Nutrients for building strong and healthy bones

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ABSTRACT: Bone is a dynamic multifunctional organ. Bone development is a lifelong concern. Dietary intake is an important lifestyle factor influencing bone health. Bones undergo a continuous process of formation and break-down. From conception to birth and throughout life, various nutrients significantly impact the process of bone formation and resorption. The process of bone mineralization is regulated by calcium, phosphorus, magnesium, vitamin D, and trace elements. Vitamin A promotes the differentiation and maturation of bone cells. Vitamin C and vitamin K are involved in the synthesis of bone matrix proteins. Imbalance of nutrients in the body negatively affects bone health. A healthy diet with an adequate and constant supply of proteins, vitamins, and minerals is required for bone formation and development. Dietary constituents such as essential fatty acids and phytoestrogens are also essential for bone health. Thus, the review thoroughly discusses the role of various nutrients on bone development and metabolism, the influence of their deficiency, and excess on bones. We suggest further exploration to assess appropriate role of trace elements, phytoestrogens, essential fatty acids, vitamin K supplementation, and other non-traditional nutrients on bone health.

Key words Bone, minerals, trace elements, vitamins

The skeletal system is composed of bones that provide internal support in all higher vertebrates. The adult skeleton is composed of 206 bones. The axial skeleton and appendicular skeleton are the two principal divisions of the skeletal system. The skull, vertebral column, and the thorax, forming the longitudinal axis of the body, are the part of the axial skeleton. Bones of arms and legs along with their respective girdles form the appendicular skeleton. Bone is a specialized type of connective tissue composed of bone matrix and bone cells. The bone matrix has about 30 per cent organic component and 70 per cent inorganic matter. Type I collagen, proteoglycans, and non-collagenous protein form the organic matrix. The crystalline salts of calcium and phosphorus form the inorganic portion of the bone matrix deposited in the form of hydroxyapatite (Jr. Marks and Odgren, 2002). There are two forms of bones: cortical (compact) and cancellous (spongy). The compact bone forms 80 per cent of the skeleton and provides mechanical functions. The other 20 per cent of the skeleton is the spongy bone which houses the bone marrow and provides metabolic functions (Clarke, 2008; Jr. Marks and Odgren, 2002). There are four types of bone cells (Table 1).

The development of bones occurs in three general phases *i.e.,* growth, modeling, and remodeling. The growth phase begins from the embryonic period and continues until the age of twenty years. The modeling phase begins after the attainment of twenty years of age and continues until the acquisition of peak bone mass by the age of thirty years. After the age of thirty years, the remodeling phase begins and consists of a constant process of bone resorption (breakdown), responsible for the decline in bone mass with age (Heaney *et al.,* 2000). The main functions of bones are movement, shape, protection, support, blood production, and mineral homeostasis. The development of bones is influenced by genetic and environmental factors such as nutrition and lifestyle (Ferrari *et al.,* 1998).

Table 1: Types, Origin, and Functions of Bone Cells

Cell type	Origin	Function	Source
• Osteoprogenitor cells	Primitive mesenchymal cells	• Differentiate into osteoblasts	Lowe and Anderson, 2015
• Osteoblasts	Mesenchymal stem cells	• Bone forming cells • Production of bone matrix • Regulate bone mineralization	Jr Marks and Odgren, 2002
• Osteocytes	Mature osteoblast	• Maintain bone matrix • Homeostasis of extracellular fluid • Local activation of bone formation and/ or resorption	Buckwalter *et al.*,1996
• Osteoclasts	Hematopoietic stem cells	• Bone resorption	Fernandes, 2004

Nutrients play a significant role during each phase of bone development. From macronutrients to trace elements, every nutrient has got a certain function in bone metabolism. Both deficiency and excess of nutrients, influence or disturb the normal physiology of bones. Since bones support the whole-body structure, imbalance of any nutrients will adversely affect mobility and quality of life. Therefore, the present review thoroughly discusses the potential role of various nutrients on bone development and metabolism, the influence of their deficiency and excess on bones, adult body mineral content, and recommended intakes of bone essential nutrients for various population groups.

