REVIEW ARTICLE

A Narrative Review on Determinants of Bone Health in Premenopausal Women: Interplay of Hormones, Nutrition, Lifestyle, and Medical Conditions

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Abstract

Bone health of premenopausal women has become an important topic due to the rising recognition of bone-related problems and early risk of osteoporosis in this age group. It is determined by several interconnected factors, including hormonal and nutritional factors, and the presence of chronic diseases. This review aims to synthesize the evidence from various studies, addressing factors that affect bone health in this population. Estrogen and progesterone play a crucial role in determining bone health, and women with low levels of serum estradiol are more prone to low bone mineral density (BMD) and osteoporosis risk. Ovulatory disturbances during the menstrual cycle lead to an estrogen–progesterone imbalance. Physical activity is consistently linked to improved skeletal integrity, whereas excessive alcohol consumption and cigarette smoking result in lower bone mass. Medical conditions such as diabetes mellitus, anorexia nervosa, hyperthyroidism, premature ovarian insufficiency, and celiac disease significantly reduce BMD. Findings show that higher protein intake poses no harm to bone health, although its benefits are inconclusive, while contradicting evidence exists regarding the association between Vitamin D and bone health in premenopausal women, and there is inconsistent evidence on the effect of calcium and Vitamin D supplementation. Any disruptions in these factors can limit peak bone mass acquisition or contribute to accelerated bone loss. Identifying and addressing these complex and sometimes contradicting factors is important for developing strategies that support bone health and reduce the risk of fracture in young women.

Key words: Premenopausal women, bone health, osteoporosis, bone mineral density, hormonal influence, nutrition, lifestyle

INTRODUCTION

Osteoporosis is a worldwide health concern characterized by diminished bone density and structural deterioration, which results in weak bones and heightened fracture risk.[1] Decreased bone mineral density (BMD) is a significant factor in the development of osteoporosis and fragility fractures.[2] Osteoporosis results from an impaired balance in bone remodeling, which leads to a reduction in bone strength. Bones lose strength due to disruption of bone architecture, thus increasing fracture susceptibility. Bone loss gradually progresses over time and can occur without any evident symptoms. An imbalance between bone resorption and formation during the remodeling process leads to the development of osteoporosis.[3]

In postmenopausal women, osteoporosis is clearly defined. Primary osteoporosis is a prevalent condition in older postmenopausal women, which is brought about by rapid natural bone loss during menopause. Elderly people usually experience a predicted age-related reduction in bone formation, together with the cumulative impact of an unhealthy lifestyle, which causes idiopathic osteoporosis,

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Received: 08-09-2025
Revised: 06-05-2026
Accepted: 20-05-2026

but this is not the case for premenopausal women. Low bone mass and idiopathic osteoporosis are rare in younger women.[4] In premenopausal women, low BMD may suggest inadequate attainment of peak bone mass, which is defined as the maximum amount of bone tissue accrued at skeletal maturity.[5] It is a crucial factor in determining osteoporosis and the risk of fractures. Several interrelated factors are believed to influence bone mass accumulation and bone health. Various nutrients and dietary factors are believed to affect bone health, including macronutrients, micronutrients, and various bioactive compounds. Bone mass is influenced by a variety of factors, which can be categorized into modifiable factors, including hormonal levels, physical activity, smoking, alcohol consumption, and dietary factors, and non-modifiable factors such as gender, age, genetic makeup, body size, and ethnicity. All these factors interact and impact both peak bone mass acquisition and post-maturity bone loss.[6]

Low BMD in premenopausal women may also result from progressive bone loss occurring after peak bone mass has been reached. Menstrual status plays an important role in achieving optimal peak bone mass and also contributes to bone loss in women before menopause. In women with normal reproductive function, subclinical reductions in gonadal steroid levels may be linked to lower peak mass and continued bone loss. Follicle-stimulating hormone levels above 20 mIU/mL are linked with both elevated bone turnover markers and accelerated bone loss in perimenopausal women.[7]

Although several studies have examined individual factors affecting bone health, the interplay of these factors in premenopausal women is not fully understood. Moreover, variability in findings across studies highlights the need for a consolidated perspective. This review aims to specifically highlight the factors influencing the bone health of premenopausal women that could lead to low BMD and osteoporosis, after providing a concise overview of bone physiology and the remodeling cycle.

