisphosphonates for osteoporosis. A dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with concomitant risk factors, for example poor oral hygiene, dental disease or glucocorticoid therapy. While on treatment, these patients should avoid invasive dental procedures if possible and good oral hygiene practices should be maintained during treatment. ONJ is extremely rare in patients receiving bisphosphonate therapy for osteoporosis and in the

vast majority the benefits of treatment outweigh the risks. Atypical fractures, mainly of the subtrochanteric and diaphyseal regions of the femur and of the femoral shaft have rarely been reported in patients taking bisphosphonates for osteoporosis. A direct causal link has not been established. These fractures may be bilateral and often heal poorly. It is currently uncertain whether there is a causal association with bisphosphonate therapy and in the vast majority of patients the benefits of bisphosphonate therapy outweigh the risks.[140,147]

5. **Denosumab** is a fully humanized monoclonal antibody against Receptor Activator of Nuclear factor Kappa B Ligand (RANKL), a major regulator of osteoclast development and activity. It is approved for the treatment of osteoporosis in postmenopausal women at increased risk of fractures and is given as a subcutaneous injection of 60 mg once every 6 month. It has been shown to reduce the incidence of vertebral, non-vertebral and hip fractures in men with osteoporosis. Denosumab is contraindicated in men with hypocalcaemia or with hypersensitivity to any of the constituents of the formulation. Its use is not recommended in pregnancy or in the paediatric population (age ≤18 years). No dose adjustment is required in patients with renal impairment. The safety and efficacy of denosumab in patients with hepatic impairment have not been studied. Hypocalcaemia should be corrected by adequate intake of calcium and vitamin D before initiating therapy. Side-effects include skin infection, predominantly cellulitis, and hypocalcaemia. ONJ has been reported rarely in clinical studies in patients receiving denosumab at a dose of 60 mg every 6 months for osteoporosis. A dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with concomitant risk factors, for example poor oral

hygiene, dental disease or glucocorticoid therapy. While on treatment, these patients should avoid invasive dental procedures if possible and good oral hygiene practices should be maintained during treatment. The condition is rare & in the vast majority of patients the benefits of treatment outweigh the risks.

6. **Strontium ranelate:** Strontium ranelate contains two atoms of strontium linked to ranelic acid. Its mode of action is incompletely understood although it appears to have anti-resorptive properties whilst maintaining bone formation. It is approved for the treatment of osteoporosis to reduce the risk of vertebral and hip fractures at a dose of 2 g daily. It has been shown to reduce the risk of vertebral and non-vertebral fractures in men with osteoporosis over a broad age range, including in men aged over 80 years. In a post hoc analysis of men aged 74 years or older with a femoral neck BMD T-score below -2.4 SD a significant reduction in hip fracture was also shown. Strontium ranelate should be used with caution in patients with a creatinine clearance below 30 ml/min and in patients with risk factors for venous thromboembolism. Side-effects include diarrhoea, headache, nausea and dermatitis. A small increase in the risk of venous thromboembolism was seen in the phase III trials and, very rarely, hypersensitivity reactions may occur. Strontium ranelate should be taken between meals and at least 2 hours after the last meal. It is usually taken at bedtime.[136]

7. **Raloxifene**

   Raloxifene is a selective oestrogen receptor modulator and inhibits bone resorption. It is approved for the treatment and prevention of osteoporosis at a dose of 60 mg daily. It has been shown to reduce vertebral fracture risk but reduction in non-vertebral and hip fractures has not been demonstrated.9

Raloxifene is contraindicated in women with child-bearing potential, a history of venous thromboembolism or unexplained uterine bleeding. Hepatic impairment and severe renal impairment are also contraindications. It should be used with caution in people with a history of stroke or with risk factors for stroke. Side-effects include leg cramps, oedema and vasomotor symptoms. There is a small increase in the risk of venous thromboembolism, mostly within the first few months of treatment and a small increase in the risk of stroke has been reported. Raloxifene is taken as a single daily dose (60 mg) and may be taken at any time without regard to meals.[136,139]

8. Parathyroid hormone peptides

Parathyroid hormone (PTH) peptides, when administered intermittently, have anabolic skeletal effects with an increase in bone formation. The effects are most marked in cancellous bone and may differ between cortical sites.[142]

9. **Teriparatide** (recombinant human PTH 1-34) is approved for treatment of osteoporosis in men at high risk of fracture and is given as a subcutaneous injection in a dose of 20 μg/day. Teriparatide is also approved for the treatment of osteoporosis associated with systemic glucocorticoid therapy in men at increased risk of fracture. The duration of treatment is limited to 18 months. It has been shown to reduce vertebral and non-vertebral fractures in people with osteoporosis but no data are available for hip fractures. Teriparatide is contraindicated in patients with hypercalcaemia, metabolic bone diseases other than osteoporosis, severe renal impairment, prior radiation to the skeleton and malignant disease affecting the skeleton. It should be used with caution in patients with moderate renal impairment. Side effects include headache, nausea, dizziness and postural hypotension. Teriparatide is given as

a subcutaneous injection in a dose of 20 µg/day. The duration of treatment is limited to 24 months.[143]

10. **Recombinant human PTH (1-84)** is approved for the treatment of osteoporosis in people at high risk of fractures. It has been shown to reduce vertebral fractures in people with osteoporosis but no data are available for non-vertebral and hip fractures. Recombinant human PTH (1-84) is contraindicated in patients with hypercalcaemia, metabolic bone diseases other than osteoporosis, severe renal or hepatic impairment, prior radiation to the skeleton and malignant disease affecting the skeleton. PTH should be used with caution in patients with previous or active urolithiasis. Hypercalcaemia and/or hypercalciuria develop in approximately 25% of treated patients and serum and urine calcium should be monitored at 1, 3 and 6 months after starting treatment, with adjustment of calcium and vitamin D supplementation ± frequency of PTH administration if required. Other side-effects include nausea and headache. Recombinant human PTH (1-84) is given as a subcutaneous injection in a dose of 100µg/day. The duration of treatment is limited to 24 months.

