2.1 Calcium

Calcium (Ca$^{2+}$) is the most abundant mineral in the human body. Nearly all (99%) of total body calcium is located in the skeleton (Food and Nutrition Board & Institute of Medicine, 2010). The remaining 1 per cent is equally distributed between the teeth and soft tissues, with only 0.1 per cent in the extracellular fluid (ECF). In the skeleton, it constitutes 25 per cent of the dry weight and 40 per cent of the ash weight. The ECF contains ionized calcium at concentrations of about 4.8mg/100ml (1.20 mmol/l) maintained by the Parathyroid–Vitamin D system as well as complexed calcium at concentrations of about 1.6mg/100ml (0.4 mmol/l). In the plasma, there is also a protein-bound calcium fraction which is present at a concentration of 3.2mg/100ml (0.8mmol/l). In the cellular compartment, the total calcium concentration is comparable with that in the ECF but the free calcium concentration is lower by several orders of magnitude (Robertson et al., 1981).

An adult female body contains approximately 1,000g of calcium (Leitch et al., 1959). The crystalline salts deposited in the matrix of bone are composed principally of calcium and phosphate in the form of hydroxyapatite {Ca$^{10}$[PO$_4$]$_6$[OH]$_2$} (Institute of Medicine, 1997).

Calcium is physiologically very important. Calcium salts provide structural integrity to the skeleton (Breslau, 1996). After crossing the intestinal wall, most of the calcium is deposited in the skeletal bones. It is continually released to maintain appropriate blood levels (Junqueria et al., 1995; Ganong, 1999). Approximately 500 mmol per day is released into the bloodstream from the interstitial fluid by diffusion of calcium ions into the hydration shell of the hydroxyapatite crystals. A small amount of calcium (7.5 mmol per day) is released into the bloodstream as a result of continuous bone remodeling (Ganong, 1999). Small amounts of calcium are excreted through the kidneys, but most of the calcium is re-absorbed (98-99%).
mainly in the proximal tubules of the kidney (60%) and to a lesser extent in the ascending limb of the loop of Henley and in the distal tubule (40%) (Junquera et al., 1995; Breslau, 1996; Ganong, 1999).

Each day, calcium is exchanged between bone mineral and extra cellular fluid. Much of this exchange reflects resorption and reformation of bone as the skeleton undergoes constant remodeling (Baron, 1996). An imbalance between bone resorption and formation will result in bone loss (Nilas et al., 1989). After the skeleton reaches its maturity at about the age of 30 years (Riggs et al., 1986), bone resorption begins to exceed its formation resulting in an age-related reduction of less than 0.5 per cent per year in cortical (i.e. long bones of arms and legs) and trabecular bone (i.e. vertebrae, neck of femur, lower end of radius) in both sexes. In the female, trabecular bone loss occurs at an accelerated rate of 1 to 8 per cent in the spinal vertebrae and 0.5 to 5 per cent in femoral head five to ten years after the menopause. These lead to a 50 per cent loss of bone mass in a female by the age of 70 (Gordan, 1984).

The skeleton acts as a storage site for calcium. When an individual does not meet daily calcium needs through diet, the body will withdraw calcium from bones over time. The amount of calcium consumed also affects the mineralization of bones throughout life. Low calcium intake was the key factor involved in bone loss (Alevizaki et al., 1973).

2.2 Bone Cycle

2.2.1 Bone as an Organ

Bone is an organ composed of cortical and trabecular bone cartilage, haemopoetic and connective tissues (Malina et al., 2004). These tissues enable the skeleton to serve its main functions that include the protection of internal organs, movement of parts of the body, and the provision of a site for hematopoiesis. In addition, the skeleton is of fundamental importance in mineral homeostasis (Institute of Medicine, 1997).

There are three types of bone cells. An osteoblast, the bone-forming cell, is of mesenchymal origin and its main function is to produce new bone
matrix, osteoid, and to mineralize it. When an osteoblast is entrapped in the bone matrix, it becomes an osteocyte (Stein et al., 1996). Bone resorption is done by the bone-resorbing cell, the osteoclast. Osteoclasts originate from the hematopoietic-macrophage lineage (Rubinacci et al., 1998).

Specialized cells called osteoclasts respond to plasma calcium levels and carefully maintain these levels through a process called resorption. Osteoclasts resorb minerals, including calcium, and organic materials from the bone. During this process, osteoclasts remove microscopic portions of minerals and organic material from the surface of the bone, thereby leaving small deficits in the bone (Prentice, 2004). In contrast, osteoblasts replace, or repair, the deficits left in bone during resorption (Confavreux, 2011). Furthermore, as one age, osteoblastic activity slows even more, sometimes taking up to a year or more to fill the deficits left by osteoclastic activity (Mahan et al., 2008).

The bones continuously undergo bone resorption and bone formation. If this process occurs at different bone locations and alters the bone morphology, it is defined as bone modeling (Ruimerman, 2005). When it is done at the same bone location it is defined as remodeling. Bone tissue is under constant reconstruction which is necessary for normal skeletal maintenance particularly during adulthood (Rubinacci et al., 1998). In a homeostatic equilibrium, resorption and formation are balanced. Old bone is continuously replaced by new tissue to ensure that the mechanical integrity of the bone is maintained. Approximately 30% of bone mass is remodeled in a year (Seeman, 2008; Malina et al., 2004).

2.2.2 Bone and Aging

In the growing individual, a positive relationship between bone mass and age reflects rapid bone deposition (Malina et al., 2004). In young and middle-aged adults, rates of bone deposition and bone resorption are typically in balance. However, during late adulthood, there is a negative association between age and bone mass in such a way that as age increases bone mass decreases, reflecting a more rapid rate of bone
resorption compared to bone deposition (Food and Nutrition Board, Institute of Medicine, 2010; Malina et al., 2004., Dawson-Hughes, 1996).

During menopause, women lose approximately 3 per cent of the total body bone mineral mass per year, followed by around 1 per cent per year bone loss after the age of 65 (Dawson-Hughes, 1996). This condition results in microarchitectural deterioration of bone tissue and consequently loss of bone strength thus making bone more fragile and easily susceptible to fracture. These characteristics explain osteopenia and osteoporosis (Brown et al., 2002).

Bone mass is believed to accrue in young adult women as a result of increased bone formation relative to bone resorption. After menopause, the balance between formation and resorption is apparently altered in favor of increased bone resorption at least in some women (Favous, 1990). It has been suggested that promoting greater bone mass in young adult women may be the most effective method of sustaining sufficient bone mass during aging (Newton et al., 1968). Maximal accrual of BMD during the adolescent years may be protective of bone and may help prevent or delay the development of bone-related diseases such as osteopenia and osteoporosis later in life (Kudlac et al., 2004).

Sowers et al. (1985) found that greater calcium intake was associated with greater bone mass, measured by single photon densitometry, in a geographically defined population of women aged 20-35 years after considering the effects of age, body size, lifestyle habits and reproductive events. Studies by Sandler et al. (1985) and Halioua et al. (1989) reported that women who had consumed milk during childhood and adolescence were more likely to have better bone mass than those whose milk consumption had ceased during childhood.

2.2.3 Time of Peak Bone Mass Attainment

Peak Bone Mass is the maximum amount of bone that an individual will attain in life (Leslie et al., 1999).

Peak bone mass (PBM) has been defined as the maximum strength
and density of bone tissue that a person has in his/her life (Heaney, 2000). The age at which PBM is achieved is not certain. Early estimates of attainment of peak total-body BMD and BMC ranged from late adolescence to mid-20s (Gropper et al., 2009; Teegarden et al., 1995; Recker et al., 1992). In a longitudinal study, Theintz et al. (1992) suggested that PBM may be attained at the age of 16 years in healthy adolescent females. In contrast, the results of the Fels Longitudinal Study showed that the age at which PBM measured as BMC and BMD were achieved between 20 and 25 years (Nguyen et al., 2001). At this age range, the bones of the human skeleton reach 90 per cent to 95 per cent of their peak bone mass. Over the next 10 years, the final 5 per cent to 10 per cent of bone mineral may be added (Lin et al., 2003).