METHODOLOGY

A literature search was carried out using Google Scholar, PubMed, and ResearchGate to identify studies related to bone health in premenopausal women. Keywords covering BMD, hormonal factors, nutrition, lifestyle, and osteoporosis were used to guide the search. Relevant studies of different types were reviewed and summarized to provide a comprehensive narrative on the factors influencing bone health in this population.

BONE PHYSIOLOGY

Bone is organized into cortical and trabecular forms, each exhibiting distinct structural, compositional, and functional characteristics. Cortical bone with a high degree of calcification plays a key role in maintaining structural integrity and offering protection. Trabecular bone has lower mineral density and higher surface area, making it more metabolically active. Bone mass grows from about 80 g at the time of birth to 3000 g by the age of 25, when peak bone mass is reached. A balance between the collagen matrix and mineral content is essential for bone strength, and alterations in either component can impair its mechanical properties and structural integrity. When the collagen is abnormal, bones become less tough, and susceptibility to fractures increases. Inadequate mineralization decreases bone stiffness, and while over-mineralization increases brittleness, both conditions increase the risk of fractures.[8]

Bones are dynamic in nature. They remain metabolically active and adapt to the physiological demands across the lifespan. This ongoing skeletal transformation is referred to as bone remodeling. It is a process of skeletal renewal that helps keep bones strong and maintains the levels of calcium and phosphorus in the body. It involves the removal of old or damaged bone through resorption, followed by the formation of new bone tissue.[9] Bone remodeling is primarily driven by osteoclasts and osteoblasts. However, osteocytes are also involved in coordinating the process. Osteoclasts are responsible for bone resorption, osteoblasts for bone formation, and osteocytes function as mechano-sensors that determine if bone remodeling is required and coordinate the action of osteoclasts and osteoblasts.[10]

The bone remodeling cycle follows a well-regulated, stereotyped sequence of five overlapping stages, namely activation, resorption, reversal, formation, and termination [Figure 1].

Bone remodeling begins with an activation phase, which depends on the regulatory inputs from local and systemic factors acting on osteoblast-lineage mesenchymal cells.

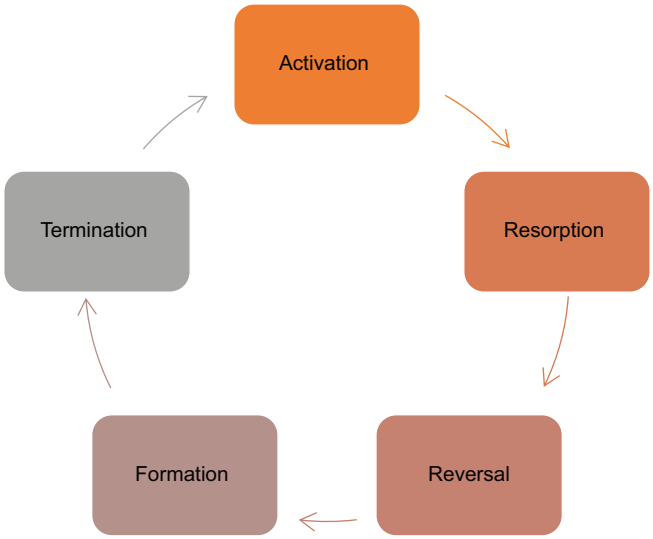

Figure 1: Bone remodeling cycle

Through interactions with hematopoietic precursors, these cells facilitate the formation of osteoclasts, initiating the resorption phase of bone remodeling.[11] Termination of the resorption phase is mediated by apoptosis of osteoclasts, preventing excessive bone resorption.[12] Following resorption, a reversal phase occurs, when single-nuclear cells occupy the surface of the bone. These cells could conclude bone resorption and generate indications that initiate the subsequent formation phase. Finally, mesenchymal cells divide into active osteoblasts in successive waves, which produce and mineralize new bone matrix in the formation phase.[11] Following the completion of mineralization, osteoblasts undergo apoptosis, transform into bone-lining cells, or differentiate into osteocytes within the mineralized matrix. Osteocytes signal the termination of the remodeling process by releasing osteogenesis inhibitors, particularly Wnt-signaling antagonists such as sclerostin.[13]

