2. REVIEW OF RELATED LITERATURE

The related literatures collected relevant to the title “A study on the prevalence and management of osteoporosis in women with special reference to diet and yoga” is presented in the following paragraphs.

2.1. Bone Physiology

2.1.1. Role of Bone in the Human Body

Bone plays an important structural role in the body. It provides mobility, support, and protection for the body, and acts as a storehouse for essential minerals. Bones are important in the production of red blood cells which carry oxygen and waste products from cellular metabolism. Red blood cells are produced in the bone marrow, or the central portion of the bones. Bone is not static, even in fully grown adults. To understand the osteoporosis which is the major bone disorder a brief note on bone physiology under the following heads: Promoting bone health is important in helping to stem the rate and risk of onslaught of osteoporosis, the most common bone disease [17].

2.1.2. Structure- Long Bone- Longitudinal Section of Haversian Canal

In describing the general structure of bone, a long bone will be used as an example as given in Fig.2.1. At each end of such a bone there is an expanded portion called an epiphysis, which forms a joint with another bone. The shaft of the bone, which is located between the epiphyses, is called the diaphysis. The bone is completely enclosed by a tough covering called the periosteum. Within the periosteum lies a bony layer called compact bone, which is solid, strong, and resistant to bending. The epiphyses are composed largely of spongy (cancellous) bone, which provides the greatest amount of elastic strength since the epiphyses are subjected to the greatest forces of compression [18].
2.1.3. Development of Bone- Ossification

In the fetus, most of the skeleton is made up of cartilage, a tough, flexible connective tissue that has no minerals or salts. As the fetus grows, Osteoblasts and osteoclast slowly replace cartilage cells and ossification begins [18].

Ossification is the formation of bone by the activity of osteoblasts and osteoclasts and the addition of minerals and salts. Calcium compounds must be present for ossification to take place. Osteoblasts do not make these minerals, but must take them from the blood and deposit them in the bone [18].

In long bones, the growth and elongation (lengthening) continue from birth through adolescence. Elongation is achieved by the activity of two cartilage plates, called epiphy seal plates, located between the shaft (the diaphysis) and the heads (epiphyses) of the bones. These plates expand, forming new cells, and increasing the length of the shaft. In this manner, the length of the shaft increases at both ends, and each head of the bone moves progressively apart. As growth proceeds, the thickness of the epiphyseal plates gradually decreases and this bone lengthening process ends. In humans, different bones stop lengthening at different ages, but ossification is fully complete by about age 25. During this lengthening period, physical activity results in the strengthening of bone tissue [18].
In contrast to the lengthening of bone, the thickness and density of bone is continually be maintained by the body. That is, old bone must be replaced by new bone all the time. This is accomplished as bone is continually deposited by osteoblasts, while at the same time, it is continually being resorbed (broken down and digested by the body) by osteoclasts. Osteoblasts are found on the outer surfaces of the bones and in the bone cavities. A small amount of osteoblastic activity occurs continually in all living bones (on about 4% of all surfaces at any given time) so that some new bone is being formed constantly. Normally, in fact, except in growing bones, the rates of bone deposition and resorption are equal to each other so that the total mass of bone remains constant [18].

2.1.4. Factors Influencing the Growth and Health of Bone: Nutrients, Hormones and Physical Exercise

Bone development is influenced by a number of factors, including nutrition, exposure to sunlight, hormonal secretions, and physical exercise. For example, exposure of skin to the ultraviolet portion of sunlight is favorable to bone development, because the skin can produce vitamin D when it is exposed to such radiation. Vitamin D is necessary for the proper absorption of calcium in the small intestine. In the absence of this vitamin, calcium is poorly absorbed, the bone matrix is deficient in calcium, and the bones are likely to be deformed or very weak. Vitamins A and C also are needed for normal bone growth and development [19]. Details of the nutrients are given later in this chapter.

Hormones that affect bone growth and development include those secreted by the pituitary gland, thyroid gland, parathyroid glands, and the ovaries and testes. The pituitary gland, for instance, secretes growth hormone (GH), also called somatotropin, which stimulates activity in the epiphyseal plates. This hormone is the main regulator of height. Somatotropin plays many roles in the body: it stimulates bone and muscle growth, maintains the normal rate of protein synthesis in all body cells, and speeds the release of fats as an energy source for growth. Other hormones play a part in maintaining the strength and health of the bone matrix by functioning to control the level of blood calcium. In fact, calcium is needed for a number of metabolic processes other than for bone formation, including blood clot formation,
nerve impulse conduction, and muscle cell contraction. When a low blood calcium condition exists, the parathyroid glands respond by releasing parathyroid hormone (PTH). This hormone stimulates osteoclasts to break down bone tissue, and as a result, calcium salts are released into the blood. On the other hand, if the blood calcium level is excessively high, the thyroid gland responds by releasing a hormone called calcitonin. Its effect is opposite that of parathyroid hormone; it inhibits osteoclast activity allowing osteoblasts to form bone tissue. As a result, the excessive calcium is stored in bone matrix. The actions of these hormones are both excellent examples of some important negative feedback loops present in our bodies. Without adequate supplies of these important chemicals, the bones will not develop or grow normally [19].

Women, especially if slim, are more prone to bone loss after menopause (when women stop menstruation, age 45-60). Race is another factor that affects ones tendency to lose bone. Usually, during bone loss, the osteoblastic activity in the bone is less than normal, and consequently the rate of bone deposition is reduced. This result in brittle bones in the elderly age, and, therefore, their bones are more susceptible to fracture. Older people may also develop a hump in the upper back, often referred to as a dowager's hump. Some women can lose as much as one-third of their skeletal structure by age 75. This is twice the rate of bone loss in older men, who have about 30% more bone mass to start with. Bone loss afflicts more people than any other bone disease [19].

2.2. Osteoporosis

2.2.1. Definition

Osteoporosis is characterized by a loss of bone mass, resulting in greater bone fragility, which increases the risk of bone breakage, also known as fracture. The fractures most commonly associated with osteoporosis occur in the hip or spine, and often result in a downward spiral in physical and mental health, which can greatly impair quality of life and can result in death [20].

The word osteoporosis literally means "porous bones." It occurs when bones lose an excessive amount of their protein and mineral content, particularly calcium.
Over time, bone mass, and therefore bone strength, is decreased. As a result, bones become fragile and break easily. Even a sneeze or a sudden movement may be enough to break a bone in someone with severe osteoporosis [21].

Osteopenia refers to decreased calcification or density of bone. Having osteopenia places a person at risk for developing osteoporosis, the more serious condition. Osteoporosis is defined as having a bone density of more than 25% below the average of young adults of the same sex and race; a bone density between 10 to 25% below average levels is termed osteopenia and reflects a milder degree of bone loss than osteoporosis [22].

Osteoporosis is a bone disease in which the amount of bone is decreased and the structural integrity of trabecular bone is impaired. Cortical bone becomes more porous and thinner. This makes the bone weaker and more likely to fracture [22].

The T-score is the number of standard deviations below the average for a young adult at peak bone density. There are different T-scores depending on which groups of young adults were used as the reference (for example, Caucasian women, Hispanic men). The Z-score is the number of standard deviations below an average person of the same age. There are also different Z-scores depending on the group used as a reference (for example, the group could include everybody of the same age, or it could be limited to people with the same age, race, gender and weight). Furthermore, a person can have one T-score at the femoral neck, another at the total hip, and another at the spine [22].

2.2.1.1. The World Health Organization (WHO) Definitions

The World Health Organization has defined the following categories based on bone density in white women:

- Normal bone: T-score better than -1
- Osteopenia: T-score between -1 and -2.5
- Osteoporosis: T-score less than -2.5
- Established (severe) osteoporosis: T-score less than -2.5 as well as the presence of a non-traumatic fracture.
The WHO committee did not have enough data to create definitions for men or other ethnic groups. It is important to realize that the T-score alone does not predict fractures, and osteopenia is not a disease. In 1994, a committee of the World Health Organization defined osteoporosis based on bone density. Using standardized bone density measurements of the total hip, "normal" bone is greater than 833 mg/cm$^2$. "Osteopenia" is between 833 and 648mg/cm$^2$. Osteoporosis is lower than 648mg/cm$^2$, and "Severe (established) osteoporosis" is when there has been a fragility fracture [22]. See fig. 2.2.

