

Risk Factors for **OSTEOPOROSIS & CELIAC DISEASE**

It has been recognized for several decades that both children and adults with celiac disease have a significantly increased frequency of osteoporosis and increased risk of fractures as compared to the age-matched, non-celiac healthy individuals. Based on published data, the prevalence of osteoporosis among celiac patients varies from as low as 4 percent to as high as 70 percent. The data from our clinic indicate that prevalence of osteoporosis among adults with gluten intolerance and celiac disease is in the vicinity of 30 to 40 percent.

Characteristics and Causes of Osteoporosis

Osteoporosis is a bone disease characterized by reduced bone mineral density and impaired bone structure that leads to an increased risk of fracture. The three main mechanisms by which osteoporosis develops include an inadequate peak bone mass, excessive bone resorption, and inadequate formation of new bone during remodeling.

Bone mass results from the amount of bone acquired during growth (the peak bone mass) minus bone loss due to a variety of reasons including age, malabsorption syndromes, chronic steroid use, etc. The rate and magnitude of bone mass gain during the pubertal years may be markedly different from one individual to another. Pediatric onset of celiac disease and poor compliance with a gluten-free diet during childhood significantly reduces peak bone mass.

One of the main causes of osteoporosis occurs during bone remodeling.

Remodeling is a process where mature bone tissue is removed (resorption) and new tissue is formed. When resorption occurs more excessively than formation, there is a reduction in bone mass and an increased risk of fractures.

Formation of new bone is facilitated by specialized cells, called osteoblasts, which actively synthesize bone matrix. Bone resorption is mediated by other specialized cells, called osteoclasts.



There are several well-characterized risk factors which contribute to the development of osteoporosis in celiac patients. These include:

1. Malabsorption of vitamin D and secondary hyperparathyroidism

Villous atrophy in celiac patients reduces the active absorption surface and induces steatorrhea (excess fat in feces), which has a chelating effect on calcium and vitamin D, making their absorption difficult. This reduces levels of the vitamin D transporting protein (calbindin and calcium binding protein) and increases parathyroid hormone synthesis which, in turn, lead to increased bone resorption, causing osteoporosis.

2. Malabsorption of vitamin K

Malabsorption of fat soluble vitamins, including vitamin K, is a common finding in celiac patients.

Three vitamin K-dependent proteins have been isolated in the bone: osteocalcin, matrix Gla-protein (MGP), and protein S.

Osteocalcin is a protein secreted by osteoblasts. Osteocalcin requires vitamin k to perform the mineralization of bones.

MGP has been found in bone, cartilage, and soft tissue, including blood vessels. The results of animal studies suggest MGP facilitates normal bone growth and development.

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The vitamin k-dependent anticoagulant, protein S, is also synthesized by osteoblasts, but its role in bone metabolism is unclear. Children with inherited protein S deficiency suffer complications related to increased blood clotting as well as decreased bone density.

3. Magnesium deficiency

Magnesium deficiency may be an additional risk factor for celiac-associated osteoporosis. This may be due to the fact that magnesium deficiency alters calcium metabolism and the hormones that regulate calcium. Several human studies have suggested that magnesium supplementation may improve bone mineral density. Magnesium deficiency is easily detected with laboratory tests (eg. low serum magnesium, low serum calcium, resistance to vitamin D) or clinical symptoms (eg. muscle twitching, muscle cramps, high blood pressure, irregular heartbeat). Screening for magnesium deficiency should be routinely included in the screening of celiac patients with osteoporosis.

4. Chronic diarrhea and metabolic acidosis

Chronic diarrhea in patients with celiac disease results in significant bicarbonate losses and development of metabolic acidosis (excess acid in the body). Because bone acts as a buffer to maintain a systemic stable pH, it acts as a major reservoir for the excess acid. To maintain a stable bicarbonate level, one of the body's main compensatory mechanisms is the dissolution of the buffer and net loss of calcium from bone.

5. Hypogonadism

Decline of estrogen production and activity is one of the main events in the development of age-related osteoporosis. It is well known that estrogen deficiency is important in the pathogenesis of osteoporosis not only in women but also in men. Increase in bone mineral density in young men and declines in older men are related to circulating free estrogen, not testosterone. In general, patients with celiac disease are characterized by low levels of circulating estrogens, which contributes to the development of premature osteoporosis.

6. Chronic use of Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are one of the most widely used classes of drugs. The commonly used PPIs include such drugs as Omeprazole (brand name: Prilosec), Lansoprazole (brand name: Prevacid), Dexlansoprazole (brand names: Kapidex, Dexilant), Esomeprazole (brand name: Nexium), Pantoprazole (brand name: Protonix) and Rabeprazole (brand name: AcipHex). Chronic use of PPIs for gastroesophageal reflux disease and other related conditions has been associated with impaired calcium and magnesium absorption and increased risk of vertebral and nonvertebral fractures.

