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VITAMIN D SUPPLEMENTATION IN BURN PATIENTS: EFFECTS ON WOUND HEALING AND CLINICAL OUTCOMES — A NARRATIVE REVIEW

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ABSTRACT

Background: Burn injury induces profound metabolic, endocrine, and immunologic disturbances associated with impaired wound healing, increased infection risk, and prolonged recovery. Vitamin D deficiency is highly prevalent in patients with moderate-to-severe burns due to impaired cutaneous synthesis and altered metabolism.
Objective: This narrative review summarizes current evidence regarding vitamin D deficiency and supplementation in burn patients, with emphasis on wound healing, infectious complications, and clinical outcomes.
Methodology: A literature review was conducted using PubMed, Scopus, Web of Science, and Google Scholar databases. Clinical trials, observational studies, reviews, and meta-analyses published primarily between 2000 and 2025 were evaluated.
Results: Available evidence demonstrated that vitamin D deficiency is common in burns involving ≥20% total body surface area and is associated with delayed wound healing, increased infectious complications, prolonged ICU and hospital stay, and long-term musculoskeletal abnormalities.
Conclusion: Vitamin D appears to contribute to wound repair, immune modulation, and systemic recovery after burn injury; however, standardized burn-specific supplementation protocols remain unavailable.

KEYWORDS

Vitamin D, Burn Injury, Wound Healing, Cholecalciferol, Critical Care, Supplementation

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Introduction

Burn injury remains a major global public health problem associated with substantial morbidity, mortality, and long-term disability. Severe burns induce a complex systemic response characterized by hypermetabolism, inflammation, immune dysregulation, endocrine alterations, and accelerated protein catabolism (Herndon & Tompkins, 2004). In addition to local tissue destruction, extensive burns affect multiple organ systems and frequently require prolonged intensive care treatment, repeated surgical procedures, and long-term rehabilitation.

Among the metabolic disturbances observed after burn injury, alterations in vitamin D homeostasis have gained increasing attention. Vitamin D is traditionally recognized for its role in calcium–phosphate metabolism and skeletal integrity; however, accumulating evidence demonstrates that it also plays an important role in immune regulation, inflammatory modulation, cellular proliferation, differentiation, and wound repair (Bikle, 2014; Hewison, 2010). Consequently, vitamin D deficiency may have clinically relevant implications in critically ill burn patients.

Vitamin D deficiency is common in patients with moderate-to-severe burns, particularly in burns involving ≥20% total body surface area (TBSA) (Al-Tarrah et al., 2018; Rousseau et al., 2013). Multiple mechanisms contribute to this phenomenon. Destruction of the skin significantly reduces the availability of 7-dehydrocholesterol, impairing endogenous vitamin D synthesis. In addition, prolonged hospitalization, limited sunlight exposure, altered hepatic and renal metabolism, systemic inflammation, and hypermetabolism further exacerbate deficiency (Klein et al., 2004; Porter et al., 2007). Persistent deficiency has been documented months to years after injury and may contribute to impaired wound healing, infectious complications, prolonged hospitalization, and long-term musculoskeletal abnormalities (Porter et al., 2007).

In recent years, interest has expanded regarding the therapeutic potential of vitamin D supplementation in burn care. Experimental studies suggest that vitamin D influences keratinocyte proliferation, antimicrobial peptide expression, angiogenesis, extracellular matrix remodeling and cytokine regulation, all of which are relevant to wound healing and infection control (Bikle, 2014; Schauber et al., 2007). Clinical studies further suggest associations between low vitamin D levels and poorer clinical outcomes, including increased sepsis risk and prolonged ICU stay (Garner et al., 2022; Lee et al., 2016).

Despite increasing research interest, important uncertainties remain regarding the clinical significance of vitamin D deficiency in burn injury and the optimal supplementation strategy. Available studies vary considerably in design, patient populations, dosing regimens, target serum concentrations, and outcome measures. Consequently, no standardized burn-specific supplementation protocols currently exist.

The aim of this narrative review is to summarize current evidence regarding vitamin D metabolism and supplementation in burn patients, with emphasis on wound healing, infection, systemic recovery, and clinical outcomes. Additionally, the review evaluates currently available supplementation strategies and highlights ongoing controversies and research gaps in this evolving field.

