Online ISSN 3007-1941

Print ISSN 3007-1933

https://msrajournal.com/index.php/Journal/issue/view/15

Multidisciplinary Surgical Research Annals

https://msra.online/index.php/Journal/about

Volume 3, Issue 3 (2025)

Role of Magnesium in Bone Health

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Article Details

Keywords: Magnesium, organs of body, bone health, hypomagnesemia, Osteopenia, bone mineralization, bone mineralization

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ABSTRACT

Mg is vital as it maintains bone health and is also beneficial for other organs of body. Many emerging studies suggest its importance in preventing and managing osteoporosis in older adults and other bone related diseases. This review examines the current and the past studies which tells us the role of magnesium in bone health including its impact on bone mineral density and bone turnover. We discuss the molecular mechanism of magnesium and its influence on hormonal pathways involved in bone remodelling through diagrams. This study highlights importance of adequate magnesium intake on overall health. Moreover, magnesium supplements have been shown to be beneficial for bone related and other body organ diseases as well. The low intake of magnesium can cause hypomagnesemia, which displays a significant outcome on bone density. The toxicity of this nutrient is rare, known as hypermagnesemia which can cause severe cardiac failure and leads towards the mineralization defects and bone loss. In diet, low intake of magnesium can contribute towards many skeletal related disorders such as Osteopenia which is related with the reduced bone mineralization. Most common diseases associated with hypomagnesemia is osteocalcin (softening of bone tissue) that further causes rickets in children. Having low magnesium levels in serum can elevate the fragility of bones and it influences osteoclast and osteoblast activity. Magnesium also contributes with stimulation of vitamin D that prevents osteoarthritis (older adults).

INTRODUCTION

Magnesium is essential mineral as it the 4th ample cation in the body and the 8th prime common element in earth's crust [1]. It is the most affluence metal after potassium [2]. It is the vital intracellular cation that's crucial for many bodily functions. Most of it is stored in the bones about 60% while 39% is found in the intracellular space and about 1% inside extracellular space [3]. Mg+2 distribution in human at birth is 760 mg, at 4–5 months is 5 g, total body amount is 20–28g. About 50–65% is in bones and 34–39% in muscles, soft tissues, and organs, and about <1–2%in blood and extracellular fluids [4]. The regulation of Mg+2 shows a very crucial role in anatomical and homeostatic roles [5]. Mg+2 helps with lots of things such as forming energy, supporting the healthy function of muscles and nerves, and even managing our blood sugar levels and blood pressure. Mg+2 is also involved within building strong bones and making important molecules like DNA and RNA. It's even needed for our heart to beat regularly [6]. 28 qualified studies were performed from which 9 investigations conducted on relation about blood and Mg, 7 investigations concluded about major Mg supplementation and lastly 12 studies concluded about magnesium intake in diet [5].

Unfortunately, magnesium intake is insufficient for many individuals, even though it's essential for over 300 metabolic processes. One of its key roles is supporting bone health and function. Interestingly, blood magnesium levels don't always demonstrate the overall magnesium levels in the body, as much is reserved in bones and cells. Mg+2 is necessary in activating enzymes that produce ATP, the energy currency of our cells. Without enough magnesium, many of these vital processes can be disrupted [3]. Magnesium is also known as forgotten cation as it's availability is not generally determined in patients. Kidneys can low the excretion of the magnesium when there is risk of hypomagnesemia. Initial symptoms of magnesium deficiency include fatigue, loss of appetite, nausea and vomiting. Severe insufficiency can cause hypokalemia and hypocalcemia [4].