**Fig.2.2. Bone Mass Density and Age**

(Standardized Total Hip BMD of a White woman mg/cm$^2$) (22)

2.2.2. Types of Osteoporosis

Individuals with osteoporosis are at high risk of suffering one or more fractures, which are often physically debilitating and can potentially lead to a downward spiral in physical and mental health. The most common form of osteoporosis is known as “primary osteoporosis.” It is the result of the cumulative impact of bone loss and deterioration of bone structure as people age. This bone loss can be minimized and osteoporosis prevented through adequate nutrition, physical activity, and, if necessary, appropriate treatment.

There are a wide variety of diseases and certain medications and toxic agents that can cause or contribute to the development of osteoporosis.
2.2.2.1. Primary Osteoporosis

Primary Osteoporosis can be further divided into two as – Post menopausal osteoporosis and Age related or senile osteoporosis

2.2.2.1.1. Postmenopausal Osteoporosis: Postmenopausal women are at greater risk hence, the term “postmenopausal” osteoporosis is also used. The loss of bone followed by menopause is faster and accelerates as age advances. This is partly due to the fact that women have two phases of age-related bone loss—a rapid phase that begins at menopause and lasts 4–8 years, followed by a slower continuous phase that lasts throughout the rest of life [23].

2.2.2.1.2. Age related or Senile Osteoporosis: Primary osteoporosis is mainly a disease of the elderly, the result of the cumulative impact of bone loss and deterioration of bone structure that occurs as people age. This form of osteoporosis is sometimes referred to as age-related osteoporosis.

Age-related osteoporosis is by far the most common form of the disease (Fig. 2.3). There are many different causes of the ailment, but the bone loss that leads to the disease typically begins relatively early in life, at a time when corrective action (such as changes in diet and physical activity) could potentially slow down its course. While it occurs in both sexes, the disease is two to three times more common in women. As a result, women typically lose more bone than do men. The rapid phase of bone loss alone in women results in losses of 5–10 percent of cortical bone (which makes up the hard outer shell of the skeleton) and 20–30 percent of trabecular bone (which fills the ends of the limb bones and the vertebral bodies in the spine, the sites of most osteoporotic fractures). The slow phase of bone loss results in losses of 20–25 percent of cortical and trabecular bone in both men and women, but over a longer period of time [23].
2.2.2.2. Secondary Osteoporosis

Secondary osteoporosis is that in which the underlying cause (e.g., steroid use) is known. Young adults and even older individuals who get osteoporosis often do so as a byproduct of another condition or medication use. In fact, there are a wide variety of diseases along with certain medications and toxic agents that can cause or contribute to the development of osteoporosis. Individuals who get the disease due to these “outside” causes are said to have “secondary” osteoporosis. They typically experience greater levels of bone loss than would be expected for a normal individual of the same age, gender, and race. Secondary causes of the disease are common in many premenopausal women and men with osteoporosis [24]. In fact by some estimates the majority of men with osteoporosis exhibit secondary cause of the
disease [25]. In addition, up to a third of postmenopausal women with osteoporosis also have other conditions that may contribute to their bone loss [26].

Approximately 20% of postmenopausal women have secondary causes of osteoporosis [27]. A wide array of medical conditions has been associated with bone loss and osteoporosis; examples include rheumatoid arthritis, multiple myeloma, hyperparathyroidism, Cushing’s syndrome, hyperthyroidism, inflammatory bowel disease, chronic kidney disease, and organ transplantation [27, 28]. Oral glucocorticoids are the most common contributor to drug-induced osteoporosis [28]. Other drugs that have been associated with detrimental effects on bone are excessive thyroid hormone, anticonvulsant medications, heparin, gonadotropin-releasing-hormone agonists, neuroleptic agents, methotrexate, and lithium [27, 29].

2.3. Different Methods of Diagnoses of Osteoporosis

2.3.1. Measurement Techniques of Bone Density

A bone mineral density test (BMD) is a non-invasive and painless test and is the best way to determine your bone density. It can identify osteoporosis, determine your risk for fractures, and monitor your response to osteoporosis treatment. Different bone density tests measure hip, spine, wrist, finger, shin bone, or heel. This test can be done using various methods [30, 31]. They are

- Dual Energy X-ray Absorptiometry (DXA or DEXA)
- Single Energy X-ray Absorptiometry (SEXA)
- Qualitative Ultrasound (QUS)
- Quantitative Computed Tomography (QCT)
- Single Photon Absorptiometry (SPA)
- Dual Photon Absorptiometry (DPA)
- Digital X-ray Radiogrammetry (DXR)

The commonly used BMD test methods are DEXA and QUS. Hence these two are explained here in detail.
2.3.1.1. Dual Energy X-ray Absorptiometry

A routine X-ray can reveal osteoporosis of the bone, which appears much thinner and lighter than normal bones. Unfortunately, by the time X-rays can detect osteoporosis, at least 30% of the bone has already been lost. In addition, X-rays are not accurate indicators of bone density. Having a Densitometer test will confirm osteoporosis. It is a Dual Energy X-ray Absorptiometry test with low radiation rills and a margin of error less than 1.4%. The appearance of the bone on X-ray is often affected by variations in the degree of exposure of the X-ray film. Dual energy X-ray absorptiometry (DEXA, formerly DXA) is considered the gold standard for the diagnosis of osteoporosis.

DEXA bone densitometry is a simple, quick and non-invasive procedure. No anesthesia is required. DEXA bone density testing is the most accurate method available for the diagnosis of osteoporosis and is also considered an accurate estimator of fracture risk. DEXA equipment is widely available making DEXA bone densitometry testing convenient for patients and physicians alike. No complications are expected with the DEXA procedure. However DEXA is a costly procedure.

2.3.1.2. Qualitative Ultrasound (QUS)

QUS for bone analysis is a non-ionizing method in which the calcaneus is the measurement site. This technique is both a cost-effective and accurate for identifying patients at risk of osteoporotic fracture. QUS has been scientifically validated in both fundamental in vitro studies and clinical in vivo studies. Clinical studies have shown that QUS parameters are sensitive to age-related changes, they may be useful in distinguishing osteoporotic subjects, and they offer a prospective prediction of fracture risk comparable to that of axial DEXA.

Apart from calcaneal QUS, measurement of Bone Mineral Density (BMD) can be carried out at the sites - Distal radius and Mid Shaft Tibia using the principle of Speed of Sound (SOS).
2.3.1.3. Other BMD Measurements

Bone-density measurements are not an effective method to monitor the response to treatment because changes in bone density may not be detected for up to 2 years. Radiation techniques to measure BMD, such as Single (SPA) and Double Photon Absorptiometry (DPA) have several limitations. The accuracy of density and attenuation coefficients for the bone mineral and soft-tissue components are also uncertain, though this limitation can partly be overcome with direct DPA and DXA measurement. The accuracy of photon absorptiometry has been estimated to be 4-8% for SPA and 4-6% for DXA. However, the accuracy can be as low as 11% and is worse for lateral projections compared with antero-posterior (AP) projections. SPA is used to measure forearm bone density, and it may not provide an accurate assessment of bone density of spine or hip. DPA is used to measure the density of the spine or hip. Soft-tissue in homogeneity affects the accuracy of Quantitative Computed Tomography (QCT).

Overall, the value of single-energy methods is in the range of 5-15%. With 2 effective beam energies, this changes to 3-10%, but at the cost of poor precision. The precision and accuracy of QCT is good, but the radiation involved is relatively high. Therefore, QCT is not a preferred technique when other methods are available. Ultrasound transmission is attenuated by the thickness and composition of tissues within and surrounding the bone. In trabecular bone, fatty marrow in the inter-trabecular spaces influences both broad and ultrasound attenuation (BUA) and velocity. If such ultrasound measurements show low bone density, the patient should be referred for DEXA because of its high accuracy and precision [31].