Different skeletal sites achieve PBM at very different times. Females attained their peak earlier than males (Nguyen et al., 2001). It has been shown in girls that during puberty, calcium absorption and bone calcium deposition rate increases, resulting in more calcium absorption and less overall calcium excretion than adults with the same calcium intake (Abrams et al., 1994; Abrams et al., 2000; Weaver et al., 1995).

Menstrual status is an important determinant of peak bone mass as well as the development of bone loss prior to onset of menopause. It has also been reported that the group of postmenopausal women has significantly lower bone mass than pre and perimenopausal women (Khan et al., 2004; Usmani et al., 2004).

Peak bone mass (the maximum bone mass attained in a person’s life) and the rate of subsequent bone loss are both important determinants of BMD in later life. In fact, premenopausal bone mass is as important as postmenopausal bone loss for prediction of fracture (Riis et al., 1996). Peak bone mass may not be reached until well into adult life (Recker et al., 1992) and a substantial amount of bone loss occurs prior to menopause through age-related bone loss (Reacker et al., 2000). Thus in premenopausal women, it is potentially possible to intervene to both improve peak bone mass as well
as slow age-related bone loss and through this maintain adequate BMD and reduce fracture risk in old age.

Adequate calcium nutrition is essential to the attainment and maintenance of peak bone mass and is critical to both the prevention and treatment of osteoporosis (NIH, 2000; Nordin, 1997; NIH, 1994). Observational studies of both pre- and post-menopausal women suggest that a higher lifetime intake of dietary calcium is associated with greater bone mineral density (Cumming et al., 1990; Welten, 1995) and reduced risk of osteoporosis-related fractures (Cumming et al., 1997; Matkovic et al., 1979).

2.3 Calcium Homeostasis

The mineralization of bone occurs in response to a high level of calcium in the blood. The blood calcium concentration is maintained at 9 to 11mg/dL or 2.5mmol/L (Bronner et al., (1999); Volpe, 1999). When serum calcium concentration rises above normal, calcitonin is secreted by the C-cells of the thyroid gland. Calcitonin serves to inhibit osteoclastic resorption of bone so that deposition of calcium into the bone matrix is allowed. This withdrawal of calcium from the blood returns serum calcium to normal while allowing bone mineralization (Delftos, 1996).

Just as readily calcium can be deposited into bone, it can be withdrawn. Hydroxyapatite provides a source of calcium when the blood calcium level is low (Volpe 1999). The major hormone involved in releasing calcium from bone is PTH. When the extracellular calcium level falls by minute increments, PTH is secreted from the parathyroid gland into circulation. The role of PTH in controlling serum calcium concentration is threefold. This hormone allows: (1) bone resorption of calcium, (2) renal reabsorption of calcium, and (3) renal synthesis of vitamin D to its active form (1, 25(OH)₂D₃) to enhance calcium absorption in the small intestine (Gropper et al., 2009; Holick 1996; Kronenberg, 1996).

When the blood calcium level falls below normal, PTH signals the kidney to increase renal tubular reabsorption of calcium so that calcium is routed back into circulation. Lastly, PTH enhances renal tubular conversion
of vitamin D to its active form (Holick 1996, Kronenberg 1996). Dihydroxy cholecalciferol, or calcitriol, enhances intestinal absorption of calcium and stimulates osteoclast production, which in turn releases calcium into circulation and mobilizes calcium stores from bone, respectively. The result of PTH activity is a return of serum calcium concentration to normal (Perez et al., 2008; Holick 1994).

Serum calcium is very tightly regulated and does not fluctuate with changes in dietary intakes; the body uses bone tissue as a reservoir for and source of calcium to maintain constant concentrations of calcium in blood, muscle, and intercellular fluids (Food and Nutrition Board, Institute of Medicine, 2010).

When oral calcium intake is lower than the recommended levels, the skeleton is “mined” for calcium to ensure adequate serum calcium levels for homeostatic functions (Bronner, 2003).

In the animal study using rats, Chen et al. (2002) showed that in rats with low dietary calcium intake, the whole body BMD, femoral weight and femoral trabecular bone decreased when compared to rats with normal calcium intake.

When calcium intake is low or ingested calcium is poorly absorbed, bone breakdown occurs as the body uses its stored calcium to maintain normal biological functions. Bone loss also occurs as part of the normal aging process, particularly in postmenopausal women due to decreased amounts of estrogen (National Osteoporosis Foundation, 2011).

Level of serum calcium was slightly increased in post menopausal as compared to premenopausal women. According to a study, when the menstrual cycles get irregular towards menopause, the serum calcium level rises rapidly and reaches maximum in 2–5 years after menopause and then slightly decreases afterwards. Level of serum inorganic phosphorus, magnesium and alkaline phosphatase were decreased in post menopausal groups as compared to the women with pre menopausal status (Sornay et al., 2005).
2.4 Calcium Absorption

Calcium is absorbed both actively and passively from the small intestine. Active absorption of calcium is dependent on numerous factors: when dietary intake is low, transcellular transport is upregulated and the active process is the predominant absorptive mechanism (Bronner et al., 1999). At dietary intake above 800 mg/d, a larger proportion of calcium is absorbed via passive transport (Pansu et al., 1993). At low dietary intakes, bioavailability of calcium from the food sources is of great importance (Heaney et al., 1990) but at higher intakes bioavailability has less importance (Deroisy et al., 1997).

Paracellular transport of calcium occurs passively down a chemical gradient throughout the small intestine, predominantly in the jejunum and ileum (Bronner et al., 1999). With high calcium intake, there is a down regulation of the active transport process (Buckley et al., 1980); thus, passive diffusion is the primary calcium transport mechanism when calcium intake is adequate or high (Pasnu et al., 1993). With older age, both passive calcium absorption and active transport of calcium become less efficient (Boonen et al., 2006).

In addition to the effect of dietary calcium intake levels on overall calcium absorption; Vitamin D, glucose and lactose, intact digestive tract integrity, and increased dietary requirements (i.e., pregnancy) enhance calcium absorption. Fiber, phytates and oxalates, encountered naturally in some high calcium containing foods, bind calcium and, thereby, decrease calcium bioavailability. Diets that are high in proteins and sodium increase urinary calcium excretion (Volpe 1999).

However, there is always loss of calcium in the faeces from the digestive juices (endogenous faecal calcium) and it follows that the net calcium absorbed (the difference between calcium intake and faecal calcium) is negative at zero intake, becomes zero when intake matches endogenous loss and then increases with intake, rapidly at first and then more slowly. This relationship is shown in the equation as:

\[ y = \left[ \frac{491x}{287 + x} \right] + 0.06x - 206 \text{ mg}, \]
Where \( y \) represents net absorbed calcium and \( x \) represents intake (Nordin et al., 1988).

The menopause is associated with a rise in obligatory calcium excretion (Prince et al., 1995; Nordin et al., 1987; Stepan et al., 1987; Gallagher et al., 1972; Young et al., 1967) and a probable decrease in calcium absorption (Nordin, 1997; Heaney et al., 1989).

2.5 Calcium Deficiency

Over the long term, inadequate calcium intake causes osteopenia which if untreated can lead to osteoporosis. The risk of bone fractures also increases especially in older individuals (Food and Nutrition Board, Institute of Medicine, 2010).