Methodology

A narrative literature review was conducted to evaluate current evidence regarding vitamin D deficiency and supplementation in burn patients, with emphasis on wound healing, infectious complications, metabolic alterations, and clinical outcomes. Literature searches were performed using PubMed, Scopus, Web of Science, and Google Scholar databases. The search strategy incorporated combinations of the following keywords and Medical Subject Headings (MeSH): “burn injury,” “burn patients,” “vitamin D,” “25-hydroxyvitamin D,” “cholecalciferol,” “wound healing,” “critical illness,” “hypermetabolism,” “burn outcomes,” “infection,” “sepsis,” and “supplementation.”

The review primarily focused on studies published between 2000 and 2025. Clinical trials, randomized controlled trials, observational cohort studies, systematic reviews, meta-analyses, and mechanistic studies evaluating vitamin D metabolism or supplementation in burn injury were included. Additional references were identified through manual review of bibliographies from relevant publications.

Studies involving adult and pediatric burn populations were considered. Priority was given to studies involving moderate-to-severe burns, particularly those with total body surface area (TBSA) involvement ≥20%, due to the greater metabolic and endocrine disturbances observed in this subgroup. Publications examining vitamin D physiology, immune modulation, wound repair, calcium–phosphate homeostasis, and long-term musculoskeletal outcomes in burn patients were also included to provide mechanistic and clinical context.

Because this review was narrative rather than systematic, formal risk-of-bias assessment and quantitative pooled analysis were not performed. However, emphasis was placed on peer-reviewed studies with clinically relevant outcomes and higher methodological quality where available.

Results

Vitamin D Physiology and Role in Skin Biology

Vitamin D is a fat-soluble secosteroid hormone with broad physiological functions extending beyond regulation of calcium–phosphate metabolism and skeletal homeostasis. In recent decades, increasing evidence has demonstrated that vitamin D also plays important roles in immune regulation, cellular differentiation, inflammatory modulation, oxidative stress response, and tissue regeneration (Bikle, 2014; Hewison, 2010).These pleiotropic effects are particularly relevant in burn injury, where wound healing and systemic recovery depend on coordinated interactions among inflammatory, immune, endocrine, and metabolic pathways (Al-Tarrah et al., 2018; Jeschke et al., 2020).

In humans, vitamin D is obtained through both endogenous synthesis and dietary intake, although cutaneous synthesis represents the major source under normal physiological conditions. Ultraviolet B (UVB) radiation converts epidermal 7-dehydrocholesterol into previtamin D3, which subsequently undergoes thermal isomerization into cholecalciferol (vitamin D3). This process occurs primarily within the epidermis, emphasizing the critical role of intact skin in maintaining vitamin D homeostasis (Bikle, 2014). Following synthesis or ingestion, vitamin D undergoes hepatic 25-hydroxylation to form 25-hydroxyvitamin D [25(OH)D], the major circulating metabolite and principal marker used to assess vitamin D status. Subsequent renal 1α-hydroxylation generates biologically active 1,25-dihydroxyvitamin D [1,25(OH)2D], which binds to the vitamin D receptor (VDR) and regulates transcription of numerous target genes.

The skin itself is not only a site of vitamin D synthesis but also an important target organ for vitamin D signaling. VDR expression has been identified in keratinocytes, fibroblasts, sebaceous glands, endothelial cells, melanocytes, and immune cells located within the skin microenvironment (Bikle, 2014). Through VDR activation, vitamin D regulates epidermal differentiation, barrier function, and cutaneous immune responses. Experimental studies demonstrate that disruption of VDR signaling impairs epidermal maturation and

compromises skin integrity, highlighting the importance of vitamin D in maintaining normal tissue homeostasis.

These functions become particularly important during wound healing. Burn wound repair involves a highly coordinated process traditionally divided into inflammatory, proliferative, and remodeling phases. During the inflammatory phase, cytokine release and immune-cell recruitment are necessary to remove pathogens and damaged tissue. However, excessive or prolonged inflammation contributes to tissue destruction and impaired healing. Vitamin D appears to modulate this balance through suppression of excessive pro-inflammatory signaling while preserving antimicrobial defense mechanisms (Hewison, 2010).

One of the best-characterized immunologic effects of vitamin D is stimulation of antimicrobial peptide production. Vitamin D directly induces expression of cathelicidin and β-defensins, which possess broad antimicrobial activity against bacteria, viruses, and fungi (Schauber et al., 2007; Wang et al., 2004). These peptides are particularly relevant in burn patients, where disruption of the skin barrier substantially increases susceptibility to wound colonization and infection (Church et al., 2006; Al-Tarrah et al., 2018). In addition to direct antimicrobial activity, vitamin D modulates macrophage and dendritic cell function and contributes to regulation of adaptive immune responses (Bikle, 2014; Al-Tarrah et al., 2018). Reduced vitamin D availability may therefore impair local immune defense while promoting dysregulated systemic inflammation (Al-Tarrah et al., 2018; Bikle, 2014).