11. **Hormone Therapy**

    With respect to the role of testosterone replacement in hypogonadal men, there are no data showing efficacy (or safety) in fracture reduction but there are data demonstrating that testosterone levels below the reference range are associated with increased fracture risk. Hormone therapy may contribute to a reduction in fracture risk for this population.[144]

Other pharmacological interventions

12. **Calcium:**

- Total calcium intake from dietary sources and supplements should exceed 1200 mg/day.76–78 Vitamin D from sunlight exposure (avoiding the middle of the day) and supplements should ensure 25-OH D levels are above 60 nmol/L

- To optimise clinical efficacy, calcium 1000–1200 mg/day should be taken in conjunction with vitamin D 700–800 IU/day77–78
- Calcium citrate does not need to be taken after meals like calcium carbonate, as it does not require an acid environment to be optimally absorbed
- There are some data suggesting that calcium supplements may be more effective if taken at night, eg. with the evening meal
- Vitamin D may be taken at any time of the day
- Recent research suggests that supplementation with calcium or vitamin D alone is not effective. They should be taken concurrently.[145,146,149,150]

13. **Calcitonin** is an endogenous polypeptide hormone that inhibits osteoclastic bone resorption. Salmon calcitonin, 200IU daily by intranasal administration, is approved for the treatment of established osteoporosis in order to reduce the risk of vertebral fracture. The approved dose has been shown to reduce vertebral fractures in people with osteoporosis but robust evidence for non-vertebral and hip fracture reduction is lacking. Calcitonin is contraindicated in patients with hypocalcaemia and should not be used in patients with nasal ulceration. The most frequently observed undesirable effects are local reactions such as rhinitis and nasal discomfort.[148]

14. **Calcitriol (1,25-dihydroxyvitamin D)** is the active form of vitamin D and is approved for the treatment of established osteoporosis in a dose of 0.25µg twice daily. It acts mainly by inhibiting bone resorption. It has been shown to reduce vertebral fracture risk in people with osteoporosis but effects on non-vertebral and hip fractures have not been established. It is contraindicated in patients with hypercalcaemia and because it may cause hypercalcaemia and/or hypercalciuria, serum calcium and creatinine levels should be monitored at 1, 3 and 6 months after starting treatment and at 6 monthly intervals thereafter.[150]
15. **Etidronate** in the formulation Didronel PMO is approved for treatment of osteoporosis and for prevention in people considered to be at risk. Etidronate is also approved for the prevention and treatment of glucocorticoid-induced osteoporosis. Etidronate has been shown to reduce vertebral fractures in people with osteoporosis but no effect on non-vertebral or hip fractures has been shown in randomized controlled trials. Didronel PMO is a long-term cyclical regimen administered in 90-day cycles. Each cycle consists of etidronate 400mg tablets for the first 14 days, followed by Cacit (calcium) 500mg tablets for the remaining 76 days. Its use has largely been supplemented by the newer bisphosphonates.[136,139]

METHODOLOGY

The present study was conducted in the department of Orthopaedics, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study design:

One year Cross Sectional Study.

Source of Data:

Data was collected from all Men aged more than 50 years undergoing DEXA scan attending outpatient & inpatient of department of Orthopaedics KLES Dr. Prabhakar Kore Hospital and Medical Research Center, Belgaum, Karnataka. & also attending osteoporotic check up camps from December 2010 to November 2011.

Sample Size

101 Men aged more than 50 years were selected who were willing to undergo a DEXA Scan.

Sampling procedure:

Sample size was calculated by using the formula $4pq/d^2$ where p is prevalence of Osteoporosis in % (In a similar study done) & was 50%, q = (100-p) %, d is absolute error taken as 10%.

SELECTION CRITERIA

Inclusion criteria:

1. Men aged more than or equal to 50 years.
2. Participants giving consent to enroll in the study
3. After ruling out all the exclusion criteria
4. All subjects with back pain more than or equal to 50 years irrespective of whether symptomatic/ asymptomatic will be included

Exclusion criteria:

1. Participants on following medication which are known to affect calcium metabolism
    a. Long term steroids
    b. Phenytoin
    c. Eltroxin
    d. Heparin
    e. Thiazide diuretics
2. Patients with following long term diseases
    a. Chronic liver/ kidney diseases
    b. Chronic skin disease
    c. Malignancy
    d. Rheumatoid Arthritis
3. Patients not willing to enroll in the study

Procedure:

The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum. After finding the suitability as per inclusion and exclusion criteria ,patients were selected for the study and briefed about the nature of the study, the interventions used and written ,informed consent was obtained (Annexure–I). The consented patients were enrolled in the present study. Further, descriptive data of the participants & risk factors were evaluated through a Questionnaire. (Annexure II).

Proforma:

The patients were evaluated through a proforma & after ruling out the patients in the exclusion criteria, the rest were enrolled in the study.

IPD/OPD No. :

Name:

Age: Age is an important factor to be noted, as the study was focused on patients aged more than 50 years.

Sex: Male

Address: Address was noted to communicate with the patient for treatment purposes if found osteoporotic & osteopenic.

Socioeconomic Status: Was determined according to BG Prasad classification.

Questionnaire:

1. Occupation:

Occupation of the individual was asked and it was further classified into manual labour, sedentary work and other group. This was to assess the amount of physical activity a patient involves in as increased bone mass is seen among men with higher physical activity.

2. Complaints of the individual

To know the reason for attending the department of orthopaedics for evaluation & treatment.

3. Medication History.

To rule out all the exclusion criteria. To advice the patient to stop calcium supplementations 48 hours prior to the scan.

4. History suggestive of following chronic diseases.

a. Chronic liver disease b. Chronic kidney disease

c. Chronic skin disease d. Rheumatoid arthritis

e. Diabetes mellitus f. Hypertension

g. Malignant conditions

5. History of alcohol Consumption.

Alcohol consumption was asked as it leads to fall in bone mineral density. If the men consumed alcohol quantity of intake was assesed.

6. History of smoking cigarettes.

Cigarette smoking was asked as it leads to fall in bone mineral density. If the men smoked cigarette, the no of cigarettes smoked per day was asked.

7. History of consumption of milk & milk products.

To assess whether the patient is on calcium rich diet as it leads to increase in BMD.

8. Diet

Patients diet was assessed whether the patient is a vegeterian or a non vegetarian.

9. Were you having Long-term bed rest
    1. Yes
    2. No

10. Sunlight exposure

A history of exposure to sunlight (number of hours per day) was solicited.

11. Family history of fractures after trivial fall or deformity of the back (Hunch Back) was asked.
12. Body mass index was calculated after determining the Height & weight

BMI: - wt (kg)/Ht (m2) _____.

Investigation:

BMD (Bone mineral density) measurement was done using DEXA Scan of make GE Wipro and 2008 Lunar model.