2.3.1.3.1. FRAX®: FRAX® is a scientifically validated risk assessment tool, endorsed by the World Health Organization and now integrated into an increasing number of national osteoporosis guidelines around the world. It is considered a major milestone in helping health professionals to improve identification of patients at high risk of fracture. The web-based FRAX® calculator assesses the ten-year risk of osteoporosis fracture based on individual risk factors, with or without BMD values. IOF supports the maintenance and development of the tool and promotes its worldwide use. FRAX® version 3.3 is currently (August 2011) available in
34 country models and in 18 languages. Further country models are being developed [32].

2.3.2. Bone Markers

Various biochemical markers are now available that allow a specific and sensitive assessment of the rate of bone formation and bone resorption of the skeleton [33]. Although these markers are not recommended for use in diagnosis of osteoporosis yet, they appear to be useful for the individual monitoring of osteoporotic patients treated with anti-resorptive agents.

A summary list of bone formation markers is as follows:
- Serum total alkaline phosphatase
- Serum bone–specific alkaline phosphatase
- Serum osteocalcin
- Serum type 1 procollagen (C-terminal/N-terminal): C1NP or P1NP

A summary list of bone resorption markers is as follows:
- Urinary hydroxyproline
- Urinary total pyridinoline (PYD)
- Urinary free deoxypyridinoline (DPD)
- Urinary collagen type 1 cross-linked N-telopeptide (NTX)
- Urinary or serum collagen type 1 cross-linked C-telopeptide (CTX)
- Bone sialoprotein (BSP)
- Tartrate-resistant acid phosphatase

Such markers can also be useful in selected cases to improve the assessment of individual fracture risk when bone mineral density (BMD) measurement by itself does not provide a clear answer. Recent studies in 2009 have shown that the combined use of BMD measurement and bone markers is likely to improve the assessment of the risk of fractures in those cases [34, 35, 36].

Serum alkaline phosphatase is the most commonly used marker of bone formation. In a study conducted by Indumathi, [37] the total ALP levels were significantly high in postmenopausal women in comparison to premenopausal
women. Ionized calcium levels were found to be significantly decreased in early postmenopausal women compared to late postmenopausal women.

2.4. Related Studies: Prevalence of Osteoporosis and Associated Risk Factors

2.4.1. Prevalence of Osteoporosis

2.4.1.1. Demographic Prevalence of Osteoporosis

Osteoporosis is a global problem occurring in every geographic area and affecting 150 million men and women worldwide. Ethnicity and race are well known determinants of skeletal health and bone mineral density. Our knowledge of the magnitude of the problem is very limited and most of the available data is from industrialized nations.

2.4.1.1.1 International Scenario: In USA, 10 million individuals already have osteoporosis and 18 million have osteopenia making it to a total of 28 million Americans affected by this condition. American women are four times more likely to develop osteoporosis than men. Osteoporosis affects 30% of postmenopausal white women in the USA and the proportion rises to 70% in women over the age of 80 year.

The incidence in Europe is projected to double in the next 50 years, and the incidence in Latin America is also expected to rise significantly. Although data on the prevalence of osteoporotic fractures are limited, hip fractures are extremely serious and are responsible for subsequent mortality. Each year, osteoporosis causes more than 1.5 million fractures, resulting in permanent disability, loss of independence, and death. It is predicted that one out of every two women and one in eight men over 50 will have an osteoporosis-related fracture in her or his lifetime. 15 - 30% of those with a hip fracture will die of complications related to the fracture, of those who survive 50% are unable to walk again independently and 1/3rd becomes totally dependent functionally [38].

Globally, osteoporosis is the highest in Whites and Asians, and lowest among Blacks. Blacks have more bone density than other racial groups, lowering their risk of osteoporosis. Hispanic-American women have somewhat greater bone
density than that of non-Hispanic whites [39]. Of all the varieties, postmenopausal osteoporosis is the commonest and the most preventable. Postmenopausal osteoporosis today is recognized to be a major public health problem and is a common cause of morbidity and mortality in women. According to World Bank report, the worldwide population of postmenopausal women which was 470 million in 1990 is expected to increase to 1.2 billion by the year 2030 and 76% of these women would be living in developing countries [40]. Few studies conducted in various countries are summarized in the table 2.1.

Table 2.1. Summary of Studies Conducted on Prevalence of Osteoporosis

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PREVALENCE RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>China 2001</td>
<td>300% increase in last 30 years. [41]</td>
</tr>
<tr>
<td>China 2002</td>
<td>In 2002 11.5% males, 19.9% females [42]</td>
</tr>
<tr>
<td>Hong Kong 2004</td>
<td>200% increase in last 20 years. Women aged &gt;65 – 45% osteoporosis 42% osteopenia. [43]</td>
</tr>
<tr>
<td>Hong Kong 2002</td>
<td>Men &gt; 65 – 13% osteoporosis, 47% osteopenia. [44]</td>
</tr>
<tr>
<td>Singapore 2004</td>
<td>800 to 900 hip fractures due to osteoporosis. [45]</td>
</tr>
<tr>
<td>Singapore 2004</td>
<td>Past 3 decades hip fractures in women aged ≥ 50 increased from 75 to 402 cases. [46]</td>
</tr>
<tr>
<td>Malaysia 2000</td>
<td>51% menopausal women had mild osteoporosis. [47]</td>
</tr>
<tr>
<td>India 2003</td>
<td>In 26 million projected to increase to 36 million by 2013. The peak incidence in India is 10 to 20 years younger compared to western countries. 70 to 80 years to 50 to 60 years. [48]</td>
</tr>
<tr>
<td>Australia 2002</td>
<td>2 millions affected increasing at a rate of 4% per annum. [49]</td>
</tr>
<tr>
<td>New Zealand 2004</td>
<td>Osteoporosis affects more than half of women and nearly 1/3 of men &gt; greater than 60 years. [50]</td>
</tr>
<tr>
<td>Korea 2002</td>
<td>2 million people suffering from osteoporosis. [51]</td>
</tr>
<tr>
<td>Indonesia 2002</td>
<td>5 major cities screened, 35% were normal, 36% osteopenia, 29% osteoporosis. [31]</td>
</tr>
<tr>
<td>Sri Lanka 2004</td>
<td>42.4% women had osteoporosis and over 50 years &gt; 61.5% women. [52]</td>
</tr>
<tr>
<td>Thailand 2002</td>
<td>Osteoporosis in women at FN and LS is 19.3% and 24.7%. [53]</td>
</tr>
<tr>
<td>America 2007</td>
<td>1.5 millions suffer from osteoporosis. [54]</td>
</tr>
</tbody>
</table>
2.4.1.1.2. Prevalence of Osteoporosis in India (National Scenario): Digital X-ray radiogrammetry results revealed that in Indian 29.9% women and 24.3% men between the age of 20 and 79 years had low bone mass. About 50% women and 36% of men over 50 years of age were noted to have low bone mass. The observations of this study suggest that there is higher prevalence of low bone mass in the Indian population compared to the western population.

In India, it is projected that by the year 2030, the population of postmenopausal women will be second highest in the world, next to China. Thus, the burden of osteoporosis in the Indian scenario will also be immense. Osteoporosis is highly prevalent in India [55, 56, 57]. An estimated 61 million people in India are reported to be affected by it [58]. The life span of an average Indian has also increased and this also contributes to the increased incidence of osteoporosis. Recent data indicate that Indians have lower bone density than their North American and European counterparts [55, 59, 60]. It is reported that osteoporotic fractures occur 10-20 years earlier in Indians as compared to Caucasians [55]. In regard to the burden of osteoporosis in the Indian scenario, 50% women have osteoporosis and in actual numbers it accounts for 30 million women. A study conducted to evaluate the burden of osteoporosis among 450 urban healthy women between 25-75 years of age by determining the bone mineral density revealed that only 29% had normal T score[61].

