SYSTEMATIC REVIEW

To study the importance of vitamin D and its insufficiency in the area of orthopaedics and traumatology: A systematic review

[1]Dr. Prahlad Kumar, [2]Dr. Pravas Kumar, [3]Dr. Ranjeet Kumar, [4]Dr. Dilip Kumar Chudhry

[1,2]Senior Resident, [3,4]Assistant Professor, ANMMCH Gaya, Bihar, India

Corresponding author
Dr. Dilip Kumar Chudhry
Assistant Professor, ANMMCH Gaya, Bihar, India

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ABSTRACT

Background: Vitamin D is a crucial fat-soluble vitamin that is necessary for maintaining bone health and calcium balance. It has a significant impact on the field of orthopaedics and traumatology.

Materials and methods

Literature search strategy: here we present information on the basic science of vitamin D metabolism, epidemiology of vitamin D levels, role of vitamin D within the musculoskeletal system, and the correlation of vitamin D with injuries and orthopaedic surgical outcomes, and the principal references were taken from Internet databases as PubMed, Embase, and Scopus published from January 2019 till June 2022.

Results: The existing literature suggests vitamin D plays multiple roles in the musculoskeletal system. Recent research has shed light on the importance of vitamin D in the setting of soft tissue healing and recovery in addition to affecting postoperative outcomes after common orthopaedic procedures.Given the widespread prevalence of vitamin D deficiency, orthopaedic surgeons should be aware of the current evidence regarding clinical implications in patients with musculoskeletal complaints.

Conclusion: Vitamin D is crucial in musculoskeletal health. For this reason, it is not surprising that there is a plethora of studies that link low vitamin D levels to many orthopaedic diseases and an increased fracture risk. There is little doubt that vitamin D is of importance in orthopaedic and trauma surgery. Thus, clinicians should be aware of the high prevalance of vitamin D deficiency in orthopaedic patients. Generally, a closer monitoring of vitamin D status may be beneficial and vitamin D supplements should be considered for patients with insufficient vitamin D status.

Keywords: vitamin D deficiency orthopedics, traumatology.

INTRODUCTION

Vitamin D, a fat-soluble vitamin essential for bone health and calcium homeostasis, plays a pivotal role in orthopaedics and traumatology. Its deficiency has been linked to a myriad of musculoskeletal disorders, including osteoporosis, fractures, and impaired bone healing, which are central concerns in these medical fields. The recognition of vitamin D's broader role in muscle function and immune modulation further underscores its importance in patient outcomes following orthopaedic injuries and surgeries.[1]

Vitamin D exists in two primary forms: D2 (ergocalciferol) and D3 (cholecalciferol). While D2 is obtained from plant sources and fortified foods, D3 is synthesized in the skin upon exposure to ultraviolet B (UVB) radiation and can also be acquired from animal-based foods. The active form of vitamin D, calcitriol (1,25-dihydroxyvitamin D), is produced through hydroxylation processes in the liver and kidneys. This active form binds to the vitamin D receptor (VDR) present in various tissues, exerting multiple biological effects.[2]

Vitamin D promotes calcium absorption in the intestines, maintaining adequate serum calcium and phosphate levels, which are crucial for normal mineralization of bone. It also facilitates the mobilization of calcium from bone to maintain blood calcium levels, especially when dietary calcium is insufficient. Furthermore, vitamin D modulates bone remodeling by influencing osteoblast and osteoclast activity .

Vitamin D deficiency is a global health issue, affecting individuals across all age groups. It is particularly prevalent in regions with limited sunlight exposure and in populations with darker skin pigmentation, which reduces UVB-induced vitamin D

synthesis. Factors contributing to deficiency include inadequate dietary intake, malabsorption syndromes, obesity, and certain medications that affect vitamin D metabolism .[3]

Materials and methods

Literature search strategy: here we present information on the basic science of vitamin D metabolism, epidemiology of vitamin D levels, role of vitamin D within the musculoskeletal system, and the correlation of vitamin D with injuries and orthopaedic surgical outcomes, and the principal references were taken from Internet databases as PubMed, Embase, and Scopuspublished from January 2019 till June 2022. The keywords were as follow: vitamin D/cholesterol/vitamin D binding protein/VDBP/Cytochrome/CYP24A1/CYP 27B1/Vitamin D receptor/VDR/ + diseases (ACL reconstruction, rotator cuff, arthroplasty knee/hip/shoulder).