Vitamin D also contributes to cellular proliferation and tissue regeneration through regulation of multiple intracellular signaling pathways. Experimental evidence suggests involvement of Wnt/β-catenin, MAPK, and PI3K/Akt pathways, which are associated with keratinocyte migration, fibroblast proliferation, angiogenesis, and extracellular matrix remodeling (Bikle, 2014). Keratinocyte migration is essential for wound epithelialization, whereas fibroblasts contribute to collagen synthesis and structural repair. Through modulation of these pathways, vitamin D may facilitate more efficient wound closure and tissue regeneration following burn injury.

Angiogenesis represents another critical component of wound healing influenced by vitamin D signaling. Adequate vascularization is required to ensure oxygen delivery, nutrient transport, and removal of metabolic byproducts from healing tissue. Experimental evidence suggests that vitamin D may regulate endothelial cell activity, angiogenic signaling, and vascular remodeling, thereby supporting the proliferative phase of tissue repair (Bikle, 2014; Piotrowska et al., 2016).

Oxidative stress is a major contributor to tissue injury following severe burns. Extensive burn injury induces the production of reactive oxygen species and inflammatory mediators that promote cellular damage and impair wound healing (Chen et al., 2025). Emerging evidence suggests that vitamin D may exert antioxidant effects through modulation of pathways associated with nuclear factor erythroid 2–related factor 2 (Nrf2), thereby enhancing cellular antioxidant defenses and attenuating oxidative injury (Bikle, 2014; Süntar, 2021). By limiting oxidative stress and inflammatory damage, vitamin D may contribute to a more favorable environment for tissue repair and recovery (Al-Tarrah et al., 2018; Bikle, 2014).

In addition to local effects on wound repair, vitamin D may influence systemic recovery after burn injury. Vitamin D deficiency has been associated with muscle weakness, impaired immune competence, prolonged hospitalization, and increased susceptibility to critical illness complications (de Haan et al., 2014).Because severe burns induce profound hypermetabolism and protein catabolism, maintenance of adequate vitamin D status may be important for preserving musculoskeletal function and supporting rehabilitation during prolonged recovery (Al-Tarrah et al., 2018; Rousseau et al., 2019).

Overall, current evidence indicates that vitamin D functions as a multifunctional regulator of cutaneous homeostasis, immune defense, inflammatory modulation, and tissue regeneration. These biologic properties provide a strong mechanistic rationale for investigating vitamin D deficiency and supplementation in burn patients, particularly in those with extensive injuries and prolonged critical illness.

Pathophysiology of Burn Injury and Vitamin D Metabolism

Severe burn injury produces extensive metabolic and endocrine disturbances that significantly alter vitamin D homeostasis. These changes begin immediately following injury and may persist for months or years after the acute phase (Herndon & Tompkins, 2004; Porter et al., 2007).

One of the most important mechanisms underlying vitamin D deficiency in burn patients is destruction of the skin itself. The epidermis contains high concentrations of 7-dehydrocholesterol, the precursor required for endogenous vitamin D synthesis. Extensive cutaneous damage reduces available substrate and markedly impairs UVB-mediated cholecalciferol production (Klein et al., 2004). Studies demonstrate that healed burn

scars and grafted skin exhibit substantially reduced capacity for vitamin D synthesis compared with normal skin, contributing to persistent deficiency long after wound closure (Klein et al., 2004).

Reduced sunlight exposure may further exacerbate vitamin D deficiency following severe burn injury. Patients often require prolonged ICU care and extended hospitalization, resulting in minimal ultraviolet (UV) exposure, while dressings, compression garments, and scar coverage may further limit cutaneous vitamin D synthesis (Al-Tarrah et al., 2018; Rousseau et al., 2019).

Burn injury is also associated with profound hypermetabolic catabolic state. Severe burns induce sustained increases in resting energy expenditure, protein breakdown, and inflammatory mediator release (Finnerty et al., 2013; Herndon & Tompkins, 2004). These changes alter vitamin D turnover and increase physiologic demand. Hypermetabolism may also affect vitamin D binding proteins and distribution within tissues, potentially contributing to lower circulating 25(OH)D concentrations.