Hormones, particularly estrogen and progesterone, regulate osteoclast and osteoblast activity during bone remodeling, while nutritional factors, including calcium and Vitamin D, are essential for proper mineralization and efficient remodeling. Lifestyle factors such as physical activity and smoking also influence the efficiency and balance of this process. The balance in the remodeling cycle is central to sustaining bone strength and quality. Any disturbances in the process can compromise bone health and increase susceptibility to low BMD and osteoporosis. In premenopausal women, this balance is especially important, as this life phase corresponds to the consolidation and preservation of the peak bone mass. Any imbalance in tightly coupled activities of bone cells can therefore make the skeleton vulnerable to low bone mass and fragility. The process of remodeling is regulated by multiple factors, both intrinsic and extrinsic. A comprehensive understanding of these factors is critical for identifying the risk factors and developing effective preventive strategies. The following section, therefore, will focus on various factors that influence the bone health of premenopausal women.

FACTORS INFLUENCING BONE HEALTH IN PREMENOPAUSAL WOMEN

Bone health during the premenopausal period is shaped by a complex interplay of biological, nutritional, lifestyle, and medical factors. Adequate intake of calcium, Vitamin D, and protein is essential for maintaining BMD mineral density, while hormonal regulation, particularly estrogen and progesterone, plays a pivotal role in bone remodeling. Lifestyle behaviors such as physical activity, smoking, alcohol consumption, and stress management further contribute to skeletal strength. In addition, underlying medical conditions, genetic predisposition, and emerging biomarkers influence the risk of early bone fragility. Understanding these determinants is critical for optimizing peak bone mass and preventing osteoporosis later in life.

Hormonal factors

Estrogen helps maintain bone by reducing osteoclast-mediated bone resorption, and progestogens act by binding to specific progesterone receptors,[14] promoting the formation of new bone. When present at physiological levels that are either moderate or high, estradiol reduces the process of bone resorption[15] by the synthesis of osteoprotegerin in osteoblasts, higher absorption of calcium in the intestines, along with additional mechanisms, therefore preventing bone loss.[16] Lower estradiol levels were associated with bone mass differences in healthy women during the maximal bone accumulation period.[17] Recent evidence has reinforced this association through a cross-sectional study of 270 premenopausal women from the health workers cohort study. Analysis of linear regression indicated that estradiol levels, Vitamin D intake, physical activity, and body mass index (BMI) were positively associated with BMD. The likelihood of low BMD was significantly higher in premenopausal women with reduced serum estradiol levels.[18] Progesterone encourages the production of new osteoblasts from mesenchymal stem cells and further promotes osteoblasts to produce additional bone matrix. It is the hormone that promotes bone growth in women.[19]

Research from the two separate studies explored the relationship between serum insulin-like growth factor 1 (IGF-1) and bone health in premenopausal women, but their findings differ. In a 2010 study,[20] healthy premenopausal women aged 20–50 years were examined. Hip BMD, IGF-1, bone turnover markers, and mineral levels declined with age while parathyroid hormone (PTH) increased. IGF-1 showed a positive association with minerals, bone turnover markers, and BMD and negative correlations with age, BMI, and PTH. After adjusting IGF-1 levels for age and BMI, weak but statistically significant correlations with serum PTH, N-terminal propeptide of type 1 procollagen (P1NP), and bone alkaline phosphatase (AP) remained. Overall, age-related decline in IGF-1 levels was linked to a gradual reduction in bone formation markers in premenopausal women. In contrast to this, a 2022 study[21] in premenopausal women with idiopathic osteoporosis reported that increased IGF-1 levels were correlated with decreased bone formation, greater body fat, and reduced BMD response to teriparatide treatment. Together, the findings of the study highlighted that these unexpected associations between serum IGF-1, bone, and fat might play a role in the development of idiopathic osteoporosis in premenopausal women.