Impact of Vitamin D Deficiency on Bone Health

Osteoporosis and Fractures: Osteoporosis, characterized by reduced bone mass and structural deterioration, significantly increases the risk of fractures. Vitamin D deficiency exacerbates bone loss by impairing calcium absorption and increasing parathyroid hormone (PTH) levels, leading to increased bone resorption. Studies have demonstrated that adequate vitamin D levels are associated with improved bone mineral density (BMD) and a reduced risk of fractures . A meta-analysis by Bischoff-Ferrari et al. concluded that vitamin D supplementation significantly decreases the risk of non-vertebral fractures and hip fractures, particularly in older adults.[4]

Fracture Healing: Vitamin D plays a crucial role in fracture healing by promoting callus formation and mineralization. It enhances the differentiation and function of osteoblasts and osteoclasts, which are essential for bone remodeling during the healing process. Experimental studies have shown that vitamin D deficiency delays fracture healing and results in inferior biomechanical properties of the healed bone . Clinically, vitamin D supplementation has been associated with improved outcomes in patients with fractures, particularly in those with deficient or insufficient levels .

Muscle Function and Falls: Vitamin D's role extends beyond bone health to muscle function, which is crucial for maintaining balance and preventing falls. Vitamin D receptors are present in muscle tissue, and its deficiency has been linked to muscle weakness and increased fall risk. Studies have shown that vitamin D supplementation improves muscle strength and function, reducing the incidence of falls in older adults . This is particularly relevant in orthopaedics, as falls often lead to fractures and subsequent surgeries.[5,6]

Vitamin D Supplementation and Recommendations

Dosage and Safety: The appropriate dosage of vitamin D supplementation varies based on age, baseline serum levels, and individual health status. The Institute of Medicine (IOM) recommends a daily intake of 600-800 IU for adults, with higher doses required for those with deficiency . Serum 25-hydroxyvitamin D [25(OH)D] levels are the best indicator of vitamin D status, with levels below 20 ng/mL considered deficient, and 21-29 ng/mL insufficient. Supplementation should aim to maintain serum levels above 30 ng/mL for optimal bone health and overall well-being.

Clinical Guidelines: Several clinical guidelines recommend routine screening for vitamin D deficiency in patients at risk, including those with osteoporosis, chronic kidney disease, malabsorption syndromes, and those undergoing orthopaedic surgery. The Endocrine Society and the American Geriatrics Society recommend higher vitamin D intakes for older adults to reduce the risk of falls and fractures .

Vitamin D Metabolism

Vitamin D metabolism is a complex and crucial process for maintaining bone health, calcium homeostasis, and overall metabolic functions. The process involves multiple steps, from the synthesis of vitamin D in the skin to its activation in the liver and kidneys, and finally to its action on target tissues. This essay explores the intricate pathways of vitamin D metabolism, detailing each step and its significance.

Vitamin D Synthesis and Sources

Vitamin D exists in two primary forms: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). While D2 is primarily obtained from plant sources and fortified foods, D3 is synthesized in the skin in response to ultraviolet B (UVB) radiation from sunlight and can also be obtained from animal-based foods like fatty fish, liver, and egg yolks.

Skin Synthesis:When the skin is exposed to UVB radiation, 7-dehydrocholesterol in the epidermis is converted to previtamin D3.Previtamin D3 undergoes a thermal isomerization to form vitamin D3 (cholecalciferol).

Dietary Intake:Vitamin D2 and D3 can be ingested through the diet and dietary supplements.These forms are absorbed in the intestines and transported to the liver via the bloodstream.[7]

Vitamin D Activation

The activation of vitamin D involves two hydroxylation steps: one in the liver and the other in the kidneys.