Hepatic and renal dysfunction observed in critically ill burn patients may further impair vitamin D metabolism. Because hepatic 25-hydroxylation and renal 1α-hydroxylation are required for the generation of biologically active vitamin D metabolites, organ dysfunction may reduce vitamin D activation (Bikle, 2014; Al-Tarrah et al., 2018). Inflammatory cytokines and acute-phase responses may additionally alter vitamin D metabolism and interfere with enzymatic conversion pathways (Al-Tarrah et al., 2018; Rousseau et al., 2019).

Disturbances in calcium–phosphate metabolism are common following severe burns. Burn patients frequently develop hypocalcemia, altered phosphate balance, elevated urinary calcium losses, and secondary hyperparathyroidism (Klein, 2016). Increased bone resorption and suppression of osteoblastic activity contribute to progressive bone mineral density loss during prolonged recovery (Porter et al., 2007). Vitamin D deficiency may exacerbate these abnormalities by impairing intestinal calcium absorption and promoting compensatory parathyroid hormone secretion.

Persistent endocrine and musculoskeletal consequences have also been described in long-term survivors. Chronic vitamin D deficiency following severe burns has been associated with reduced bone mineral density, osteopenia, muscle weakness, and impaired rehabilitation outcomes (Porter et al., 2007). These observations suggest that disruption of vitamin D metabolism represents not only an acute metabolic abnormality but also a contributor to long-term morbidity after burn injury.

The combination of impaired synthesis, altered metabolism, increased catabolism, and prolonged critical illness creates a multifactorial state of vitamin D deficiency in burn patients, particularly in individuals with extensive TBSA involvement.

Clinical Consequences of Vitamin D Deficiency in Burn Patients

Prevalence of Vitamin D Deficiency in Burn Injury

Vitamin D deficiency is common among patients with moderate-to-severe burns. Multiple observational studies report deficiency or insufficiency in the majority of hospitalized burn patients, particularly in those with burns involving ≥20% total body surface area (TBSA) (Al-Tarrah et al., 2018; Rousseau et al., 2013). In retrospective cohorts, prevalence rates of suboptimal serum 25(OH)D concentrations frequently exceed 70–80% during hospitalization (Lee et al., 2016). Persistent deficiency has additionally been documented months to years after injury, indicating that vitamin D dysregulation often extends beyond the acute recovery phase (Porter et al., 2007).

Several factors contribute to this high prevalence. In addition to impaired cutaneous synthesis resulting from skin destruction, burn patients experience prolonged hospitalization, limited ultraviolet exposure, hypermetabolism, altered hepatic and renal metabolism, and increased inflammatory burden. Nutritional deficiencies and impaired gastrointestinal absorption may further exacerbate vitamin D depletion in critically ill individuals.

Notably, the severity of deficiency appears to correlate with burn size and clinical severity. Patients with extensive burns, prolonged ICU stay, and multiple complications generally demonstrate lower circulating vitamin D concentrations than patients with smaller injuries (Al-Tarrah et al., 2018).

Effects on Wound Healing

Wound healing is a complex process involving inflammatory regulation, keratinocyte migration, fibroblast proliferation, angiogenesis, extracellular matrix remodeling, and collagen deposition. Vitamin D appears to influence several of these processes, suggesting that deficiency may contribute to impaired wound repair following burn injury. Burn wound healing involves overlapping inflammatory, proliferative, and remodeling phases. During the proliferative phase, keratinocyte migration, fibroblast proliferation, angiogenesis and granulation support tissue repair, whereas extracellular matrix turnover and collagen

maturation during the remodeling phase determine scar quality and long-term tissue integrity (Eming et al., 2014; Guo & DiPietro, 2010; Pastar et al., 2014).

Experimental studies demonstrate that vitamin D promotes keratinocyte proliferation and differentiation while facilitating fibroblast migration and collagen synthesis (Bikle, 2014). Additionally, vitamin D signaling regulates angiogenesis, extracellular matrix remodeling, and cellular differentiation, processes that are fundamental to wound closure and graft integration (Bikle, 2014; Piotrowska et al., 2016). Activation of the vitamin D receptor (VDR) has further been linked to improved epithelial barrier integrity and modulation of inflammatory responses during tissue repair, supporting the potential role of vitamin D in cutaneous regeneration (Bikle, 2014; Piotrowska et al., 2016).

Clinical evidence supports a potential relationship between vitamin D status and wound healing outcomes. Observational studies report associations between lower serum 25(OH)D concentrations and delayed wound closure, impaired graft integration, and prolonged recovery (Al-Tarrah et al., 2018). A randomized controlled trial conducted by Ghadimi et al. (2025) demonstrated that daily vitamin D3 supplementation improved wound healing indices and recovery parameters in hospitalized burn patients, with greater improvement observed in patients receiving 3000 IU/day compared with lower-dose supplementation.