Bone is an incredibly unique and versatile material, known for its strength, toughness, and ability to adapt to various conditions. It is structurally dynamic and constantly changing, responding to the mechanical and physiological demands placed on it. The strength, structure, and size of bones are influenced by the stresses they encounter, and bone can adjust based on both internal and external forces, as well as factors like immobilization [7]. Bone health is crucial aspect of comprehensive health which aims at maintaining dense and strong bones throughout life. Bones are made up of collagen, calcium and bone marrow. Its working is affected through various elements including hormones, lifestyle factors, age, and genetics. Bones store calcium and phosphate [8]. Bone health is a essential component of overall well-being. The skeleton not only contributes to structural aid and defense while also playing a vital role in essential physiological functions needed in daily life. Overall, the skeleton serves three main purposes: blood formation, calcium metabolism maintenance, and structural support.

Magnesium acts as an essential cofactor for enzymes required for the synthesis of bone matrix and bone formation. In some research, men and women who have a high intake of magnesium have a low risk for fractures. A study suggests that a high intake of magnesium is correlated with a high risk of hip fractures. Magnesium absorbs calcium, which is essential for healthy bones. Magnesium helps to regulate the parathyroid hormone, which is responsible for maintaining bone density [9]. Mg+2 aids our body in utilizing calcium and vitamin D. It assists minerals, such as calcium, in hardening and strengthening your bones. Magnesium helps form bones and regulate bone strength. Many studies have shown that low magnesium levels increase the risk of osteoporosis and osteopenia. Magnesium decreases the likelihood of bone fracture and osteoporosis, particularly in postmenopausal and elderly women [10]. It supports bone development by boosting the activity of bone-forming cells. It also helps regulate the enzymes involved in bone mineralization. Magnesium also helps in regulating calcium levels in the body, which are crucial for bone density and strength. A deficiency of magnesium can lead to weaken bones, making them more prone to fractures and diseases like osteoporosis [11].

Magnesium is an essential mineral that enables numerous bodily functions, including its important role in bone health. Approximately 60% of the magnesium is stored in bones, which contributes to skeletal strength and bone mineral density. In contrast to calcium and vitamin D, magnesium's role in bone metabolism has received less attention. Among the aging population, osteoporosis and bone fractures are becoming more frequent, then it is important to study magnesium in bone health and structure. According to recent studies, taking a sufficient amount of magnesium can maintain bone health and reduce the risk of osteoporosis; however, further investigation is needed.

To review already existing studies on magnesium and its effect on bone strength and density. To understand the biological functions through which magnesium aids in osteoclast and remodeling and explore the potential role of Mg+2 in reducing osteoporosis and other bone diseases. In recent years, there has been an increasing awareness of the pathophysiology and clinical importance of Mg+2, which also provides a deep understanding of its beneficial effects on various human diseases. Magnesium deficiency has been linked to the development of vast conditions, prompting further research into the therapeutic potential of Mg+2 supplementation and its role in disease prevention and management. This review provides an overview of Mg+2 and its benefits in bone health. It's also setting the stage for a comprehensive exploration of magnesium's impact on human health.

LITERATURE REVIEW

Mg+2 plays a vital role in bone health through supporting the bone formation and maintaining bone density. It aids in calcium absorption and metabolism, which are crucial for strong bones. Magnesium also influences the activity of bone-building cells and bone-resorbing cells, helping to balance bone remodeling. Additionally, it contributes to the activation of vitamin D, which further enhances calcium utilization.

Magnesium helps to prevent bone demineralization by interacting with calcium and phosphorus, supporting the preservation of bone structure. Other than regulating Calcium homeostasis through secretion of parathyroid hormone (PTH), Magnesium plays an essential role in strengthening the bones by aiding in synthesis of crucial protein like osteocalcin, which is crucial for bone mineralization and stability. A magnesium deficiency may lead to weakened bones and a greater likelihood of osteoporosis and other bone-related diseases.

OVERVIEW OF OTHER MINERALS WITH BONE HEALTH

Minerals are essential in various physiological processes, including bone health, nerve impulse propagation, fluid balance, and catalytic reactions [12]. Minerals, which are needed in smaller quantities are referred as micro-minerals. Fluoride [13], zinc [14] and copper [15] are micro-minerals. And minerals that are needed in relatively large quantities are referred to as macro-minerals. Magnesium, calcium, and phosphorus are macro-minerals [16].