NUTRIENTS FOR BONE HEALTH

Proteins

The proteins play an essential role to lay down the organic bone matrix by synthesizing collagenous and non-collagenous proteins. Dietary proteins provide necessary amino acids for an optimal bone mass gain during childhood and adolescence, and preservation of bone mass during aging. Protein is involved in calcium metabolism in the body by providing vitamin D-dependent calcium-binding protein (CaBP) which enhances intestinal calcium absorption (Thakker *et al.,* 2016). Protein intake improves muscle mass, contributes

Table 2: Influence of Trace Elements on Bone Health

Trace Element	Positive Effects	Deficiency	Source
Fluoride	• Stimulates osteoblastic bone formation • Inhibits bone crystal dissolution	-	Farley *et al.,* 1983; Prentice 2004
Copper	• Cofactor for enzyme lysyl oxidase involved in cross-linking of collagen	• Menkes' kinky hair syndrome: skeletal changes such as scurvy, fractures, or delayed bone age • Acquired Copper deficiency: osteopenia, fractures	Turnland 1999; Blumenthal *et al.*, 1980; Sutton *et al*., 1985
Zinc	• Increase the bone protein content • Synthesis of insulin-like growth factor-1 and transforming growth factor-β • Osteoblastic activity, collagen synthesis, and alkaline phosphatase activity • Infant bone growth	• Reduced bone growth and maturation • Short stature • Low bone mineral density • Fracture risk	Ma and Yamaguchi 2001; Igarashin and Yamaguchi 2001; Ma *et al*., 2001; Palacios 2006; Prentice & Bates 1994; New *et al*., 1997; Elmståhl *et al*.,1998; Abrams and Griffin, 2004; Prasad *et al*., 1962
Selenium	• Antioxidant • Selenoproteins are expressed in mesenchymal stem cells which form bone, cartilage, and tendons as well as osteoclasts	• Kashin Beck disease: osteoarthritis	Kohrle *et al.,* 2005; Ebert *et al.*, 2006; Jakob *et al*., 2002; Moreno-Reyes *et al.*, 2003
Boron	• Enhance bone mineral balance • Proliferation and mineralization of bones • Bone regeneration	-	Abrams and Griffin, 2004; Hakki *et al*., 2010
Silicon	• Enhance bone formation • Decrease bone resorption	-	Abrams and Griffin, 2004
Strontium	• Decrease bone resorption • Enhance bone mineralization	-	Abrams and Griffin, 2004
Manganese	• Biosynthesis of mucopoly-saccharides in bone matrix formation • Cofactor for several enzymes in bone tissue	-	Palacios, 2006
Iron	• Cofactor in enzymes such as prolyl and lysyl hydroxylases involved in collagen bone matrix synthesis • Cofactor in 25-hydroxy cholecalciferol hydroxylase, which is involved in transforming vitamin D to an active form	-	Palacios, 2006

towards increased bone density and strength with decreased risk of bone fracture. Dietary proteins play an essential role in connecting the endocrine axis to skeletal growth. The formation of osteotrophic hormone, insulin-like growth factor 1 (IGF-1) which is synthesized by hepatic and osteogenic cells, depends upon protein intake (Bonjour *et al.,* 1996). The longitudinal bone growth is stimulated by IGF-1, as it promotes proliferation and differentiation of chondrocytes and osteoblasts (Ohlsson *et al.,* 2009). IGF-1 promotes intestinal absorption of calcium and phosphorus by synthesizing active form of vitamin D. Furthermore, by its direct action on renal cells, it increases renal tubular reabsorption of phosphorus (Caverzasio *et al.,* 1990).

Inadequate supply of proteins impairs bone development and synthesis of IGF-1. Protein undernutrition results in delayed skeletal growth, reduced bone mineral mass, and strength, by uncoupling the process of bone formation and bone resorption (Rizzoli *et al.,* 1999; Ammann *et al.,* 2000). Protein deficiency causes muscle weakness, reduced calcium absorption, and secondary hyperparathyroidism. This results in accelerated bone loss and increased risk of fractures (Kerstetter *et al.,* 2001). Several epidemiological studies support the positive association between protein intake and bone health. A population-based Framingham Osteoporosis study reported an inverse correlation between dietary protein intake and bone loss in both women and men (Hannan *et al.,* 2000).