Calcium deficiency leads to osteoporosis (Miwa et al., 1898; Wu, 1990; Nordin, 1960; Hess, 1929). This deficiency is easily induced because of the obligatory losses of calcium via the bowel, kidneys and skin. In growing animals it may impair growth, delay consolidation of the skeleton and in certain circumstances give rise to rickets but the latter is more often due to deficiency of vitamin D. In adult animals, calcium deficiency causes mobilization of bone and leads sooner or later to osteoporosis i.e. a reduction in the "amount of bone in the bone" or apparent bone density (Nordin, 1997).

A deficiency of calcium intake in itself is considered a major risk factor for osteoporosis (Sugimoto, 2001). Low calcium intake causes secondary hyperparathyroidism as the calcium homeostasis in blood must be kept stable. This causes resorption of calcium from the bone with ensuing bone loss and an increased susceptibility to fractures. There is a lack of studies on calcium intake in patients with hip fractures (Dvorak et al., 2004; Shoback, 2007).

Low dietary intake of calcium in adulthood could be involved in the pathogenesis of osteoporosis. Optimal peak bone mass could be achieved with adequate calcium intake which is necessary for the prevention of osteoporosis. In fact, optimal calcium intake is necessary to maximize peak
bone mass, maintain adult bone mass and minimize bone loss in the later years (Welton et al., 1995; Cumming, 1990).

Dietary calcium deficiency may be a dangerous factor for osteoporosis which may induce the risk of osteoporotic fractures (Langdahl et al., 1996). After the age of 50, bone mineral density (BMD) decreases at a rate as high as 3% per year in postmenopausal women who often have negative calcium balance due to decrease in body calcium absorption, insufficient dietary calcium ingestion as well as increase in urinary calcium loss associated with estrogen deficiency during menopause (Kaplan et al., 2004).

According to Lau et al. (1996) low calcium has been found to be one of the risk factors for osteoporosis amongst Asian women.

Adequate calcium consumption throughout the lifecycle may help in the prevention of chronic diseases such as osteoporosis, hypertension and certain types of cancer later in life (Gropper et al., 2009).

2.6 Osteopenia/Osteoporosis

Resorption is the digestion of old bone; this is done by the osteoclasts. If there is “excessive resorption, bones weaken (osteopenia) and over time can become brittle and prone to fracture (osteoporosis)” (International Osteoporosis Foundation, 2007). The balance of osteoclasts and osteoblasts determines if bone is made, lost or maintained.

Osteopenia is a condition of low bone mass that, if not detected and treated may lead to osteoporosis. Despite the decreased density, the osteopenic bone in osteoporosis is normally mineralized (National Osteoporosis Foundation, 2010; Glase et al., 1997).

Osteopenia - refers to BMD that is lower than normal peak BMD but not low enough to be classified as osteoporosis. It can be a precursor to osteoporosis; having a T-scores between -1.0 and -2.5 (www.webmd.com).

Osteoporosis is a progressive disease characterized by abnormal loss
of bone density, leading to bone fragility and an increased susceptibility to fractures (Anderson et al., 1998).

Consensus Development Conference (1993) defined osteoporosis as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of the skeleton, leading to enhanced bone fragility and increased fracture risk. Osteoporosis causes no symptoms until a fracture occurs (National Osteoporosis Foundation, 2009).

Osteoporosis is caused by an imbalance in the normal bone remodeling process whereby excessive osteoclast resorption occurs without adequate new bone formation. The trabecular struts become thin and eventually resorb altogether leading to a reduction in bone strength and an increased likelihood of fractures of the spine, hip and wrist in sufferers (Cummings et al., 2002). These fractures are generally attributed to the reduction in the bone mass and trabecular connectivity.

Osteoporosis refers to a group of diseases in which bone absorption outpaces bone deposition. Bone becomes incredibly fragile that something as simple as a hearty sneeze or stepping off a curb can cause them to break. Though it affects the whole skeleton but the spongy bones of vertebra, wrist and femur neck are more vulnerable (Elaine, 2006).

The World Health Organization defines osteoporosis as a BMD “≥2.5 standard deviations below the young-adult, gender-matched mean” (WHO, 1994). There are four general diagnostic categories of bone mass for adult women (Lane, 1999). These categories include: normal (T- scores greater than or equal to 1 SD below young-adult average); osteopenia (T- scores less than 1 but greater than 2.5 SD below young-adult average); osteoporosis (T-scores greater than or equal to 2.5 SD below young adult average); and severe osteoporosis (T- scores greater than or equal to 2.5 SD below young-adult average plus the presence of one or more osteoporotic fractures).
Table 2.1
Criteria for the Diagnosis of Osteoporosis Based on the Measurement of Bone Density

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone Density Criteria</th>
<th>T-score Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Not more than 1 SD below the average peak young adult value</td>
<td>Better than or equal to -1</td>
</tr>
<tr>
<td>Osteopenia (low bone mass)</td>
<td>More than 1 but not yet 2.5 SD below the average peak young adult value</td>
<td>Poorer than -1 but better than -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2.5 SD or more below the average peak young adult value</td>
<td>-2.5 or poorer</td>
</tr>
<tr>
<td>Severe (established) fracture osteoporosis</td>
<td>2.5 SD or more below the average peak young adult value + a fracture</td>
<td>-2.5 or poorer +</td>
</tr>
</tbody>
</table>

Source: World Health Organization (WHO), 1994

The NIH consensus conference defines osteoporosis as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength reflects the integration of two main factors, bone density and bone quality (NIH, 2001).

Osteoporotic fractures occur predominantly in populations aged over 65 years (Dhesi et al., 2006). Elderly populations have lower daily intakes of vitamins and minerals compared with younger populations partly because of a lower food intake (Mowe et al., 2002).

In osteoporosis, bone mineral density (BMD) is decreased partly due to decreased osteoblast bone formation (Kloppmeyer, 2005). The consequences of osteoporosis are well known with regard to the risk of fractures (Kanis, 2002). In particular, hip fractures are a growing problem worldwide. Half of all women will eventually suffer from a fracture after the age of 50 (Keen, 2007). An adequate intake of these nutrients is also necessary to ensure optimal benefit from drugs (Nievis, 2005). A deficiency of calcium intake in itself is considered a major risk factor for osteoporosis (Sugimoto, 2001).
Pathogenic factors favoring the osteoporotic process are those impairing bone mass accumulations during growth and those accelerating bone losses during later life. Individuals vary markedly in peak bone mass, which is mainly determined by body size. Genetics is also a determinant of peak bone mass, as are the degree of physical activity and calcium intake (Arden et al. 1996; Gueguen et al., 1995).

### 2.6.1 Prevalence of Osteopenia/Osteoporosis

It has been estimated that 1.7 million people globally suffered from osteoporotic hip fractures in 1990. The number might increase to 6.3 million by 2050 (Johnell, 1997).

Based on 2001 census, approximately 163 million Indians above the age of 50 are suffering from osteoporosis; this number is expected to increase to 230 million by 2015 (Nordin, 1966).

Osteoporosis is a disorder linked with ageing. It usually occurs in elderly people, especially postmenopausal females (Delmas et al., 1999). In Asia, osteoporosis is rapidly becoming a major public health problem with increasing life expectancy. Osteoporosis is presenting a serious problem in epidemic proportions in Asia (Lau et al., 1996) because consumption of milk is poor, as the traditional Asian diet is considered to be low in calcium content (Lau et al., 2001).

In India, osteoporosis is highly prevalent with an estimated 30 million women diagnosed to have osteoporosis. Studies suggest that Indians have lower bone density than their North American and European counterparts and that osteoporotic fracture occur 10-20 years earlier in Indians (Shah et al., 2005).

According to WHO (1994), it is estimated that as a whole about 30 per cent of postmenopausal women are osteoporotic. In India, it is assumed that approximately 35 per cent of postmenopausal women develop osteoporosis coupled with the increasing number of postmenopausal women; the problem would soon assume large proportions (Peotia et al., 1996). However, in US osteoporosis affects more than 25 million people, 80% of which are women.
and it accounts for more than 1.3 million fractures annually including more than 500,000 of the spine, 250,000 of the hip and 240,000 of the wrist (Gums, 1996).