DEXA Scan Evaluation technique:

A dual energy X-ray absorptiometry (DEXA) scan uses X-ray equipment and a computer to measure bone density. Bone mineral density is the most important tool in the diagnosis of osteoporosis . It allows for accurate , precise and reproducible assessment of bone mineral density and enables the detection of osteoporosis before the occurrence of fractures. DEXA Scan is the gold standard in the assessment of BMD.

Pre Scan Requisites

1. Completion of the questionnaire
2. Selection of the study group after ruling out the exclusion criteria
3. Filling of the informed consent.

Instructions prior to the scan

1. Stoppage of calcium supplements 48 hours before the scan.
2. Removal of clothes that have metal buttons or other metal accessories & change to a gown if necessary.
3. To remain still during the procedure.

Procedure:

The procedure was quick , painless and time taken was about 10 minutes. It involved exposing the body to a small dose of X-ray radiation. Patient was taken to the Dexa scan room and asked to lie down on the Dexa scan machine table. A radiographer operated the scanning equipment.

Scan was carried out at two sites the lumbar spine followed by the hip joint. Patient legs were flexed & placed over a large block for scanning of the lumbar spine. This was done to achieve straightening of the spine. For scanning of the hip joints patient was made to lie supine only. The scanning apparatus was then passed over the patients lumbar spine & the hip joints respectively and it will project X rays beam. Some of this radiation travels straight through the bones and a certain amount is absorbed by them - how much depends on how dense the bones are.

A detector measured how much radiation passes through the bones and sends the information to a computer. A printed report was then obtained stating the BMD, 'T' & 'Z' scores.

Assessment of data:

The Bone Mineral Density (BMD in g/cm2) and 'T' and 'Z' scores was determined. 'T' score compares the BMD result with that of a young adult of the same gender with a peak bone mass while 'Z' score compares the BMD result with people of the same age group size and gender.

Data was analyzed as follows.

- Normal BMD: T scores not more than 1 SD below the adult mean.
- Osteopenia: T score between -1.0 and- 2.5.
- Osteoporosis: T score <- 2.5 with or without fragility fracture.

Data was collected and recorded and diagnosis based on the BMD score was done. BMD data was correlated with the data of various risk factors obtained through the questionnaire and correlations were derived.

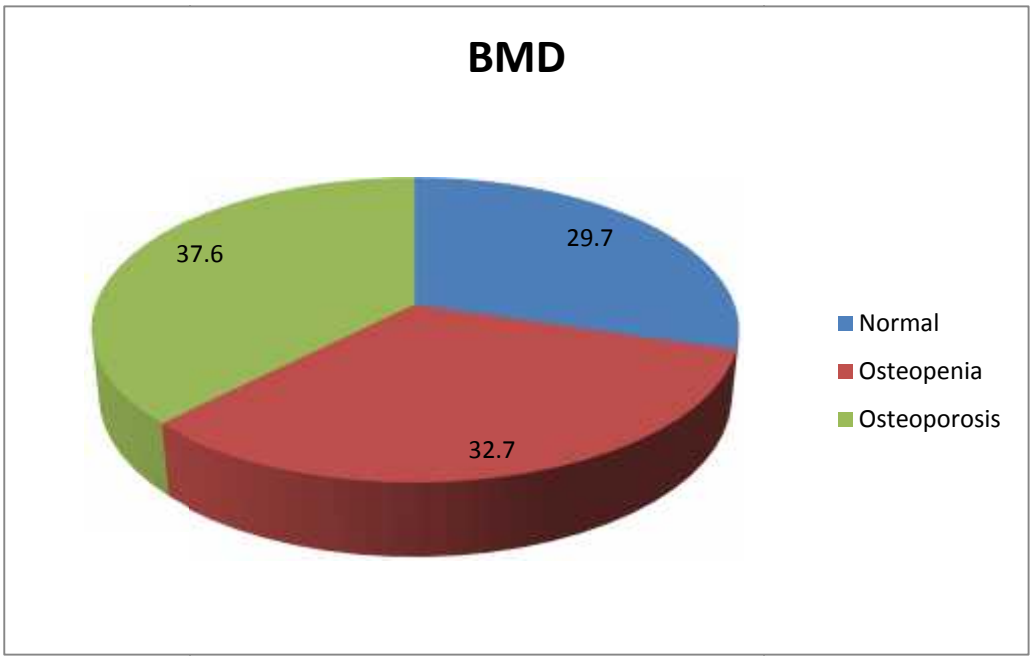
RESULTS

In this series of 101 patients were evaluated. Following are the observations made.

Table 1: BMD Distribution

Normal (%)	Osteopenia (%)	Osteoporosis (%)
29.7	32.7	37.6

The overall prevalence of osteoporosis was 37.6%, osteopenia 32.7% and men with normal BMD were 29.7%. This study was conducted in Men aged ≥ 50 Years.



Graph 1: BMD Distribution

Table 2: Age & BMD

AGE	Normal n(%)	Osteopenia n (%)	Osteoporosis n (%)	Total
50-54	4(26.7)	4(26.7)	7(46.6)	15
55-59	3(17.7)	8(47.1)	6(35.2)	17
60-64	5(29.4)	8(47.1)	4(23.5)	17
65-69	5(29.4)	6(35.3)	6(35.3)	17
≥70	13(37.1)	7(20)	15(42.9)	35
Total	30	33	38	101

Age of all the patients in this study was ≥50 years. Majority of the patients were aged > 70 years.15 patients (14.85%) were in the age group 50 to 55 years. There were 17 patients (16.83 %) in the age group of 55 to 59 years, 17 patients (16.83%) in age group 60 to 64 years, 17 patients in the age group 65 to 69 years and 35 patients aged more than 70 years (34.66 %). Highest numbers of osteoporotic individuals 15 were aged more than 70 years.