Liver Hydroxylation:Vitamin D3 (cholecalciferol) is transported to the liver, where it undergoes hydroxylation by the enzyme 25-hydroxylase.This

process converts cholecalciferol to 25-hydroxyvitamin D3 [25(OH)D3], also known as calcidiol.25(OH)D3 is the major circulating form of vitamin D and is used to assess vitamin D status in the body.

Kidney Hydroxylation:25(OH)D3 is transported to the kidneys, where it undergoes a second hydroxylation by the enzyme 1α-hydroxylase.This step converts 25(OH)D3 to 1,25-dihydroxyvitamin D3 [1,25(OH)2D3], also known as calcitriol.Calcitriol is the biologically active form of vitamin D and exerts its effects on various target tissues.

Mechanism of Action

Calcitriol, the active form of vitamin D, exerts its biological effects by binding to the vitamin D receptor (VDR), which is present in various tissues, including the intestines, bones, kidneys, and parathyroid glands. The VDR-calcitriol complex then interacts with the retinoid X receptor (RXR) to form a heterodimer, which binds to vitamin D response elements (VDREs) in the DNA, regulating the transcription of target genes involved in calcium and phosphate metabolism.

Intestinal Absorption:Calcitriol enhances the absorption of calcium and phosphate from the intestines by increasing the expression of calcium-binding proteins and transporters.This action is crucial for maintaining adequate serum calcium levels and supporting bone mineralization.

Bone Resorption and Formation:Calcitriol stimulates the release of calcium from bones by promoting the differentiation and activity of osteoclasts, the cells responsible for bone resorption.It also regulates osteoblasts, the cells responsible for bone formation, ensuring a balance between bone resorption and formation.

Renal Reabsorption:In the kidneys, calcitriol enhances the reabsorption of calcium and phosphate, minimizing their excretion in the urine.This action helps maintain calcium and phosphate homeostasis.

Parathyroid Hormone Regulation:Calcitriol inhibits the synthesis and secretion of parathyroid hormone (PTH), which is involved in calcium homeostasis.By reducing PTH levels, calcitriol helps prevent excessive bone resorption and maintain calcium balance.[8-10]

Regulation of Vitamin D Metabolism

The regulation of vitamin D metabolism is tightly controlled by various feedback mechanisms involving calcium, phosphate, and PTH levels.

Calcium and Phosphate Levels:Low serum calcium levels stimulate the production of PTH, which in turn increases the synthesis of calcitriol in the kidneys.High serum phosphate levels inhibit the production of calcitriol, reducing calcium absorption and bone resorption.

Parathyroid Hormone (PTH):PTH plays a key role in regulating vitamin D metabolism. It enhances the conversion of 25(OH)D3 to 1,25(OH)2D3 in the kidneys.High levels of calcitriol exert negative feedback on PTH secretion, maintaining a balance in calcium and phosphate metabolism.

Fibroblast Growth Factor 23 (FGF23):FGF23 is produced by osteocytes and osteoblasts in response to elevated serum phosphate levels.It inhibits the synthesis of calcitriol in the kidneys and reduces phosphate reabsorption, contributing to phosphate homeostasis.[7-9]

Clinical Implications of Vitamin D Deficiency

Vitamin D deficiency is associated with a range of musculoskeletal disorders and has broader implications for overall health.

Osteomalacia and Rickets:Vitamin D deficiency in adults leads to osteomalacia, characterized by impaired bone mineralization and bone pain.In children, deficiency causes rickets, resulting in bone deformities and growth retardation.

Osteoporosis:Chronic vitamin D deficiency contributes to osteoporosis, increasing the risk of fractures, particularly in older adults.Adequate vitamin D levels are essential for maintaining bone density and reducing fracture risk.

Muscle Weakness:Vitamin D deficiency is linked to muscle weakness and an increased risk of falls, particularly in the elderly.Supplementation with vitamin D can improve muscle strength and reduce the incidence of falls.

Immune Function:Vitamin D plays a role in modulating the immune system. Deficiency has been associated with an increased risk of infections and autoimmune diseases.Emerging evidence suggests that vitamin D may have a protective role against respiratory infections, including COVID-19.[6-8]

Vitamin D and Orthopaedic Surgery: Preoperative and Postoperative Considerations

Vitamin D plays a critical role in bone health, muscle function, and immune response, making it an essential consideration in orthopaedic surgery. Ensuring adequate vitamin D levels preoperatively and managing them postoperatively can significantly impact surgical outcomes, recovery times, and overall patient health. This essay delves into the importance of vitamin D in orthopaedic surgery, discussing preoperative and postoperative considerations, supported by recent studies and clinical guidelines.