As life expectancies increase in the United States, osteoporosis rates are expected to continue to increase (Oden et al., 1998). It is anticipated that the number of individuals affected by osteoporosis will rise to 12 million by 2010 and to 14 million by 2020 unless greater efforts are made to reduce the risk of this debilitating disease (A Report of the Surgeon General, 2009). Osteoporosis is more prevalent among women than men with 80 percent of those affected by osteoporosis being females (American Bone Health, 2008).

According to the third National Health and Nutrition Examination Survey (NHANES III) data and prevalence data from the National Osteoporosis Foundation, over 10 million men and women aged 50 and older in the United States are affected by osteoporosis. An additional 34 million men and women are affected by low bone mass (osteopenia). Overall 44 million people affected by either osteoporosis or osteopenia represent 55 per cent of the population 50 years of age or over in the United States (American Bone Health, 2008; Looker et al, 1997).

According to the WHO up to 70 percent of women older than 80 years of age have osteoporosis (Robert et al., 2002). Worldwide the incidence of fractures associated with osteoporosis is higher in women than men and there is an increase with age in both sexes (Melton et al., 1999).

Osteoporosis, not only causes fractures, it also causes people to become bedridden with secondary complications that may be life threatening in the elderly (WHO, 2003). It is one of the leading health problems of the older adult women today and expectation is that more than 41 million women worldwide will be affected within the next 20 years (Kass, 2004).

The number of elderly individuals is increasing more rapidly in the developing countries like Asia and Middle East, Africa and South America. It has been estimated that about 70 percent of the 6.26 million cases of hip
fracture in the year 2050 will occur in these populations (Cooper et al., 1992).

2.6.2 Diagnostic Criteria for Osteopenia/ Osteoporosis

2.6.2.1 Bone Mineral Density

Bone Mineral Density (BMD) is a two-dimensional projection measurement defined as the average concentration of mineral per unit area expressed in grams per square centimeter (Gourlay et al., 2004).

Various bone mineral density (BMD) tests are available. The T-score from these tests compares an individual's BMD to an optimal BMD (that of a healthy 30-year old adult). A T-score of -1.0 or above indicates normal bone density, -1.0 to -2.5 indicates low bone mass (osteopenia), and lower than -2.5 indicates osteoporosis (National Osteoporosis Foundation, 2011).

Osteoporosis is clinically diagnosed through the use of BMD measurements at specific skeletal sites. When bone is fully mineralized, measurements of BMD can provide estimates of skeletal mass. Since mass is the one of major determinants of bone’s compressive and torsional strength, lower bone mass ultimately leads to greater risk of fracture (Kanis, 1994). BMD which indirectly measures bone strength accounts for 60-70% of the variation in bone strength (Ammann, 2003).

Bone mineral density (BMD) is a major predictor of osteoporotic fracture (Marshall et al., 1996; Nguyen et al., 1993). Peak bone mass (the maximum bone mass attained in a person’s life) and the rate of subsequent bone loss are both important determinants of BMD in later life. In fact, premenopausal bone mass is as important as post-menopausal bone loss for prediction of fracture (Riis et al., 1996).

BMD measurement is widely used for diagnosis of osteoporosis and determination of its severity (Cummings et al., 1995; Orwoll et al., 1995; Miller et al., 1996; Kanis et al., 1997; Melton et al., 1998; Krog et al., 1999). The Surgeon General's “Report on Bone Health and Osteoporosis” (2004), and the National Osteoporosis Foundation’s (NOF) “Physician’s Guide to
Prevention and Treatment of Osteoporosis” (2003) identify osteoporosis as a major public health concern, and emphasize the importance of using BMD testing as a clinical tool to diagnose patients at high risk of fracture before the first fracture occurs. Low BMD is an important risk factor for osteoporosis and its related fractures (Consensus Development Conference, 1993).

WHO (1994), established BMD as a diagnostic measure for osteoporosis. In order to diagnose osteoporosis, BMD threshold values were defined in order to capture the most patients with osteoporotic fractures. By comparing the BMD values to a standard reference population, standard deviation (SD) threshold values in the form of T-scores for normal bone, osteopenia and osteoporosis were established. After accretion of a peak bone mass around the age of 30 years a gradual loss continues until the more abrupt loss around the menopause and a more gradual loss later in life (Riggs et al., 1995).

Values of Bone Mineral density are measured in g/cm² and then converted into T- scores. T- scores are related to the young mean peak bone mass (the young normal healthy mean BMD) of the reference population of the same gender and are calculated according to the following formula:

\[
T\text{-scores} = \frac{\text{Patients' BMD - young adult mean BMD of the reference population}}{\text{Standard deviation (SD) of the young mean peak BMD}}
\]

Table: 2.2

T- scores are used for the densitometric diagnosis of osteoporosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>T-score Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>$\geq -1$</td>
</tr>
<tr>
<td>Osteopenia (low bone mass)</td>
<td>$&lt;-1$ and $&gt;-2.5$</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>$\leq -2.5$</td>
</tr>
<tr>
<td>Severe (established) fracture osteoporosis</td>
<td>$\leq -2.5 + \text{presence of one or more fragility fracture}$</td>
</tr>
</tbody>
</table>

Source : Alexeeva et al., 1994; Faulkner, 2005.
T-scores appear to be good predictors for fracture risk. T scores are equally helpful in postmenopausal patients and those with senile osteoporosis. The definition of osteoporosis as established by WHO (a score of 2.5 SD below the mean) effectively defines patients at risk and predicts fracture risk in an Indian population (Vaidya et al., 2010).

Marci et al. (2000) found that BMD results were the most significant predictor of changes in calcium intake.

### 2.6.2.2 Bone Mineral Density Measurement

The optimal method for diagnosing osteoporosis is to measure bone mineral density by (DEXA) dual-energy x-ray absorptiometry at the hip and lumbar spine. However, it is very difficult to apply this procedure in community-based studies because of its lack of portability and its cost. Furthermore, the procedure exposes subjects to low but significant doses of ionizing radiation. Quantitative ultrasound (QUS) measurement, a technique for measuring the peripheral skeleton, has been proposed because it can be performed quickly, is relatively inexpensive, portable and involves less radiation. Thus, QUS could be an ideal tool to screen for osteoporosis at the community level (Hans et al., 1996; Kim et al., 2001).

Quantitative ultrasound (QUS) measurement may provide some additional data on fracture risk because QUS parameters express both bone mass and bone quality. QUS measures two parameters: speed of sound (SOS) and broadband ultrasound attenuation (BUA). SOS is believed to express elasticity and bone mass and higher SOS values are obtained in denser and more elastic bone tissue. BUA is a function of absorption and dispersal of ultrasound wave and is associated with density and structure of trabecular bone (Gluer et al., 1993).

Several types of quantitative ultrasound devices are commonly used for screening individuals for osteoporosis. Quantitative ultrasound transducers use either wet (water) systems or dry (gel) systems. Most devices are designed to make measurements at one site. Common sites include the calcaneus, the finger phalanges, the tibia, and the radius. The
Sunlight Omnisense (Sunlight Technologies, Rehovot, Israel) is the first commercial quantitative ultrasound device allowing measurement at multiple skeletal sites. The Clinical Sunlight Omnisense 7000S model allows measurement at the finger phalanges and the distal radius. The Omnisense software calculates a T-score and Z-score from SOS values for each individual screened based upon the reference population used to develop the software. The Omnisense software utilizes the same WHO guidelines for osteopenia and osteoporosis. The reference population consisted of 1521 Israeli women between the ages of 20-90 years with a BMI < 35 kg/m2 (Weiss et al., 2000).