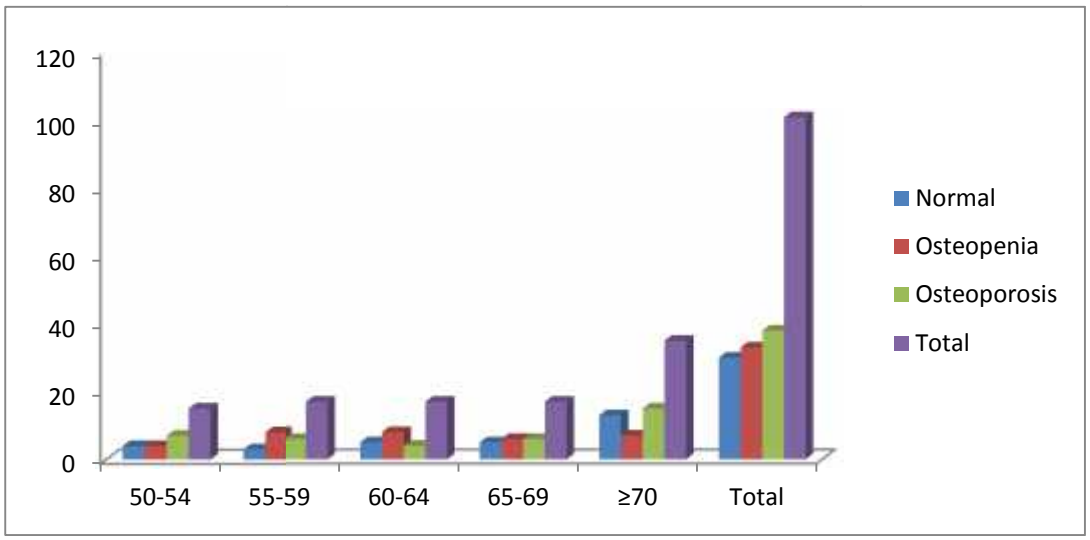
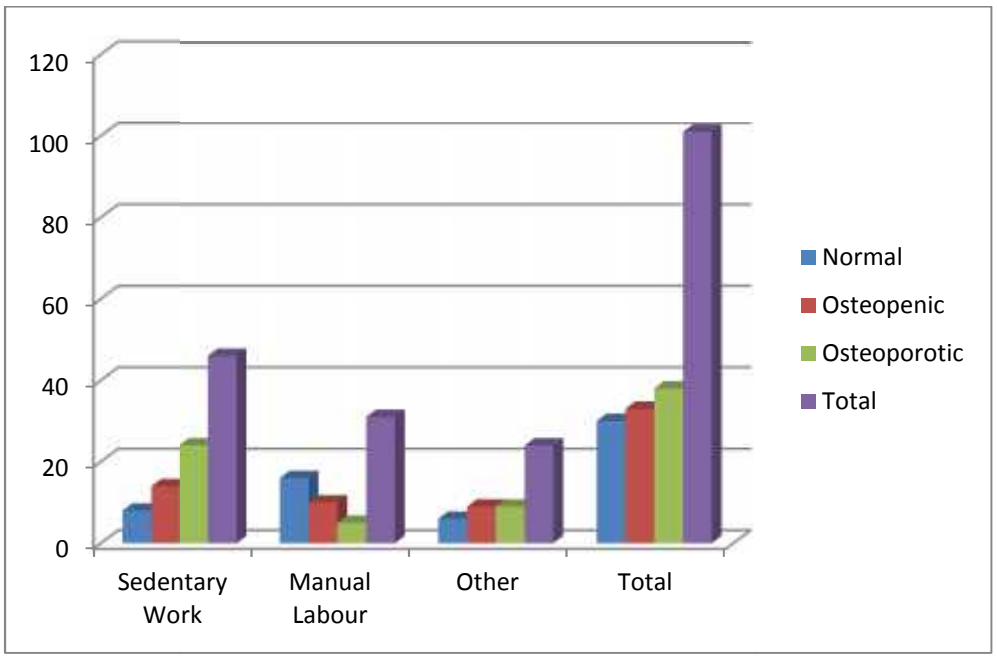


Table 2: Age & BMD

Table 3: Occupation & BMD

Occupation	Normal n (%)	Osteopenic n (%)	Osteoporotic n (%)	Total
Sedentary Work	8 (17.4)	14 (30.4)	24 (52.2)	46
Manual Labour	16 (51.6)	10 (32.3)	5 (16.1)	31
Other	6 (25)	9 (37.5)	9 (37.5)	24
Total	30	33	38	101

The prevalence of osteoporosis was highest among men involved in sedentary work (office work, retired from jobs) where in 24 men (52.2%) had osteoporosis. (51.6%) of men among manual Labour group had normal BMD.

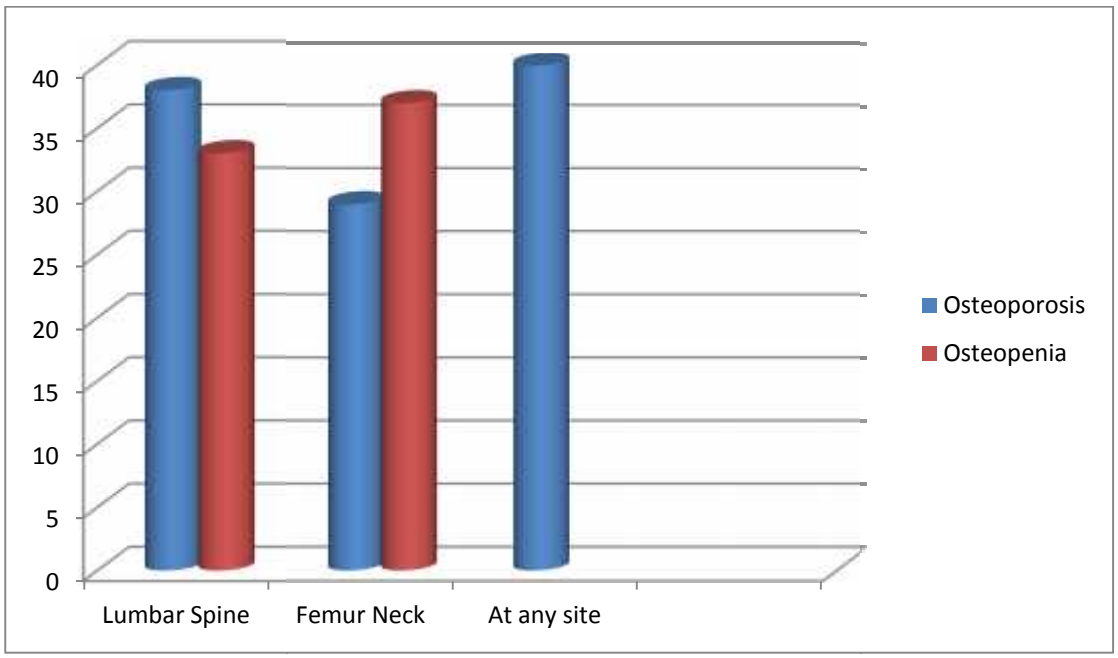


Graph 3: Occupation & BMD

Table 4: Percentage of Study Subjects with Osteoporosis and Osteopenia at Various Anatomic Sites

Lumbar Spine		Femur Neck		Osteoporosis at any site
Osteoporosis	**Osteopenia**	**Osteoporosis**	**Osteopenia**	
38	33	29	37	40

Determination of BMD at Lumbar spine was more sensitive for osteoporosis with 38 men having osteoporosis, where as dual hip joint DEXA evaluation showing 29 men with osteoporosis.