The data obtained by Indian investigators showed that BMD values in the Indian population were approximately 15% lower than those in Caucasian women [62, 63, 64, 65, 66]. Such a variation was also seen among Asian women residing in America [67]. Studies also indicate a lack of awareness among Indian women. Osteoporosis mostly affects women, as its victims are 80 percent female and 20 percent male. One quarter of all women above 60 years old are afflicted by the condition. In India, one out of two women over the age of 45 years is affected. It is caused by poor calcium and vitamin D intake and absorption, as well as being a side effect of hormone replacement therapy. The most serious health implication of osteoporosis is frequent fractures, which can be caused by even routine activities like bending to lift a bucket or even just coughing or sneezing. Repeated fractures can cause to lose several inches in height as the posture becomes stooped [68].
2.4.2. Non Modifiable Risk Factors and their Related Studies

2.4.2.1. Advanced Age (in both men and women)

Bone mass peaks at age 25 years. Thereafter, the bone mass in both sexes remains stable until age 45-55 years, when accelerated bone loss begins in women and a more gradual loss commences in men. The accelerated bone loss in women causes the loss of 25-30% of skeletal mass over 5-10 years, followed by a slower phase with stable loss rates of 0.5-1% per year. Males do not have an accelerated bone loss, but rather, a stable loss rate. The percentage of decrease in BMD increases with age and mainly at the duration of menopause [69]. Osteoporosis is a debilitating disease that affects many older people. Fragility fractures are the hallmark of osteoporosis [70].

Increasing age is one of the strongest predictors of future fracture. Some of the age related change in fracture risk is related to a reduction in BMD; however, both age and decreasing BMD add independently to fracture risk. In the Rotterdam study (and using national hip fracture data), when comparing an 80-year-old woman with average bone density with a 60-year-old woman the Relative Risks (RR) for hip fracture was 13.6; age contributed 7.1 to this risk while the age-related decline in bone density contributed only 1.9. For men the results were broadly similar [71].

2.4.2.2. Sex and Sex Hormone

Osteoporosis predominantly affects postmenopausal women, but both sexes can be affected. Bone loss is greater in women than in men because the rate of loss significantly increases after menopause. Because women have lighter, thinner bones than men, osteoporosis is much more frequent in women. At age 35, men have 30% more bone mass than women. Bone loss also occurs much more slowly in men than women [72].

Estrogen deficiency following menopause is correlated with a rapid reduction in BMD, while in men a decrease in testosterone levels has a comparable (but less pronounced) effect. Menopause occurs approximately at age 51-52 years (range, 42-60 year). Following menopause, levels of circulating estradiol significantly decrease by around 25% and 75%, respectively. Estrogen or testosterone deficiency during
adolescence (due to Turner’s, Kallman’s, or Klinefelter’s syndrome, anorexia nervosa, athletic amenorrhea, cancer, or any chronic illness that interferes with the onset of puberty) leads to low peak bone mass [23]. Estrogen deficiency that develops after peak bone mass is achieved but before normal menopause (due to premature ovarian failure for example) is associated with rapid bone loss. Low sex steroid levels may also be responsible for reduced bone density in patients with androgen insensitivity or acromegaly. By contrast, excess thyroid hormone (thyrotoxicosis), whether spontaneous or caused by over treatment with thyroid hormone, may be associated with substantial bone loss [73]; while bone turnover is increased in these patients, bone resorption is increased more than bone formation. Likewise, excess production of glucocorticoids caused by tumors of the pituitary or adrenal glands (Cushing’s syndrome) can lead to rapidly progressive and severe osteoporosis, as can treatment with glucocorticoids. The relationship between diabetes and osteoporosis is more controversial. For example, hip fractures are increased in some studies of diabetic patients, but not in others. In general, patients with type 1 (insulin-dependent) diabetes, particularly those with poor control of their blood sugar [74], are at greater risk of osteoporosis than are those with type 2 (non-insulin dependent) diabetes [75].

2.4.2.3. Ethnicity

Though osteoporosis occurs in people from all ethnic groups, European or Asian ancestry predisposes for osteoporosis. Caucasian and Asian women are at the highest risk of developing the disease. African-American and Hispanic women have a lower, but still significant risk.

In people of African descent, rates of fractures are lower than those in white populations. Although Asian women have lower bone mass than white women, they have a lower rate of hip fractures. Hispanic women also have half as many fractures as white women despite similar peak bone masses.

There are substantial geographic differences in the prevalence of vertebral deformities in Europe, with a range of 6-20%. The highest rates occur in Scandinavian countries. The incidence of osteoporotic fractures is lower in Japanese individuals than in whites.
2.4.2.4. Family History

Family History of fracture or osteoporosis are at an increased risk; the heritability of the fracture as well as low bone mineral density is relatively high, ranging from 25 - 80%. There are at least 30 genes associated with the development of osteoporosis.

About 60% of a person’s peak bone mass is genetically determined. A woman whose mother has osteoporosis is more likely to have the condition. The remaining 40% of one’s peak bone mass is attributed to dietary factors, physical activity, medication use, and lifestyle.

2.4.2.5. Personal History of Fracture

Those who have already had a fracture are at least twice as likely as to have another fracture compared to someone of the same age and sex.

2.4.2.6. Diseases and Disorders

2.4.2.6.1. Hypogonadal States: In females, the effect of hypogonadism is mediated by estrogen deficiency. It can appear at early menopause (<45 years) or from prolonged premenopausal amenorrhea (>1 year). A bilateral oophorectomy (surgical removal of the ovaries) or a premature ovarian failure can cause deficient estrogen production. In males, testosterone deficiency is one of the causes.

2.4.2.6.2. Endocrine Disorders: Primary hyperparathyroidism is a relatively common condition in older individuals, especially postmenopausal women, caused by excessive secretion of parathyroid hormone. Most often, the cause is a benign tumor in one or more parathyroid glands; very rarely the cause is parathyroid cancer [76]. Typically, cortical bone is affected to a greater extent than trabecular bone in primary hyperparathyroidism [77]. It is presumed that the reduction in bone mass is associated with the increased risk of fracture seen in these patients.

2.4.2.6.3. Nutritional and Gastrointestinal Disorders: Diseases that reduce intestinal absorption of calcium and phosphorus, or that impair the availability of vitamin D, can also cause bone disease. Moderate malabsorption results in osteoporosis, but severe malabsorption may cause osteomalacia. Celiac disease, due
to inflammation of the small intestine is a commonly overlooked cause of secondary osteoporosis [78]. Bone loss is seen after gastric bypass surgery even in morbidly obese women who do not have low bone mass initially [79]. Increased osteoporosis and fractures are also seen in patients with Crohn's disease and ulcerative colitis [80]. Glucocorticoids commonly used to treat both disorders, probably contribute to the bone loss. Similarly, diseases that impair liver function may result in disturbances in vitamin D metabolism and cause bone loss. Primary biliary cirrhosis is associated with particularly severe osteoporosis. Fractures are more frequent in patients with alcoholic cirrhosis than other type of liver disease, although this may be due to increased risk of falling among drinkers [81]. HIV infected patients also have a higher prevalence of osteopenia or osteoporosis [82]. This may involve multiple endocrine, nutritional, and metabolic factors and may also be affected by the antiviral therapy that HIV patients receive.

2.4.2.6.4. Autoimmune and Neurological Disorders: Autoimmune and allergic disorders are associated with bone loss and increased fracture risk not only due to the effect of immobilization and the damage to bone by the products of inflammation from the disorders themselves, but also from the glucocorticoids that are used to treat these conditions [83]. Rheumatic diseases have been associated with lower bone mass and an increased risk of fractures. 12% of women with systemic lupus erythematosus are reported at least one fracture since the onset of disease, a 4.7-fold higher risk of fracture than in typical women. Fractures in these women were found to be associated with older age at diagnosis, longer disease duration, longer duration of steroid use, and post-menopausal status [84].

Many neurologic disorders are associated with impaired bone health and an increased risk of fracture [85]. This may be due to the effects of these disorders on mobility and balance or due to the effects of drugs used in treating these disorders on bone and mineral metabolism. Patients with stroke, spinal cord injury, or neurologic disorders show rapid bone loss in the affected areas [86]. Children and adolescents with these disorders are unlikely to achieve optimal peak bone mass, due both to an increase in bone resorption and a decrease in bone formation. In some cases very rapid bone loss can produce a large increase in blood calcium levels to produce
symptoms [87]. Bone loss can be slowed, but not completely prevented by antiresorptive therapy.