MACRO-MINERALS

Magnesium: It promotes activity of osteoblasts by stimulating phosphate group involved in bone formation process. Mg+2 is stored in bones and plays an important role in mineral, bone homeostasis [17].

Calcium: Total calcium in human body is about 1200g and 99% of it is found in the bones and teeth. It is responsible for tissue mineralization. The intake of calcium during growth period may cause bone maturity and there is elevated likelihood of bone density-related fractures later in life. High dietary calcium enhances bone mineral density in short time [18].

Phosphorus: It is next to calcium and component of bone tissue. Inorganic phosphorus intake helps in activity of osteoblasts and osteoclast in mineralization. Dietary phosphorus plays a role in bone formation [18].

MICRO-MINERALS

Fluoride: It directly influences mineralized bones by integrating apatite crystals through ion exchange. It helps to stimulate bone formation. There is no effect of fluoride on osteoclast has been reported [13].

Zinc: It is engaged in the formation of bone tissue and aids in the proper functioning of skeletal system. About 30% zinc is present in bones. Its major function is to slow down the process of osteoclast cells in the bones. And it also promotes the activity of osteoblast cells [14].

Copper: Copper is a vital nutrient in human health. It plays a crucial role in the formation of soft bone tissue like collagen and elastin. Its deficiency can cause severe bone remodeling and fracturing in infants [15].

While various minerals are crucial for maintaining strong bones, magnesium stands out as a vital substance that performs a multifaceted role in bone. Unlike other minerals, Mg+2 participates in over 300 cellular reactions including those that regulate bone mineralization, density, and structure [19]. Its unique ability to influence osteoblast and bone forming activity, as well as its role in vitamin D metabolism, make magnesium an indispensable mineral for maintaining optimal bone health [20]. Furthermore, magnesium's impact on muscle function and nerve transmission helps prevent falls and fractures, reducing the risk of osteoporosis. As the second most abundant magnesium's importance cannot be overstated, making it an essential nutrient for maintaining strong, healthy bones throughout one's lifetime.

IMPORTANCE OF MAGNESIUM IN HUMAN PHYSIOLOGY

Brain: Low extracellular Mg2+ levels in the neural system in that lead to contributes to the hyper excitability of NDMA receptors that can cause epilepsy, neuron cell death. It also plays a key role in regulating the oxidative stress and release of neuropeptide like calcitonin gene-related peptides. Patients with low magnesium concentration in cortex, white matter, basal ganglia and brainstem have most likely to have Parkinson’s disease in older age [21].

Lungs: Magnesium reduces the airways inflammation at the root of various lung ailments including asthma, chronic lung disease and genetic lung disease. Only few studies discuss the anti- inflammatory role of Mg+2 [21].

Heart: Magnesium plays a significant role in heart function by manipulating the myocardial metabolism. There are five phases of cardiac action potential. In each phase many nutrients are important. Mg2+ is important in phase 2, 3 by applying its effect on the potassium and calcium channel. An important role of magnesium is the substantial vasodilatory effect. Low level of magnesium is associated with high risk of myocardial infarction [21].

Muscle: Magnesium works as an antagonist for Ca2+ in muscles. It can compete for the Calcium binding sites. When there is deficiency of magnesium only a small amount of Ca2+ is required for the replacement of magnesium that can cause hyper contractibility which can cause muscle cramps [21].

Pancreas: Mg+2 is essential for proper glucose consumption and insulin transmission. Low magnesium levels can cause many problems in pancreas leading to lessen pancreatic beta cell activity and elevated insulin resistance. low serum level of magnesium contributes to type-2 diabetes [21].

Liver: Magnesium may play a role in liver regeneration, particularly during the proliferative phase, by advancing hepatocytes in the cell cycle. Mg2+ deficiency is associated with various liver diseases, including alcoholic liver disease, and intensifies liver pathology and disease progression. Some studies suggest that magnesium intake may be associated with a reduced risk of liver cancer [21].