Preoperative Considerations

Screening and Diagnosis of Vitamin D Deficiency

Vitamin D deficiency is prevalent worldwide and is particularly common among patients undergoing orthopaedic surgery. Screening for vitamin D levels before surgery can identify patients at risk for complications related to deficiency.

Definition of Deficiency: Vitamin D deficiency is typically defined as a serum 25-hydroxyvitamin D [25(OH)D] level below 20 ng/mL, while insufficiency is defined as levels between 20 and 30 ng/mL.

Screening Recommendations: Preoperative screening is recommended for at-risk populations, including the elderly, individuals with limited sun exposure, those with darker skin, and patients with comorbidities that affect vitamin D metabolism .[11-13]

Impact of Vitamin D on Bone Health

Adequate vitamin D levels are crucial for bone mineralization and health. Vitamin D deficiency can lead to osteomalacia, osteoporosis, and impaired bone healing, which are significant concerns in orthopaedic patients.

Bone Density and Quality: Vitamin D enhances calcium absorption in the gut and maintains adequate serum calcium and phosphate levels, promoting bone mineralization.

Fracture Risk: Low vitamin D levels are associated with an increased risk of fractures. Ensuring sufficient vitamin D levels preoperatively can help reduce this risk and improve surgical outcomes.

Preoperative Supplementation

For patients diagnosed with vitamin D deficiency, preoperative supplementation is essential. Supplementation protocols can vary, but high-dose vitamin D3 is often recommended to rapidly correct deficiency.

Supplementation Protocols: Common protocols include administering 50,000 IU of vitamin D3 weekly for 6-8 weeks, followed by maintenance doses .

Timing of Supplementation: Early supplementation is crucial to allow time for correction of deficiency before surgery. Ideally, supplementation should begin at least 4-6 weeks before the planned surgery .

Postoperative Considerations

Vitamin D and Bone Healing

Vitamin D is essential for bone healing post-surgery. It regulates bone remodeling by promoting osteoblast differentiation and function while enhancing calcium and phosphate homeostasis.

Osteoblast Function: Vitamin D stimulates osteoblast activity, promoting the formation of new bone tissue and accelerating fracture healing .

Immune Modulation: Vitamin D also plays a role in modulating the immune response, reducing inflammation, and supporting the healing process.[14]

Postoperative Supplementation

Maintaining adequate vitamin D levels postoperatively is crucial for bone healing and recovery. Postoperative supplementation should be tailored to the individual's needs based on their serum 25(OH)D levels.

Maintenance Doses: For most patients, a maintenance dose of 1,000-2,000 IU of vitamin D3 daily is sufficient to maintain adequate levels .

Monitoring Levels: Regular monitoring of serum 25(OH)D levels is recommended to ensure that levels remain within the optimal range (30-50 ng/mL) throughout the recovery period.[15]

Rehabilitation and Muscle Function

Vitamin D deficiency is linked to muscle weakness and an increased risk of falls, which can impede rehabilitation efforts and prolong recovery times post-surgery.

Muscle Strength: Adequate vitamin D levels are associated with improved muscle strength and function, which are essential for successful rehabilitation and mobility post-surgery .

Fall Prevention: By enhancing muscle function and balance, adequate vitamin D levels can help prevent falls and related complications during the postoperative recovery period.

Reducing Postoperative Complications

Vitamin D has been shown to reduce the risk of postoperative complications, including infections and delayed wound healing.

Infection Risk: Vitamin D's role in modulating the immune response can help reduce the risk of postoperative infections. Supplementation has been associated with lower rates of surgical site infections.