Despite these findings, evidence remains heterogeneous. Differences in burn severity, timing of supplementation, outcome definitions, and nutritional protocols complicate direct comparison between studies. However, the overall direction of evidence suggests that adequate vitamin D availability may support more favorable wound healing conditions following severe burn injury.

Infection and Sepsis

Infection remains a major cause of morbidity and mortality following severe burn injury. Disruption of the skin barrier, burn-induced immune dysfunction, prolonged hospitalization, invasive procedures, and critical illness collectively increase susceptibility to local and systemic infections (Church et al., 2006; Zhang et al., 2021).

Vitamin D may influence infection risk through modulation of both innate and adaptive immune responses. Vitamin D–VDR signaling stimulates expression of antimicrobial peptides such as cathelicidin and β-defensins, which enhance local antimicrobial defense and reduce bacterial colonization (Schauber et al., 2007; Wang et al., 2004). Additionally, vitamin D modulates inflammatory cytokine production and may reduce excessive inflammatory responses associated with sepsis.

Several clinical studies have demonstrated associations between vitamin D deficiency and infectious complications in burn patients. Garner et al. (2022) reported increased infectious complications among vitamin D–deficient burn patients, while a recent systematic review and meta-analysis demonstrated that adequate vitamin D status was associated with significantly lower risk of bacteremia and septicemia (Madarshahian et al., 2025). Deficient patients also exhibited prolonged hospitalization and more severe clinical courses.

Although direct causal relationships remain difficult to establish, current evidence suggests that vitamin D deficiency may contribute to impaired immune defense and increased infection susceptibility in burn populations (Al-Tarrah et al., 2018; Madarshahian et al., 2025).

ICU Stay, Hospitalization, and Systemic Recovery

Burn injury induces a prolonged hypermetabolic state associated with increased resting energy expenditure, muscle catabolism, systemic inflammation, and endocrine dysregulation (Herndon & Tompkins, 2004). Recovery often requires prolonged ICU treatment, repeated surgical interventions, nutritional support, and rehabilitation.

Lower vitamin D concentrations have been associated with poorer systemic recovery and increased healthcare utilization. Lee et al. (2016) demonstrated that vitamin D deficiency correlated with significantly longer ICU and hospital length of stay in adult burn patients. Similarly, meta-analytic evidence indicates that vitamin D–sufficient patients experience shorter hospitalization and reduced ICU duration compared with deficient individuals (Madarshahian et al., 2025).

The relationship between vitamin D and systemic recovery is likely multifactorial. Potential contributing mechanisms include modulation of inflammation, enhancement of immune competence, support of muscle metabolism, and facilitation of tissue repair (Al-Tarrah et al., 2018; Bikle, 2014). In critically ill patients, vitamin D may additionally influence cardiovascular stability, endothelial function, oxidative stress regulation, and overall metabolic homeostasis (Al-Tarrah et al., 2018; Zheng et al., 2025).

However, evidence regarding mortality remains inconsistent. While some observational studies suggest increased mortality among severely deficient patients, pooled analyses generally fail to demonstrate a clear mortality benefit associated with supplementation or higher vitamin D levels (de Haan et al., 2014; Han et al.,

2020). These observations suggest that vitamin D deficiency may act partially as a marker of illness severity rather than an isolated determinant of survival.

Long-Term Musculoskeletal Consequences

Long-term musculoskeletal complications are increasingly recognized among burn survivors. Severe burns are associated with persistent hypermetabolism, prolonged immobilization, inflammatory activation, and endocrine disturbances that contribute to progressive bone and muscle loss (Porter et al., 2007).

Vitamin D deficiency appears to exacerbate these effects through impaired calcium absorption and secondary hyperparathyroidism. Increased bone resorption and suppression of bone formation may lead to reduced bone mineral density, osteopenia, osteoporosis, and increased fracture risk, particularly in patients with extensive burns and prolonged rehabilitation (Klein, 2016).

Muscle weakness and muscle wasting are also common after severe burns. Hypercatabolism promotes accelerated protein breakdown and loss of lean body mass, while vitamin D deficiency may impair muscle function and recovery. Reduced muscle strength contributes to delayed rehabilitation, impaired mobility, and prolonged functional disability.