The reference population has been validated in North America in several studies. In a study by Drake et al. (2001), the researchers found that the peak SOS values occurred around the age of 40 in a population of 545 healthy Caucasian females aged 20-90 years from five North American sites. This is somewhat later than the time that peak BMD occurs in different skeletal sites but quantitative ultrasound measures different structural properties. The researchers found that maximal rate of decline in SOS was seen in 10 years post-menopause in all sites measured (-12.4, -9.2, -12.1, and -18.8 m/s at the radius, tibia, metatarsal, and phalanx, respectively).

The use of multisite quantitative ultrasound has been evaluated in several diverse populations in order to validate its use as a screening tool. Weiss et al. (2000) utilized the Omnisense in a population of elderly women (76.1 ± 6.0 years) who had a known osteoporotic hip fracture. SOS scores obtained from the distal radius were significantly lower in the hip fracture group compared to the control group (3860 ± 150 v. 3969 ±142 m/s).

Knapp et al. (2001) examined the relationship between SOS measurements obtained with the Omnisense and BMD measured using DEXA in a cohort of 409 Caucasian women (236 premenopausal and 173 postmenopausal) in the United Kingdom. Correlations between SOS measurements at the distal radius and BMD at the lumbar spine and femoral neck ranged from $r = 0.43$-0.47 for the entire cohort. When mean T-scores
were plotted versus age for the lumbar spine and femoral neck DEXA sites and distal radius QUS site, changes in mean T-scores showed a similar, expected trend of BMD maintenance until menopause. The researchers suggested that SOS measurements obtained from the Omnisense are capable of measuring BMD trends similar to DEXA for pre- and post-menopausal women.

2.7 Calcium Rich Sources

It is possible to meet calcium recommendations by consuming a variety of foods (Weaver et al., 1999). Milk products are known as one of the best source of dietary calcium due to high calcium content, bioavailability of the calcium and other nutrients which may facilitate absorption (US DHHS, 1996).

For adults, dairy products supply 72 per cent of the calcium in the U.S. diet, grain products about 11 per cent and fruits and vegetables about 6 per cent (US Department of Agriculture, 1989). Milk drinkers get 80 per cent more calcium in their diet compared to non-milk-drinkers (Fleming et al., 1994).

Dairy products provide the most readily available sources of dietary calcium, primarily with milk, yogurt, and cheese. Most American adolescents obtain their dietary calcium primarily from milk products (Institute of Medicine 1997; Subar et al., 1998).

Natural calcium-rich foods, calcium fortified foods or calcium supplements are dietary sources of calcium. Natural calcium-rich foods are ideal sources of calcium since they provide a variety of nutrients which are necessary for bone health (Dawson- Hughes 2003; Institute of Medicine, 1997).

Calcium is present in a variety of different foods. However, some foods are better sources of calcium than others. The best sources of dietary calcium are dairy products (milk, cheese, and yogurt), fish with bones, clams and oysters. Other sources of calcium include broccoli, leafy greens, dried fruits, and legumes (Gropper et al., 2009).
Vegetables high in dietary calcium include broccoli, bok choy (Chinese cabbage), spinach and rhubarb (Kass –Wolf, 2004). However, the ability of calcium from these sources is lower compared to animal sources due to their high fiber and oxalate content. Both fiber and oxalate content are known to inhibit dietary calcium absorption (Nordin, 1997; Wahlqvist et al., 2000).

According to Weaver et al. (1994) sources of well-absorbed calcium for vegans include calcium-fortified soy milk and juice, calcium-set tofu, soybeans and soynuts, bok choy (Chinese cabbage), broccoli, collards, Chinese cabbage, kale, mustard greens and okra.

Table 2.3
Calcium content of popular Indian dishes (mg/100g)

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Quantity</th>
<th>Cal(mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapati</td>
<td>Thin flatbread</td>
<td>3-4 pieces</td>
<td>27</td>
</tr>
<tr>
<td>Plain Parantha</td>
<td>Flatbread without any filling</td>
<td>3 medium</td>
<td>27</td>
</tr>
<tr>
<td>Aloo Parantha</td>
<td>Potato-stuffed flatbread</td>
<td>3 medium</td>
<td>54</td>
</tr>
<tr>
<td>Gobhi ka Parantha</td>
<td>Cauliflower-stuffed flatbread</td>
<td>3 medium</td>
<td>65</td>
</tr>
<tr>
<td>Mooli Parantha</td>
<td>White radish-stuffed flatbread</td>
<td>3 medium</td>
<td>79</td>
</tr>
<tr>
<td>Poori</td>
<td>Deep-fried unleavened bread</td>
<td>4-5 small</td>
<td>20</td>
</tr>
<tr>
<td>Palak poori</td>
<td>Poori of dough made with pureed spinach</td>
<td>4-5 small</td>
<td>70</td>
</tr>
<tr>
<td>Plain Kichdi</td>
<td>Mixture of rice and lentils</td>
<td>1 small bowl</td>
<td>20</td>
</tr>
<tr>
<td>Idli</td>
<td>Savory cake made with black beans &amp; rice</td>
<td>3-4 small</td>
<td>27.5</td>
</tr>
<tr>
<td>Suji ki Idli</td>
<td>Made of black bean and semolina</td>
<td>3 small</td>
<td>42</td>
</tr>
<tr>
<td>Dish</td>
<td>Description</td>
<td>Quantity</td>
<td>Price</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td>Plain Dosa</td>
<td>Crepe made from rice and black beans</td>
<td>2 dosas</td>
<td>35</td>
</tr>
<tr>
<td>Masala Dosa</td>
<td>Crepe with spicy potato filling</td>
<td>2 small dosas</td>
<td>56</td>
</tr>
<tr>
<td>Uttappam</td>
<td>Indian pizza</td>
<td>2 medium</td>
<td>49</td>
</tr>
<tr>
<td>Appam</td>
<td>Pancakes made of fermented rice flour</td>
<td>3 medium</td>
<td>15</td>
</tr>
<tr>
<td>Mung ki dal</td>
<td>Boiled green lentil preparation</td>
<td>1 bowl</td>
<td>46</td>
</tr>
<tr>
<td>Dal Makhani</td>
<td>Creamy black beans, garlic and tomatoes</td>
<td>1 bowl</td>
<td>67</td>
</tr>
<tr>
<td>Curried lentils with kale</td>
<td>Modified traditional dish: lentils &amp; spinach</td>
<td>1 bowl</td>
<td>142</td>
</tr>
<tr>
<td>Sambhar</td>
<td>Vegetable stew with tamarind &amp; red gram</td>
<td>1 bowl</td>
<td>52</td>
</tr>
<tr>
<td>Channa masala</td>
<td>Chickpea curry</td>
<td>1 bowl</td>
<td>61</td>
</tr>
<tr>
<td>Rajmah curry</td>
<td>Red kidney bean curry</td>
<td>1 bowl</td>
<td>63</td>
</tr>
<tr>
<td>Matar aloo curry</td>
<td>Pea-potato curry</td>
<td>1 bowl</td>
<td>76</td>
</tr>
<tr>
<td>Ghia kofta curry</td>
<td>Fried balls with chickpea flour in gravy</td>
<td>3-4 koftas</td>
<td>74</td>
</tr>
<tr>
<td>Palak kofta curry</td>
<td>Fried balls of spinach</td>
<td>3-4 koftas</td>
<td>169</td>
</tr>
<tr>
<td>Sarson ka saag</td>
<td>Mustard greens and spinach based curry</td>
<td>1 bowl</td>
<td>230</td>
</tr>
<tr>
<td>Aloo kale</td>
<td>Modified traditional dish: palak aloo</td>
<td>1 bowl</td>
<td>154</td>
</tr>
<tr>
<td>Mushroom matar</td>
<td>Mushroom-pea curry</td>
<td>1 bowl</td>
<td>54</td>
</tr>
<tr>
<td>Baingan bhartha</td>
<td>Roasted and mashed eggplant</td>
<td>1 small bowl</td>
<td>30</td>
</tr>
<tr>
<td>Bharwan bhindi</td>
<td>Okra slit and filled with spices</td>
<td>1 small bowl</td>
<td>98</td>
</tr>
<tr>
<td>Aloo gobhi</td>
<td>Spicy potato and cauliflower mixture</td>
<td>1 small bowl</td>
<td>38</td>
</tr>
</tbody>
</table>

2.8 Calcium Fortification in Food Products

According to Devadas et al. (1980) a cereal based diet supplemented with sweet potato, field beans, drumstick leaves, sesame seeds, groundnut and cottonseed flours was found best in terms of weight gain, calcium absorption and calcium retention. These results showed a positive correlation between calcium in diet and calcium absorption and calcium retention.

