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Interdisciplinary Nursing, Radiologic, Health Information, and Nutritional Perspectives in the Assessment and Management of Osteomalacia

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Abstract

Background: Osteomalacia is a metabolic bone disease characterized by defective bone mineralization, leading to softened bones and an increased risk of pain, deformity, and fracture. It is primarily caused by prolonged and severe vitamin D deficiency, which disrupts calcium and phosphate homeostasis. Other etiologies include malabsorption syndromes, chronic kidney or liver disease, certain medications, and hereditary phosphate-wasting disorders.

Aim: This article aims to provide a comprehensive, interdisciplinary review of the assessment and management of osteomalacia, integrating perspectives from nursing, radiology, health information, and nutrition to optimize patient diagnosis, treatment, and long-term care.

Methods: The review synthesizes current clinical knowledge, detailing the pathophysiology of vitamin D metabolism, the evaluation through biochemical testing (e.g., serum 25-hydroxyvitamin D, calcium, phosphate, alkaline phosphatase) and radiologic imaging (e.g., identification of Looser zones), and the principles of management.

Results: Diagnosis relies on a combination of clinical symptoms (e.g., bone pain, proximal muscle weakness), characteristic biochemical abnormalities, and radiographic findings. Treatment is centered on correcting the underlying cause and replenishing vitamin D and calcium stores through high-dose supplementation, followed by lifelong maintenance therapy. The successful management of this condition is highly dependent on a collaborative, interprofessional team.

Conclusion: Osteomalacia is a largely reversible disorder with a favorable prognosis when diagnosed and treated promptly. An interdisciplinary approach is crucial for accurate diagnosis, effective treatment, patient education, and prevention of long-term complications.

Keywords: Osteomalacia, Vitamin D Deficiency, Metabolic Bone Disease, Hypophosphatemia, Interdisciplinary Care, Bone Mineralization, Nutritional Supplementation.

1. Introduction

Vitamin D deficiency is widely recognized as the most prevalent nutritional deficiency among both children and adults and remains a major global public health concern.[1] In adults, one of the most clinically significant skeletal consequences of prolonged vitamin D deficiency is osteomalacia, a disorder characterized by defective mineralization of osteoid leading to "softening" of bone. In osteomalacia, the organic bone matrix is produced in normal or near-normal amounts, but insufficient incorporation of calcium and phosphate results in undermineralized bone that is mechanically weak and prone to pain, deformity, and fracture.[1][2] By contrast, in children, the analogous process manifests as rickets, in which defective mineralization occurs primarily at the cartilage of the growth plates, leading to impaired linear growth, skeletal deformities, and characteristic radiologic changes in the metaphyses of long bones.[2][3] Together, osteomalacia and rickets represent a continuum of metabolic bone disease driven largely by impaired vitamin D metabolism, inadequate calcium and phosphate availability, or both. Normal bone integrity depends on the dynamic and tightly regulated process of bone remodeling, which involves continuous cycles of resorption and formation. This process is mediated by several specialized cell types, most notably osteoclasts and osteoblasts. Osteoclasts are multinucleated, bone-resorbing cells that degrade mineralized bone and

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osteoid by secreting proteolytic enzymes such as collagenase, thereby creating microscopic resorption pits.[1] Osteoblasts, the bone-forming cells, subsequently synthesize and deposit osteoid, a collagen-rich organic scaffold into which inorganic salts—predominantly calcium and phosphate in the form of hydroxyapatite—are deposited to form mineralized bone.[2] The balance between these processes is modulated by systemic hormones, including parathyroid hormone (PTH) and calcitonin, which respond to fluctuations in serum calcium levels, as well as by active vitamin D metabolites that facilitate intestinal calcium absorption and directly influence bone cells.[1][3]

In states of chronic vitamin D deficiency, intestinal absorption of calcium is reduced, leading to a tendency toward hypocalcemia. To preserve normal or near-normal serum calcium concentrations, a compensatory increase in PTH secretion occurs, a response known as secondary hyperparathyroidism.[1][2] Elevated PTH acts on bone to enhance osteoclastic resorption and mobilize calcium and phosphate from the skeletal reservoir, thereby restoring serum calcium at the expense of bone mineral content. Over time, this adaptive mechanism becomes maladaptive, as persistent recruitment of calcium from bone leads to progressive undermineralization of newly formed osteoid. The result is the characteristic histologic hallmark of osteomalacia: excessive unmineralized osteoid lining trabecular and cortical bone surfaces.[2][3] Clinically, adults affected by disorders that impair vitamin D production, activation, or bioavailability—such as inadequate sunlight exposure, malabsorption syndromes, chronic liver or kidney disease, certain medications, or dietary insufficiency—are at heightened risk for developing osteomalacia and its attendant manifestations. These may include diffuse bone pain, muscle weakness, difficulty walking, and an increased propensity for insufficiency fractures, particularly in weight-bearing bones.[2][3] From a pathophysiological standpoint, osteomalacia thus represents the culmination of prolonged disturbances in mineral metabolism and vitamin D homeostasis, in which hormonal mechanisms maintain serum calcium at the cost of skeletal strength. Early recognition and correction of vitamin D deficiency, along with appropriate nutritional and metabolic management, are therefore essential in preventing the progression to osteomalacia and mitigating its long-term skeletal consequences.[1][2][3]

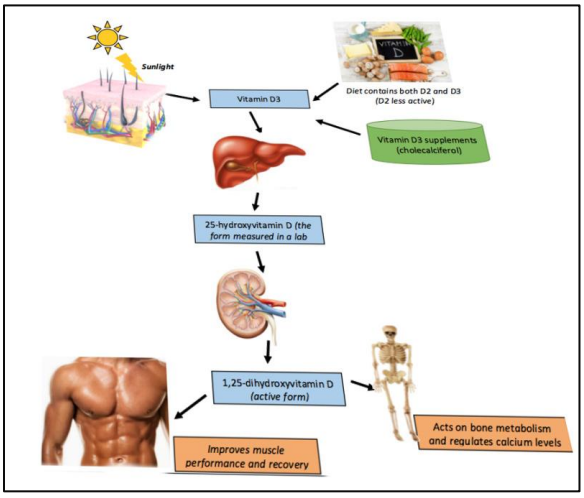

Fig. 1: Vitamin D Metabolism.