Longitudinal studies demonstrate that vitamin D abnormalities may persist long after acute recovery. Porter et al. (2007) reported persistent skeletal and vitamin D abnormalities months to years after severe burn injury, emphasizing the importance of long-term metabolic monitoring in this population.

Vitamin D Supplementation Strategies in Burn Patients

Supplementation Approaches and Dosing Regimens

Current evidence regarding vitamin D supplementation in burn patients remains limited but increasingly supportive of targeted replacement strategies. Most available studies evaluate cholecalciferol (vitamin D3) administered through oral or enteral routes, with dosing regimens varying considerably between studies. Randomized controlled trials and meta-analyses in critically ill populations demonstrated that vitamin D supplementation may improve selected secondary outcomes, including ICU length of stay, although mortality benefits remain inconsistent (Amrein et al., 2014; Putzu et al., 2017; Langlois et al., 2018).

Daily supplementation strategies are most commonly reported. Standard supplementation protocols frequently utilize doses ranging from 800 to 2000 IU/day, while higher doses are often used in patients with confirmed deficiency or extensive burns (Al-Tarrah et al., 2018). A randomized controlled trial by Ghadimi et al. (2025) compared 1000 IU/day and 3000 IU/day supplementation in hospitalized burn patients and demonstrated greater improvement in wound healing and recovery parameters in the higher-dose group.

Some critically ill patient studies have evaluated high-dose bolus regimens designed to rapidly correct deficiency. However, evidence from ICU populations indicates that large single-dose strategies may normalize serum concentrations without consistently improving clinical outcomes (National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, 2019). Consequently, daily supplementation approaches may be more physiologically appropriate in burn populations experiencing sustained hypermetabolic stress.

Enteral administration remains the preferred route in critically ill burn patients receiving nutritional support through feeding tubes. Oral supplementation is commonly used in stable hospitalized and outpatient populations. Parenteral administration has been described in selected critically ill patients with impaired gastrointestinal absorption, although burn-specific evidence regarding intravenous or intramuscular administration remains limited.

Monitoring and Target Serum Levels

Monitoring of vitamin D status in burn patients remains an important but insufficiently standardized aspect of clinical management. Because severe burn injury significantly alters vitamin D metabolism and calcium–phosphate homeostasis, serial biochemical assessment may provide clinically relevant information regarding nutritional status, endocrine function, and response to supplementation.

The primary laboratory marker used to assess vitamin D status is serum 25-hydroxyvitamin D [25(OH)D], which reflects total body vitamin D stores and remains the most widely accepted indicator of deficiency and sufficiency. Most studies involving burn patients define deficiency as serum concentrations below 20 ng/mL (50 nmol/L), while concentrations between 20–30 ng/mL are generally considered insufficient (Han et al., 2020). Concentrations ≥30 ng/mL have historically been targeted in critically ill populations based on earlier guideline recommendations and the proposed extra-skeletal effects of vitamin D, although the optimal threshold remains controversial (Zheng et al., 2025).

However, interpretation of vitamin D levels in severe burn injury may be more complex than in healthy populations. Hypermetabolism, systemic inflammation, altered protein binding, fluid shifts, hepatic

dysfunction, and renal impairment may influence circulating vitamin D concentrations and tissue utilization (Al-Tarrah et al., 2018; Rousseau et al., 2019). Consequently, serum 25(OH)D levels may not always fully reflect functional vitamin D activity within tissues (Bikle, 2014; Rousseau et al., 2019). Some investigators have proposed that burn patients may require higher circulating 25(OH)D concentrations than non-burn populations to achieve comparable biological effects, although definitive target levels have not been established (Al-Tarrah et al., 2018; Rousseau et al., 2019).

In addition to serum 25(OH)D, monitoring protocols frequently include assessment of calcium–phosphate metabolism and endocrine markers. Commonly evaluated laboratory parameters include serum calcium, phosphate, parathyroid hormone (PTH), and alkaline phosphatase (ALP). These markers help identify secondary hyperparathyroidism, altered bone turnover, and disturbances in mineral metabolism that commonly develop after severe burns (Klein, 2016).

Hypocalcemia is frequently observed during the acute phase of burn injury and may result from inflammatory-mediated alterations in calcium homeostasis, increased urinary calcium losses, hypoalbuminemia, and impaired vitamin D metabolism (Klein, 2008; Rousseau et al., 2019). Although reduced calcium availability normally stimulates PTH secretion to preserve calcium balance, severe burns may disrupt this adaptive response through cytokine-mediated alterations in parathyroid calcium sensing, contributing to persistent abnormalities in mineral metabolism and skeletal health (Klein et al., 2004; Klein, 2008). Monitoring PTH concentrations may therefore provide additional insight into the physiologic consequences of vitamin D deficiency and calcium dysregulation following burn injury (Al-Tarrah et al., 2018; Rousseau et al., 2019).