Pahwa et al. (1980) concluded that the utilization of calcium was negatively related to the oxalate content of leafy vegetables. The retention of calcium from leafy vegetables was increased when these were consumed with skim milk powder.

According to Gupta et al. (1992) the supplementation of bengal gram to wheat based diets significantly improved the calcium absorption. They reported that in vivo calcium absorption was less in wheat chapati as compared to bengal gram supplemented wheat chapati. The supplementation of legumes to cereals improved the calcium utilization and it was concluded that there will be no risk of occurrence of protein induced hypercalciuria and osteoporosis in old age.

Muhrbauer et al. (1999) reported that several common vegetables in the diet of man altered bone metabolism in the rat. It was concluded that if this also occurred in man then including an appropriate amount of these vegetables in the daily diet could be an effective and inexpensive way to decrease the incidence of osteoporosis. Weaver (1999), examined that calcium fortified foods, such as milk products, were likely to play an increasingly important role in helping consumers to achieve newer calcium requirements aimed at reducing the risk of osteoporosis.

Soybean milk is an inexpensive high quality vegetable protein. It contains equal amount of protein to a comparable amount of cow’s milk but only 1/5th of the calcium. In a study of Chaiwanon et al. (2000) soybean milk was fortified with calcium carbonate and tri-calcium phosphate at similar level of calcium to cow’s milk. Results revealed that calcium bioavailability
was improved in fortified milk compared to control.

Korstanje (2001) reported that calcium fortified juice products were a major trend in the USA. About eight big juice companies like, Minute Maid and Tropicana positioned their calcium fortified orange juice as a substitute to milk. In Israel, calcium citrate had been recommended for food enrichment as a source of calcium in juice, drink mixes, infant formulas, sports beverages, diet products and cereals (Koder et al., 2001).

Calcium is a popular ingredient to add to orange juice, soymilk, breads, biscuits, cereal and popcorn. In UK, the current trend is to add calcium and other nutrients to snack foods. The low pH carbonated or non-carbonated beverages can be fortified with calcium and vitamin D by making suspension of water-soluble vitamin D and vegetable oil and a gum (Timmcke, 2002).

Pocket type flat bread (Pita) loaves were prepared from flours fortified with calcium carbonate, calcium sulfate and tricalcium dicitrate at eight ascending levels in the ranges of 800 to 2500, 700 to 1500 and 400 to 2000 mg of added calcium/100 g flour, respectively. The calcium fortified bread analogues provided 61 to 126.5 per cent of the recommended daily intakes for calcium for middle Eastern population and these are potentially good source of calcium for vegetarians and other population groups that do not consume dairy products in Europe and North America (Ziadeh et al., 2005).

2.9 Dietary Calcium Intake in Indian Women

Dietary calcium intake has been shown to vary widely in global nutrition (FAO/WHO, 2004). Many studies in Asia and Africa have reported the inadequate intake of dietary calcium in different populations where, milk and milk products are limited in the usual diet or such food items are not consumed habitually (Prentice et al., 1993; ACC/SCN, 1997). According to the Food and Nutrition Board, the recommended daily allowance of calcium for female adults in Asia is 400-500 mg/day, although a number of investigators believed that this level of intake is extremely low for postmenopausal women (Hickler et al., 1984; Heaney et al., 1989).
Food and Agriculture Organization’s report in 1990 demonstrated that
the mean calcium intake in the developing world was 344 mg day (Hejazi et
al., 2009). It has also been shown that the Asian diet, especially in the
elderly is low in calcium. A study published in 2004 found that an elderly Thai
rural population had a mean daily calcium intake of 236 mg/day
(Pongchaiyakul et al., 2004).

Ho et al. (1994) and Hu et al. (1993) observed that the average
calcium intake has been low among Asian people, who consume less dairy
products. The mean dietary calcium intakes among Hong Kong and Chinese
population were between 350-450 mg/day. These values of calcium intake
were about half of that found in a Western population.

The lowest calcium intake occurs in developing countries, particularly
in Asia and the highest in developed countries particularly in North America
and Europe (FAO, 1991). Calcium intake in India is also far below western
recommendations (Bathia, 2008).

The small number of studies on dietary calcium intake within the
Indian population has found mean calcium intakes below RDI. As quoted in
the study of Shatrugana et al. (2005) mean dietary calcium intake in a
sample of 289 Indian women (mean age of 41 years) was 270±57mg/day as
measured by a food frequency questionnaire (FFQ) & a 24hour recall.
Moreover, the main food sources of dietary calcium came from plant sources
such as cereals and green leafy vegetables. Both these sources have a
lower bioavailability compared to animal sources. In this study, the women
were recruited from a large urban slum (Addagutta) in Hyderabad, South
India.

Further, a low calcium intake in Indian women was also reported by
Harinarayan et al. (2004). Both dietary calcium and vitamin D levels were
measured in 316 men and women living in rural (n= 191; mean age of
44.0years) and urban (n=125; mean age of 45.5years) area. Area of
investigation was Tirupati, located in the extreme southeast and southern
part of India. Participants were asked to recall their diet of the previous five
to seven days, which was recorded by a single observer. Analysis of data showed a mean dietary calcium intake ±SEM in rural and urban area was 264±1.94mg/day and 354± 5mg/day respectively.

Harinarayan et al. (2007) showed similar findings. In this study, a larger cohort was obtained (n=1,148) from the same region of South India. Mean age of the participants in rural and urban groups were 43.0 years and 46.0 years respectively. Mean dietary calcium intake ±SEM in rural and urban females were 262±3mg/day and 306±2mg/day respectively. Once again, dietary calcium intakes were below RDI.

2.10 Nutritional Calcium Supplements

Calcium is a fundamental part of any treatment program to reduce osteoporosis-associated fracture risk. The majority of patients treated for osteoporosis are postmenopausal women (National Osteoporosis Foundation, 2002), who often lack sufficient dietary calcium to meet daily requirements (Feskanich, 2003). Calcium supplements provide additional alkali salts and since the maintenance of acid–base balance is crucial to preserving bone health, calcium supplements may be important for also providing additional alkali salts (New et al., 2003).

Postmenopausal women are at high risk for fracture (Papaioannou et al., 2010) and are not meeting adequate calcium intake levels (Vatanparast et al., 2009) The regular use of calcium supplements is thus important in reducing fracture risk related to inadequate calcium intake (Spangler et al.,2011).

When baseline habitual calcium consumption is low, larger increments in BMD occur with increased dietary calcium intake (Du et al., 2002) and sustained beneficial effects of higher intake are more likely to occur in individuals with previously low habitual calcium intake (Bonjour et al., 1997).
Adequate calcium intake from food sources and supplements promote bone health. When food sources do not provide enough calcium, supplements can be used to meet this goal. Bioavailability of calcium in food sources and supplements are important aids in achieving daily calcium recommendations.

Calcium supplements offer a convenient alternative to women unable to consume enough calcium from diet alone. Many forms of dietary calcium supplements are widely available, the two most often used calcium salts are calcium carbonate and calcium citrate (Levenson et al., 1994; Heller et al., 1999; Porter, 2003). A wide variety of calcium salts is found in calcium supplements, including calcium acetate, calcium citrate maltate, calcium gluconate, calcium lactate, calcium lactogluconate, and calcium phosphate.