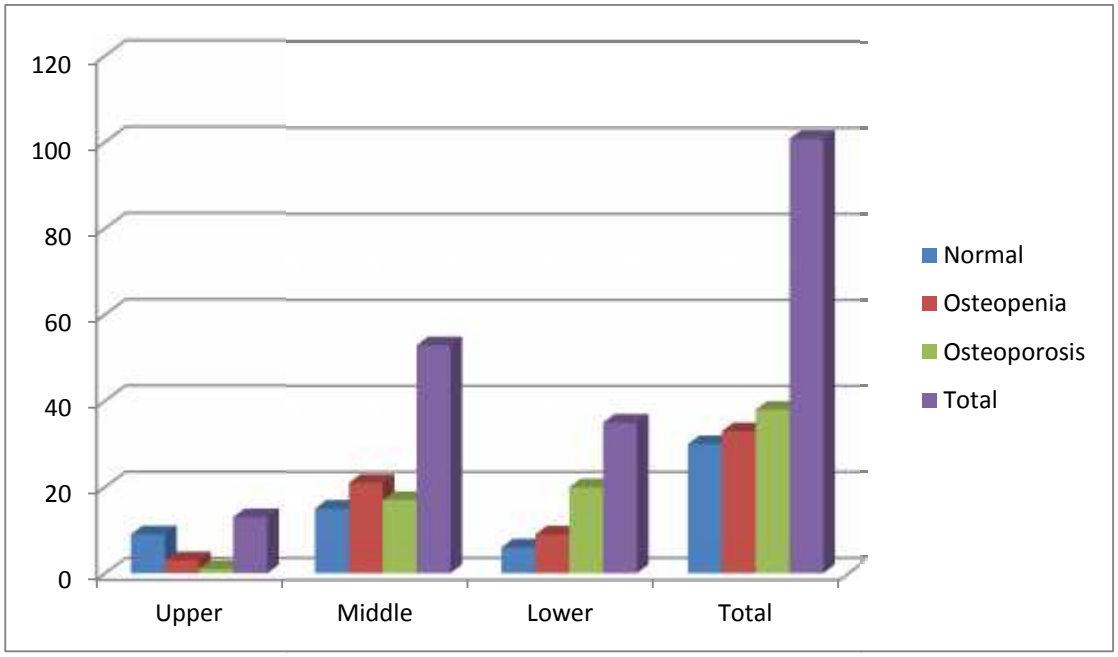


Graph 4: Osteoporosis and Osteopenia at Various Anatomic Sites

Table 5: Socioeconomic status and BMD

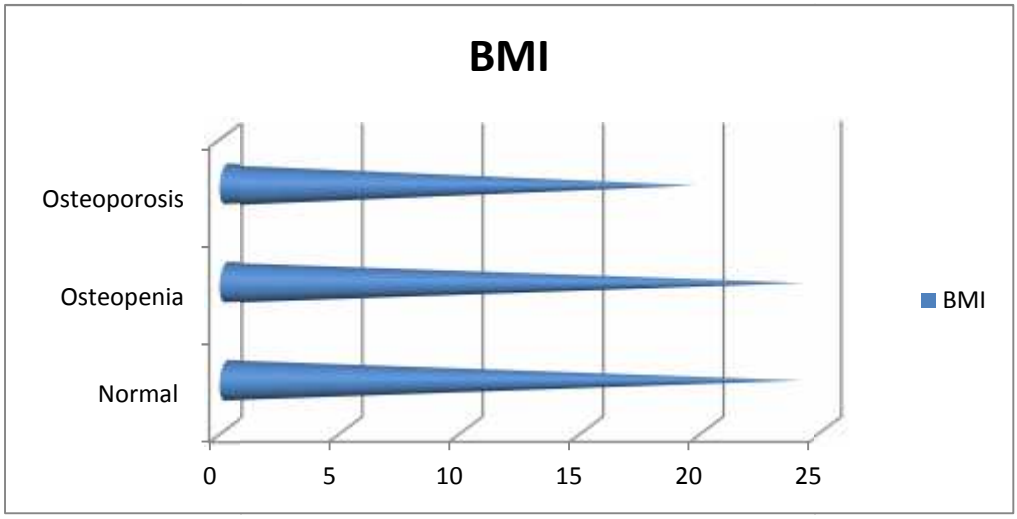
Socioeconomic status	Normal	Osteopenia	Osteoporosis	Total
Upper	9 (69.2%)	3 (23.1%)	1(7.7%)	13
Middle	15(28.3%)	21(39.6%)	17(32.1%)	53
Lower	6 (17.2%)	9(25.7%)	20(57.1%)	35
Total	30	33	38	101

The number of osteoporotic men in the lower socio economic group was the highest 20 (57.1%). Percentage of men having normal BMD was highest in the upper socio economic group (69.2%).