Alkaline phosphatase is another potentially useful marker, particularly during prolonged recovery and rehabilitation. Elevated ALP concentrations may reflect increased bone turnover and ongoing skeletal remodeling associated with hypermetabolism and prolonged immobilization. In long-term burn survivors, persistent endocrine and skeletal abnormalities may contribute to reduced bone mineral density and increased fracture risk (Porter et al., 2007).

The optimal frequency of laboratory monitoring has not been standardized. In critically ill patients with extensive burns, many clinicians perform baseline assessment during early hospitalization followed by repeat measurements every several weeks during ICU treatment and rehabilitation, particularly in patients receiving supplementation. More frequent monitoring may be necessary in patients receiving higher supplementation doses or exhibiting renal dysfunction, hypercalcemia, or severe metabolic abnormalities.

Despite increasing recognition of vitamin D deficiency in burn populations, important uncertainties remain regarding ideal target serum concentrations and supplementation thresholds. Most currently used cutoffs are extrapolated from general medical populations rather than burn-specific evidence. Consequently, future research is needed to determine whether burn patients require individualized target ranges reflecting the unique metabolic and inflammatory environment associated with severe injury.

Discussion

The available evidence demonstrates a consistent association between severe burn injury, reduced vitamin D status, and adverse clinical outcomes. Patients with burns involving ≥20% total body surface area (TBSA) exhibit markedly increased prevalence of vitamin D deficiency compared with both healthy populations and patients with smaller burns (Al-Tarrah et al., 2018; Rousseau et al., 2013). This deficiency appears multifactorial, resulting from destruction of vitamin D–producing skin, prolonged hospitalization, limited ultraviolet exposure, altered metabolism, systemic inflammation, and sustained hypermetabolism (Klein et al., 2004; Herndon & Tompkins, 2004). Overall, current findings support the concept that burn severity is closely linked to progressive disruption of vitamin D homeostasis and that this disruption may contribute to impaired recovery.

One of the most clinically relevant observations emerging from the literature is the association between vitamin D deficiency and infectious complications. Multiple studies report increased rates of wound infection, bacteremia, and sepsis among deficient burn patients (Garner et al., 2022; Madarshahian et al., 2025). These findings are biologically plausible considering the known immunomodulatory role of vitamin D. Vitamin D–VDR signaling enhances innate immune responses through induction of antimicrobial peptides such as cathelicidin and β-defensins while simultaneously modulating excessive inflammatory activation (Hewison, 2010; Schauber et al., 2007). In critically ill burn patients, where immune dysfunction and systemic inflammation contribute substantially to morbidity, these mechanisms may partially explain the observed relationship between vitamin D deficiency and infectious outcomes.

The role of vitamin D in wound healing represents another important area of interest. Experimental evidence demonstrates that vitamin D contributes to keratinocyte proliferation, fibroblast migration, angiogenesis, and extracellular matrix remodeling, all of which are essential components of tissue repair (Bikle, 2014). Furthermore, vitamin D appears to regulate signaling pathways involved in cellular proliferation and differentiation, including Wnt/β-catenin, MAPK, and PI3K/Akt pathways. These mechanisms support the hypothesis that adequate vitamin D availability may facilitate wound epithelialization and graft integration following burn injury.

Clinical studies evaluating wound healing outcomes have produced generally favorable but heterogeneous results. Observational studies frequently associate lower vitamin D concentrations with delayed wound closure and prolonged recovery, while randomized supplementation trials suggest potential improvement in healing indices and hospital outcomes with daily cholecalciferol administration (Ghadimi et al., 2025). However, methodological variability among studies limits direct comparison. Differences in burn severity, timing of supplementation, nutritional support protocols, and outcome definitions likely contribute to inconsistent findings regarding wound healing endpoints.

In addition to local wound effects, vitamin D deficiency appears associated with broader systemic consequences in burn patients. Lower serum 25(OH)D concentrations correlate with prolonged ICU stay, increased hospital length of stay, and delayed overall recovery (Lee et al., 2016; Madarshahian et al., 2025). These relationships may reflect the influence of vitamin D on inflammatory regulation, immune competence, oxidative stress modulation, and musculoskeletal metabolism. Hypermetabolism and accelerated protein catabolism following severe burns contribute substantially to muscle wasting and functional decline (Finnerty et al., 2013). Vitamin D deficiency may further exacerbate muscle dysfunction and impair rehabilitation outcomes.