Recommended calcium levels refer to “Elemental calcium” (North American Menopause Society, 2006). Different calcium salts may contain different percentage of elemental calcium. The calcium content of several popular supplements was given in (Table 2.4).

Guidelines have been published by the National Osteoporosis Foundation (1999), the National Institutes of Health Consensus Development Panel on Osteoporosis (2000), and others all recommending 1200–1500 mg of elemental calcium and 400–800 IU of vitamin D to be taken daily through a combination of diet and supplementation.

US Department of Health and Human Services, (2004), suggested that calcium supplements should be taken with meals and best absorbed by the body when taken in doses of 500 mg or less. Supplement doses above this level should be divided so that they are not consumed in a single setting.

There is some evidence that taking calcium supplements in the evening may work to advantage by suppressing the nocturnal rise in bone resorption but it has also been suggested that divided dose regimens (one-third in the morning, two-thirds in the evening) may lead to a greater total calcium absorption (Scopacasa et al., 2002).
Table 2.4
Comparison of selected calcium supplements

<table>
<thead>
<tr>
<th>Supplements</th>
<th>Elemental calcium Per tablet (mg)</th>
<th>Vitamin D Per tablet (IU)</th>
<th>Tablets Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium carbonate+D</td>
<td>600</td>
<td>200</td>
<td>2</td>
</tr>
<tr>
<td>Caltrate + D</td>
<td>600</td>
<td>200</td>
<td>2</td>
</tr>
<tr>
<td>Os- Cal +D</td>
<td>500</td>
<td>200</td>
<td>2</td>
</tr>
<tr>
<td>Tums Ultra</td>
<td>400</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Viactiv</td>
<td>500</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>Calcium Citrate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citracal + D</td>
<td>315</td>
<td>200</td>
<td>3</td>
</tr>
<tr>
<td>Calcium citrate</td>
<td>250</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Calcium complex (Carbonate, Lactate, Gluconate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcet</td>
<td>150</td>
<td>100</td>
<td>7</td>
</tr>
<tr>
<td>Calcium Phosphate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posture D</td>
<td>600</td>
<td>125</td>
<td>2</td>
</tr>
</tbody>
</table>


According to the study by Heaney et al. (2000) the bioavailability of calcium carbonate vs. calcium citrate was found to be identical in 23 vitamin D–sufficient postmenopausal women. In another study, the absorption of calcium carbonate and calcium citrate was found to be equivalent when taken with a meal (Heaney et al., 1999).

The bioavailability of calcium carbonate was found to be equivalent to skim milk and orange juice fortified with calcium-citrate malate in 12 elderly subjects. Changes in serum, urinary calcium, and PTH were not significantly different between sources including skim milk, calcium carbonate, or orange juice fortified with calcium citrate malate (Martini et al., 2002).
Calcium carbonate is the most widely used and least expensive form of calcium supplement with adequate absorbability when consumed with meals (Dawson, 2003). Cost is a consideration for many patients. A study assessing the cost of calcium from food and supplements found that calcium carbonate was the least expensive form of calcium at approximately one-third the cost of the least expensive food source which includes skim milk and calcium-fortified orange juice made from frozen concentrate (Recker, 1985).

Calcium lactate and calcium gluconate are less concentrated forms of calcium (Hendler et al., 2001). Because calcium lactate and calcium gluconate contain a small concentration of elemental calcium, many tablets have to be consumed to reach desirable doses.

2.11 Clinical Trials of Nutritional Calcium Supplements

Several studies have shown that calcium supplementation increases bone loss in premenopausal females. In a meta-analysis study completed by Welton et al. (1995) suggested that calcium supplementation prevented bone loss in pre menopausal females. For women who were previously consuming between 700-1,000 mg calcium/day, the supplementation of roughly 1,000 mg/day prevented approximately 1 per cent of bone loss per year at all sites except the ulna.

Dawson-Hughes et al. (1990) showed that in postmenopausal women whose dietary calcium intake was lower than 400 mg/day, calcium supplementation of 500 mg/day prevented bone loss at both the hips and the spine.

According to Mazess et al., (1991) the impact of calcium supplementation in premenopausal women had been found to be greater in those whose calcium intake was low.

Studies also show that Calcium supplements are effective in reducing bone loss in women in late post menopause (>5 years post menopause) particularly in those with low habitual Ca intake (<400 mg/d) (Heaney, 2000).
In a Canadian hospital-based case-control study, Kreiger et al. (1992), found a statistically significant reduction in the risk of wrist fractures in women who consumed more than 1,000 mg/day of calcium.

Some randomized control trials (Chapuy et al., 1992; Chevalley et al., 1994; Recker et al., 1996; Dawson et al., 1997) showed the benefit of calcium plus vitamin D supplementation in the elderly for prevention of bone loss and reduction of fracture rates. Bendich et al.(1999) supported the benefit of calcium supplementation (1,200 mg/d) in postmenopausal women for prevention of hip fracture.

Heaney et al. (1993) found a positive correlation between calcium intake and calcium balance in both premenopausal and postmenopausal women; they claimed that daily calcium intakes of 1000 and 1500 mg respectively would achieve calcium balance and that larger intakes would result in positive calcium balance. Horsman et al. (1997) and Riggs et al. (1998) also claimed that calcium supplementation leads to increased bone mass.

Kanis (1994) found that calcium supplements in excess of 1 g daily have been found to slow the rate of bone loss in postmenopausal women and decrease the risk of hip fractures.

A few studies have now shown that in postmenopausal women who already have osteoporosis and vertebral fractures and who were treated with calcium supplements and dietary calcium of over 1,500 mg per day for two years, new vertebral fractures decreased (Recker et al., 1996; Reid at al., 1990). Calcium also decreases the risk of hip fracture in women who start taking it even in their late 70s, which is important because hip fractures are common among this age group (Cummings et al., 1995).

Reid et al. (1995) studied the effects of calcium supplements of 1 g/day on women with usual daily calcium intake of 750mg. The mean rate of bone loss decreased by 43% in the calcium group as compared with the placebo group.

A systematic review of the literature to assess the effectiveness of calcium supplementation and/or dietary calcium for the prevention of
osteoporotic fractures in postmenopausal women showed that calcium supplementation (1,050 mg/day) could reduce the risk of osteoporotic fracture from 2-70 per cent (Cumming et al., 1997).

Devine et al. (1997) described a sustained reduction in the rate of BMD loss at the ankle and hip in postmenopausal women who took a calcium supplement of 1 g/day. In North America, Storm et al. (1998) showed that calcium supplementation by either calcium carbonate or dietary means prevented seasonal bone loss. Calcium supplementation also was found to be associated with reduction in femoral medullary expansion, secondary hyperthyroidism, and high bone turnover in addition to preventing loss of BMD.

Patrice et al. (1998) found that two month of calcium supplementation in postmenopausal women was efficient in reducing markers of bone turnover with a greater effect in women with a low dietary calcium intake.

An analysis of 20 major calcium trials in postmenopausal women also demonstrated that calcium supplementation (500–1200 mg/d) decreased bone loss (Nordin, 1997). Women who received calcium supplementation lost bone at the rate of 0.014% per year. Women who did not receive calcium supplementation lost bone at the rate of 1% per year. A review of both investigator-controlled calcium intervention trials and observational studies from 1975 to 1998 found that calcium from diet or supplements decreased age-related bone loss (Heaney, 2000).

Short clinical trials of calcium supplementation show that calcium reduces the loss of bone in postmenopausal women and the risk of fracture. A meta-analysis of 15 trials that included a total of 1806 participants randomized to either calcium supplementation or usual calcium dietary intake over a 2-year period showed an increase in bone density for the lumbar spine of 1.66%, 1.64% for the hip, and 1.91% for the distal radius in the calcium-supplemented group (Shea et al., 2000).