Etiology

Osteomalacia is a metabolic bone disease characterized by defective mineralization of the osteoid matrix, resulting in structurally weakened bone that is prone to pain, deformity, and fracture.[4] Under normal physiological conditions, bone formation proceeds through the orderly deposition of hydroxyapatite crystals—composed mainly of calcium and phosphate—onto an organic matrix of collagen and other proteins produced by osteoblasts. Any sustained disturbance in the availability of vitamin D, calcium, or phosphate, or in the enzymatic pathways that activate vitamin D, can disrupt this process and lead to the accumulation of unmineralized osteoid, which is the hallmark of osteomalacia.[4] The etiological factors underlying this disorder are diverse and often interrelated, encompassing impaired vitamin D production, reduced intestinal absorption, altered vitamin D metabolism, and conditions associated with hypophosphatemia or hypocalcemia, as well as the effects of specific medications. One of the most frequent and sometimes overlooked mechanisms contributing to osteomalacia is decreased cutaneous production of vitamin D. Ultraviolet-B radiation from sunlight is essential for the conversion of 7-dehydrocholesterol in the skin to cholecalciferol, the precursor of active vitamin D. Inhabitants of cold-weather climates often experience reduced sun exposure due to heavy clothing and limited outdoor activity, thereby decreasing cutaneous synthesis of vitamin D.[4] Similarly, individuals with darker skin have higher melanin content, which competes with 7-dehydrocholesterol for ultraviolet-B photons; this reduces the efficiency of vitamin D synthesis and places such populations at higher risk of deficiency, particularly in regions with limited sunlight. Obesity represents another factor in decreased vitamin D bioavailability. In obese individuals, vitamin D is sequestered in adipose tissue, effectively lowering the circulating pool of calcidiol (25-hydroxyvitamin D) available for subsequent hydroxylation to the active hormone. Moreover, aging is associated with a decline

in the capacity of the skin to produce vitamin D, accompanied by diminished stores and altered metabolism, making older adults particularly vulnerable to osteomalacia when additional risk factors coexist.[4]

Even when cutaneous production is adequate, decreased intestinal absorption of vitamin D can precipitate deficiency. Poor dietary intake, especially in populations with limited access to fortified foods or at-risk dietary patterns, can result in nutritional deficiency despite reasonable sunlight exposure.[4] Malabsorptive syndromes represent a major etiological category in this context. Chronic inflammatory conditions such as Crohn disease, hereditary disorders like cystic fibrosis, and immune-mediated conditions such as celiac disease all impair fat absorption and thus reduce the uptake of fat-soluble vitamins, including vitamins A, D, E, and K.[4] Cholestatic liver diseases further compromise micelle formation and fat-soluble vitamin absorption, while surgical modifications of the gastrointestinal tract—such as gastric bypass or extensive bowel resection—can severely limit absorptive surface area. In these scenarios, vitamin D deficiency may be profound and prolonged, contributing significantly to the development of osteomalacia if not recognized and treated. Alterations in vitamin D metabolism also play a central role in the pathogenesis of osteomalacia. The conversion of calcidiol (25-hydroxyvitamin D) to calcitriol (1,25-dihydroxyvitamin D), the hormonally active form, occurs predominantly in the kidney via 1-alpha-hydroxylase. Chronic kidney disease disrupts this process by causing nephron loss, structural damage, and reduced expression and activity of 1-alpha-hydroxylase.[4] Hyperphosphatemia, a common feature of advanced renal failure, further suppresses the enzyme's activity, compounding calcitriol deficiency and impairing calcium absorption from the gut. Nephrotic syndrome contributes through a different mechanism: excessive urinary loss of vitamin D–binding protein, which carries calcidiol in the circulation, leading to reduced availability of substrate for activation. Liver disease, including cirrhosis and metabolic dysfunction-associated steatotic liver disease, impairs the hepatic 25-hydroxylation of cholecalciferol to calcidiol, thereby undermining the first critical step in vitamin D activation and predisposing to osteomalacia.[4]

Physiological states such as pregnancy can also alter vitamin D homeostasis. Pregnancy is associated with increased maternal and fetal demands for calcium and vitamin D, and decreased calcidiol levels have been documented in pregnant women, particularly when baseline vitamin D status is suboptimal. In recognition of this, the American College of Obstetricians and Gynecologists recommends supplementation with at least 1000 to 2000 international units of vitamin D daily when deficiency is identified, in order to reduce maternal skeletal complications and support fetal bone development.[4] Beyond vitamin D itself, disturbances in mineral metabolism, particularly hypophosphatemia and hypocalcemia, are important etiological drivers of osteomalacia. Renal tubular acidosis, as seen in Fanconi syndrome, leads to impaired reabsorption of phosphate and other solutes, promoting urinary phosphate waste and systemic hypophosphatemia.[4] Phosphate is a critical component of hydroxyapatite; its deficiency directly impairs bone mineralization. Notably, multiple intravenous iron infusions, especially with certain formulations, have been associated with hypophosphatemia and subsequent osteomalacia, likely via mechanisms that increase fibroblast growth factor 23 (FGF23), a hormone that promotes renal phosphate wasting.[5] Tumor-induced osteomalacia, or oncogenic osteomalacia, represents a rare but instructive acquired cause. This paraneoplastic syndrome is characterized by hypophosphatemia, inappropriately elevated or normal levels of FGF23 relative to phosphate level, and renal phosphate wasting.[6][7][8][9] The culprit lesions are usually small, often benign mesenchymal tumors located in the skin, muscles, bones of the extremities, or paranasal sinuses, which secrete excess FGF23 and thereby disrupt normal phosphate homeostasis and bone mineralization.[10]

A number of commonly used medications further contribute to the etiology of osteomalacia by interfering with vitamin D metabolism. Classic antiepileptic drugs such as phenobarbital, phenytoin, and carbamazepine induce hepatic cytochrome P450 enzymes, which accelerate the catabolism of calcidiol and reduce circulating levels of 25-hydroxyvitamin D.[11] As a result, long-term therapy with these agents can lead to progressive vitamin D depletion and secondary osteomalacia if supplementation is not provided. Other drugs, including isoniazid, rifampicin, and theophylline, may precipitate vitamin D deficiency through similar enzyme-inducing mechanisms, again increasing calcidiol breakdown and blunting its biological availability. Antifungal agents such as ketoconazole inhibit steroidogenic enzymes, including 1-alpha-hydroxylase, thereby increasing vitamin D requirements and potentially tipping borderline patients into deficiency. Prolonged corticosteroid use has multiple adverse skeletal effects, including stimulation of bone resorption, impairment of osteoblast function, and reduction in calcium absorption. Corticosteroids may also enhance 24-hydroxylase activity, leading to increased degradation of both calcidiol and calcitriol and further contributing to vitamin D deficiency and osteomalacia.[12][13][14][15] In clinical practice, osteomalacia often arises from a convergence of these etiological factors rather than a single isolated cause. For example, an older adult living in a cold climate with limited sun exposure, chronic liver disease, and

long-term anticonvulsant therapy embodies multiple overlapping risks for vitamin D deficiency and impaired bone mineralization. Similarly, a patient with chronic kidney disease and secondary hyperparathyroidism may also be receiving corticosteroids or phosphate-binding therapies that further disturb mineral metabolism. Therefore, a comprehensive etiologic assessment, including detailed history, medication review, and evaluation for gastrointestinal, hepatic, renal, and endocrine disorders, is essential for identifying correctable factors and preventing or reversing osteomalacia.[4][5][11][12][13][14][15]