The hormonal fluctuations that occur throughout the menstrual cycle also influence skeletal metabolism with alterations in bone turnover markers. In a study conducted by Gass *et al*.,[22] 55 premenopausal women were examined for bone turnover marker profiles during the menstrual cycle. The findings indicated that serum C-terminal telopeptide of type-I collagen (sCTX) was significantly higher in the early-mid follicular phase compared to the mid-late luteal phase. Urinary N- terminal telopeptide of type I collagen showed a similar pattern to sCTX, but it was less significant. P1NP levels were

significantly reduced during the follicular phase compared to the luteal phase. No significant variation was observed in levels of osteocalcin or bone-specific AP. Furthermore, subclinical ovulatory disturbances, characterized by anovulation or short luteal phases within normal menstrual cycles, result in lower progesterone-to-estrogen levels. The meta-analysis of prospective studies assessed the relationship between ovulatory disturbances and BMD changes in healthy premenopausal women.[23] Data suggested that women experiencing more frequent ovulatory disturbances showed a greater decline in spine BMD, and they lost more mass, highlighting the importance of unrecognized estrogen-progesterone imbalances.

The adrenal stress hormone, cortisol, which is found in both men and women, is important for human existence. Cortisol, at high amounts, induces bone resorption by preventing absorption of calcium and central inhibition of gonadal steroid synthesis, resulting in decreased estradiol levels, and it also prevents the development of bones by preventing the effects of progesterone and testosterone on osteoblasts.[16]

An overview of studies of hormonal influence on bone health in premenopausal women is summarized in Figure 2.

Nutritional factors

Calcium

Recommendations for the prevention of fragility fractures include a balanced diet providing optimal protein and calcium, along with sufficient Vitamin D and active participation in weight-bearing physical activity. Dairy products are a rich source of both protein and calcium. The risk of hip fractures reduces in those consuming dairy products, particularly fermented dairy products.[24] While prior studies indicated a link between calcium, Vitamin D, and protein and BMD, recent evidence suggests no direct relationship.

Bailey *et al*.[25] aimed to evaluate the change in bone density at the lumbar spine and hip region, and fracture risk in relation to calcium supplement use, among participants in the study of Women's Health Across the Nation. In fully adjusted models, calcium supplement was linked to reduced annual BMD loss at the femoral neck for the total cohort. The role of calcium supplementation in preventing BMD loss was observed in premenopausal women, and no notable change was observed in women who were in early perimenopause. Méndez-Sánchez *et al*.[26] assessed the potential benefits and risks of supplementing with calcium and Vitamin D, either separately or in combination, on BMD, fracture incidence, and adverse effects in healthy premenopausal women compared with placebo. Results of the study provided no evidence to support the combined and isolated administration of calcium and Vitamin D in healthy premenopausal women as a health strategy to increase total hip or lumbar spine BMD.

Vitamin D

Adami *et al*.[27] indicated that inadequate Vitamin D was associated with lower spinal BMD and higher bone AP. Dar *et al*.[28] conducted a study to determine bone health status in