Excess dietary protein intake has been cited to have a detrimental effect on bone health and negatively affect bone calcium levels. A higher intake of animal proteins induces systemic acidosis by increasing the production of sulfuric acid in the body (Dawson-Hughes *et al.,* 2004). In response to the increased net endogenous acid production (NEAP), dissolution of calcium salts occurs from bones to buffer dietary-induced acid load. This increases net renal acid excretion, increased calcium excretion, and decreased renal tubular re-absorption of calcium (Kerstetter *et al.*, 2003). A cross-sectional study conducted among middle-aged and elderly women in China reported a positive correlation between urinary calcium excretion and animal protein intake (Hu *et al.,* 1993). However, in contrast to the theory suggesting the detrimental impact of animal protein on bone health is not supported by various experimental evidences. The Framingham Osteoporosis study, conducted among elderly women and men, reported that the decrease in bone mineral density was not associated with a higher intake of animal protein (Hannan *et al.,* 2000).

The Recommended Dietary Allowance (RDA) for proteins for normal Indian adults was set at 60 g/d and 55 g/d for males and females, respectively (ICMR, 2010). For the American and Canadian populations, the protein recommendations were established at 56 g/d and 46 g/d for adult males and females, respectively (USDA and HHS, 2010; IOM, 2006). The Population Reference Intake (PRI) of adult males and females was established at 0.83 g/kg/ body weight per day in Europe (EFSA, 2017).

Calcium

If we look at the mineral content of the adult human body, the most abundant mineral is calcium. Approximately, 1,200 g of calcium is present in the body of an adult human.Calcium is the major building block of the skeleton and 99 per cent of the body's calcium resides in bones and teeth. Adequate intake of calcium helps in the attainment of peak bone mass and reducing bone loss with aging. A three-year, double-blind, placebo-controlled trial conducted among prepubertal children reported a significant increase in bone mineral density with calcium supplementation (Johnston *et al.,* 1992). A meta-analysis examining the effect of calcium on bone density and fractures in postmenopausal women reported a small positive effect of calcium supplementation on bone density with a reduction in vertebral fractures (Shea *et al.,* 2002).

During pregnancy and lactation, the calcium requirements of the mother increases. The calcium absorption increases to approximately 60 per cent during the third trimester (Ritchie *et al.,* 1998). During lactation, approximately 250 mg per day of calcium is lost to breast milk (Laskey *et al.,* 1998). Increased intestinal calcium absorption, increased renal calcium conservation, and increased bone mobilization, are the physiological adaptations that occur during pregnancy and lactation to meet these increased demands (Cross *et al.,* 1995; Ritchie *et al.,* 1998). Recovery of bone calcium occurs during weaning by increasing intestinal calcium absorption and decreasing renal calcium excretion (Kalkwarf *et al.,* 1996). During the third trimester, calcium deposition in bones was estimated to be 90–120 mg per kg of foetal body weight per day (Ziegler *et al.,* 1976). Total body bone mineral density increases at a rate of about 1 per cent per year and 4 per cent per year during childhood and adolescence, respectively (Matkovic *et al.,* 1991) which indicates increased calcium requirements during these life stages. Calcium supports bone formation phase of bone re-modeling in adults. About 200 mg of calcium is removed from the adult skeleton and replaced each day (Dawson-Hughes, 2004). The rate of bone re-modeling and bone loss in older individuals is influenced by calcium intake (Dawson-Hughes, 2006). Calcium deficiency results in intrauterine growth retardation during pregnancy, rickets in childhood, bone fragility fracture during adolescence, inadequate peak bone mass in adulthood, and osteoporosis in old age (Chan *et al.,* 1984; Goulding *et al.,*

1998; Matkovic *et al.,* 1979).

The calcium recommendations for Indians were set at 800 mg/d for adolescents, 600 mg/d for adults, and 1200 mg/d during pregnancy and lactation (ICMR, 2010). For American and Canadian populations, the RDA for calcium was higher as compared to Indians and established at 1300 mg/d for adolescents, 1000 mg/d for adults, and 1200 mg/d for 51 y and older (USDA and HHS, 2010; IOM, 2006). The Population Reference Intake of calcium in Europe for adolescents, 18-24 y, and ≥25 y adults were 1150 mg/d, 1000 mg/d, and 950 mg/d, respectively (EFSA, 2017).