Long-term musculoskeletal consequences are particularly important in survivors of extensive burns. Persistent hypermetabolism, prolonged immobilization, endocrine abnormalities, and inflammatory activation contribute to progressive bone loss and reduced bone mineral density after severe burn injury (Porter et al., 2007). Vitamin D deficiency may intensify these effects through impaired calcium absorption and secondary hyperparathyroidism. Studies demonstrate that skeletal abnormalities may persist months to years after injury, emphasizing the long-term implications of altered vitamin D metabolism in burn populations (Klein, 2016).

Despite increasing evidence supporting a role for vitamin D in burn recovery, important limitations and inconsistencies remain. Much of the available literature is observational, limiting the ability to establish causality. Vitamin D deficiency may partially reflect burn severity, systemic inflammation, nutritional status, or overall critical illness rather than functioning as an isolated pathophysiologic driver. Patients with larger burns and prolonged ICU courses are more likely to demonstrate both lower vitamin D concentrations and worse outcomes, making confounding difficult to eliminate completely.

Considerable heterogeneity also exists among supplementation studies. Investigators have utilized differing dosing regimens, administration routes, supplementation timing, and target serum concentrations. Some studies employ physiologic daily supplementation, whereas others utilize high-dose bolus approaches. Evidence from broader ICU populations suggests that large single-dose supplementation may rapidly normalize serum concentrations without consistently improving meaningful clinical outcomes (Han et al., 2020; National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, 2019). Consequently, the optimal supplementation strategy in burn patients remains uncertain.

An additional limitation is the absence of standardized burn-specific target serum concentrations for vitamin D. Thresholds currently used in clinical practice are generally extrapolated from non-burn populations. However, the hypermetabolic and inflammatory environment associated with severe burns may alter vitamin D utilization and physiologic requirements, suggesting that standard definitions of sufficiency may not fully reflect functional adequacy in this population.

Potential bias within the existing literature should also be considered. Many studies involve relatively small sample sizes and single-center populations, limiting generalizability. Publication bias may additionally favor positive findings regarding supplementation efficacy. Variability in laboratory measurement techniques, timing of vitamin D assessment, and adjustment for confounding variables such as nutritional status, renal dysfunction, and comorbidities further complicates interpretation.

However, despite these limitations, the overall body of evidence supports a clinically relevant relationship between vitamin D status and burn recovery. Mechanistic, observational, and early interventional data collectively suggest that vitamin D deficiency may contribute to impaired wound healing, increased infection risk, prolonged hospitalization, and long-term musculoskeletal complications in burn patients. Although current evidence does not yet support definitive standardized supplementation protocols, vitamin D represents a promising adjunctive target in the multidisciplinary management of severe burn injury.

Conclusions

Vitamin D deficiency is common among patients with moderate-to-severe burns, particularly in individuals with burns involving ≥20% total body surface area. Severe burn injury disrupts vitamin D homeostasis through impaired cutaneous synthesis, hypermetabolism, altered hepatic and renal metabolism, prolonged hospitalization, and reduced sunlight exposure. Available evidence suggests that reduced vitamin D availability is associated with adverse clinical outcomes, including increased infectious complications, delayed wound healing, prolonged ICU and hospital stay, and long-term musculoskeletal abnormalities.

Vitamin D appears to influence multiple biological processes relevant to burn recovery, including keratinocyte proliferation, inflammatory regulation, antimicrobial peptide production, extracellular matrix remodeling, and calcium–phosphate metabolism. Experimental and clinical findings therefore support a biologically plausible role for vitamin D in both local wound repair and systemic recovery following severe burns.

Available supplementation studies suggest that vitamin D replacement, particularly through daily cholecalciferol administration, may improve biochemical status and selected clinical outcomes. However, substantial heterogeneity persists regarding supplementation dose, timing, route of administration, and target serum concentrations. Consequently, no standardized burn-specific supplementation protocol currently exists.

Further research is required to establish evidence-based clinical guidelines for vitamin D supplementation in burn populations. Large randomized controlled trials evaluating standardized dosing regimens, optimal serum targets, wound healing outcomes, infection risk, and long-term musculoskeletal recovery are needed. Improved understanding of burn-specific vitamin D metabolism and physiologic requirements may help optimize supportive care strategies in patients with severe burn injury.

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