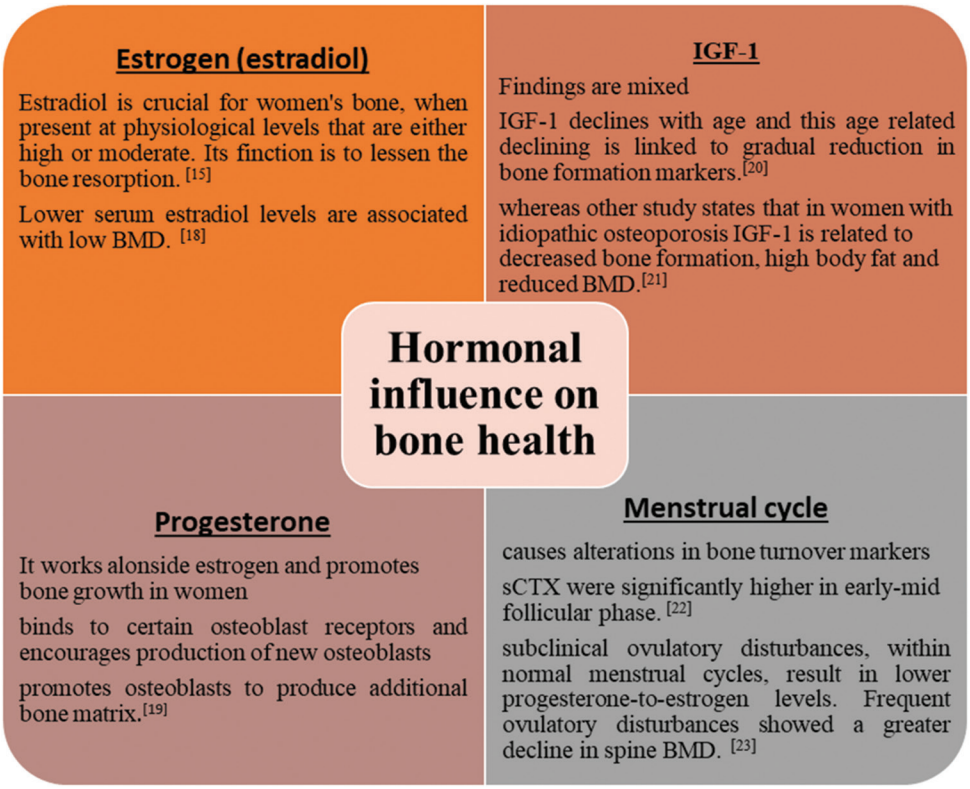

Figure 2: Overview of hormonal influence on bone health of premenopausal women

healthy females by analyzing biochemical markers of bone metabolism, specifically N-telopeptide of type-1 collagen, 25-hydroxyvitamin D, and plasma intact PTH. The results highlighted that elevated bone turnover and prevalent Vitamin D deficiency in apparently healthy premenopausal women predispose them to increased risk of developing osteoporosis.

On the other hand, Zareef *et al*.[29] evaluated the adequacy of Vitamin D intake among Saudi women relative to estimated average requirements, to identify major dietary sources and potential determinants of intake, and to evaluate bone health in relation to calcium and Vitamin D consumption and BMD, in 257 premenopausal women (20–50 years). Calcium intake was positively linked to lumbar spine BMD after adjusting for BMI and energy intake. There was no statistical variation in Vitamin D intake between women with low bone mass and those with normal bone mass. In a recent Mendelian randomization analysis, no causal association between 25-hydroxyvitamin D levels and BMD at different skeletal sites was found across different stages of life. No difference was observed between the overall and specific effects of Vitamin D on BMD after BMI adjustment. The study found no causal effect of genetically predicted Vitamin D on BMD.[30]

Protein

Various studies suggest that higher protein intake may be associated with reduced fracture risk when calcium intake is adequate. Beasley *et al*.[31] examined the link between baseline dietary protein and BMD while assessing the influence of protein source and participant characteristics using both cross-sectional and longitudinal analysis. Longitudinal findings found no adverse effect of higher protein intake in premenopausal women, whereas cross-sectional data revealed that lower protein intake is linked to reduced BMD. Darling *et al*.[32] found no clear association between protein intake and the relative risk of osteoporosis after accounting for other influencing factors. Increasing protein intake provided minimal benefits to bone health in healthy adults but also showed no harm. Taken together, these studies imply that higher protein poses no harm to bone health, although its beneficial impact remains inconclusive.

Differences in reported effects of calcium, Vitamin D, and protein on bone health in premenopausal women can be explained by variations in study design, participant characteristics, baseline nutrient levels, and nutrient interactions. These factors account for the inconsistent findings observed across studies.

Antioxidants

One of the primary causes of bone loss is oxidative stress. Vitamin E, a popular antioxidant, can prevent osteoporosis progression. A favorable correlation was found between BMD and α-Tocopherol consumption in premenopausal women of Japan. Increasing the dietary intake of Vitamin E can help preserve bone mass in these women.[33] Another study looked into the relationship between pre and postmenopausal combined dietary intake of antioxidants and risk of osteoporosis.[34] From the study, it was found that in postmenopausal women, the composite dietary antioxidant index (CDAI) was inversely related to the risk of osteoporosis, suggesting that osteoporosis risk can be reduced in women by consuming these antioxidants. Similar conclusions were drawn by Liu *et al*.[35] In their study, 2023, they reported a favorable relationship between CDAI and BMD and a lower risk of adult osteoporosis. The relationship between estimated BMD and alpha-tocopherol was examined using Mendelian randomization. Genetically determined α-Tocopherol did not correlate with the risk of fracture. The study provided compelling evidence of a causal relationship between higher BMD and circulating α-Tocopherol.[36]