Phosphorus

Phosphorus is the second most abundant mineral in the human body. On average, a 70-kg adult human contains about 630 g of phosphorus (Heaney and Graeff-Armas, 2018). Phosphorus is an essential bone-forming element and occurs as a component of hydroxyapatite. Approximately 85 per cent of the body's phosphorus is found in bone. Phosphorus is mainly involved in the mineralization of bones with calcium during the process of ossification. It is also required for the functioning of bone-forming cells, osteoblasts (Heaney, 2001; 2004). Phosphorus and calcium metabolism are closely related. The three endocrine hormones- parathyroid hormone, vitamin D, and fibroblast growth factor-23 (FGF-23), regulates the homeostasis of calcium and phosphorus. Parathyroid hormone is released in response to the slight drop in blood calcium concentration which results in a decrease in urinary calcium excretion and an increase in urinary phosphorus excretion. The parathyroid hormone also promotes the release of calcium and phosphorus from the bones and restores the serum calcium concentrations. The parathyroid hormone promotes the synthesis of the active form of vitamin D in the kidney which in turn increases the intestinal absorption of calcium and phosphorus. Osteocytes secrete fibroblast growth factor-23 (FGF-23) in response to hyperphosphatemia. Fibroblast growth factor-23 inhibits the synthesis of the active form of vitamin D and increases urinary phosphorus excretion (O'Brien *et al.,* 2014).

High phosphorus intake may result in increased synthesis of parathyroid hormone and fibroblast growth factor-23 and impairment of osteoblasts functions. This increases the risk of extraskeletal calcification, increased rate of bone resorption, and renal osteodystrophy (Lamberg-Allardt *et al.,* 2010). But these effects have only been observed on diets that were high in phosphorus and low in calcium. Calvo *et al.,* 1988 studied the effect of high phosphorus and low calcium diets on serum parathyroid hormone among young adults aged 18-25 years. The study revealed that the diet resulted in elevated serum parathyroid hormone levels, and changes in mineral metabolism in young adults. Little evidence is available on the effect of phosphorus deficiency on osteoporosis, however inadequate phosphorus intake results in impairment in bone mineralization (Palacios, 2006).

The recommended intake of phosphorus for Indians was set at 800 mg/d for adolescents and 600 mg/d for adults (ICMR, 2010). The RDA for phosphorus was set at a level of 1250 mg/d for adolescents and 700 mg/d for adults among American and Canadian populations (USDA and HHS, 2010; IOM, 2006). In Europe, the Adequate Intake (AI) for phosphorus for adolescents and adults was set at 640 mg/d and 550 mg/d, respectively (EFSA, 2017).

Magnesium

The adult human body contains 24 g of magnesium (Jahnen-Dechent and Ketteler, 2012), of which about 50-60 per cent is located in bones. Magnesium is important in bone crystal growth and stabilization. Magnesium regulates the parathyroid hormone-vitamin D-fibroblast growth factor-23 axis and thus serves the role in mineral metabolism (Prentice, 2004). The deficiency of magnesium alters the parathyroid hormone and vitamin D synthesis. It also results in impairment in osteoblastic and osteoclastic activity, osteopenia, and bone fragility (Fatemi *et al.,* 1991). A cross-sectional study reported a positive association between magnesium intake and vitamin D status (Deng *et al*., 2013). A meta-analysis of observational studies reported a positive correlation between magnesium intake and femoral neck and total hip bone mineral density (Farsinejad-Marj *et al.,* 2016).
For Indians, the RDA for magnesium was set at 340 mg/d and 310 mg/d for adult males and females, respectively (ICMR, 2010). The RDA for American and Canadian population was established at 310 and 400 mg/d, 19–30y, and 320 and 420 mg/d, >30 y, in females and males, respectively (USDA and HHS, 2010; IOM, 2006). The Adequate Intake (AI) for magnesium in Europe was set at a level of 350 mg/d and 300 mg/d for adult males and females, respectively (EFSA, 2017).