Epidemiology

The epidemiology of osteomalacia reflects a complex interplay of environmental, cultural, nutritional, and biological factors that influence vitamin D status and mineral homeostasis across populations. Postmortem studies have revealed that histological evidence of osteomalacia may be far more common than clinically appreciated, with some European reports describing prevalence rates as high as 25% in adult cadavers, suggesting that many cases remain undiagnosed during life.[11] This disparity highlights the fact that osteomalacia is frequently under-recognized and that its global incidence is likely significantly underestimated. Mild or early forms of the disease may present with nonspecific symptoms—such as fatigue, musculoskeletal pain, or diffuse bone tenderness—leading to delays in diagnosis or misattribution to alternative causes such as fibromyalgia, arthritis, or neuropathic pain. Risk factors for osteomalacia are well documented and demonstrate considerable geographic and demographic variation. Individuals with dark skin are disproportionately affected due to increased melanin pigmentation, which reduces the efficiency of ultraviolet-B–induced cutaneous vitamin D synthesis.[16] Limited sun exposure is another major risk factor, common among persons living in northern latitudes, those who spend most of their time indoors, or individuals whose occupational environments involve minimal sunlight. Cultural practices that involve regular use of full-body clothing—particularly in regions where such attire is customary for religious or social reasons—further reduce the skin surface area available for sunlight exposure and increase susceptibility to vitamin D deficiency.

Low socioeconomic status is also associated with a higher prevalence of osteomalacia, largely due to dietary inadequacies, reduced access to fortified foods, and limited opportunities for supplementation or medical evaluation.[17] Poor diet lacking in vitamin D–rich foods such as oily fish, fortified dairy products, and eggs contributes directly to deficiency, especially when combined with inadequate sunlight exposure. Ethnicity plays an additional role, as certain populations have genetic, cultural, or lifestyle characteristics that predispose them to chronic vitamin D insufficiency. Globally, the distribution of osteomalacia varies widely depending on latitude, climate, cultural norms, and patterns of nutrition. For instance, populations in regions with prolonged winters or high air pollution levels may experience decreased ultraviolet-B penetration, while those in equatorial areas may still develop deficiency due to indoor living patterns or covering clothing. These variations emphasize the need for population-specific public health strategies and targeted screening in high-risk groups. Healthcare professionals should remain vigilant in identifying individuals at risk for osteomalacia, as early detection and intervention can prevent long-term morbidity. Clinical decisions regarding laboratory evaluation or initiation of vitamin D supplementation must therefore incorporate not only laboratory and clinical findings but also the broader contextual factors—including environmental exposure, cultural practices, and socioeconomic conditions—that influence individual patient susceptibility.[16][17]

Pathophysiology

Understanding the pathophysiological processes underlying osteomalacia requires a clear comprehension of vitamin D metabolism and its regulatory mechanisms. The synthesis of active vitamin D, or calcitriol, begins in the skin, where ultraviolet B (UVB) radiation initiates a photochemical reaction that converts 7-dehydrocholesterol, a provitamin located in epidermal keratinocytes and dermal fibroblasts, into pre-vitamin D3. This compound subsequently undergoes thermal isomerization to form cholecalciferol (vitamin D3), the primary naturally occurring form of vitamin D in humans. The efficiency of this cutaneous step depends on factors such as skin pigmentation, sunlight exposure, geographic latitude, season, and age. Any process that reduces UVB availability or impairs this photochemical conversion can significantly lower endogenous vitamin D production and predispose individuals to deficiency. Once synthesized, cholecalciferol enters the circulation and is transported to the liver, where it undergoes its first hydroxylation reaction. Hepatic 25-hydroxylase converts cholecalciferol into calcidiol, or 25-hydroxyvitamin D (25[OH]D). This metabolite is the major circulating form of vitamin D and serves as the most reliable marker of total body vitamin D status because it reflects contributions from dietary intake, cutaneous synthesis, and mobilized adipose stores.[18] Approximately 40% to 50% circulating 25(OH)D is estimated to originate from skin-derived vitamin D, underscoring the significance of sunlight exposure in maintaining adequate levels. Because liver disease—including cirrhosis, hepatitis, and steatotic liver disease—impairs the 25-hydroxylation process, patients with chronic hepatic dysfunction are at heightened risk of vitamin D deficiency and its skeletal consequences.

The second hydroxylation step, which generates the biologically active hormone calcitriol

(1,25-dihydroxyvitamin D or 1,25[OH]$_2$D), occurs in the kidney under the influence of renal 1-alpha-hydroxylase. This enzyme is tightly regulated by several hormonal and metabolic signals, including parathyroid hormone (PTH), serum phosphate concentrations, and fibroblast growth factor 23 (FGF23).[6][8] In chronic kidney disease, the diminished number and function of nephrons, combined with hyperphosphatemia and declining 1-alpha-hydroxylase activity, impair calcitriol synthesis. As calcitriol levels fall, intestinal calcium absorption decreases, leading to hypocalcemia and a compensatory rise in PTH secretion. This cascade contributes to the development of secondary hyperparathyroidism, which chronically stimulates osteoclastic bone resorption and accelerates the loss of mineralized bone, thereby promoting osteomalacia. With prolonged renal failure, these regulatory disturbances may progress to tertiary hyperparathyroidism, characterized by autonomous, excessive PTH secretion. The regulation of calcitriol synthesis is governed by an intricate system of feedback loops that maintain calcium and phosphate homeostasis. PTH exerts positive feedback on 1-alpha-hydroxylase, stimulating increased calcitriol production when serum calcium levels fall. Low serum phosphate is also a positive regulator, as hypophosphatemia signals the need for enhanced intestinal and renal conservation of minerals, thereby promoting calcitriol synthesis to restore balance. Conversely, negative feedback mechanisms act to prevent excessive accumulation of active vitamin D. FGF23, a hormone produced by osteocytes in response to increased phosphate or calcitriol levels, inhibits renal phosphate reabsorption and suppresses 1-alpha-hydroxylase activity.[8][6] This hormone plays a central role in phosphate homeostasis and is markedly elevated in tumor-induced osteomalacia, where its pathological overproduction causes profound hypophosphatemia, renal phosphate wasting, and impaired bone mineralization.