Metabolism of Mg+2: Mg+2 homeostasis in the body is primarily controlled through a combination of intestinal absorption which acts as a reservoir to store excess magnesium. The kidneys play a vital role in stimulating magnesium levels by excreting large amounts into urine. Magnesium absorption (intestines): In comparison to other minerals, intestines have finite role in regulation and absorption of Mg as it mainly depends on Mg intake. About 30-50% is absorbed in the intestine from a daily intake of 370mg. When Mg+2 is consumed in small doses about 80% is absorbed. The gut absorbs magnesium via two primary pathways: one is para-cellular transport specifically for bulk Mg absorption (in small intestine) and the other is trans-cellular transport (large intestine) [21].

Magnesium Storage (Bones): Bones functions as a key repository for magnesium as nearly 99% of the body's total Mg+2 is retained within tissues [22], with 50–60% specifically stored in bones [21]. However, below 1% of magnesium is present in RBC's and serum. Magnesium present on the bone surface is around 1/3rd and this is associated with serum magnesium levels. The other part of it is distributed in the skeletal muscles and elastic tissues. Measuring serum mg levels is not the best option for accurately representing overall magnesium since only 0.3% of body's total Mg is found in serum [22]. Magnesium on the surface of hydroxyapatite crystals in bone is continuously exchanged with Mg^{2+} in the bloodstream. This exchange influences bone structure, as Mg^{2+} enhances the solubility of phosphate (Pi) and calcium (Ca^{2+}) bone apatite, affecting crystallization and size [21]. Magnesium also supports osteoblast extraction, means that the deficiency in Mg^{2+} can cause the reduction in bone formation. Research on Mg^{2+} -deficient rats has shown a decrease in bone destroying cell numbers and bone mass. Additionally, magnesium reduction triggers an increase in inflammatory cytokines, such as tumor necrosis factor-alpha, interleukin-1 beta, and substance P, all of which are linked to higher osteoclastic bone resorption [21].

Also, low Mg^{2+} levels are often associated with decreased parathyroid hormone and vitamin D, further contributing to bone loss. Magnesium deficiency also disrupts chondrocyte column formation by reducing the expression of SRY-box 9 (SOX9), a key transcription factor for cartilage development. Interestingly, in a study examining gene expression in the Mg^{2+} moving the part of kidney, mRNA levels were significantly elevated in subjects on a low-magnesium diet. These findings indicate that SOX9 is essential for maintaining magnesium balance in both bone and kidney function [21].

REGULATION OF MAGNESIUM

Magnesium excretion (kidneys): Kidneys are the primarily regulators of Mg homeostasis [21]. During normal circumstances about, 90-95% of strained Mg+2 is retaken in the body and only 3-5% is eliminated through urine. About 15-20% of filtered Mg+2 is reabsorbed in the proximal convoluted tubules, most of the reabsorption (65-75%) occurs in thick ascending limb of loop of Henle [22].

Bone Composition: Bony structure, in decreasing order, is a complex structure consisting of both organic matrix and inorganic matrix. The mineral phase known as calcium phosphate crystal ($Ca_{10}(PO_4)_6(OH)_2$), is identical in structure to geological apatite. The organic matrix is largely made up of nearly ninety percent type 1 collagen, about five percent non-collagenous proteins (NCPs), and nearly two percent lipids by weight. Two structural proteins such as collagen and fibronectin also play crucial roles in regulating bone integrity and supporting cellular functions. Additional proteins have specialized functions, including the maintenance of hydroxy-apatite crystal formation those that control the diameter of collagen fibrils, act as signaling molecules, act as growth factors, act as enzymes, and have other roles [23].