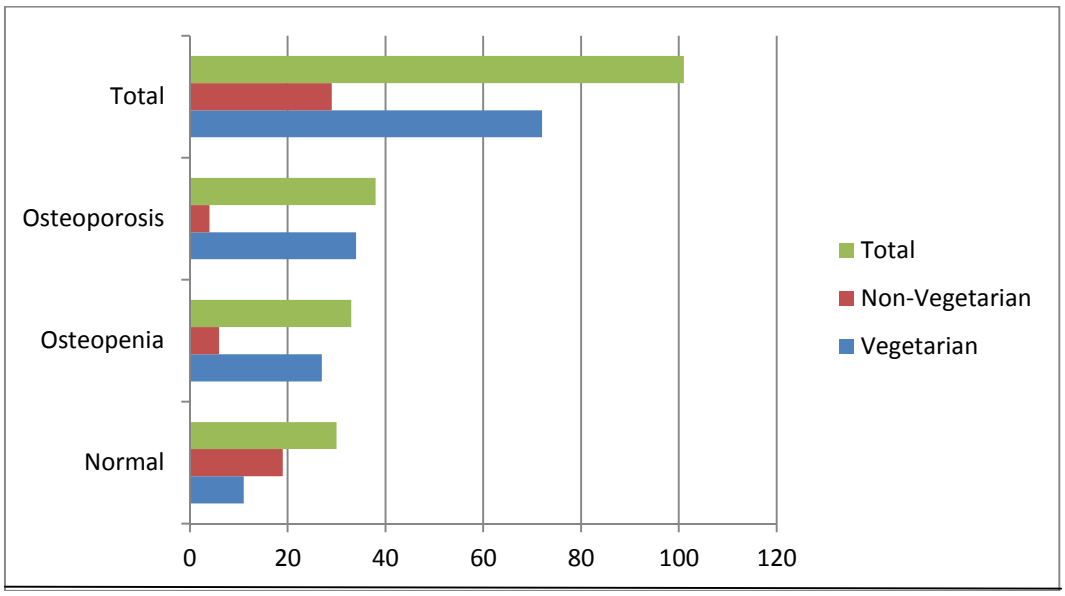
Graph 5: Socioeconomic status & BMD

6. BMI and BMD



Graph 6: BMI and BMD

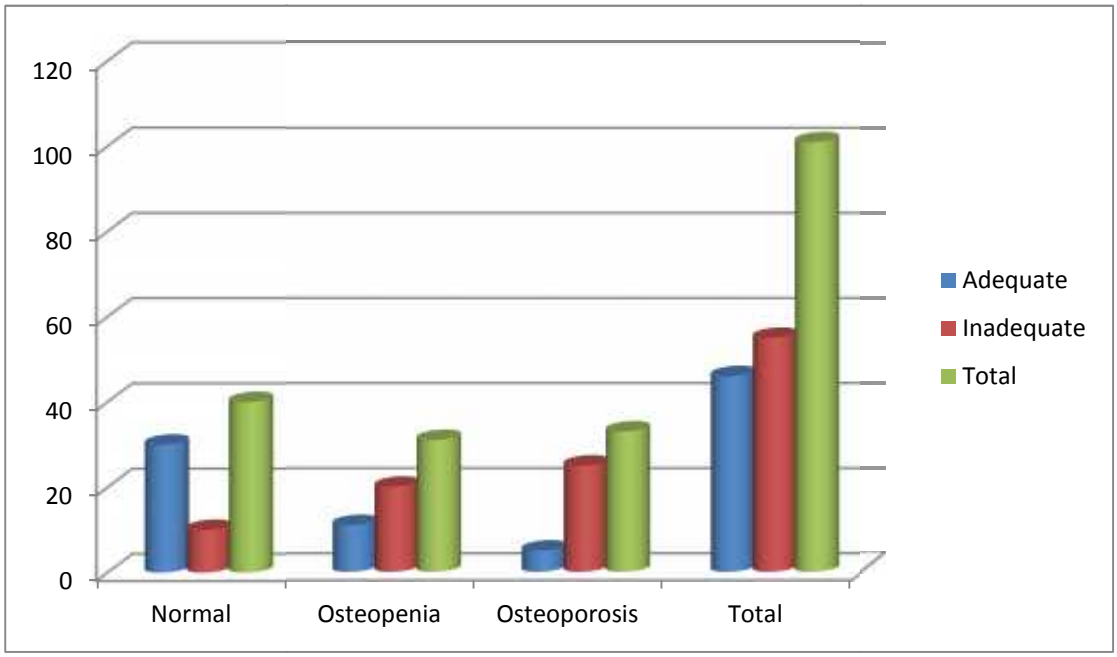
Body Mass Index ranged from 9.91 to 45.34. Men with higher body mass index had lower incidence of osteoporosis. Highest number of Men with osteoporosis had lower BMD values



Graph 7: Diet and BMD

Highest percentages of men of with osteoporosis were in the vegetarian group (47.22%). The non-vegetarian group had the higher number of men with normal BMD (65.52%).

:



Graph 8: Sunlight exposure and BMD

The number of men with adequate amount of exposure of sunlight (1 ½- 2 hrs) were 46 and men with inadequate exposure of sunlight (< 1 ½) was 55. The prevalence of osteoporosis was higher among the group with inadequate exposure to sunlight. The number men with normal BMD was highest among the group with adequate exposure to sunlight.

DISCUSSION

Osteoporosis is the commonest metabolic bone disease in clinical practice, it is a major public health problem worldwide and its prevalence is increasing with rise in the ageing population.

In this cross sectional study 101 men were evaluated with a DEXA scan for the presence of osteoporosis and various risk factors were assessed. This was significant as no other studies were carried out in this region to determine the prevalence and risk factors.

The overall prevalence of osteoporosis in this study was 37.6%, osteopenia was 32.7% & men with normal BMD values were 29.7%.

Age of all the patients in our study ranged from 50 to 85.3 years. Average age of the men in this study was 65.436 years. Highest numbers of osteoporotic men (39.47%) were aged more than 70 years.

In comparative studies they concluded that age correlated inversely with BMD values and fracture threshold reduces with age. Anburanjan et al prospectively studied the rate of loss of BMD per annum. They concluded that rates of BMD loss at the age of 65 years were 0.91%, 0.84%, 0.72%, 0.78%, 1.66%. Per annum respectively for the neck of femur, trochanter, intertrochanteric region, total hip and Ward's triangle.[151]

BMD at forearm sites (distal radius and ulna) declined by 0.49% to 0.66% per year.[152]

Changes in serum sex steroids and gonadotropins over life in a random sample of 346 men (Rochester, MN) aged 23–90 years were: Bioavailable estrogen: -47%,

Bioavailable testosterone -64%, SHBG +124%, Luteinizing hormone +285%, Follicle-stimulating hormone +505% [153,154]

Osteoporosis is predominantly a disease of men aged above 50 years. The burden of morbidity from osteoporosis has significant medical, social and financial implications.

Life style factors form the cornerstone of prevention. These include regular exercise, adequate dietary calcium (1- 1.5 Gm/day), adequate vitamin D (800 1.4./day) and cessation of smoking and alcohol intake.