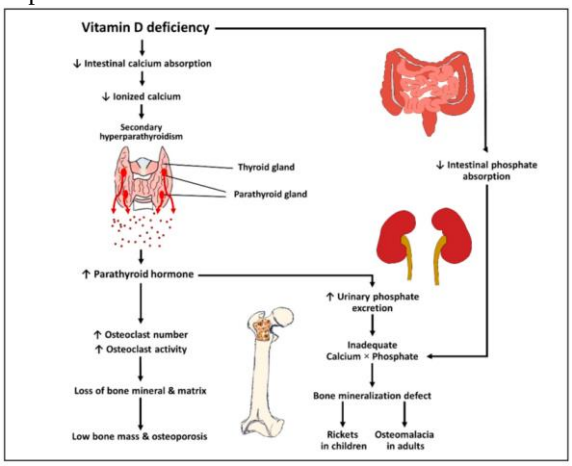

Fig. 2: Pathophysiology of Osteomalacia.

Calcitriol itself also participates in negative feedback by reducing 1-alpha-hydroxylase expression and promoting 24-hydroxylase activity. The latter enzyme converts both calcidiol and calcitriol into inactive metabolites, such as 24,25-dihydroxyvitamin D (24,25[OH]$_2$D), which are subsequently excreted.[19] This coordinated inhibition prevents excessive levels of active vitamin D, protecting against hypercalcemia and hyperphosphatemia, and ensures dynamic adjustment of the vitamin D axis in response to physiological needs. When any component of this metabolic system fails—whether due to impaired cutaneous synthesis, reduced dietary intake, defective hepatic conversion, renal insufficiency, or abnormal hormonal regulation—the downstream consequences converge on bone. Without adequate calcitriol, the intestine absorbs insufficient calcium and phosphate, and serum calcium may transiently normalize only because PTH mobilizes minerals from bone. Over time, however, the newly formed osteoid matrix cannot mineralize properly, resulting in its accumulation along trabecular and cortical surfaces. Histologically, this appears as widened osteoid seams and delayed mineralization fronts. Clinically, the failure of mineral deposition manifests bone pain, proximal muscle weakness, difficulty ambulating, and an increased susceptibility to fractures, particularly of the ribs, pelvis, and femoral neck. Thus, the pathophysiology of osteomalacia reflects the downstream expression of chronic disturbances in vitamin D metabolism and mineral homeostasis. It is a final common pathway of diverse etiological processes—nutritional, environmental, gastrointestinal, hepatic, renal, endocrine, and oncogenic—all of which ultimately impair the body's ability to mineralize bone appropriately. Understanding these mechanisms is essential for accurate diagnosis, risk assessment, and formulation of targeted therapeutic strategies aimed at correcting underlying metabolic derangements and restoring skeletal integrity.[18][19]

History and Physical

A thorough and methodical clinical evaluation is essential when assessing a patient for suspected osteomalacia. The medical history should begin with a detailed review of the patient's past medical, surgical, and family history, as certain inherited or chronic conditions may predispose individuals to vitamin D deficiency or disorders of mineral metabolism. Attention should be given to any history of gastrointestinal disease, bariatric surgery, chronic liver or kidney disease, or long-term medication use, particularly drugs known to interfere with vitamin D metabolism. The clinician should also inquire about dietary habits, including restrictions related to cultural practices, allergies, or vegetarian/vegan diets, which may contribute to inadequate intake of vitamin D or calcium. Socioeconomic factors are equally relevant, as limited access to nutrient-rich foods, fortified products, or outdoor physical activity may significantly increase

the risk of osteomalacia. Patients often present with vague or nonspecific complaints that evolve gradually, making early diagnosis challenging. Diffuse bone pain is one of the hallmark symptoms and typically involves the lower back, pelvis, hips, and legs—areas subjected to the greatest mechanical load. This pain often worsens with movement or weight-bearing and may be described as a deep, aching discomfort. Muscle weakness, particularly of the proximal muscles of the thighs and shoulders, is another prominent feature and may lead to difficulty rising from a seated position, climbing stairs, or maintaining balance. As weakness progresses, patients may report frequent falls or general instability during ambulation. Fatigue, myalgias, arthralgias, and malaise are common and can be mistaken for rheumatologic or neurologic conditions. In more severe or prolonged disease, fractures or bone deformities may occur with minimal trauma, reflecting the underlying structural fragility of poorly mineralized bone.

Physical examination findings, while often subtle, can provide important diagnostic clues. Proximal muscle weakness, particularly involving the hip girdle, is frequently observed and may be accompanied by visible muscle waste. Diffuse bone tenderness is a notable sign and is most pronounced in weight-bearing regions such as the lumbar spine, pelvis, and long bones of the lower extremities. Some patients exhibit an antalgic or "waddling" gait due to pain and weakness. Long-standing osteomalacia may lead to skeletal deformities, including genu varum (bowed legs), spinal curvature abnormalities, and pelvic deformities resulting from chronic undermineralization. Fractures or pseudofractures—also known as Looser zones—are characteristic radiologic and clinical findings. These transverse, incomplete fractures commonly appear in the ribs, femoral neck, pubic rami, and scapula and may be painful or asymptomatic. Additionally, the physical exam may reveal muscle spasms, especially in the presence of hypocalcemia. Neuromuscular irritability, manifesting as positive Chvostek or Trousseau signs, can further support the presence of underlying calcium or vitamin D deficiency. In severe cases, hypocalcemia may precipitate tetany or hypocalcemic seizures, indicating a significant disturbance in mineral homeostasis.[20] Overall, the gradual and nonspecific nature of symptoms necessitates a high index of suspicion, especially in individuals with known risk factors. Early identification based on comprehensive history-taking and focused physical examination is crucial to preventing progression, minimizing complications, and initiating timely diagnostic evaluation and treatment.