Potassium

The total potassium content in the adult human body is about 135 g. (Navarro and Vaquero, 2003). Potassium-rich foods promote the alkaline environment and reduce the release of skeletal salts to buffer the endogenous acid production. High potassium intake preserves the calcium of bones and may help to prevent osteoporosis. Supplementation of potassium bicarbonate to post-menopausal women has been shown to neutralize net endogenous acid and a decrease in urinary calcium excretion (Wood, 1994). Thus, balancing the protein intake with the alkalinizing effect of fruits and vegetables

could protect from the detrimental effect of excess protein intake on bone health.

The recommended intake of potassium for Indians was set at 3750 mg/d and 3225 mg/d for adult males and females, respectively (ICMR, 2010). The potassium recommendations for American and Canadian population was established at 4700 mg/d for ages 19 and older (USDA and HHS, 2010; IOM, 2006). In Europe, the Adequate Intake (AI) for potassium was set at a level of 3500 mg/d for adults (EFSA, 2017).

Sodium

The mean sodium content in the adult male is about 92 g, of which ~35 g is located in the skeleton (Strazzullo, 2014). High sodium intake increases urinary calcium excretion. Sodium competes with calcium for renal tubular reabsorption. Sodium also increases parathyroid hormone secretion and thus leading to bone resorption. A study conducted among postmenopausal women to investigate the adaptive mechanisms in response to changes in salt and calcium intake found a significant increase in urinary calcium excretion with the moderately high salt intake (Teucher *et al.,* 2008). Another study reported an increase in bone turnover markers with high dietary sodium intake in postmenopausal women with low bone mass (Park *et al*., 2015). Most of the studies have reported the deleterious effect of excess sodium on bone health with low calcium intake. Thus, increasing calcium intake while reducing sodium intake will be a good strategy to support bone health.

The sodium recommendation for Indian adult male and female was set at 2092 mg/d and 1902 mg/d, respectively (ICMR, 2010). The dietary guidelines for American and Canadian populations recommend reducing daily sodium intake to less than 2300 mg/d (USDA and HHS, 2010; IOM, 2006). Sodium intake of 2 g/d is recommended as safe and adequate intake by the European Food Safety Authority, 2017.

Trace Elements

Trace elements are the minor building components of the skeleton and play an important functional role in bone metabolism. The microminerals are needed in trace amounts, the body contains approximately 2 g zinc and 0.1 g copper (Bost *et al.,* 2016; WHO and FAO, 2005). On average, 1-3 g of iron is stored in an adult body (Abbaspour *et al.,* 2014). The selenium and manganese content of normal adult human ranges from 3 to 20 mg and 10 to 20 mg, respectively (Kieliszek, 2019; Nielsen, 2012). The total silicon content in a man weighing 70-kg ranges from 0.14 to 0.7 g (Sripanyakorn *et al.,* 2005).

Fluoride is deposited in the skeleton during the growth phase. Fluoride promotes bone formation and inhibits the dissolution of bone crystal. Copper is involved in the synthesis of bone matrix protein. Copper serves as a cofactor for the enzyme, lysyl oxidase, which is involved in the cross-linking of collagen. Collagen along with non-collagenous proteins, constitute the organic matrix of bone. Zinc serves as a cofactor for numerous enzymes involved in bone metabolism. Zinc stimulates the activity of bone-forming cells, osteoblasts. Zinc promotes the synthesis of collagen, bone proteins, and insulin like growth factor-1. Manganese serves as a cofactor for several enzymes in bone tissue. Manganese promotes bone matrix formation, through its role in the biosynthesis of mucopolysaccharides. Iron also serves as a cofactor for enzymes involved in bone metabolisms such as prolyl hydroxylase, lysyl hydroxylase, and 25-hydroxy cholecalciferol hydroxylase. Boron, silicon, and strontium have a positive effect on bone mineralization. Excess of fluoride may cause skeletal fluorosis; however, the adverse effects of trace mineral toxicity on bones are generally not reported (Table 2).