The human skeleton is made up of two primary components: a mineralized matrix and an organic framework. The mineralized part is mainly composed of Ca-phosphate compound, primarily in form of bone mineral crystals, which gives the bone its strength and rigidity, allowing it to support the body. The organic part consists mostly of collagen fibers, which provide flexibility and resilience, preventing the bones from becoming brittle. Additionally, bone contains other substances, like proteoglycans and non-collagenous proteins, that further contribute to its structure and function. This unique combination of materials allows bone to be durable and adaptable, capable of withstanding mechanical stresses while also facilitating movement and protecting critical organs [24].

Magnesium Deficiency: Magnesium deficiency happens due to inadequate levels in the body [25]. Around 50–60% of the body's magnesium is contained in bones, its deficiency can significantly impact bone health. Magnesium plays an essential role in bone metabolism, influencing both skeletal formation and resorption. A deficiency can weaken bones, increasing the risk of fractures [26].

The body closely controls the magnesium levels through absorption in intestines and excretion via the kidneys. However, prolonged low intake or conditions that increase magnesium loss can lead to a deficiency [26]. Experimental studies suggest that magnesium deficiency causes a 30– 40% reduction inside bone magnesium content [25]. Additionally, it directly causes a reduction in osteoblastic bone formation [27], affecting the bone remodeling process.

Further research has demonstrated that magnesium deficiency can trigger chronic disease, low- grade inflammation, which is linked to several health issues, including osteoporosis, cardiovascular disease, hypertention, and diabetes. When $Mg+2$ levels are too low, immune cells like leukocytes and macrophages become activated, releasing inflammatory molecules and increasing free radical production. This inflammation is often caused by an imbalance in calcium levels within cells, which heightens the inflammatory response. As a result, markers of inflammation such as tumor necrosis can rise. Long-term $Mg+2$ shortage is a known risk factor for chronic inflammatory conditions, further contributing to bone loss and systemic diseases.

Clinical research also indicates that osteoporotic individuals, particularly postmenopausal women, result to have a low serum magnesium level compared to non-osteoporotic individuals [28]. Furthermore, magnesium reduction has been observed to delay the mineralization in newly formed cartilage bones, further compromising skeletal integrity [29]. Notably, magnesium deficiency is prevalent in individuals with osteopenia and osteoporosis, conditions that increase the risk of fractures. Magnesium deficiency can occur indirectly through decreased vitamin D levels, increased parathyroid hormone biosynthesis, oxidative stress, and elevated pro- inflammatory cytokines [30].

Interestingly, magnesium deficiency can happen regardless of normal serum magnesium levels, as most of the magnesium is stored in bones and tissues. For example, a study found that 84% of post menstruation women with osteoporosis exhibited low magnesium trabecular bone content and were diagnosed with magnesium deficiency through tests like the throne magnesium load test. Similarly, approximately 20% of 381 elderly individuals were found to have low erythrocyte potassium and magnesium levels despite normal serum levels [31]. This highlights the challenges in detecting magnesium deficiency and underscores the importance of thorough testing to assess magnesium status beyond blood levels.

In summary, magnesium deficiency not only affects bone health by reducing osteoblast activity and delaying mineralization but also contributes to systemic inflammation and increases the risk of bone diseases like osteoporosis. Ensuring adequate magnesium intake through diet or supplementation is crucial to maintaining bone strength, preventing fractures, and reducing the long-term health complications associated with magnesium deficiency [32].

BONE DISORDERS

Bone health is also affected by magnesium deficiency. When magnesium levels are low, it is often linked to bone thinning, which makes the bones weaker and more prone to fractures. Many people, especially postmenopausal women, struggle with magnesium insufficiency, which increases the risk of losing bone density and developing fractures. Research has shown that lower blood magnesium levels are strongly associated with poor bone health, resulting in weakened bones and a higher risk of breaks [33].

Magnesium is vital for maintaining the structure and strength of bones. Without enough magnesium, the bones become more fragile and susceptible to damage, contributing to conditions like osteoporosis. Ensuring adequate magnesium intake through diet or supplementation has been shown to help improve bone density and reduce the likelihood of fractures [33].