In our study the prevalence of osteoporosis was highest among men involved in sedentary work (office work, retired men) where in 24 men (52.2%) osteoporosis had. Cross sectional studies show weight bearing exercises have beneficial impact on the bone mass, development of peak bone mass and reduces the bone loss and the mechanical stress.[155] Thus lower rate of osteoporosis prevalence was seen among men involved in laborious professions in our study. The cohort studies showing Physical inactivity in the old age populations are responsible for decline of bone mass and the major risk factor for Osteoporosis fractures.[156]

Osteoporosis itself has no specific symptoms; its main consequence is the increased risk of bone fractures. Osteoporotic fractures are those that occur in situations where healthy people would not normally break a bone; they are therefore regarded as fragility fractures. Typical fragility fractures occur in the vertebral column, rib, hip and wrist. The most common complaints the patients presented with in our study with was backache (66.34%).Rest had complaints of knee pain, sciatica, generalized weakness & diffuse body ache.

The number of osteoporotic men in the lower socio economic group was the highest 20 (57.1%). Several risk factors contribute to low bone mass. These include non-modifiable factors like old age, small thin built, Caucasian/Asians and family history of fractures. Ethnic differences in bone mineral density (BMD) are strongly influenced by body weight. Behavioral risk factors for osteoporosis and fractures include functional impairment, physical inactivity,[157-159] sedentary work,[160] low calcium intake,[161] high caffeine intake, smoking,[157] and high alcohol intake.[162]

Body Mass Index of the men in our study ranged from 9.91 to 45.34. Prospective studies, including one from the Osteoporotic Fractures in Men Study (MrOS) cohort, have established that low hip bone mineral density (BMD) is an independent risk factor for fracture among older men.[163] Underweight has consistently been reported as a risk factor for fracture when compared to normal weight.[164] the correlation between BMI and BMD is moderate, many overweight and obese individuals have relatively low BMD, and bone strength may not increase in proportion to increases in total or fat mass.[165]

It was found that highest percentage of men with osteoporosis were in the vegetarian group (47.22%). Various Indian studies have shown that vegetarians have 50% risk of osteoporosis and 98.82% are osteopenic.[166]

Important modifiable risk factors include calcium and vitamin D deficiency, sedentary life style, smoking, excessive alcohol and caffeine intake. Only 9 men in this study gave history of drinking alcohol of which 2 were osteopenic. 10 men gave history of smoking 4 had Osteopenia & 3 had Osteoporosis. Prospective and cohort studies show smoking decreases the bone mineral density and leads to the risk of

osteoporosis fractures in both men and women and also studies demonstrating that quitting smoking may help to reduce the fractures.[167]

The prevalence of osteoporosis was higher among the group with inadequate exposure to sunlight. The number of men with normal BMD was highest among the group with adequate exposure to sunlight. The multi centric and cross sectional studies show there is a strong association between less exposure to sun light leading to the hip fractures in the age groups of above 50 years.[168]

Genetic factors have a role on Bone mineral Density.[169] Fifty percent of the Peak bone mass, bone geometry, bone strength, bone architecture depends on genetic predisposition.[170] In our study 4 men had positive family history for fracture of the wrist and hip after trivial fall and all the 4 men had osteoporosis in this study.

It is important to distinguish between diagnostic and prognostic use of bone mineral density measurement. As a diagnostic tool, it gives information concerning the presence or absence of the disease with the cut off values chosen. Its potential as a prognostic tool is to determine the future probability of osteoporosis.

Central DEXA, a proven technology for the diagnosis and management of bone mineral loss, is now widely used all over the world.

As the diagnosis and long term treatment of osteoporosis and consequent fractures are expensive for the individual as well as the health system, there is a need for careful consideration in determining the risk factors as well as the future course of action on scientific evidence.

The presence of a key risk factor should alert the physician to the need for further assessment and intervention, pharmacologic as well as non pharmacologic, to prevent fracture.

Like most other public health problems of widespread magnitude, treatment alone cannot help a society or nation to cope with the scourge of osteoporosis. Also, since no therapy fully restores lost bone mass, the importance of prevention cannot but be underscored.

Life style factors form the cornerstone of prevention. These include regular exercise, adequate dietary calcium (1- 1.5 Gm/day), adequate vitamin D (800 1.4./day) and cessation of smoking and alcohol intake.

Osteoporosis and related fractures have a multifactorial genesis; as a result their management is complex. The goals of treatment of established disease are to arrest bone loss, maintain skeletal integrity and prevent fragility fracture. All this necessitate early intervention.

Global research on treatment and prevention of osteoporosis in the past decade employing randomized controlled trials has made it possible to apply various therapeutic options. These options include non-pharmacologic approaches for all groups of patients and specific drugs for different subgroups.

CONCLUSION

In this cross sectional study 101 men were evaluated with a DEXA scan for the presence of osteoporosis and various risk factors were assessed.

The overall prevalence of osteoporosis in this study was 37.6%, osteopenia was 32.7% & men with normal BMD values were 29.7%.

Age of all the patients in this study ranged from 50 to 85.3 years. Average age of the men in this study was 65.436 years. Highest number of osteoporotic men 39.47%) were aged more than 70 years.

The number of osteoporotic men in the lower socio economic group was the highest 20 (57.1%). Percentage of men having normal BMD was highest in the upper socio economic group (69.2%).

The most common complaints the patients presented with was backache (66.34%).Rest had complaints of knee pain, sciatica, generalized weakness & diffuse body ache.

In our study 46 men doing sedentary work & 31 men worked in the fields & 24 were involved in other jobs. The prevalence of osteoporosis was highest among men involved in sedentary work (office work, retired men) where in 24 men (52.2%) had osteoporosis.

Body Mass Index ranged from 9.91 to 45.34. Average BMI of men in this study was 22.31. Men with higher body mass index had lower incidence of osteoporosis.

The number of men who were vegetarian in this study were 72 and non vegetarian were 29. Highest percentages of men with osteoporosis were in the vegetarian group (47.22%). The non vegetarian group had the higher number of men with normal BMD (65.52%).

The number of men with adequate amount of exposure of sunlight (1 ½- 2 hrs) were 45.55% and men with inadequate exposure of sunlight(< 1 ½) were 54.45%. The prevalence of osteoporosis was higher among the group with inadequate exposure to sunlight. The number of men with normal BMD was highest among the group with adequate exposure to sunlight.

Only 8.91% men in this study gave history of drinking alcohol of which 1.98% were osteopenic. 9.9% men gave history of smoking, of which 3.96% were osteopenic & 2.97% were osteoporotic.