VITAMINS FOR BONE HEALTH

Vitamin D

Vitamin D is essential for bone development and maintenance. Vitamin D assists in intestinal calcium absorption by stimulating the synthesis of calcium-binding protein (DeLuca, 2004). It also stimulates osteoclast activity and enhances the expression of alkaline phosphatase, osteopontin, and osteocalcin (Holick, 2004). Vitamin D decreases the expression of the parathyroid hormone gene (Dawson-Hughes, 2004). Vitamin D also regulates phosphorus homeostasis. Deficiency of vitamin D causes rickets in infants and children, osteomalacia in adults, and osteoporosis in elderly individuals. Vitamin D deficiency in pregnancy and infancy has adverse health outcomes such as low birth weight, neonatal hypocalcemia, poor postnatal growth, bone fragility, and hyperparathyroidism (Mulligan *et al.,* 2010). A global study conducted among postmenopausal women showed a significant positive relation between 25-hydroxy cholecalciferol and bone mineral density in the trochanteric area of the hip with a threshold below 50 nmol/l (Kuchuk *et al.,* 2009). A recent clinical trial reported significantly lower radial bone mineral density with daily supplementation of high doses of vitamin D among healthy adults (Burt *et al.,* 2019). Thus, both less and higher intake of vitamin D has adverse effects on bone health.

Indian Council of Medical Research (ICMR) 2010, recommends a daily supplement of 400 IU/day of vitamin D for Indians under situations of minimal exposure to sunlight. The RDA for vitamin D for all age groups was established at 15 µg/d for American and Canadian

populations (USDA and HHS, 2010; IOM, 2006). In Europe, the Adequate Intake (AI) for vitamin D was set at a level of 10 µg/d for infants and 15 µg/d for ages 1 and older (EFSA, 2017).

Vitamin A

Vitamin A is essential for the growth and differentiation of all the cells in the body. Vitamin A is required for the activity of osteoblasts and osteoclasts as they have the nuclear receptor for retinoic acid (Palacios, 2006). Excessive intake of vitamin A through supplements has negative effects on bone health. Skeletal effects of hypervitaminosis include suppression of osteoblasts activity, decreased rate of bone formation, stimulation of osteoclasts formation, increase in bone resorption, fracture risk, hypercalcemia, bone pain, and hyperostosis (Barker and Blumsohn, 2003; Hathcock *et al.,* 1990). A prospective study assessed vitamin A intake of 72,337 postmenopausal women and found a positive association between hip fracture and high retinol intake (Feskanich *et al.,* 2002). However, a cohort study conducted among 75,747 women found no association between vitamin A or retinol intake and the risk of hip or total fractures among postmenopausal women (Caire-Juvera *et al.,* 2009).

The RDA for vitamin A for Indian adults was set at a level of 600 µg of retinol and 4800 µg of β-carotene per day (ICMR, 2010). For American and Canadian populations, 900 µg/d and 700 µg/d of Retinol Activity Equivalents (RAE) is recommended for adult males and females, respectively (USDA and HHS, 2010; IOM, 2006). The Population Reference Intake of vitamin A in Europe for adult males and females was established at 750 µg RE/d and 650 µg RE/d, respectively (EFSA, 2017).

Vitamin K

Vitamin K serves as a cofactor for the γ-carboxylation of specific glutamic acid residues in certain proteins which confers mineral binding properties (Furie & Furie, 1997). Vitamin K is required for the synthesis of two bone proteins, osteocalcin and matrix Gla protein, and the synthesis is regulated by vitamin D. Osteocalcin is the non-collagenous protein of bone produced by osteoblasts during bone matrix formation. Vitamin K-dependent γ-carboxylation of three glutamic acid residues in osteocalcin provides hydroxyapatite binding capacity (Price, 1989). Matrix Gla protein is present in bones and cartilage and it binds to both organic and mineral components of bone (Booth and Charette, 2004). A cross-sectional study reported a positive association between vitamin K intake and bone mineral density in women (Booth *et al.,* 2003). However, another study found no effect of Vitamin K supplementation on bone mineral density in older men and women (Booth *et al.,* 2008).

The recommended intake of 55 µg of vitamin K per day for Indians was based upon WHO guidelines as limited data are available on the content of this vitamin in foods of Indian origin (ICMR, 2010). For American and Canadian populations, 90 µg/d and 120 µg/d of vitamin K for adult females and males are recommended as Adequate Intake, respectively (USDA and HHS, 2010; IOM, 2006). The Adequate Intake of vitamin K for Europeans was set at a level of 70 µg/d for adults (EFSA, 2017).