Osteoporosis: Magnesium (Mg) plays a vital role in maintaining bone health and is closely linked to the development and progression of osteoporosis—a condition marked by weakened bones, reduced density, and increased fracture risk [34]. Magnesium is essential for bone development and mineralization, as it regulates calcium homeostasis, a key element in bone structure [34, 35]. A deficiency in magnesium can disrupt calcium regulation by affecting parathyroid hormone and vitamin D levels [35]. Parathyroid hormone influences the expression of RANKL and OPG in osteoblasts, which are critical for osteoclast formation through the RANK/RANKL/OPG signaling pathway [35]. This axis is central to bone remodeling, balancing bone formation and resorption [35]. Magnesium also supports bone formation by activating enzymes necessary for healthy bone metabolism. When magnesium is insufficient, the balance between bone breakdown and formation is disturbed, enhancing osteoclast activity and accelerating bone loss and structural deterioration [34, 35]. These effects are particularly concerning in older or postmenopausal individuals, who are already at higher risk for osteoporosis [34]. Clinical research indicates that adequate magnesium intake or supplementation may help preserve bone strength and mitigate osteoporosis-related symptoms [34, 35].

A healthy diet is especially crucial for young people before skeletal maturity is reached, as osteoporosis generally reflects peak bone mass that is determined by factors prior to skeletal maturity [36]. About 50-60% magnesium resides in skeleton and this skeleton reflects magnesium status [37]. By 2050 it is anticipated that over 30 million people in Europe will have osteoporosis [36, 37]. A low, normal, high bone Mg is found in osteoporosis. Mg deficiency can cause osteoporosis in premenopausal and postmenopausal women [38].

A number of other food components, including phytoestrogens, flavonoids, vitamins A, B, C, E, and folate, as well as minerals, including copper, zinc, selenium, iron fluoride, and magnesium (Mg), are known to be significant, even though calcium and vitamin D have been the primary focus of nutritional prevention of osteoporosis [39].

The function of bone density reduction for osteoporosis begins with inadequate magnesium nutritional needs that results for reduction in bone mineral concentration. In comparison with case study performed on animals shows that, insufficient intake of dietary magnesium facilitates the occurrence of osteoporosis, moreover it lowers bone density and shows reduction in amounts of PTH and 1,25(OH)2-VD in epithelial tissues. And the finding displayed such as it illustrated that hypomagnesaemia be able to suppress the production of biosynthesis of PTH that can cause organ damage [40]. Dietary magnesium restriction has been shown to promote osteoporosis in various studies on various species. Animals lacking magnesium exhibit brittle and fragile bones, detectable trabeculae micro fractures, and significantly compromised mechanical properties. As a result, it is not unexpected that a diet low in magnesium has a detrimental impact on the peri-implant cortical bone markedly decreasing the depth of the tibial cortical. The impact of low magnesium level on bone density are caused through a number of direct and indirect mechanisms. Additionally, it should be remembered that reduced magnesium intake delays matrix calcification and the differentiation of connective tissue and bone [41]. Reduced osteoblastic activity contributes to decreased bone formation in rodents with experimental magnesium deficiency. Endothelial dysfunction is encouraged by magnesium deficiency, and bone health is known to depend on endothelial health [42]. It is tempting to hypothesize that osteoporosis could be regarded as a bone vascular condition is based on these grounds. The above figure presents the knowledge of the mechanisms that link magnesium reduction and osteoporosis. Interestingly, comparable events are involved in both research models and humans. Since the blood vessels are essential in bone remodeling, we hypothesize that low Mg induces endothelial dysfunction, which affects bone mass loss.

Osteopenia: Osteopenia defined by reduced bone density which is beneath the normal range but not that much insufficient to be classified as severe bone loss, is most often seen in women after menopause and it usually becomes more severe with advancing age [43]. Mg+2 is vital for production of organic framework of bone and its shortage can impact bone integrity by inhibiting bone formation [43].