Psychiatric disorders can also have a negative impact on bone health. While anorexia nervosa is the psychiatric disorder that is most regularly associated with osteoporosis, major depression, a much more common disorder, is also associated with low bone mass and an increased risk of fracture [88]. Many studies show lower BMD in depressed patients [89].

One factor that may cause bone loss in severely depressed individuals is increased production of cortisol, the adrenal stress hormone. While the response of individuals with major depression to calcium, vitamin D, or antiresorptive therapy has not been specifically documented, it would seem reasonable to provide the preventive measures to patients at high risk [85].

2.4.2.6.5. Medication and Therapy Induced Disorders: Glucocorticoid induced Osteoporosis (GIO) is by far the most common form of osteoporosis produced by drug treatment. Glucocorticoids, which are used to treat a wide variety of inflammatory conditions (e.g., rheumatoid arthritis, asthma, emphysema, chronic lung disease), can cause profound reductions in bone formation and may, to a lesser extent, increase bone resorption [90] leading to loss of trabecular bone at the spine and hip, especially in postmenopausal women and older men.

2.4.3. Modifiable Risk Factors and their Related Studies

2.4.3.1. Low Body Mass Index

Body weight and rates of hip fracture are inversely related. Lifestyle factors are associated with osteoporosis in lean women but not in normal and overweight women. The women with BMI < 25.1 kg m² had lower Broadband Ultrasound Attenuation BUA (p < 0.0001) and radial BMD values (p < 0.0001) than women with higher BMI [91]. In the Framingham study [92], the relative risk of fracture was 0.63 in individuals who were 114-123% overweight and 0.33 in individuals more than 138% overweight. Obesity appears to protect the skeleton in several ways: by increased the production of estrogen in fatty tissue, by improving vitamin D storage in fatty tissues, by exerting a cushioning effect in association with falls, and
by creating a larger skeleton as a result of increased weight bearing. Being overweight protects against osteoporosis, either by increasing load or through the hormone leptin.

Body Mass Index (BMI) is a good indicator for measurements of Bone Mineral Density (BMD) which measures the density of minerals present in the bones using a special scan. This study was conducted to assess the association between BMI and status of BMD among 101 individuals who underwent Dual-Energy X-ray Absorptiometry (DEXA) scan. 39 subjects had normal and 62 had low bone mineral density. BMD was low in 82.4% of people with normal BMI, 78.1% among overweight, and 44.2% among obese.

Eight Surgical post menopausal women (SPMW) and 27 Natural postmenopausal women (NPMW) who underwent systemic DEXA scan were chosen for the cross sectional study. The prevalence of osteopenia was comparatively high in young SPMW as shown by their low bone mass which predicts their vulnerability to develop osteoporosis in future [93].

A cross-sectional study was conducted by Kofi Asomaning in 2006. The study was among women aged 50–84 years referred by their physicians for a bone mineral density (BMD) examination at Baystate Medical Centre between October 1998 and September 2000. BMI was determined prior to the BMD examination. Odds ratios (OR) for low, high, and obese compared with moderate BMI women were 1.8 (95% CI 1.2-2.7), 0.46 (95% CI 0.29-0.71), and 0.22 (95% CI 0.14-0.36), respectively, with a significant linear trend (p < 0.0001) across BMI categories. Women with low BMI are at increased risk of osteoporosis. To help reduce the risk of osteoporosis, patients should be advised to maintain a normal weight [94].

2.4.3.2. Low Calcium and Vitamin D Intake

Diet assessment helps to detect those at low calcium intake who need calcium supplementation. Calcium and/or vitamin D deficiency from malnutrition increases the risk of osteoporosis. The problem occasionally arises in calcium deficient adolescents. Calcium is an essential mineral in maintaining nerve function, muscle function, and bone mineralization, and it is involved in the control of several intracellular processes. Vitamin D is essential for the absorption of calcium from the
gut. During periods of calcium deficiency from decreased intake or decreased absorption, bone acts as a buffer, maintaining a constant level of calcium in the blood. Data from the Third National Health and Nutrition Examination Survey shockingly revealed that 75% of men and 87% of women did not meet the recommended daily calcium intake of 1000 mg per day [95]. Calcium can be removed from bone either through transport over the osteocyte-lining cell system, which is responsible for the rapid regulation of serum calcium, or via the liberation from the bone matrix through osteoclastic resorption. Calcium loss also occurs through the gut, kidney, and skin. The kidney plays an important role in calcium homeostasis by affecting PTH levels.

Calcium is an essential mineral found in great abundance in the body. 99% of all the calcium in the body is found in the bones and teeth. The remaining one percent is in the blood. Calcium plays important roles in nerve conduction, muscle contraction, and blood clotting. If calcium levels in the blood drop below normal, calcium will be taken from bone and put into the blood in order to maintain blood calcium levels. Table 2.2 represents the RDA of calcium for different groups with respect to ICMR and NIH data.

<table>
<thead>
<tr>
<th>Particulars</th>
<th>Recommended Calcium Intake/day for Indians (ICMR) in mg</th>
<th>Recommended Calcium Intake/day for Americans (National Academy of Sciences) in mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-50 yrs</td>
<td>600</td>
<td>1000</td>
</tr>
<tr>
<td>Over 50 yrs</td>
<td>600</td>
<td>1200</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1200</td>
<td>1000</td>
</tr>
<tr>
<td>Lactation</td>
<td>1200</td>
<td>1000</td>
</tr>
</tbody>
</table>

The calcium in a compound is called elemental calcium. During digestion, the calcium compound dissolves and the elemental calcium becomes available to be absorbed into the blood. If a tablet contains 500 milligrams of calcium carbonate, it contains only 200 milligrams of elemental calcium. This is because only 40% of the calcium compound is elemental calcium. The other 60%, or 300 milligrams, would be from the carbonate ingredient. Most calcium supplements list the elemental calcium content on the label.
Peak bone mass, which is attained during adolescence/young adulthood, can be compensated by raising calcium intake to the adequate intake levels. Higher calcium intakes have been related to higher bone mass in children, young adult and post menopausal women in observational epidemiological studies[96].

Post menarcheal adolescent girls(<15.5 years of age) with baseline low calcium intakes (<800 mg/day) who were given calcium supplementation (100mg/day) had enhanced bone mineral acquisition as compared with girls given placebo, especially in girls more than 2 years past the onset of menarche[97].

The benefits of added calcium on bone mass disappears when supplementation is halted[98, 99], although one trial showed a persistent benefit persisting after 3-4 years [100]. These data suggest that adequate calcium intake needs to be maintained throughout childhood, adolescence and young adulthood to have a lasting impact on peak bone mass. Over 20 studies have concluded that calcium supplementation can decrease bone loss by approximately 1% per year[101].

Calcium balance studies[102] demonstrated that calcium requirements increase after menopause in women and this, together with an early epidemiologic study [103]associating increased hip fracture rates with low calcium intake, strongly suggested the importance of adequate calcium nutrition with regard to osteoporosis, particularly in postmenopausal women.

Calcium supplementation has been shown to be effective in retarding bone loss in post-menopausal women. The beneficial effect of calcium intake on bone loss in post menopausal women may be modified by factors, including age, number of years since menopause, baseline calcium intake before supplementation and possibly physical activity level. The effect of calcium may be greater at the skeletal sites with more cortical bone, in elderly and late post-menopausal women, and in women with low baseline calcium intakes [104, 105].

The people in Africa live on a low protein vegetable diet consuming less than 47 grams of protein per day and 400 mg of calcium, but they are to all intents and purposes free of osteoporosis and calcium deficient diseases [106]. On the other hand, their genetic relatives living in the USA consuming a western diet high in meat
and dairy food suffer from osteoporosis to similar levels as white people [107]. Eskimos also consume a high protein diet (250-400gm per day from fish, walrus and whale meat), along with an extremely high intake of calcium (2,000mg or more from fish bones) and despite being physically active, they have one of the highest rates of osteoporosis in the world.

2.4.3.3. Low Physical Activity and Excess Physical Activity

Physical activities continue to stimulate increase in bone diameter throughout the lifespan. These exercise-stimulated increases in bone diameter diminish the risk of fractures by mechanically counteracting the thinning of bones and increases in bone porosity.