Evaluation

The evaluation of osteomalacia requires a comprehensive integration of clinical findings, biochemical abnormalities, and radiographic features. No single laboratory test is pathognomonic for the condition, reflecting the complexity of its underlying metabolic disturbances. Nonetheless, characteristic patterns in serum and urine markers can strongly suggest the diagnosis when interpreted in conjunction with symptoms and imaging studies. In most patients, osteomalacia is marked by hypophosphatemia, hypocalcemia, or a combination of both, reflecting impaired mineral availability for bone formation.[18] These abnormalities arise from disruptions in vitamin D metabolism, phosphate handling, or calcium absorption, all of which compromise proper osteoid mineralization. A key biochemical marker is elevated alkaline phosphatase (ALP), particularly bone-specific ALP, which increases in response to the accumulation of unmineralized osteoid and heightened osteoblastic activity. Many experts emphasize that low phosphate or calcium levels paired with elevated ALP should prompt strong suspicion of osteomalacia, especially in symptomatic patients. Radiographic abnormalities often emerge later in the disease course, paralleling the progression of osteoid accumulation and skeletal fragility. Low bone mineral density (BMD), observed on dual-energy X-ray absorptiometry (DEXA), reflects impaired mineralization and may involve the spine, hip, and forearm.[21] More specific radiologic findings include Looser zones, also known as pseudofractures—transverse radiolucent lines perpendicular to the cortex that represent areas of incomplete fracture healing. These classically appear symmetrically in the femoral necks, long bone shafts, and pelvic bones. Bone scintigraphy may reveal focal increased tracer uptake corresponding to these pseudofractures, supporting the diagnosis when radiographs are inconclusive. To improve diagnostic clarity, Fukumoto et al proposed a set of criteria that categorize osteomalacia as definite or possible.[18] According to their model, definite osteomalacia is diagnosed when five key findings are present: hypocalcemia or hypophosphatemia, elevated bone alkaline phosphatase, muscle weakness or bone pain, BMD less than 80% of the young adult mean, and multiple areas of increased uptake on scintigraphy or radiographic evidence of Looser zones. Possible osteomalacia is defined by the presence of the first two laboratory findings in addition to any two of the remaining three criteria. Although useful for clinical guidance, these criteria require further validation, and their applicability may be limited in cases with overlapping metabolic or endocrine abnormalities.

Another set of diagnostic criteria was proposed by Uday and Hogler, particularly aimed at identifying nutritional osteomalacia in the absence of significant hepatic or renal disease.[22] These criteria include elevated parathyroid hormone (PTH), elevated ALP, low urinary calcium excretion, and either low calcium intake (typically less than 300 mg/day) or markedly reduced calcidiol levels (<30 nmol/L). These markers highlight key physiological responses to calcium and vitamin D deficiency, such as secondary hyperparathyroidism, reduced calcium conservation, and impaired bone mineralization.

Importantly, these criteria are less reliable in patients with chronic kidney disease or liver dysfunction, where PTH, ALP, and calcidiol levels may be influenced by underlying pathology. The measurement of serum 25(OH)D remains central to the evaluation because it is the most reliable indicator of vitamin D status. Patients with nutritional osteomalacia typically exhibit severely low 25(OH)D levels, often falling below 10 ng/mL. Additional biochemical indicators include elevated PTH in response to hypocalcemia and decreased urinary calcium due to reduced intestinal calcium absorption. These findings help differentiate osteomalacia from other metabolic bone disorders and underscore the impacts of mineral deprivation on endocrine regulation. Radiographic studies provide further corroboration. Beyond pseudofractures, plain radiographs may reveal decreased cortical thickness, osteopenia, and blurring of vertebral trabecular patterns due to undermineralized osteoid.[21][23] However, these features can overlap with osteoporosis, making clinical correlation essential. Bone scintigraphy serves as a sensitive adjunctive tool and may detect early or subtle lesions not visible on X-ray. Although rarely necessary, iliac crest bone biopsy with tetracycline labeling remains the gold standard for diagnosing osteomalacia. Histologic examination reveals an increased volume of unmineralized osteoid and prolonged mineralization lag time. Given its invasive nature, biopsy is typically reserved for unclear cases, atypical presentations, or instances in which noninvasive studies fail to identify the underlying cause.[21][23] In most clinical scenarios, the diagnosis can be confidently established through biochemical evaluation, imaging studies, and careful clinical assessment.

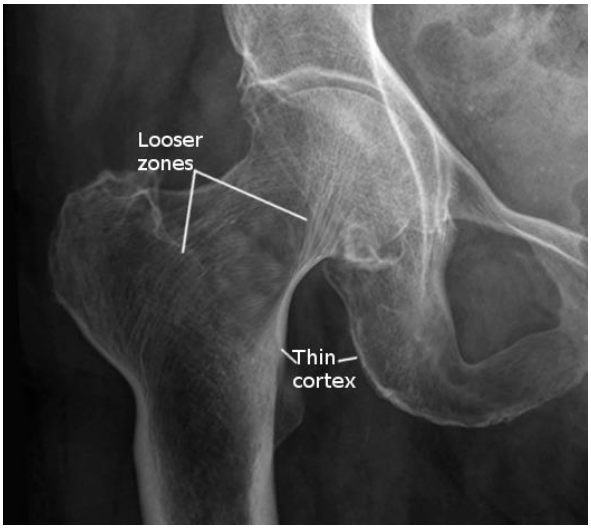

Fig. 3: Osteomalacia of Hip Joint.

Treatment / Management

Effective management of osteomalacia requires a dual approach: the correction of underlying etiologies and the restoration of normal vitamin D, calcium, and phosphate levels to promote proper bone mineralization. Because osteomalacia can arise from diverse mechanisms—including malabsorption, chronic kidney or liver disease, medication effects, or nutritional deficiencies—an individualized treatment plan must be developed based on the specific contributing factors identified during the diagnostic process. Once vitamin D deficiency has been established as the primary mechanism, therapeutic intervention often results in rapid clinical improvement. Many patients experience enhanced muscle strength, better mobility, and relief from bone tenderness within several weeks of initiating treatment, reflecting the skeletal system's responsiveness to restored mineral availability. Monitoring biochemical parameters is essential during the early phases of therapy. Serum calcium and urine calcium excretion should be assessed at approximately 1 month, then at 3 months, and subsequently every 6 to 12 months until 24-hour urine calcium levels normalize. These measurements help ensure that adequate mineralization is occurring while preventing potential complications such as hypercalcemia or hypercalciuria. Serum 25-hydroxyvitamin D (25[OH]D) levels can be rechecked after 3 to 4 months of supplementation to verify therapeutic response and guide dose adjustments. If signs of vitamin D excess arise—such as elevated serum calcium or increased urinary calcium—doses should be reduced to avoid toxicity. For individuals with severe vitamin D deficiency, high-dose loading regimens are often employed to replenish depleted stores efficiently. A commonly recommended strategy consists of administering 50,000 IU of ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3) orally once weekly for 8 to 12 weeks. This loading phase is followed by a maintenance regimen of 800 to 2000 IU of vitamin D3 daily, although higher maintenance doses may be necessary in patients with ongoing risk factors, persistent deficiency, or malabsorptive conditions. Cholecalciferol is generally preferred over ergocalciferol because vitamin D3 has a higher affinity for vitamin D–binding protein, resulting in a longer half-life and greater potency in raising serum vitamin D concentrations. Ergocalciferol, derived primarily from plant sources and fortified foods, remains an acceptable alternative when D3 is unavailable or contraindicated, but most evidence supports superior outcomes with cholecalciferol during long-term supplementation.