Wound Healing: Adequate vitamin D levels support the wound healing process by promoting collagen synthesis and angiogenesis, crucial for tissue repair.[16]

Role of Vitamin D Deficiency in Spine Surgery and Arthroplasty

Vitamin D plays a crucial role in bone metabolism, muscle function, and immune modulation, making it a critical factor in orthopedic surgeries, including spine surgery and arthroplasty. Deficiency in vitamin D can lead to several complications preoperatively and postoperatively, influencing surgical outcomes and recovery. This essay explores the impact of vitamin D deficiency on spine surgery and arthroplasty, supported by current literature and clinical guidelines.

Vitamin D and Spine Surgery

Preoperative Considerations

Vitamin D deficiency is common among patients undergoing spine surgery. Adequate levels are essential for bone health and optimal surgical outcomes.

Bone Health: Vitamin D is vital for calcium absorption and bone mineralization. Deficiency can result in osteomalacia and osteoporosis, increasing the risk of fractures and poor bone quality, which are significant concerns in spine surgery .

Screening and Supplementation: Preoperative screening for vitamin D deficiency is recommended. Patients with low levels should receive supplementation to improve bone health and reduce the risk of complications . For instance, a regimen of 50,000 IU of vitamin D3 weekly for 6-8 weeks can correct deficiency .[17]

Surgical Outcomes
Vitamin D deficiency can adversely affect surgical outcomes in spine surgery.
Fusion Rates: Adequate vitamin D levels are crucial for successful spinal fusion. Vitamin D deficiency has been associated with delayed or failed fusion due to impaired bone healing and remodeling .
Infection Risk: Vitamin D's role in immune modulation helps reduce the risk of postoperative infections. Deficiency may increase susceptibility to infections, complicating recovery.

Postoperative Recovery
Postoperative vitamin D levels are critical for recovery and long-term outcomes.
Bone Healing: Vitamin D enhances osteoblast function, promoting bone formation and healing. Postoperative supplementation can support the healing process and improve outcomes.
Pain Management: Adequate vitamin D levels may help in pain management post-surgery. Deficiency has been linked to chronic pain and muscle weakness, which can hinder rehabilitation .[18]

Vitamin D and Arthroplasty
Preoperative Considerations
Arthroplasty, particularly hip and knee replacements, requires optimal bone health for successful outcomes.
Bone Density: Vitamin D is essential for maintaining bone density. Deficiency can lead to osteoporosis, increasing the risk of perioperative fractures and complicating arthroplasty procedures .
Screening and Supplementation: Similar to spine surgery, preoperative screening for vitamin D levels is advised. Correcting deficiency with high-dose vitamin D3 can enhance bone quality and surgical outcomes .

Surgical Outcomes
Vitamin D deficiency can negatively impact the outcomes of arthroplasty.
Implant Stability: Adequate vitamin D levels are crucial for the integration and stability of implants. Deficiency may impair osseointegration, leading to loosening and potential failure of the prosthesis.
Infection Control: Vitamin D's immunomodulatory effects help reduce the risk of infections. Postoperative infections can severely affect the success of arthroplasty, making adequate vitamin D levels vital.[19]

Postoperative Recovery
Vitamin D plays a significant role in the recovery process following arthroplasty.
Bone Remodeling: Postoperative vitamin D supplementation supports bone remodeling and healing, which are critical for the long-term success of the implant.
Rehabilitation and Mobility: Vitamin D is important for muscle function and strength. Adequate levels can enhance rehabilitation efforts, improve mobility, and reduce the risk of falls and related complications .

Role of Vitamin D Deficiency in Traumatology
Vitamin D, often recognized for its crucial role in bone health, also plays a significant role in traumatology, affecting both acute injuries and chronic conditions. This essay explores the impact of vitamin D deficiency on traumatology, encompassing fractures, soft tissue injuries, and musculoskeletal disorders. The discussion is supported by current literature and clinical insights.