Rickets: Magnesium helps in vitamin D activation, which helps to manage Ca and phosphate homeostasis that affects the growth and maintenance of bones. Mag+2 deficiency does not directly cause rickets, but it can contribute to the condition. Rickets are mainly caused by a lack of vitamin D, calcium, or phosphate. However, magnesium is crucial for healthy bones and for activating vitamin D. Without enough magnesium, the body may have difficulty activating vitamin D, which is vital for calcium absorption to strengthen the bone tissues. While magnesium deficiency alone doesn't cause rickets, it can increase the risk, especially when combined with other deficiencies [44]. A 4-year-old boy with untreated vitamin D-resistant rickets showed normal magnesium metabolism, despite exhibiting typical calcium and phosphorus abnormalities associated with this disease. This finding contradicts a previous report of disturbed magnesium metabolism in an adolescent with rickets. The discrepancy may be attributed to differences in the underlying disease process between the two age groups or variations in disease severity, which are discussed as possible explanations [45].

Osteomalacia and Hypomagnesemia: Magnesium deficiency can cause osteomalacia the softening of bones and also interfere with Ca and vitamin D metabolism which is essential for bone mineralization. Osteomalacia can caused by altered or impaired skeletal tissue mineralization. Osteomalacia is usually associated with impaired bone mineralization in adults, related to pathological features and can be seen during skeletal development often overlapping with rachitic changes in growing bones. Osteomalacia is characterized by altered bone quality and quantity making the bone strength weaker and easily breakable [46]. Osteomalacia and rickets and hypomagnesemia are somehow linked because magnesium is essential for bones and helps the body properly use vitamin D. As vitamin D is needed for calcium absorption, which is crucial for strong bones. Without enough magnesium, the body cannot activate vitamin D which leads towards poor calcium absorption and weaker bones. In children, this causes rickets, resulting in elastic bones, while in adults, it causes osteomalacia. Treating magnesium deficiency along with vitamin D and calcium issues is important to improve bone health and prevent these conditions [47].

Fractures: As magnesium is primary constituent of bone, it is found that less levels of magnesium in serum are linked with the increased risk of fracture. In human and animal experiments magnesium deficiency decreases the bone forming and destroying activity, osteopenia and bone fragility [48]. Magnesium deficiency ca0ntributes in bone fragility and elevate the risk of fractures by affecting bone mineralization and interfering with calcium and vitamin D metabolism. As magnesium is necessary for preserving bone density and strength, its deficiency can result in weaker bones, making them more prone to fractures. Fragility fractures pose a major public health concern, affecting health, quality of life, and imposing social and financial burdens. As the population ages, the risk of these fractures increases, with a 22% lifetime risk in men and 46% in women at age 50 [49]. Without a doubt, fragility fractures are a prevalent and pertinent public health issue that affects patients' health, quality of life, and financial and social burden [50]. The prevalence of fragility fractures rises sharply with age, contributing to their ongoing rise as the global population ages [51].

Because it may be modifiable, this is another pertinent target for prevention. Although there are numerous minerals and dietary components that may also play a role in bone health, the majority of the evidence in this area has concentrated on calcium and vitamin D. Experimental research has demonstrated that changes in the quantity and activity of osteoclasts and osteoblasts are linked to magnesium (Mg) deficiency [52]. Consistent evidence points to magnesium's positive effects on bone health. However, very few studies discuss serum magnesium concentrations, and the majority discusses dietary magnesium exposure. In this context, there is strong evidence linking dietary magnesium to higher bone mineral density (BMD); however, the evidence for fractures is less consistent [53]. Our findings of a strong correlation between serum magnesium and incident fractures may be explained by a number of mechanisms. This includes the way that Mg has been shown to modulate osteoclastic and osteoblastic activity [54].