3.96% men had positive family history for fracture of the hip and wrist after trivial fall and all the 3.96% men had osteoporosis in this study.

SUMMARY

In this study 101 men aged above 50 years were evaluated to determine the prevalence of osteoporosis using a DEXA scan.

A structured questionnaire was used to assess the risk factors leading to osteoporosis. 38 men were found to be osteoporotic, 33 were osteopenic and 30 men had normal bone mineral density values.

Highest numbers of osteoporotic men were above 70 years of age. Thus increasing age was significant risk factor for osteoporosis.

Other significant risk factors were sedentary work, thin individuals and lower body mass index. Increase in age correlated directly with increase risk of osteoporosis and lower body mass index was a significant risk factor for osteoporosis.

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ANNEXURE I

INFORMED CONSENT

Mr/Mrs/Ms_____

You are invited to participate in this study.

"A HOSPITAL BASED ONE YEAR CROSS SECTIONAL STUDY TO KNOW THE PREVALENCE OF OSTEOPOROSIS IN MEN AGED MORE THAN 50 YEARS USING DUAL ENERGY X-RAY ABSORPTIOMETRY SCAN (DEXA)"

Principal Investigator: BL0110002

Why am I being asked to take part in this study?

All men attending Ortho OPD and IPD aged 50 years and above are eligible to participate in this study. As you fall under this age group you are eligible to participate. Other men of the same age group are participating in this study. The decision to participate is entirely your own. The study is being done to find out the prevalence rate and factors affecting osteoporosis as mentioned in the objectives. BL0110002 is the principal investigator.

PROCEDURE

If you consent to be in this study, the relevant data is collected as per the proforma provided to you. BMD (Bone mineral density) measurement would be done using Central DEXA Scan (Dual energy X ray absorptiometry) of make GE Wipro and 2008 Lunar model. You will undergo a DEXA Scan after ruling out all the exclusion criteria. This test is painless and can be performed within 5 to 15 minutes. You will be asked to undergo this procedure only once.

BENEFITS

To the patient in the study.

1. It will act as a diagnostic tool for the patients in the study by providing information regarding the presence of the disease.
2. Will help to initiate therapy for osteoporosis once the diagnosis is confirmed.
3. As a prognostic tool it will help to determine future probability of osteoporosis.

To the community at large.

1. The data obtained from the study will help to provide information on the epidemiology of the osteoporosis which will be then basis for initiation for various programs for osteoporosis prevention.
2. It will help create awareness regarding osteoporosis.

RISKS

There are no risks associated with this study.

ALTERNATIVES

If you decline to participate decision it will not change the present or future health care or other services that you will receive. The treatment given out to you will be the standard treatment for your condition.

WITHDRAWING / REMOVAL FROM THE STUDY:

You can withdraw from the study during anytime you want and you will not be penalized for the same. You can be removed from the study if you do not fulfil the inclusion criteria.

PRIVACY AND CONFIDENTIALITY:

All information about the subject during the course of the study will be kept confidential to the extent permitted by law. The code numbers will identify the subject in this research record. Information from this study may be published but the subject's identity will be confidential in any publication.

COSTS

Cost of each DEXA Scan will cost around Rs 850/-(Lumbar/Hip region) to 2000/-(Total Body Scan). There will be no reimbursement for your expenses.

QUESTION

If any enquiries in the future or in case of study related problems you may contact principle investigator.

STATEMENT OF CONSENT:

The details of the research study in which I am expected to participate, for which I have to undergo DEXA Scan have been explained to me. I willingly, under no pressure from the researcher agree to take part in this study, and agree to participate in all investigations. I may withdraw at any time. I am not giving up any of my legal rights by signing this form.

My signature below indicates that I have read this entire consent form or it has been read to me, and had all my questions answered. I will be given a copy of this consent form.

Signature of the participant or legally authorized representative

Participants Name : Signature :

Name of the legally : Signature :

authorized representative

Witness's name : Signature :

Investigators Name : Signature :

Date:

Place:

ANNEXURE II

STUDY TITLE: "A HOSPITAL BASED ONE YEAR CROSS SECTIONAL STUDY TO KNOW THE PREVALENCE OF OSTEOPOROSIS IN MEN AGED MORE THAN 50 YEARS USING DUAL ENERGY X-RAY ABSORPTIOMETRY SCAN (DEXA)"

I.P/ OPD NO:

Name: Age:

Address: Phone no:

1. What kind of work do you do on a daily basis? Name of the activity ☐

a. Household (retired) b. Manual labour c. Office work

d. Others specify_____

2. Do you have any of the following complaints? ☐

a. Backache b. Easy fatigability c. Fractures after trivial fall.

d. Others specify._____

3. Do you use any medications? ☐

a. Yes b. No

If yes then specify _____

4. Have you been diagnosed with any of the following conditions? ☐

a. Chronic liver disease b. Chronic kidney disease

c. Chronic skin disease d. Rheumatoid arthritis

e. Diabetes mellitus f. Hypertension

g. Malignant conditions

5. Whether you consume alcohol? ☐

a. Yes b. No

If yes then how much quantity per day? _____

6. Do you smoke cigarettes? ☐

a. Yes b. No

If yes then how many per day? _____

7. Do you consume milk and milk products daily? ☐

a. Yes b. No

If yes then quantity per day._____

8. Do you take any calcium / Vitamin D supplements? ☐

a. Yes b. No

If yes then dosage per day._____

9. Are you a vegetarian or non vegetarian? ☐

a. Vegetarian b. Non Vegetarian

10. Does he have any spinal deformities? ☐

a. Yes b. No

11. Have either of your parents been diagnosed with osteoporosis or broken a bone after a minor fall (a fall from standing height or less)? ☐

a. Yes b. No

12. Did either of your parents have a hunchback? ☐

a. Yes b. No

13. Were you having Long term bed rest ☐

a. Yes b. No

14.Do you have very little physical activity ☐

a. Yes b. No

15. Determination of Body Mass Index

Height: - _____m.

Weight: - _____Kg.

BMI: - wt (kg)/Ht (m^2)_____.

COMPUTER WITH DEXA SCAN SOFTWARE & DEXA SCAN MACHINE WITH PATIENT

STATISTICS FOR DEXA 2008-2010

DEXA SCAN OF LUMBAR SPINE REGION

DEXA SCAN OF DUAL HIP REGION