Calcium supplementation is a critical adjunct to vitamin D therapy because insufficient calcium intake can impair bone mineralization even when vitamin D levels are adequate. Most adults being treated for osteomalacia require at least 1000 mg of elemental calcium per day. Higher doses may be needed for individuals with absorptive limitations, such as those with gastrointestinal disorders or post-bariatric surgery anatomy, who may also need increased doses of vitamin D to achieve therapeutic

levels. Diet should be reviewed to ensure adequate intake of calcium-rich foods, though supplementation remains necessary for many patients. Patients with chronic liver or kidney disease present unique challenges because their ability to convert vitamin D into its active forms is diminished. In liver disease, impaired 25-hydroxylation limits the production of calcidiol, whereas renal disease diminishes 1-alpha-hydroxylase activity, reducing conversion to calcitriol. Consequently, patients with hepatic impairment may benefit from calcidiol supplementation, while those with renal dysfunction may require activated forms of vitamin D such as calcitriol, bypassing the need for renal conversion.[24] These formulations must be used with caution due to their potency and higher risk of inducing hypercalcemia. Monitoring the response to treatment involves both clinical and biochemical indicators. Serum calcium and phosphate often normalize within several weeks of therapy initiation, reflecting early correction of mineral imbalances. However, alkaline phosphatase—particularly bone-specific ALP—typically declines more slowly. Elevated ALP may persist for several months despite adequate treatment, as it reflects ongoing bone remodeling and the gradual mineralization of previously accumulated osteoid.[25] Improvement in bone mineral density (BMD) is another key marker of recovery, and increases in urinary calcium excretion often serve as a physiologic indicator that bone mineralization has resumed. Radiologic healing of pseudofractures, when present, may take several months to over a year depending on severity. Ultimately, successful management of osteomalacia hinges on identifying and addressing the underlying disorder—whether through vitamin D and calcium repletion, correcting malabsorption, modifying medication regimens, or treating renal or hepatic disease. With timely intervention and appropriate monitoring, most patients experience substantial improvement in musculoskeletal symptoms, functional capacity, and overall bone health [24][25].

Differential Diagnosis

The differential diagnosis of osteomalacia is broad and must be approached systematically, as many metabolic, neoplastic, and endocrine disorders can mimic its clinical and biochemical presentation. Because the symptoms of osteomalacia—such as diffuse bone pain, muscle weakness, gait disturbances, and fragility fractures—are nonspecific, clinicians must integrate detailed medical history, physical examination, laboratory analysis, and appropriate imaging to distinguish it from other disease processes. Several conditions share overlapping features with osteomalacia and must therefore be considered and excluded through targeted diagnostic evaluation. One major diagnostic consideration is metastatic bone disease, particularly osteoblastic metastases, which may present bone pain, reduced mobility, and multifocal skeletal abnormalities. These lesions can produce laboratory findings similar to osteomalacia, including elevated alkaline phosphatase, and may also display multiple zones of increased uptake on bone scintigraphy, thereby mimicking pseudofractures. In such cases, further evaluation—including advanced imaging such as CT, MRI, or PET scans, and possibly biopsy—is often required to rule out malignancy, especially in patients with a known cancer history or systemic symptoms suggestive of metastatic spread. Multiple myeloma is another important differential diagnosis due to its characteristic manifestations of bone pain, generalized weakness, and skeletal fragility. While osteomalacia often results in poorly mineralized bone, multiple myeloma typically produces distinct lytic lesions visible on radiographs. Additional distinguishing features include anemia, hypercalcemia, elevated serum protein levels, renal impairment, and the presence of monoclonal proteins on serum or urine electrophoresis. These findings help differentiate myeloma-related bone disease from metabolic bone disorders such as osteomalacia.

Primary hyperparathyroidism can also share clinical overlap with osteomalacia and warrants consideration. Like osteomalacia, it may present with bone pain, elevated bone alkaline phosphatase, and increased scintigraphic uptake. However, the biochemical hallmark of primary hyperparathyroidism is hypercalcemia, in contrast to the hypocalcemia or normocalcemia, which is more commonly seen in osteomalacia. Serum phosphate levels also differ significantly; hypophosphatemia is typical of both conditions, but the persistent and often profound hypercalcemia of hyperparathyroidism provides a key point of distinction. Renal osteodystrophy represents another condition that can resemble osteomalacia, particularly in patients with advanced chronic kidney disease. It encompasses a spectrum of bone abnormalities arising from impaired mineral metabolism, secondary hyperparathyroidism, and decreased calcitriol production. Unlike osteomalacia caused by nutritional or malabsorptive deficiencies, renal osteodystrophy typically presents with hyperphosphatemia rather than hypophosphatemia due to reduced phosphate excretion by the kidneys. Elevated PTH levels, metabolic acidosis, and evidence of progressive renal dysfunction further support this diagnosis. Additional conditions that may enter the differential diagnosis include osteoporosis, which causes decreased bone density but lacks the hallmark defect in mineralization; Paget disease of bone, distinguished by abnormal bone remodeling and characteristic radiographic findings; and chronic musculoskeletal disorders such as fibromyalgia, which may present with widespread pain but show no objective skeletal abnormalities on imaging or laboratory evaluation. In summary, differentiating osteomalacia from these overlapping conditions requires careful correlation of clinical findings with biochemical markers and imaging. Identification of hypocalcemia or hypophosphatemia combined with elevated alkaline phosphatase, reduced 25(OH)D

levels, and characteristic radiologic findings strongly supports the diagnosis of osteomalacia, while deviations from this pattern should prompt consideration of alternative diagnoses such as malignancy, hyperparathyroidism, or renal osteodystrophy.