Exercise works for osteoporosis prevention because it places stress on bones, which results in increased bone mass. This is especially true for weight bearing and weight training types of exercises. Weight bearing exercises have most positive effect on bone. Physical activity has its greatest impact during adolescence, affecting peak bone mass most. In adults, physical activity helps maintain bone mass, and can increase it by 1 or 2%. Physical fitness in later life is associated more with a decreased risk of falling than with an increased bone mineral density. Conversely, people who are bedridden are at a significantly increased risk. Prolonged immobility, such as bed rest, decreases bone mineral density through the loss of bone minerals [108].

An increasingly sedentary lifestyle has been suggested as a significant contributing factor for the increased prevalence of osteoporosis. Bone performs remodeling in response to physical stress. People who remain physically active throughout life have a lower risk of osteoporosis.

Lack of physical activity leads to decreased mechanical (muscle) stress on the bone. This appears to increase bone resorption without a corresponding increase in osteoblastic activity [109]. Conversely, athletes who have larger muscle mass than non athletes tend to have greater bone density, supporting an association between mechanical stress and bone density [110]. Repetitive mechanical stress seems to be the most beneficial type of activity so weightlifting and weight-bearing exercise, such as walking and running, are examples of exercise which may increase bone
mineral density. It is difficult to ascertain, however, how much and what kind of exercise is most beneficial in preventing osteoporosis. Nevertheless, a recent comprehensive study [111] on physical activity and mortality in postmenopausal women found that both vigorous and moderate physical exercise significantly reduced mortality in this age group. Therefore, some form of weight-bearing exercise is recommended for the overall health of postmenopausal women.

Excessive exercise can lead to constant damages to the bones which can cause exhaustion of the structures. There are numerous examples of marathon runners who developed severe osteoporosis later in life. In females, heavy exercise leads to amenorrhea (suppression of the menstrual cycle).

2.4.3.4. Tobacco and Cigarette Smoking

Tobacco smoking inhibits the activity of osteoblasts, and is an independent risk factor for osteoporosis. Smokers are known to experience menopause earlier than nonsmokers, and because they are slimmer than nonsmokers, they have reduced extra endocrine production of estrogens, as in adipose tissue. Smokers may also have increased metabolic clearance rate of estrogens. Smoking puts women at risk for osteoporosis because smoking decreases serum estrogen. Estrogen most likely has an effect on osteoblasts, which causes an increase in new bone formation [112]. Loss of estrogen leads to decreased osteoblastic action progressing to an imbalance between resorption and formation. Estrogen also plays a role in the absorption of calcium, an essential nutrient in forming strong bones [113].

Increased weight is also associated with increased bone density presumably because of increased stress on weight-bearing bones. Smokers tend to have lean body masses [114] perhaps because of the interference of smoking with eating. The combination of decreased estrogen and low body weight leads to increased risk for osteoporosis.

It is important to note that estrogen replacement therapy will not protect against osteoporosis as well in women who smoke as opposed to women who do not smoke [115]. Therefore, women who continue to smoke and wish to take estrogen replacement therapy for preventing osteoporosis will need their doses adjusted accordingly.
Pacock conducted a study on effects of tobacco use on axial and appendicular bone mineral density. Tobacco use has been identified as being a risk factor for the development of osteoporosis. There was however no difference in the cross-sectional studies and no significant deleterious effect detected of tobacco use on forearm bone mineral content [116].

Pooled data from three population studies conducted in Copenhagen with detailed information on smoking habit [117]. A total of 13393 women and 17379 men were initially examined between 1964 and 1992, were followed until 1997 for first admission due to hip fracture. The RR of hip fracture associated with smoking was estimated by means of multiplicative Poisson regression models. Female current smokers had an RR of hip fracture of 1.36 (95% CI : 1.12–1.65) and male smokers 1.59 (95% CI : 1.04–2.43) relative to never smokers. In both sexes, the RR of hip fracture gradually increased by current and accumulated tobacco consumption.

We measured bone density (BMD) at the lumbar spine and proximal femur in 709 elderly men and 1080 women participating in the Dubbo Osteoporosis Epidemiology Study (DOES), a community-based, longitudinal, epidemiologic study of osteoporosis in men and women over the age of 60. BMD was significantly higher in men than in women (20% at all sites). Tobacco consumption was associated with a reduction in BMD at both sites in both sexes (5-8%), and this effect was independent of calcium intake or body weight. Exsmokers had BMD intermediate between that of current smokers and never smokers, suggesting the influence of tobacco was partially reversible [118].

A population-based cohort study by the Framingham Study in 34700 woman-examinations of observation, current smoking did not appear to increase hip fracture risk (adjusted odds ratio (AOR), 1.22; 95% CI, 0.76 to 1.95;P > 0.2). Also overall, current estrogen use appeared to be protective (AOR, 0.38; CI, 0.12 to 1.21, P= 0.10). Overall, smoking does not appear to increase the risk for hip fracture in women. Although estrogen replacement protects non-smokers from fracture, smoking may negate the protective skeletal effects of estrogen replacement therapy [119].
2.4.3.5. Alcoholism

Previous or present alcoholism is a risk factor for the development of osteoporosis. Moreover, inebriation increases the risk of falls and thus potentiates fractures. Alcohol affects osteoblast proliferation in vitro and reduces matrix protein synthesis in vivo. It exerts a direct toxic effect on other bone cells as well. Alcohol intake increases women’s susceptibility to osteoporosis by three different mechanisms. First, excessive alcohol consumption depresses bone formation by decreasing osteoblastic activity. This leads to an imbalance between the resorptive osteoclastic activity and the formative osteoblastic activity progressing to decreased bone mineral density. Excess alcohol intake also leads to interference with proper nutrition, especially calcium and vitamin D intake.

Jilich [120] conducted a study to determine relationship between alcohol caffeine and bone mineral density of different skeletal sites in elderly women. A cross-sectional study in 136 Caucasian women, mean ± SD age 68.6 ± 7.1 years, all healthy and free of medications affecting bones, including estrogen. In the correlation analysis, alcohol was positively associated with spine BMD (r = 0.197, p = 0.02), 25-OHD and negatively with PTH. Smoking was negatively related to Ca intake, 25(OH)D and number of reproductive years. The past smokers who smoked on average 24 years of ~1 pack cigarettes/day had lower BMD in total body, spine and femur than never-smokers. Caffeine (average ~2.5 6-fl oz cups/day or 200–300 mg caffeine/day) had negative association with most of the skeletal sites. The results support the notion that consumption of small/moderate amount of alcohol is positively, while caffeine and past smoking are negatively associated with most of the skeletal sites, which might be attenuated with Ca intake above 750 mg/day.

Spencer [121] conducted a radiographic survey on 96 fully ambulatory male patients who were admitted to a rehabilitation center for patients with chronic alcoholism in an attempt to estimate the incidence of skeletal demineralization in these patients. The age of the patients ranged from 24 to 62 years. The radiographic survey of the 96 patients indicates the high incidence of extensive bone loss, most
likely osteoporosis, in relatively young and middle-aged ambulatory men with chronic alcoholism.

Kanis [122] conducted a study on alcohol intake as a risk factor. High intakes of alcohol have adverse effects on skeletal health, but evidence for the effects of moderate consumption is less secure. Alcohol intake was associated with a significant increase in osteoporotic and hip fracture risk, but the effect was nonlinear. No significant increase in risk was observed at intakes of 2 units or less daily. Above this threshold, alcohol intake was associated with an increased risk of any fracture (risk ratio [RR]=1.23; 95% CI, 1.06–1.43), any osteoporotic fracture (RR=1.38; 95% CI, 1.16–1.65), or hip fracture (RR=1.68; 95% CI, 1.19–2.36). It was concluded that reported intake of alcohol confers a risk of some importance beyond that explained by BMD. The validation of this risk factor on an international basis permits its use in case-finding strategies.

2.4.3.6. Soft Drinks

Some studies indicate that soft drinks (many of which contain phosphoric acid) may increase risk of osteoporosis; others suggest soft drinks may displace calcium-containing drinks from the diet rather than directly causing osteoporosis. Cola may increase women’s osteoporosis risk. “Women, who consumed five carbonated drinks a week, including four colas, had a decreased bone mineral density at the three hip sites” [123]. However, the results were not the same among men. Men were not affected as much as women. “The bone density among daily cola drinkers was as much as 4 percent less than women who did not consume as much cola. The more cola women drank, the lower their bone mineral density”[124].