Osteoarthritis: Osteo-arthropathy is a deliberating illness marked by joint cartilage breakdown and harm to other joint components [55]. It is one of the widely seen condition linked to disability seen in older individual resulting in reduced life quality [56]. Osteoarthritis is a frequently observed bone disorder related to aging. Blood magnesium levels are negatively correlated to osteoarthritis. Research shows that patients with intense Osteoarthritis had notably reduced blood magnesium levels than those with minor osteoarthritis. Although, there is no significant correlation found between magnesium levels and two specific markers of inflammation. $Mg+2$ is vital micronutrient derived from leafy green vegetables like spinach, kale, natural grains and pulses. Insufficient magnesium intake related to elevated pain levels and reduced mobility in individual with osteoarthropathy. Research shows that insufficiency of magnesium may cause range of age-related conditions like weakened bones, cerebrovascular accident attack and inflammation joint disease [57].

Supplementation: Low magnesium intake has been associated with low bone density both in pre and postmenopausal. Dietary intake of magnesium is beneficial for bone health but it is seen that magnesium supplementation suppress bone turnover [58]. Supplements like vitamin K2 and magnesium could contribute to the maintenance of skeletal health [59]. Research suggests that magnesium intake have positive effect on bone mineral density and bone mineral content. Magnesium supplements play an important role in stabilizing bone health which reduces the risk of osteoporosis and fracture.

Toxicity: Studies have shown that both magnesium deficiency and toxicity have adverse effects on bones [60]. While magnesium plays a key role for bone health its excessive levels can cause toxicity in bones and cause bone mineralization and negative impact on bone quality and leading to bone lesions and reduce bone mineral density. High magnesium level can affect the bones. Moreover, High magnesium level can influence the bone metabolism as the balance well between minerals and the bone matrix leading to reduce bone quality [61]. Its toxicity can lead to hypermagnesemia. Life threatening as electrolyte imbalance resulting from elevated amount of magnesium in blood [60]. When the serum Mg2+ amount increases above 1.1mM this condition is generally considered as hypermagnesemia. The symptoms of this type of toxicity are similar to other nutrients. The sign and symptoms include flu-like symptoms, headache and flushing. When the level rises above 3.0 mM it may impact cardiac function Extreme toxicity can cause coma, asystole and even death. Hypermagnesemia can be caused due to magnesium citrate was frequently used as a laxative. Mg2+ compounds increase intestinal osmotic pressure. Mg2+ affects aquaporin-3 expression, enhancing water permeability. Magnesium has been utilized in enemas for constipation relief. However, using Mg2+ as a laxative or enema can lead to life- threatening hypermagnesemia. Genetic cause: It is a very rare condition. A patient with genetic hypermagnesemia can be treated by the infusion of Ca2+ salts that act as antagonists for Mg2+. Drug induced: Only few cases have been reported. Out of them few are discussed here.

Epsom Salt: It is commonly used as home remedy for treating abdominal pain.it includes a very fair amount of Mg2+ that can cause hypermagnesemia. Cathartics, Laxative and Enemy Magnesium citrate [Mg3 (C6H5O7)2] was the most commonly used cathartic. Mg2+ substances elevate the intestinal osmotic pressure and also act on aquaporin-3 expression and thus increase water permeability. Mg2+ has been used as a component of enemas to treat constipation. However, both use of Mg2+ as a laxative and as an enema may result in fatal hypermagnesemia [21].

CONCLUSION

In conclusion, magnesium plays an important role in maintaining the skeletal system of the body. Adequate magnesium intake supports bone mineral density, regulates bone remodeling, and impact the activity of bone forming cell and bone destroying cells. The mineral's involvement in numerous biochemical reactions emphasize its importance in overall bone health. As research continues to magnesium effects on bone metabolism, it is clear that providing the sufficient magnesium intake, through a balanced diet or with the supplements essential for maintaining strong, healthy bones and preventing conditions such as osteoporosis. magnesium, individuals can take a healthy approach to supporting their bone health and reducing the risk of bone-related disorders. It also plays a critical role in maintaining various body functions such as energy production, enzyme activation and cellular signaling. Deficiency of Mg also linked to other chronic diseases such as heart disease, diabetic issues and musculoskeletal disorder making it crucial to maintain the adequate level.

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