Prognosis

Osteomalacia is, in principle, a preventable and largely reversible metabolic bone disorder, and its overall prognosis is generally favorable when the underlying cause is identified and adequately treated. In most patients, vitamin D deficiency represents the predominant etiologic factor, and timely correction of this deficiency can halt disease progression and allow for substantial, often complete, skeletal recovery. When the disorder results solely from nutritional or lifestyle-related vitamin D deficiency, appropriate supplementation and dietary optimization may be sufficient to normalize biochemical parameters, improve bone mineralization, and resolve symptoms to the extent that osteomalacia may be considered functionally cured. In more complex cases, where additional clinical factors such as malabsorption syndromes, chronic liver or kidney disease, or medication effects contribute to the pathogenesis, prognosis depends on the extent to which these conditions can be modified or controlled. Management must therefore be tailored to address both the primary deficiency and any comorbid conditions that impair mineral metabolism or vitamin D activation. Once treatment is initiated, improvements in biochemical markers such as serum calcium and phosphate, as well as a decline in secondary hyperparathyroidism, may begin to emerge within weeks. Patients often report early symptomatic relief, including reduction in bone pain, improved muscle strength, and enhanced mobility, which can significantly improve quality of life and functional status. Nevertheless, the pace of skeletal healing is variable and depends on factors including the severity and duration of deficiency, age, comorbid illnesses, and adherence to therapy. Normalization of bone mineral density and complete remineralization of previously undermineralized osteoid may require many months to more than a year. During this period, interval laboratory monitoring of serum calcium, phosphate, alkaline phosphatase, 25(OH)D, and urinary calcium excretion is essential to guide ongoing therapy and prevent overtreatment. Long-term prognosis is most favorable when osteomalacia is recognized early, before recurrent fractures or significant deformities have occurred. Delayed diagnosis can result in chronic skeletal pain, structural deformities such as bowing of the long bones or spinal curvature, and persistent functional impairment. In these situations, even with optimal therapy, residual disability may persist due to irreversible architectural changes in bone. However, appropriate treatment can still prevent further deterioration, reduce fracture risk, and stabilize or improve functional capacity. Overall, the prognosis is closely linked to clinical vigilance, timely intervention, and sustained patient engagement with therapy and follow-up. When these elements are in place, osteomalacia can be effectively managed with a high likelihood of symptomatic and structural recovery.

Complications

If left untreated, osteomalacia can progress to a range of clinically significant complications that reflect the structural fragility of inadequately mineralized bone. One of the hallmark complications is the development of insufficiency fractures, often referred to as Looser zones or pseudofractures. These lesions arise in areas of repetitive mechanical stress where undermineralized bone is unable to withstand normal loading forces. Clinically, they may present with localized bone pain, tenderness, and functional limitation, even in the absence of major trauma. Radiographically, pseudofractures appear as transverse or oblique radiolucent lines oriented perpendicular to the cortex, frequently bilateral and symmetrical, and most commonly involving the femoral necks, pubic and ischial rami. Reports also describe Looser zones in the ribs, scapulae, and clavicles, where they may be misinterpreted as traumatic or stress fractures if the underlying metabolic bone disease is not recognized. Spinal compression fractures, though more typically associated with osteoporosis, may also occur in patients with long-standing osteomalacia in whom vertebral bodies have been significantly weakened by chronic undermineralization. Such fractures can contribute to progressive height loss, back pain, and spinal deformity. In severe or prolonged disease, kyphoscoliosis has been reported, reflecting cumulative architectural distortion of the spine over time.[26] These deformities can impair respiratory mechanics, reduce exercise tolerance, and further compromise quality of life, especially in older adults or those with coexisting cardiopulmonary disease.

Beyond fractures and deformities, the functional consequences of untreated osteomalacia are considerable. Persistent bone pain, muscle weakness, and fatigue may lead to marked reductions in mobility and independence, predisposing patients to falls, secondary injuries, and deconditioning. Chronic pain can also contribute to mood disturbances, sleep disruption, and diminished social engagement. Recurrent fractures and delayed healing increase healthcare utilization, including hospitalizations, surgeries, and rehabilitation services. In some cases, misdiagnosis or failure to recognize osteomalacia may lead to inappropriate or incomplete management, allowing complications to progress despite medical attention. Importantly, many of these complications are preventable when osteomalacia is identified and treated early. Once adequate vitamin D and mineral repletion are achieved, bone strength gradually

improves, and the risk of new insufficiency fractures diminishes. Existing pseudofractures may heal with appropriate therapy and activity modification. However, established deformities, especially those that develop over long periods, may be only partially reversible and sometimes require orthopedic intervention. Consequently, early detection and intervention are critical not only for symptom relief but also for averting long-term structural and functional complications.

Consultations

The evaluation and management of osteomalacia are inherently multidisciplinary and frequently require input from several clinical specialties to ensure accurate diagnosis, targeted treatment, and comprehensive follow-up. In many cases, patients initially present to primary care or family medicine clinicians with vague complaints such as fatigue, diffuse musculoskeletal pain, or recurrent fractures. These frontline providers play a pivotal role in recognizing risk factors for vitamin D deficiency, ordering initial laboratory tests, and initiating basic supplementation. When osteomalacia is suspected or confirmed, referral to subspecialists may be warranted to address complex etiologies or to manage coexisting conditions. Endocrinologists and rheumatologists are often involved in the care of patients with metabolic bone disorders and are well positioned to differentiate osteomalacia from other entities such as osteoporosis, hyperparathyroidism, renal osteodystrophy, and inflammatory musculoskeletal diseases. They may guide advanced diagnostic workup, interpret nuanced laboratory abnormalities, and tailor treatment regimens, particularly in cases involving hormonal or mineral balance disturbances. Nephrologists should be consulted in patients with chronic kidney disease or suspected renal tubular defects contributing to phosphate wasting or impaired vitamin D activation, while hepatologists may be needed for individuals with significant liver dysfunction affecting vitamin D metabolism.

Radiology specialists are integral to the diagnostic process. They interpret plain radiographs, bone scintigraphy, CT, or MRI studies, helping to identify pseudofractures, osteopenia, and other structural changes characteristic of osteomalacia. Their expertise is particularly important when distinguishing these findings from metastatic disease, multiple myeloma, or other focal bone pathologies. Orthopedic surgeons should consider osteomalacia in patients presenting with fractures after minimal trauma or with atypical radiographic patterns. Awareness of underlying metabolic bone disease can influence surgical decision-making, fixation strategies, and postoperative rehabilitation planning, as well as prompt referral for metabolic evaluation to prevent future fractures. Dietitians and nutritionists also have an important consultative role, particularly in patients with dietary restrictions, eating disorders, malabsorptive conditions, or socioeconomic barriers to adequate nutrition. They can provide individualized counseling on vitamin D– and calcium-rich foods, safe supplementation strategies, and long-term dietary planning. In more complex cases, coordination among primary care clinicians, subspecialists, radiologists, orthopedic surgeons, and nutrition professionals ensures that all aspects of the patient's condition are addressed. Effective communication between these team members facilitates accurate diagnosis, optimizes therapeutic interventions, and supports sustained recovery and fracture prevention in individuals with osteomalacia.