2.4.3.7. Cola and Caffeinated Drinks

Cola beverages contain phosphoric acid, which might interfere with the body’s ability to use calcium and speed up bone loss. One theory suggests that cola drinkers’ risk of osteoporosis occurs because they tend to replace bone-building calcium with colas. However, Tucker, points out that, women who drank a lot of cola did not consume less milk than women who drank less cola. But, women who drank the most cola did consume lower levels of calcium from all sources, including dark, green leafy vegetables and beans. Tucker conducted a study on colas
association with low bone mineral density. BMD was measured at the spine and 3 hip sites in 1413 women and 1125 men in the Framingham Osteoporosis Study by using dual-energy X-ray absorptiometry [124].

Cola intake was associated with significantly lower \( P < 0.001 – 0.05 \) BMD at each hip site, but not the spine, in women but not in men. The mean BMD of those with daily cola intake was 3.7% lower at the femoral neck and 5.4% lower at Ward’s area than of those who consumed <1 serving cola/mo. Total phosphorus intake was not significantly higher in daily cola consumers than in non consumers; however, the calcium-to-phosphorus ratios were lower [124].

2.4.3.8. Heavy Metals

A strong association between cadmium, lead and bone disease has been established. Low level exposure to cadmium is associated with an increased loss of bone mineral density readily in both genders, leading to pain and increased risk of fractures, especially in elderly and in females. Higher cadmium exposure results in osteomalacia (softening of the bone).

To find out the iron overload a study was conducted by Sultan and his team in the year 2011 to find any correlation between serum iron level and low bone mass in sickle cell anemia (SCA). Patients’ ≥18 years of age with sickle cell anemia. The data of 100 patients was analyzed, 48 males and 52 females. The mean age was 27.5 ± 6.1 years. In 64 patients (32 males and 32 females) serum iron level was 319.35 μg/dl and the mean serum ferritin level in males and females was within the normal range. Bone mineral density measurement was done using dual energy X-ray absorptiometry (DEXA) at upper femur and lumbar spine. Sixty-eight percent of females and 71.8% of males patients in whom serum iron was high had lower bone mass \( P = < 0.001 \). SCA patients in whom serum iron level was higher than normal effected bone mass [125].

2.5. Related Studies: Management of Osteoporosis

The landmark publication of Potter [126], which found a significant bone-sparing effect (BMD increased 2.2%) at the lumbar spine of a soy protein diet with
an intake of 90 mg/d isoflavones over a 6-moperiod but not with 45 mg/d, set the benchmark for the choice of “dosing” in subsequent studies.

In older women, calcium supplementation is associated with a higher BMD, by around 1–3%, and with reductions in bone loss. Calcium supplementation of women within 5 years of the menopause has little or no effect on the BMD of trabecular regions of the skeleton, where the greatest loss of bone is occurring at that time.

2.5.1. Diet

2.5.1.1. Foods

There is general agreement that the best form of calcium is food sources, simply because bone, like other tissues, requires balanced nutrition. Milk and dairy products, such as cheese, yogurt and ice cream, contain the highest levels of calcium. Although many people tend to avoid milk because of its fat content, which predispose them to heart disease, especially those with hypercholesterolemia, low-fat dairy products such as skim and 1% milk are safe and contain high levels of calcium. Non-dairy food sources of calcium generally contain much lower levels, but significant amounts occur in canned salmon and sardines when the bones are also eaten. Some green vegetables (such as kale, broccoli and spinach) as well as legumes (such as soya beans and common beans) either contain much less calcium than dairy products or the calcium is poorly absorbed by the body or both.

A variety of population-based studies published in the latter part of the twentieth century and more recently between 2001 and 2003 has demonstrated a beneficial effect of fruit and vegetable/potassium intake on indices of bone health in young boys and girls, pre-menopausal women, peri-menopausal, post-menopausal women, and elderly men and women [127].

In DASH, diets rich in fruit and vegetable were associated with a significant fall in blood pressure compared with baseline measurements [128]. The explanation put forward by Barzel, was a reduction in the ‘Acid load’ with the fruit and vegetable diet compared with the control diet [129]. This study is the first
population-based fruit and vegetable intervention trial showing a positive effect on calcium economy.

Lemann and colleagues demonstrated that potassium bicarbonate administration resulted in a decrease in urinary calcium and phosphorus, with overall calcium balance becoming less negative (or more positive) [130]. The ‘acid-forming’ diet increased urinary calcium excretion by 74% and bone resorption, as measured by C-terminal peptide excretion by 19% in comparison with the alkaline-forming diet, both at baseline and after an oral calcium load [131].

Ecological studies indicate that the world-wide per capita intake of animal protein is associated with higher hip fracture risk in women who are aged more than 55 years [132]. Furthermore, women with a high ratio of animal/vegetable protein have been shown to have a higher rate of bone loss at the femoral neck than those with a low ratio, as well as a greater risk of hip fracture [133].

Cross-sectional and longitudinal population-based studies published in the last two decades suggest no differences in lumbar spine BMD between omnivorous and vegetarian premenopausal women [134]. In a 5-year prospective study of changes in radial bone density of elderly white America women (mean age 81 years) living in residential communities, no differences were seen in bone loss rates between the lacto-ovo-vegetarians and the omnivorous group [135].

2.5.1.2. Nutrients

2.5.1.2.1 Calcium: Absorption does not vary significantly among various supplements and is roughly equivalent to absorption from milk. The amount of elemental calcium in different calcium salts varies widely [136]. Calcium supplements are better absorbed when taken with food and may be better absorbed when taken in divided doses rather than all at once.

A positive calcium balance is mandatory to achieve adequate prevention against osteoporosis. Calcium supplementation (1000 mg per day) reduces bone loss and decreases fractures, especially in individuals with low daily intakes [137]. Women not on estrogen require a daily supplement of at least 1000 mg calcium. Even with the commonly used therapeutic doses of calcium, nearly 40% of
postmenopausal women will have inefficient absorption [138]. Improved calcium intake in adolescent results in significant increase in bone density and skeletal mass, providing protection against osteoporosis later in life, [139, 140]. Calcium supplementation is far more important during adolescence than in the reproductive years when bone formation is minimal. Up to the age of 25, \textit{i.e.}, during the years of bone accumulation, the daily calcium intake should be 1500 mg [141]. This amount, 1500 mg/day, is also recommended during pregnancy and lactation.

There are dozens of calcium supplements on the market, containing calcium carbonate, calcium lactate, calcium phosphate, or calcium gluconate, [142]. Calcium carbonate tablets contain 13% calcium, and calcium gluconate only 9%.

Calcium citrate does not require gastric acid for absorption and is the best choice for older patients with reduced gastric acid production. Calcium supplementation is most efficient when single doses do not exceed 500mg and when taken with a meal. Excess calcium supplementation (especially not with meals) is associated with a slight increase in risk for kidney stones, [143].

A study on calcium intake and serum calcium levels of women approaching menopause, conducted by Sudan on 125 female subjects of age 40-50 years and 20-40 years concluded that serum calcium levels of the middle aged women were low (8.21mg\%) and they also had lower calcium intake (404 mg/day) against the young adults where serum calcium was 9.2mg\% and calcium intake was 561mg/day. Hence it was observed that calcium levels are influenced by the calcium intake and age, [144].

Adequate calcium intake is important in achieving optimal peak bone mass and an increased calcium intake is of benefit if the baseline dietary calcium intake is low. In later life, low calcium intake is associated with an increased risk of fractures [145], including in Asian men and women,[146]. Dietary calcium intake declines with ageing and many people consume less than the recommended daily allowance. In addition, there is a decline in efficiency of calcium absorption with ageing.