Lifestyle factors

Physical activity

Physical activity plays a significant role in determining bone mass.[37] A cohort study including 530 healthy premenopausal women was conducted, and a significant association between physical activity levels and bone formation markers – osteocalcin and P1NP – was observed, but no association of physical activity with serum C-telopeptide of type-1 collagen was found. Following a 1-month exercise intervention, serum osteocalcin levels and P1NP increased by approximately 25% in the active group depicting that even the modest increase in physical activity can significantly influence bone formation biomarkers.[38] Another study was conducted that aimed to compare bone mass and the effects of physical activity in premenopausal women with rheumatoid arthritis versus healthy counterparts.[39] The study included 71 patients with rheumatoid arthritis and 29 healthy premenopausal women. Logistic regression identified that a sedentary lifestyle was associated with increased risk of osteopenia, while the risk of osteopenia was reduced by 50% in those who were engaged in moderate physical activity. Low body weight and a sedentary lifestyle both contribute to bone loss, whereas regular physical activity reduces its progression. Recent data show that middle-aged premenopausal female football and volleyball players had higher bone mineral density of the lumbar spine and femoral neck in comparison to those who do not exercise. The football group showed the highest serum 25-OHD levels, significantly exceeding both the volleyball and the non-exercise group.[40] Overall, weight-bearing and resistance exercises, such as walking, football, and volleyball, help improve BMD.

Alcohol consumption

Excessive intake of alcohol adversely impacts bone metabolism and contributes to reduced bone mass, which is a key factor in the development of osteoporosis. The recent study[41] highlighted a potential impact of alcohol use

disorder on bone health in young to middle-aged women, through Vitamin D deficiency and elevated bone resorption markers. While the comprehensive nutritional assessments are needed, the study could confirm that there can be an underrecognized impact of alcohol use disorder on the bone health of these women and should be considered at high risk of osteoporosis, irrespective of age. Another study was carried out to quantitatively analyze the dose-response relationship between alcohol consumption levels and changes in BMD as well as risk of osteoporotic fractures.[42] In a total of 11 studies, comprising 46916 individuals assessed for BMD, and eight studies with 240871 individuals focused on the fracture risk. The findings of the study indicated a clear association between higher levels of alcohol drinking and elevated osteoporotic hip fracture risk. Conversely, low to moderate alcohol intake was linked to greater BMD in certain regions, suggesting a non-linear relationship. However, the benefits of low alcohol consumption remain inconclusive, and the study indicated that there is a potential need to clarify its role in bone health.

Smoking

Tobacco smoking disrupts bone turnover, resulting in lower bone mass and raising the likelihood of osteoporosis and fractures. Tobacco smoke affects bone mass indirectly through its effects on body weight, alterations in the PTH-vitamin D axis, adrenal and sex hormones, and increased oxidative stress within bone tissue. In addition, tobacco smoke affects bone mass by disrupting both osteogenesis and angiogenesis. Exposure to both active and passive smoking adversely impacts bone mass.[43]

A baseline survey was conducted among a representative group of women from Japan in 1996, assessing the impact of both present and past smoking in 789 premenopausal women aged 20–40 years.[44] Using multiple regression with stepwise selection, ever-smokers showed a notable reduction in lumbar BMD after controlling for age, height, and weight. Ever-smokers had a 2.03-fold higher odds of low lumbar spine bone status, after further adjustment for parity. Women with <3 pack years of tobacco use had an odds ratio of 1.59 for lower spine bone status, rising to 2.55 in those with ≥3 pack years. The findings suggest that cumulative smoking exposure could increase the risk of reduced bone status in premenopausal women. The consistency of earlier findings was further supported by a recent study[45], which revealed that women who smoked had markedly reduced bone parameters. Physical activity and BMI were positively associated, whereas years of environmental tobacco exposure were negatively associated, with distal BMD and Bone mineral content. For distal T-scores, metabolic equivalent of task minutes per week showed a positive association, and years of active smoking and exposure to environmental tobacco smoking showed negative associations. Proximal T-scores were significantly predicted by physical activity, BMI, and age of smoking initiation in a positive direction and by active smoking and years of environmental smoking exposure in a negative direction. A high incidence of low BMD was noted despite high socio-economic status, highlighting smoking and exposure to tobacco smoke in the environment as modifiable risk factors for poor bone in young women.