According to recent evidence, supplementation with calcium or vitamin D or both has been reported to exert a significant favorable effect on
BMD and on several bone-remodeling biomarkers (Weisman et al., 2005; Baekgaard et al., 1998; Meier et al., 2004) and has been associated with a lower risk of fracture (Weisman et al., 2005).

The Women's Health Initiative (WHI), a recent large randomized trial, studied >36,000 women ages 50–79 over a 7-year period and evaluated the effect of calcium and vitamin D on fracture rates. Hip fractures were significantly reduced in women who were adherent to calcium and vitamin D treatment. A 29% relative decrease in hip fracture rates was found in women who were compliant with taking 1000 mg of elemental calcium as carbonate and 400 IU of vitamin D per day (Jackson, 2006).

Tang et al., (2007), suggested that calcium supplementation rendering a total calcium intake of 1,200 mg/day may slow the rate of bone loss. A review of over twenty studies has shown that calcium supplementation can decrease bone loss by approximately 1% per year (Goulding et al., 2007).

Heike et al. (2008), showed that four years of supplementation with 1200mg elemental calcium is associated with a reduction in risk of all fracture and minimal trauma fractures among healthy community- dwelling older men and women.

The Osteoporosis Risk Factor and Fracture Prevention Study (OSTPRE-FPS) was a randomized population-based open trial ($n=593$). In this trial the supplementation group ($n=287$) received daily cholecalciferol 800 IU + calcium 1,000 mg for 3 years while the control group ($n=306$) received neither supplementation nor placebo. The results showed that daily vitamin D and calcium supplementation have a positive effect on the skeleton in ambulatory postmenopausal women (Kärkkäinen et al., 2010).

2.12 Clinical Trials on Effect of Nutrition Education on Calcium Intake

Nutrition education is the foundation for any programme intended for nutritional improvements (Devdas et al., 1970).
Jelliffe (1966) stated that education which is geared to improve the local conditions and is based on local and free from the local cultural beliefs is most likely to be successful. He stressed that the most single aim of nutrition education is to persuade mothers in the tropics to make the best use of foods locally available for feeding children in the early years of life.

Albanese (1971) defines nutrition education as a means of translating nutritional requirements into food and adjusting the food choices to satisfy nutritional, cultural, psychological and economic needs.

Nutrition education has been defined as educational measure for inducing desirable behavioural changes for the ultimate improvement in the nutritional status of individual and family (Deshpande et al., 2003). All the above definitions suggest that nutrition education aims at bringing in nutrition behaviours which promote health of an individual.

Educational interventions without a food or supplement also increase calcium intake (Tussing et al., 2005; Bonjour et al., 2009; Wong et al., 2004). Decades of research on nutrition education have found that education would be more effective if focused on specific behaviors and if appropriate theory was used for designing the intervention (Contento, 2008).

Nutrition education researchers have explored the usefulness of a number of social-psychological theories in explaining dietary behavior. Among the theories and theoretical models that have been used by nutrition education researchers are the Health Belief Model (Maiman et al., 1974), Fishbein and Ajzen’s Theory of Reasoned Action (Fishbein et al., 1975) and Bandura’s Social Cognitive Theory (Bandura, 1977). Work done by researchers using each of these models has added to our understanding of the mental processes influencing dietary behavior.

Manios et al. (2007) found an intervention program based on Health Belief Model and the Social Cognitive Theory Which significantly increase dietary calcium intake. The Social Cognitive Theory was first developed by Bandura et al. (1977), illustrated in Fig.2.1.
Figure 2.1: The Social Cognitive Theory (Bandura et al 1977)

Personal factors include knowledge, skills, expected outcomes, goal setting, problem solving skills and stress management. Environmental factors include the social environment, such as family and friends, as well as the physical environment, such as availability of food.

Tussing et al. (2005) designed an educational intervention program using the Health Belief model as well as Theory of Reasoned Action Model (Fishbein et al., 1986), illustrated in fig. 2.2. The intervention resulted in a significant increase in dietary calcium intake, primarily due to increase in perceived benefits of calcium intake, susceptibility to osteoporosis as well as increased calcium self efficacy.

Figure 2.2: The Theory of Reasoned Action Model (Fishbein et al., 1986)
According to Peterson et al. (2000) nutrition education is a preferred approach to achieve increased calcium intake through dietary strategies to enhance the consumption of local calcium-rich foods. It is also proved that nutrition education can improve calcium intake and retard bone loss in women.

Riberio et al. (2001) reported increased calcium intake (1179mg/d to 1319mg/d) in 138 women having mean age 45-69 years after 6 months of educational intervention.

Further, Aree et al. (2005) conducted a four weeks intervention programme on 47 elderly Thai women (mean age 69 years). He took follow ups for six months which showed significant increase in dietary calcium intake from 491mg/d to 647mg/d. Similarly, Manios et al. (2007) showed a positive outcome of educational intervention program on 75 postmenopausal women from Athens, Greece. The subjects were having mean age of 60 years. After the intervention he found the mean dietary calcium intake was increased from 681.6mg/d to 1248mg/d.

According to Turner et al. (2004), to increase the likelihood of an increased dietary calcium intake can be increased through intervention trials which need to consist of workshops actively involving the participants, such as group discussions and problem solving exercises. This will help to enhance self efficacy and overcome any barrier to calcium intake women may be facing which has been found to predict dietary calcium intake (Schmiege et al. 2007, Von Hurt et al. 2007, & Wham et al. 2003).

Hein et al., (2009) conducted a controlled trial in two groups as intervention and control. The intervention group was given nutrition education during 18 months to improve calcium intake while the control subjects had the usual diet. Calcium intake and bone mass were evaluated every 6 months. He found changes in the mean calcium intake at baseline and every 6 months thereafter. Calcium intake in the control group did not change significantly over time. In interventions, calcium intake increased significantly with time from 345 ± 54 mg/d at baseline to 657 ± 64mg/d after
18 months (P<0.01). The mean calcium intake of interventions was also significantly higher than that in controls at 18 months (P<0.01). This finding is similar to a previous nutrition education study in young women with low calcium intake conducted by Peterson et al. (2000).

2.13 Terminology

WHO Scientific Group (1981) proposed definitions on the menopause as follows:

a) The term natural menopause is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. Natural menopause is recognized to have occurred after 12 consecutive months of amenorrhea for which there is no other obvious pathological or physiological cause. Menopause occurs with the Final Menstrual Period (FMP) which is known with certainty only in retrospect a year or more after the event.

b) The term induced menopause is defined as the cessation of menstruation which follows either surgical removal of both ovaries (with or without hysterectomy) or iatrogenic ablation of ovarian functions (eg. Chemotherapy or radiation).

c) The term perimenopause should include the period immediately prior to the menopause (when the endocrinological, biological and clinical features of approaching menopause commence) and the first year after menopause.

d) The term premenopause is often used ambiguously either to refer to the one or two years immediately before the menopause or to refer the whole of the reproductive period prior to the menopause.

e) The term postmenopause is defined as dating from the Final Menopausal Period (FMP), regardless of whether the menopause was induced or spontaneous.

The whole process of transition into menopause can be divided into different phases as Premenopause, Perimenopause and Postmenopause.
Few studies have defined premenopause and perimenopause based on the regularity of the menstruation only (Sayed 2000). Women are considered as postmenopausal if they have more than 12 months amenorrhoea (Sayed, 2000; Ismail et al., 1998) or sometimes just 6 months of amenorrhoea (Rizk, 1998).

Very few studies have tried to analyse the mean age at menopause in India and they estimated it between 44 to 47 years (Singh et al., 1980; Sharma et al., 1985; Randhawa et al., 1987).