Vitamin C

Vitamin C is required for the cross-linking of collagen fibers in the bone as it serves as a cofactor in the hydroxylation of lysine and proline. Vitamin C also stimulates the activity of alkaline phosphatase, a marker for osteoblast formation (Palacios, 2006). A population-based study reported the beneficial effect of vitamin C supplementation on bone mineral density among postmenopausal women (Morton *et al.,* 2001). Higher dietary vitamin C intake was found to be associated with lower bone mineral density loss among elderly men participants from the Framingham Osteoporosis Study (Sahni *et al.,* 2008).

For Indian adults, 40 mg/d of vitamin C intake is recommended as RDA (ICMR, 2010). As per the American and Canadian dietary guidelines, the RDA for vitamin C was set at a level of 90 mg/d for adult males and 75 mg/d for adult females (USDA and HHS, 2010; IOM, 2006). The Population Reference vitamin C intake in Europe for adult males and females was established at 110 mg/d and 95 mg/d, respectively (EFSA, 2017).

OTHER DIETARY CONSTITUENTS

Essential Fatty Acids

The essential fatty acids have been reported to contribute to bone metabolism. A 2012 systematic review examined the effect of omega 3 fatty acids on osteoporosis from ten randomized controlled trials. Four studies reported significantly favourable effects of omega 3 fatty acids on bone mineral density or bone turnover markers (Orchard *et al.,* 2012). A cross-sectional study conducted among 1865 female subjects, aged 20-79 years old, reported a positive association between long-chain omega-3 polyunsaturated fatty acid intake and bone mineral density among normal and osteopenic women (Lavado-Garcva *et al.,* 2018). A pilot study conducted among elderly patients reported beneficial effects of dietary supplementation of gamma-linolenic acid and eicosapentaenoic acid along with calcium on bone mineral density (Kruger *et al.,* 1998).

Phytoestrogens

Phytoestrogens are the plant chemicals that mimic the effect of estrogen and its metabolites. Isoflavones, lignans, and coumestans are the three main classes of phytoestrogens. Phytoestrogens may exhibit antagonist or agonist effect depending upon endogenous estrogen levels (Fitzpatrick, 2004). A 2016 systematic review determined the effect of phytoestrogens on bone mineral density in postmenopausal women. The results showed a beneficial effect of phytoestrogens on bone health in menopausal women (Abdi *et al.,* 2016). A cross-sectional study conducted among 650 southern Chinese women, aged 19-86 years, found a positive association between high dietary isoflavone intake and bone mineral density in postmenopausal women. However, no such association was reported between dietary phytoestrogen intake and bone mineral density in premenopausal women (Mei *et al.,* 2001).

CONCLUSION

Nutrition plays a critical role in the development and maintenance of bones throughout life. During the process of bone formation, calcium, magnesium, and phosphorus are required for bone mineralization. Potassium promotes alkalinity and prevents bone loss. Excess intake of sodium negatively affects bone calcium content. Vitamin D regulates the calcium and phosphorus metabolism and also the synthesis of bone matrix proteins. Bone matrix proteins, collagen, and osteocalcin, synthesis is regulated by vitamin C and vitamin K, respectively. Differentiation of bone cells, osteoblasts, and osteoclasts is regulated by vitamin A. However, excess intake of vitamin A supplements increases the risk of bone fractures. Trace elements mainly serve as a cofactor for several enzymes in bone tissue. Trace elements such as fluoride, zinc, boron, copper, manganese, selenium, silicon, iron, and strontium, positively affect bone mineral balance. The favourable effect of various dietary constituents such as essential fatty acids and phytoestrogens on bone mineral density have been reported in the literature. A balanced diet with adequate intake of proteins, calcium, vitamin D, plenty of fresh fruits and vegetables are required for optimal bone health. The role of trace elements, phytoestrogens, essential fatty acids, vitamin K supplementation, and other non-traditional nutrients needs to be further studied to assess their appropriate role in bone health.

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