Medical conditions

Diabetes mellitus

Diabetes mellitus is related to reduced quality of bone, leading to a higher risk of fractures. Both bone growth and resorption markers, serum P1NP and serum CTX, are reported to be reduced in type-2 diabetes mellitus (T2DM). The study[46] evaluated these markers as indicators of bone turnover in premenopausal women with and without type 2 diabetes and concluded that women with T2DM exhibited reduced bone turnover compared to women without diabetes. The reduction in bone turnover begins relatively early in premenopausal age and is irrespective of the duration of disease. Another study was carried out in Japan in which it was discovered that in premenopausal women with type 1 diabetes, heel BMD Z-scores were significantly lower and levels of tartrate-resistant acid phosphatase −5b were significantly higher compared with premenopausal controls, but no such differences were observed in postmenopausal women. PTH levels were considerably lower in both premenopausal and postmenopausal women with type 1 diabetes compared with controls. Thus, indicating that osteoporosis precautions should be considered in premenopausal women with type 1 diabetes as they approach menopause.[47]

Anorexia nervosa

People affected by Anorexia Nervosa commonly suffer from low BMD and a greater likelihood of fractures, primarily due to low body mass and compromised gonadal activity.[48] In an observational cohort study,[49] a total of 98 young females aged between 16 and 24 years, all within the normal to underweight range, were included. The study group comprised 30 age-matched healthy controls and 68 anorexia patients. According to the International Society for Clinical Densitometry criteria, a significantly higher proportion of anorexic patients fall below the expected range for age than controls. According to World Health Organization standards, 20% and 18% of patients displayed osteoporotic T-scores at the lumbar and femoral sites, respectively. In terms of lean body composition, significantly lower skeletal muscle mass index (SMI) and Total Lean Mass Index were observed in the anorexic population, and 24% of individuals showed SMI values that suggested pre-sarcopenia. Moreover, only SMI demonstrated a significant association with BMD at both the lumbar spine and femoral neck. Haines *et al*.[50] assessed BMD and microarchitecture in 28 women with atypical anorexia nervosa and 27 controls aged 21–46 years. Findings showed that even when body weight falls in the normal range,

women with atypical anorexia nervosa exhibit compromised bone density, structure, and strength compared to controls.

Hyperthyroidism

Hyperthyroidism is connected to lower BMD and an elevated risk of osteoporotic fractures. A study was conducted on 80 Portuguese premenopausal women, divided into overt hyperthyroidism ($n = 40$) and control ($n = 40$) groups, to assess the effects of hyperthyroidism on BMD, soft body tissue composition, trabecular bone score (TBS), and occurrence of silent vertebral fractures. After evaluation, it was found that the mean BMD, the total lean mass, and TBS in the hyperthyroidism group were significantly lower, along with a higher rate of vertebral fractures and a tendency toward low BMD.[51] Another study specifically aimed to assess BMD and bone turnover markers in premenopausal women with subclinical thyrotoxicosis (SCH) and investigated whether differences exist according to the condition's etiology.[52] This cross-sectional analysis of premenopausal women with SCH showed no significant change in hip or spine BMD, irrespective of whether the condition was endogenous or exogenous. In the short term, SCH may not adversely affect bone health in young females with adequate levels of serum 25-hydroxyvitamin D. The two studies together highlight stage-dependent skeletal effects of hyperthyroidism. Overt hyperthyroidism was associated with low mean BMD, the total lean mass, and TBS, along with a higher rate of vertebral fractures, whereas subclinical hyperthyroidism does not appear to significantly reduce BMD in the short term with adequate Vitamin D.

Premature ovarian insufficiency (POI)

POI, which is a disorder of the reproductive endocrine system in which ovarian function ceases before women turn 40, also influences the bone health of young women. Individuals with POI experience reduced BMD, primarily due to suboptimal accumulation of peak bone mass. This condition is mainly driven by hypoestrogenism and hypoandrogenemia in young women affected by POI. Moreover, reduced BMD is related to accelerated bone remodeling, specifically bone resorption.[53] In the combined research of both skeletal and body composition characteristics, it was found that women with POI are more likely to have reduced BMD and deficits in spinal trabecular structure in comparison to women of the same age without POI. These women were also vulnerable to muscle mass loss, but these changes can be reduced through estrogen replacement therapy (ERT). Consistent ERT increased appendicular lean mass while preventing reductions in bone measures.[54]

Celiac disease (CD)