7. Chronic use of Selective Serotonin Reuptake Inhibitors

Selective Serotonin Reuptake Inhibitors (SSRIs) are frequently used in celiac patients for treatment of depressive disorders. The commonly used SSRIs include such drugs as Citalopram (brand name: Celexa), Escitalopram (brand name: Lexapro), Fluoxetine (brand name: Prozac), Fluvoxamine (brand name: Luvox), Paroxetine (brand name: Paxil) and Sertraline (brand name: Zoloft). It has been demonstrated that SSRIs increase extracellular 5-HTP (5-Hydroxytryptophan) levels that have deleterious skeletal effects because 5-HTP restrains osteoblastic activity, thus leading to bone loss.

8. Autoimmune mechanisms

Autoimmune mechanisms have been long suspected as risk factors contributing to development of osteoporosis in celiac patients. Nearly a decade ago, it was demonstrated that blood from celiac patients with osteoporosis contained significantly high titers of antibodies against bones as compared to non-celiac osteoporotic patients. Recently, it has been described that a subset of patients with celiac disease has autoantibodies to osteoprotegerin. Osteoprotegerin is a protein that is needed to inhibit high bone turnover.

9. Chronic inflammation

Chronic inflammatory diseases, including celiac disease, are associated with overproduction of proinflammatory cytokines such as TNF- α , interleukin(IL)-1, IL-6, IL-11, IL-15, and IL-17, among others, which activate osteoclasts and accelerate bone resorption leading to osteoporosis.

Traditional Therapy for Osteoporosis

Based on mechanism of activity, the drugs for osteoporosis are divided into two main groups: antiresorptive and anabolic.

Antiresorptive medications slow down the breakdown of bone. This helps to prevent bone loss and lower the risk of fracture.

Bisphosphonate antiresorptive medications:

- Alendronate (brand name: Fosamax™, Fosamax™ Plus D)
- Risedronate (brand name: Actonel™, Actonel™ with Calcium)
- Ibandronate (brand name: Boniva™)
- Zoledronic acid (brand name: Reclast™)

Other antiresorptives:

- Estrogen therapy or hormone therapy
- Raloxifene (brand name: Evista™)
- Denosumab (brand name: Prolia™)

Anabolic medications help to make new bone, increase bone density, and can also reduce the risk of broken bones.

- Teriparatide (brand name: Forteo™)

The advertisement features a central image of several cookies on a cooling rack. In the foreground, three packages of Mina's Gluten-Free mixes are displayed: Bread Mix, All-Purpose Baking Mix, and Flourless Cake Mix. The top left corner contains a logo for Mina's Purely Divine Gluten-Free. The bottom right corner includes the text: "Use Mina's Gluten Free Mixes on ALL your Favorite Recipes! For delicious recipes or to place an order, Please Visit; WWW.NOGLUTENINC.COM". On the right side, there are four certification logos: Celiac Support Association, Non-GMO Verified, Vegan, and Gluten Free Natural.

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In general, we are trying to avoid the use of oral bisphosphonates in patients with celiac disease due to the relatively high risk of bisphosphonate-associated gastric ulcers.

Integrative Therapy for Osteoporosis

Integrative therapy incorporates the use of dietary supplements such as calcium and magnesium in combination with vitamin D and K2. In addition, we frequently use *Drynaria fortunei* extract and strontium citrate.

Drynaria fortunei: Scientific research on *Drynaria* demonstrated its ability to improve bone rebuilding in excessive bone loss via various mechanisms, including inhibition of osteoclast function, stimulation of osteoblast function, and stimulation of osteogenesis (a process by which mesenchymal cells in bone marrow differentiate to become new osteoblast cells capable of producing new bone tissue).

Strontium citrate: Stimulates new bone formation and delays bone resorption. Due to competition for absorption, Strontium should be consumed separately from calcium and magnesium by at least two hours. It should not be consumed by people with a history of heart diseases or blood clots.

Important notice: Any of the drugs and calcium, magnesium, vitamin D, and vitamin K2 can be taken together at the same time, but the drugs **should not be taken** with *Drynaria* or strontium citrate. There needs to be at least a one month wash out period between taking drugs and *Drynaria* or strontium.

Osteoporosis associated with celiac disease is not a coincidental problem. Knowing about the aforementioned risk factors is a first step in correcting and reversing the development of osteoporosis and reducing the risk of osteoporosis-associated fractures. 

To see the references used in this article, visit simplygluten-free.com/osteoporosis-references.

As always, consult a medical professional before beginning any new protocol.



ABOUT THE AUTHOR:

Dr. Alexander Shikhman, founder of the Institute for Specialized Medicine, is board certified in internal medicine and rheumatology. Dr. Shikhman also launched *Gluten-Free Remedies™*, a line of all natural supplements which help treat the complications that can arise from celiac disease. Find Dr. Shikhman at ifsmc.com and glutenfreeremedies.com.