\textbf{2.5.1.2.2. Sodium:} Dietary salt (sodium chloride) has been considered potentially detrimental because increasing salt intake within the usual range is associated with increased urinary calcium loss (also referred to as caliuria), [147, 148].
In a 2 year longitudinal study of healthy post menopausal women, urinary excretion of sodium was negatively correlated with changes in BMD at the introchanteric (femoral end line) and hip sites. [149]. The authors suggested that, based on their findings on regression analysis of the data, no bone loss occurred at the total hip when urinary sodium excretion was 92 mmol/day or less (approximately 2.1g sodium intake.). On the other hand, Jones et al. reported that while urinary sodium was correlated with urinary calcium in 154 adults (34 males and 120 females, aged 20-70 [mean 47 years], it was not associated with bone mineral content (BMC) or BMD (adjusted for sex, age, body weight and smoking) at the spine, femur or total body [150].

2.5.1.2.3. Phosphorus: There has been some controversy over the role of dietary phosphorus and, in particular, the dietary ratio of calcium to phosphorus, on bone health. The debate has been fuelled by relatively recent data to suggest that dietary phosphorus intakes have risen 10-15% over the past 20 years because of the increased use of phosphorus salts in food additives and cola beverages [151].

While excess phosphorus appears to influence circulating PTH, an important mediator of bone turnover, its effect on bone per se is less clear. Several studies in which dietary phosphorus was increased have shown declines [152, 153] or no change in the markers of bone formation. In one study, women given a low calcium diet but high phosphorus intake, had significantly elevated PTH but in addition had changes in other bone biomarkers that were indicative of increased bone resorption [154].

2.5.1.2.4. Vitamin D: Although India is a tropical country, women—particularly those in the older age group—confine themselves indoors most of the time; minimal exposure to sunlight makes them susceptible to vitamin D insufficiency. Vitamin D deficiency is rampant throughout India. Postmenopausal women residing in Southern India showed varying degrees of vitamin D status. This ranged from severely deficient to just adequate with 52% of the population showing a mean level of 37.5 nmol/L (15ng/ml), a conservative cut-off level for Vitamin D deficiency Bandgar (2010) [155]. According to Kalra (2011) the prevalence of vitamin D deficiency or insufficiency has been shown to be 66.67% in asymptomatic, healthy postmenopausal women in Haryana. [156].
A recent systematic review by Gaugris[157] concluded that the prevalence of inadequate 25(OH)D levels in serum appears to be high in postmenopausal women and especially those with osteoporosis and a history of fracture. In a study by Bruyère[158] on 8532 postmenopausal osteoporotic European women, 79.6% were found to have vitamin D insufficiency where the serum 25(OH)D threshold was considered to be 80 nmol/l, and 32.1% if the threshold was set at 50 nmol/l (1.0nmol/l= 0.4ng/ml).

Lips [159] had proposed a ‘functional health based reference value’ based on the levels of vitamin D. He defined Hypovitaminosis D as follows: severe vitamin D deficiency - <5ng/ml of 25(OH)D, moderate vitamin D deficiency – 5-10ng/ml of 25(OH)D and mild vitamin D deficiency – 10.1-20ng/ml of 25(OH)D.

Prevention of osteoporosis and bone fractures requires modification of multiple risk factors one of which is Vitamin D. Evidence suggests that for the greatest reduction in osteoporosis and fracture risk, women at increased risk should be given both calcium and vitamin D supplements, in the order of 1000–1200 mg calcium (depending on baseline status) and 800 IU vitamin D daily Rizzolia (2008) [160]. The ICMR (2010) recommendation for calcium and vitamin D is 600mg and 400IU for Indian women [161].

2.5.1.2.5. Vitamin K: The function of vitamin K is to serve as a cofactor for the vitamin K-dependent carboxylase, a microsomal enzyme that facilitates the post-translational conversion of glutamyl to y-carboxyglutamyl (Gla) residues[162]. The identification of Gla-containing proteins in bone, notably osteocalcin and matrix Gla protein, has generated much interest in the role of vitamin K in bone metabolism and bone health. The recent findings of two large, prospective cohort studies (the Nurses’ health study)[163] and the Framingham heart study [164] support an association between relative risk of hip fracture and vitamin K intake. In the Nurses’ health study, vitamin K1 intakes less than 109 µg/day were associated with an increased risk of hip fracture in 72327 women [165]. In the Framingham heart study, elderly men and women in the highest quartile of vitamin K1 intake(median 254µg/day) had significantly lower adjusted relative risk of hip fracture than did those in the lowest quartile of intake(median 56µg/day)[164]. In the recent study of post menopausal women (aged 50 and 60 years), women who received vitamin K1
supplementation (co-administered with minerals and vitamin D) for 3 years had significantly reduced bone loss of the femoral neck compared with that in women who received either the same supplement without vitamin K1 or placebo [165].

2.5.1.2.6. Vitamin A: Vitamin A (retinol) is present in food sources such as liver, kidney and milk. Dairy foods are fortified with small amounts of vitamin A and D. Chronic vitamin A toxicity affects bone and mineral metabolism [166]. Several groups of investigators have examined the possibility that excessive dietary intake of vitamin A is associated with decreased BMD and an increased risk of hip fracture. Melhus et al. showed in their multivariate analysis that, once adjusted for the body mass index, energy intake, level of physical activity, smoking status, oestrogen status and use of oestrogen, vitamin A intake was related to BMD at various skeletal sites (lumbar spine, femoral neck, and trochanter, as well as total body) in Swedish and Norwegian population [167]. The BMD was 10% lower in persons with a vitamin A intake that exceeded 1.5 mg/day, than in those with an intake of 1.5 mg/day or less. The relative risk of hip fracture was 2.1 for persons with a vitamin A intake that exceeded 1.5 mg/day, as compared with those whose intake was less than 0.5 mg/day.

Michaelsson et al. provided data on possible deleterious effects of vitamin A on bone, from a long term, prospective study of 2322 Swedish men in whom serum retinol and β-carotene levels were measured at baseline [168]. During the 30 year follow-up period, fractures were reported in 266 men. The relative risk was 1.64 for any fracture and 2.47 for hip fracture among men in the highest quintile for serum retinol (>2.64 µmol/l), as compared with the middle quintile (2.17-2.36 µmol/l). The relative risk of any fracture was 7.14 among men with a serum retinol level that exceeded 3.60 µmol/l. β-carotene level was not associated with the risk of fracture [168].

2.5.1.2.7. Vitamin B and C: Hall and Greendale compared dietary vitamin C intakes with BMD measurements in 775 post menopausal women who were participating in a study of hormone replacement therapy [169]. They found a statistically significant positive association between vitamin C intake and BMD at the hip and a similar, though non-significant association at the spine. It is also found that vitamin C supplement use appeared to have a beneficial effect on BMD in post menopausal
women. Deficiency of folate and vitamins B2, B6 and B12 *per se*, which are major determinants of homocysteine concentrations, rather than the homocysteine concentration itself, may be responsible for the observed effect on risk of osteoporotic fracture. For example, pernicious anemia has been shown to increase bone loss and risk of osteoporotic fracture [170, 171], while recently vitamin B12 status has been shown to be associated with BMC and BMD in older women [172] and frail elderly women (but not men), [173].

### 2.5.2. Exercise and Yoga

The physical activity and exercise in maintains bone quality/strength thus reduces the risk of osteoporosis and fractures. It is widely accepted that physical activity is vital in both the development of a healthy skeleton and in the maintenance of skeletal health in adulthood [174]. Many epidemiological studies have shown that regular activity in adulthood reduces the risk of fractures [175].

Regular exercise would delay the point at which osteopenia progress to clinically significant osteoporosis. Once exercise is stopped normal bone loss continues and the benefits are not maintained [176].

Yoga has been shown to reduce back pain, arthritis, and anxiety and to improve gait, neural plasticity associated with motor learning, all capacities that militate against the falls that produce osteoporotic fractures.

Fishman LM in the pilot study conducted in 2009 found that, the hip BMD increased 54% more than the spine BMD, lending further credence to the efficacy of yoga in building bone. The hypothesis was accepted with the result that practicing yoga for 8-10 minutes will improve the t-score values [177].

Thus it may be stated that from the review of related literatures, very few studies have been conducted in India on the prevalence and management of osteoporosis. Therefore the present study was proposed to study the prevalence and management of osteoporosis with simple life style interventions [diet and exercise (yoga)] and education.