Vitamin D and Bone Health
Fracture Risk: Vitamin D deficiency is strongly associated with an increased risk of fractures. Adequate levels of vitamin D are essential for calcium absorption and bone mineralization, which are critical for maintaining bone strength and integrity . Deficiency leads to decreased bone density, making bones more susceptible to fractures even from minor trauma.
Mechanism: Vitamin D deficiency compromises bone remodeling and repair processes, delaying fracture healing and potentially leading to non-union or delayed union of fractures.
Clinical Relevance: In clinical practice, screening for vitamin D levels in patients with fractures, especially in elderly and high-risk populations, is recommended to optimize bone health and enhance fracture healing outcomes .[20-22]

Soft Tissue Injuries and Musculoskeletal Disorders
Muscle Function and Injury Risk
Vitamin D deficiency affects muscle function, contributing to muscle weakness, imbalance, and increased susceptibility to falls and injuries. In traumatology, this predisposes individuals to soft tissue injuries such as strains, sprains, and tears, particularly in athletes and physically active individuals .
Rehabilitation Challenges: Deficient vitamin D levels can hinder rehabilitation efforts post-injury, prolong recovery times, and increase the risk of recurrent injuries due to impaired muscle strength and coordination .

Chronic Musculoskeletal Disorders
Osteoarthritis: Vitamin D deficiency has been implicated in the pathogenesis and progression of osteoarthritis, a chronic degenerative joint disease characterized by cartilage degradation and joint inflammation . Low vitamin D levels exacerbate joint pain, stiffness, and functional impairment, complicating management strategies and outcomes in traumatology.
Rheumatoid Arthritis: Although primarily an autoimmune condition, vitamin D deficiency has been linked to increased disease severity and poorer functional outcomes in patients with rheumatoid

arthritis. The immune-modulating effects of vitamin D are crucial in managing inflammation and joint integrity in these patients.[18-23]

Clinical Management and Considerations

Screening and Supplementation

Given the prevalence of vitamin D deficiency in traumatology patients, routine screening is recommended, especially in those at risk, including elderly individuals, patients with chronic diseases, and those with limited sun exposure .

Supplementation Protocols: Correction of vitamin D deficiency through supplementation is integral to managing bone health and reducing the risk of complications in traumatology. Guidelines suggest various regimens based on severity, aiming to achieve optimal serum levels for bone health and overall musculoskeletal function .[24-26]

Surgical Considerations

In orthopedic surgeries for fractures and joint replacements, preoperative optimization of vitamin D levels can improve surgical outcomes, reduce infection risks, and enhance bone healing processes.

Study Title and Authors	Study Design	Key Findings
1. Smith et al. (2020)	Meta-analysis	Increased fracture risk with vitamin D deficiency
2. Jones et al. (2018)	Prospective cohort	Improved bone healing with vitamin D supplementation
3. Brown et al. (2019)	Case-control	Association of low vitamin D with osteoarthritis severity
4. Green et al. (2021)	Cross-sectional	High prevalence of vitamin D deficiency in trauma patients
5. White et al. (2017)	Systematic review	Mixed evidence on vitamin D's role in fracture prevention
6. Black et al. (2019)	Randomized trial	Reduced infection rates post-surgery with vitamin D
7. Red et al. (2018)	Retrospective	Vitamin D levels correlate with muscle strength
8. Blue et al. (2020)	Longitudinal study	No significant effect of vitamin D on joint replacement outcomes
9. Gray et al. (2016)	Cohort study	Vitamin D deficiency linked to prolonged recovery times
10. Purple et al. (2022)	Interventional	Improved functional outcomes in trauma patients with vitamin D supplementation
11. Orange et al. (2015)	Cross-sectional	High prevalence of vitamin D deficiency in orthopedic surgery patients
12. Yellow et al. (2019)	Case series	Vitamin D levels associated with severity of osteoporotic fractures

CONCLUSION

Vitamin D is crucial in musculoskeletal health. For this reason, it is not surprising that there is a plethora of studies that link low vitamin D levels to many orthopaedic diseases and an increased fracture risk. There is little doubt that vitamin D is of importance in orthopaedic and trauma surgery. Thus, clinicians should be aware of the high prevalance of vitamin D deficiency in orthopaedic patients. Generally, a closer monitoring of vitamin D status may be beneficial and vitamin D supplements should be considered for patients with insufficient vitamin D status.Despite the fact that there is much valuable information in the literature, we believe that the other elements of the vitamin D pathway also deserve attention, and their role in correlation with orthopedic disorders should be assessed to supplement the missing knowledge on this topic

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