Individuals with CD are more likely to have decreased BMD. Osteopenia and osteoporosis are more common in patients with reduced BMI, Basal Metabolic Rate, muscle mass, fat-free mass, and reduced body mass.[55] A comprehensive study consisting of 563 premenopausal women and men

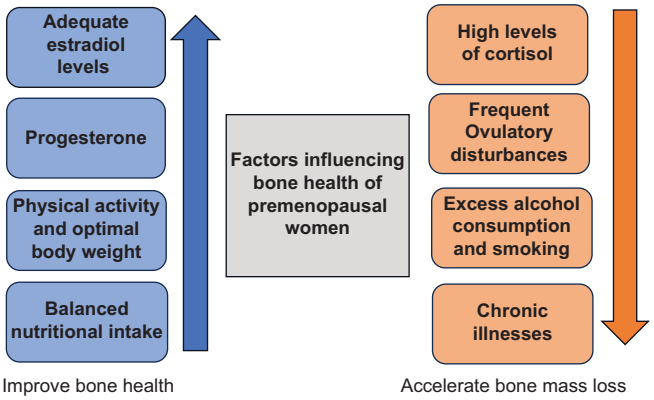

Figure 3: Factors correlated positively and negatively with the bone health of premenopausal women

estimated that 39.6% of celiac patients had osteopenia and 14.4% had osteoporosis.[56] From the nutritional point of view, in individuals with CD in its classic form, there is a decrease in the intestinal absorption of calcium, due to its binding to unabsorbed fatty acids, which leads to higher calcium losses in the feces and lower calcium excretion in the urine.[57] Metabolism of bones can be negatively influenced by other mineral and vitamin deficiencies, also. Magnesium, Vitamin B12, Vitamin D, iron, calcium, copper, and zinc are common dietary deficiencies observed in recently discovered and untreated CD patients.[58] In individuals with CD that is asymptomatic, factors associated with long-term CD (i.e., autoimmune alterations, higher cytokine production, and deficiencies in growth factors) could be primary factors responsible for the decline in BMD.[59,60]

Figure 3 presents a summary of factors that improve bone health and the factors that increase the risk of bone loss in premenopausal women.

CONCLUSION

The bone health of premenopausal women is influenced by several interconnected factors, including hormonal factors, nutritional factors, and medical conditions. Many factors, such as adequate estrogen levels, progesterone, adequate calcium intake, antioxidants, and physical activity, indicated a positive association with BMD, whereas excessive alcohol consumption, smoking, high cortisol levels, and chronic illnesses are negatively correlated. Subtle hormonal fluctuations, particularly in the menstrual cycle, can significantly influence the bone health of women. Findings related to IGF-1 remain inconsistent. Some evidence linked age-related decline in IGF-1 with a gradual reduction in bone formation markers, whereas other research points out that higher IGF-1 levels in idiopathic osteoporosis could paradoxically reduce bone formation. Apart from this, evidence for the independent impact of certain nutrients remains mixed. While some studies linked Vitamin D

insufficiency to low BMD, others did not find any direct causal association. Similarly, evidence regarding calcium and Vitamin D supplementation is also mixed, with some indicating benefits and others showing no effect. Ensuring hormonal stability, proper nutrition, and consistent physical activity helps maintain bone strength and prevent early bone loss in premenopausal women.

Summary

This review highlights the multifactorial determinants of bone health in premenopausal women, with emphasis on hormonal balance, nutritional adequacy, lifestyle behaviors, and medical conditions. Recent evidence has shown the role of estradiol, progesterone, and IGF-1 as critical biomarkers influencing bone remodeling, while nutrition, particularly calcium, Vitamin D, protein, and antioxidants, remains central to bone maintenance. Advances in imaging techniques and biochemical markers are enhancing the early detection of bone fragility, whereas digital health tools and personalized interventions are opening new avenues for prevention. The findings highlight the importance of precision approaches that integrate hormonal profiles, nutritional status, and lifestyle monitoring to design individualized strategies for optimizing peak bone mass. Future research must focus on integrating multi-omics data, refining biomarker-based diagnostics, and developing targeted interventions to mitigate osteoporosis risk in women. Ethical and social considerations, particularly regarding early screening and preventive therapies in young women, also warrant careful attention.

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Source of Support: Nil. **Conflicts of Interest:** None declared.