Patient Education

Deterrence and patient education are central pillars in both the prevention and long-term management of osteomalacia. Because the majority of cases arise from modifiable risk factors—most notably inadequate vitamin D, calcium, and sometimes phosphate intake—comprehensive counseling can significantly reduce disease burden. Patients should be informed about the importance of maintaining sufficient vitamin D levels through a combination of safe sun exposure, dietary intake, and supplementation when appropriate. Education should emphasize that regular, moderate sunlight exposure to the face, arms, and legs can contribute meaningfully to endogenous vitamin D synthesis, while also acknowledging the need for skin cancer precautions and individualized guidance based on skin type and geographic location. Dietary education is equally important. Patients should understand which foods naturally contain or are fortified with vitamin D, such as fatty fish, egg yolks, fortified milk, yogurt, cheese, certain plant-based milk alternatives, orange juice, bread, and ultraviolet B–enhanced mushrooms. Calcium-rich foods, including dairy products, fortified plant-based alternatives, leafy green vegetables, and certain nuts and seeds, should also be highlighted. Those following vegetarian or vegan diets may be at particular risk if they avoid fish and other animal products; therefore, clinicians should discuss alternative fortified foods and appropriate supplementation strategies. Patients with malabsorptive syndromes, chronic liver or kidney disease, or a history of bariatric surgery should receive tailored counseling and often require higher-dose supplementation and closer monitoring.

Certain populations are at especially high risk for vitamin D deficiency and, consequently, osteomalacia. These include individuals with dark skin, those who have limited skin exposure to sunlight due to cultural or religious clothing practices, people with diets low in vitamin D, patients taking medications that accelerate vitamin D metabolism, individuals with obesity, older adults, and those with malabsorptive, renal, or hepatic disorders. Although routine screening of asymptomatic individuals remains controversial, clinicians should maintain a high index of suspicion in these at-risk groups and consider measuring serum 25(OH)D levels when

clinical circumstances warrant. Education should focus not only on risk recognition but also on practical, culturally sensitive strategies to reduce risk, such as modest increases in sun exposure when acceptable, use of fortified foods, and adherence to supplementation regimens. Patients should also be taught to recognize early symptoms of osteomalacia, including diffuse bone pain, muscle weakness, difficulty climbing stairs or rising from a chair, and frequent falls. Prompt medical evaluation of these symptoms can lead to earlier diagnosis and intervention, preventing progression to fractures and deformities. Encouraging regular weight-bearing and strengthening exercises is another key preventive strategy, as physical activity supports bone health and reduces fracture risk. Ultimately, effective deterrence depends on ongoing dialogue between patients and healthcare providers, in which information is tailored to individual needs, beliefs, and circumstances. By empowering patients with knowledge and practical tools, clinicians can significantly reduce the incidence and impact of osteomalacia and its complications.

Enhancing Healthcare Team Outcomes

Optimal care for individuals with osteomalacia requires a coordinated, interprofessional approach that leverages the expertise of a diverse healthcare team. Physicians, advanced practice clinicians, nurses, pharmacists, dietitians, and other allied health professionals each contribute unique skills that, when integrated, improve diagnostic accuracy, treatment effectiveness, and patient satisfaction. Clinicians must be adept at recognizing the often subtle clinical manifestations of osteomalacia, interpreting relevant laboratory results—such as serum 25(OH)D, calcium, phosphate, alkaline phosphatase, and PTH—and understanding the appropriate use of imaging modalities including plain radiographs, bone density scans, and bone scintigraphy. This diagnostic acumen is essential for distinguishing osteomalacia from conditions with overlapping presentations and for identifying underlying etiologies that require specific interventions. A patient-centered approach emphasizes shared decision-making, where treatment plans are aligned with the patient's values, preferences, and lifestyle. Physicians and advanced practitioners should clearly explain the nature of osteomalacia, its causes, potential complications, and therapeutic options, including the role of vitamin D and calcium supplementation, dietary changes, sunlight exposure, and management of comorbid conditions. Nurses play a key role in reinforcing this education, assisting patients with practical aspects of supplement administration, monitoring adherence, and recognizing early signs of adverse effects or treatment failure. They also help coordinate follow-up visits, ensuring that laboratory tests and imaging studies are performed at appropriate intervals.

Pharmacists are crucial in evaluating medication regimens, identifying potential drug–nutrient interactions, and recommending suitable vitamin D formulations and dosing strategies based on individual patient factors such as renal or hepatic function. Their expertise is especially important when higher-dose regimens or active vitamin D analogs are required, as these agents carry an increased risk of hypercalcemia and require careful monitoring. Dietitians provide detailed nutritional assessments and counseling, guiding patients in selecting vitamin D– and calcium-rich foods, incorporating fortified products, and addressing barriers related to cultural practices, food availability, or socioeconomic constraints.[29] The interprofessional team must also stay abreast of evolving evidence regarding food fortification and public health strategies to combat vitamin D deficiency. Randomized controlled trials have demonstrated that fortified foods—such as dairy products, bread, orange juice, and ultraviolet B–enhanced mushrooms—can effectively increase circulating 25(OH)D levels without significant adverse events. National policies on food fortification vary, and current fortification levels may not fully meet physiological needs, particularly among high-risk groups. Research on vitamin D–enriched feed for animals has shown promising increases in vitamin D content in meat, eggs, and fish, offering additional avenues to improve population-wide status. Interprofessional teams should be aware of these developments to provide informed counseling and advocate for evidence-based public health measures. Long-term follow-up is essential because complete skeletal recovery from osteomalacia can take many months. Regular assessments allow the team to monitor biochemical response, BMD improvements, symptom resolution, and adherence to lifestyle modifications. Open communication among all team members ensures that changes in patient status, new comorbidities, or potential complications are promptly recognized and addressed. Referral to specialists such as endocrinologists, nephrologists, gastroenterologists, or orthopedic surgeons may be necessary in complex cases or when standard interventions are insufficient. By integrating clinical expertise, continuous education, and collaborative decision-making, the interprofessional team can significantly enhance patient-centered care, reduce morbidity, and optimize long-term outcomes for individuals with osteomalacia.

Conclusion:

In conclusion, osteomalacia is a preventable and highly treatable metabolic bone disease whose successful management hinges on a comprehensive, interdisciplinary approach. While its primary driver is often profound vitamin D deficiency, a thorough evaluation is essential to identify and address diverse underlying causes, including malabsorption, renal disease, and medication effects. The cornerstone of

treatment involves aggressive repletion of vitamin D and calcium, followed by lifelong maintenance supplementation and dietary optimization to restore normal bone mineralization and alleviate debilitating symptoms like bone pain and muscle weakness. The prognosis for patients with osteomalacia is generally excellent with timely intervention, leading to the resolution of biochemical abnormalities and the gradual healing of skeletal defects. However, achieving this optimal outcome requires the coordinated efforts of an interprofessional team. Physicians, nurses, pharmacists, dietitians, and radiologists must collaborate seamlessly to ensure accurate diagnosis, tailor treatment regimens, provide robust patient education on sun exposure and nutrition, and conduct long-term monitoring to prevent recurrence and complications. Through this integrated, patient-centered model of care, healthcare providers can effectively reverse the course of osteomalacia and significantly improve patient quality of life.

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