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THE HIDDEN ROLE OF MALNUTRITION IN THE PATHOGENESIS OF DIABETIC GANGRENE

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ABSTRACT

Diabetic foot ulcers (DFU) that progress to gangrene are associated with more than 50 percent mortality over a five-year period when obscured by Peripheral Arterial Disease. Current standard procedures prioritize glycemic control and mechanical offloading. However, these clinical guidelines do not address systemic nutritional deficiencies as the underlying mechanism that drives tissue necrosis and immunity failure. This review seeks to discover the critical role of Medical Nutrition Therapy and micronutrient supplementation, such as Vitamin B12, Vitamin D, Zinc, and Vitamin C, to prevent superficial ulcers from progressing into limb threatening gangrene in Type 2 Diabetes patients. A synthesis of literature was performed from scholarly databases, including ScienceDirect, PubMed, and Oxford Academic, focusing on clinical cohorts, systematic reviews and Mendelian randomization studies that correlate diabetic wound progression with systemic nutritional biomarkers, physical frailty and genetic susceptibility. Many clinical data show a profound correlation between systemic malnutrition and gangrene progression. Vitamin D deficiencies affect over half of DFU patients. Moreover, depleted levels of Vitamin B12, which are worsened by long term metformin use, seriously impair peripheral nerve integrity. Baseline protein malnutrition reduces wound healing rates from 50 percent down to 24 percent. Intensive Nutritional Support successfully prevents lean body mass loss without disrupting glycemic control. The progression of gangrene is heavily driven by systemic metabolic breakdown rather than localized infection alone. Integrating standardized nutritional screening, addressing physical frailty, and using targeted micronutrient therapy within multidisciplinary primary care are essential biological prerequisites for limb salvage.

Keywords: Diabetic foot ulcers, Gangrene, Peripheral arterial disease, Micronutrient supplementation, Levels of Vitamin B_{12}, Physical frailty

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INTRODUCTION

The Epidemic of the Non-Healing Wound

Diabetes Mellitus (DM) is a global endemic currently affecting millions of individuals, resulting in an inevitable rise in microvascular and macrovascular complications. One of the most debilitating of these is the Diabetic Foot Ulcer (DFU), a primary precursor to permanent disability and limb loss. Despite advances in surgical debridement, hyperbaric oxygen therapy and antimicrobial wound dressings, the recurrence rate of DFUs is remarkably high. Furthermore, vulnerability to gangrenous progression is heavily governed by genetics; recent Mendelian randomization analyses confirm a direct causal link between genetic susceptibility to both Type 1 and Type 2 diabetes and a significantly higher risk of gangrene, largely via disruptions of NOD-like receptor and RAGE signaling pathways [**1**]. This highlights a fundamental dysfunction in the current healthcare model, placing an over emphasis on physical wound management that does not account for the internal metabolic and genetic environment that is needed for tissue regeneration.

The Paradox of "Glycemic Blindness" and Metabolic Collapse

Current clinical guidelines are heavily anchored in a glycemic paradigm. The prevailing assumption is that standardizing blood glucose and mechanically offloading the foot will naturally lead to wound closure. However, undernutrition in diabetic patients

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can present unique and dangerous phenotypes (such as an unusually low body mass index or resistance to ketosis) which alter standard metabolic responses and severely complicate the direct effects of the disease [**2**]. When a patient with an active ulcer is subjected to a restrictive diabetic diet without addressing the massive demand for amino acids and micronutrients, the body falls into a severe catabolic state. Clinically significant involuntary weight loss and protein-energy malnutrition signal a physiological environment where the body lacks the metabolic resources to heal [**3**].

The Nutrition Gap in Multidisciplinary Teams

This segregation of nutrition science from clinical podiatric practice creates a blind spot in diabetic care. Research writes down an estimated 85 percent of diabetes-related amputations could be prevented if wounds were detected early and managed comprehensively [**4**]. Standard protocols rarely mandate the inclusion of registered dietitians or comprehensive nutritional screening in primary DFU triage. Consequently, severe micronutrient deficiencies, ranging from Vitamin D insufficiency to Metformin-induced Vitamin B12 malabsorption, go completely unmonitored until the patient needs limb-sparing surgery. A unified interdisciplinary treatment plan that aggressively incorporates clinical nursing care, physical rehabilitation and targeted medical nutrition therapy is essential for reducing complications and improving long term functional recovery.

The Global and Socioeconomic Burden of Diabetic Foot Disease

The rapid escalation of diabetic foot complications is heavily influenced by systemic socioeconomic factors and unequal access to multidisciplinary medical care. Global health data suggests the burden of foot disease and later amputations are escalating, disproportionately overwhelming middle to lower income countries [**2**]. Due to vast differences in local economies, cultural practices and available levels of medical care across different regions, preventive methods and curative outcomes for diabetic foot conditions vary greatly. When patients do not have access to basic nutritional screening, they are significantly more vulnerable to rapid tissue necrosis. Establishing standardized, globally applicable clinical guidelines is therefore critical to reducing the immense financial and physical burden that DFUs place on the global healthcare infrastructure.

Objectives and Rationale of Review

The primary aim of this review is to dismantle the purely glycemic focused approach to DFU management and set up the biological necessity of Intensive Nutritional Support (INS) for limb salvage. By synthesizing current clinical guidelines, Mendelian randomization studies and nutritional cohort data, this paper aims to expose the hidden role of systemic malnutrition in the pathogenesis of diabetes-induced gangrene. Specifically, this review will detail the physiological consequences of protein-energy malnutrition on wound healing [**3**], evaluate the genetic susceptibility to gangrenous progression [**1**] and highlight the compounding dangers of specific micronutrient deficiencies, such as metformin-induced Vitamin B12 malabsorption [**5, 6**]. Ultimately, this manuscript advocates a mandatory change toward multidisciplinary care models that incorporate localized wound management with aggressive systemic nutritional therapy to prevent non-traumatic amputations.

PATHOPHYSIOLOGY OF DIABETIC FOOT AND SYSTEMIC METABOLIC COLLAPSE

The progression to gangrene is not an absolute assurance of diabetes, but rather the result of unmitigated cellular and systemic failures. To find the pathogenesis of diabetic foot ulcers (DFUs), clinicians must look beyond localized tissue damage and report the systemic metabolic collapse leading it. These wounds are clinically categorized according to the Wagner Ulcer Classification System, ranging from Grade 0 (intact skin in a high-risk foot) to Grade 1 (superficial ulcers), then progressing into deep tissue and bone involvement (Grades 2 and 3), and ultimately culminating in either localized or full-foot gangrene (Grades 4 and 5). This deterioration is driven by a triad of physiological failures: vascular, neuropathic and immunological.

Chronic Hyperglycemia and Cellular Toxicity

Prolonged, uncontrolled hyperglycemia causes a severe state of systemic cellular toxicity through the accumulation of Advanced Glycation End products. These toxic compounds degrade the integrity of the extracellular matrix, effectively halting the proliferative stage of wound healing and significantly multiplying the risk of localized infection. This systemic vulnerability is heavily underpinned by genetics; recent analysis using Mendelian randomization confirms a direct causal relationship between genetic susceptibility to both Type 1 and Type 2 diabetes and significantly higher risk of gangrene. This progression is often mediated through disruptions to NOD-like receptor and RAGE (Receptor for Advanced Glycation End products) signaling pathways [**1**]. Arresting this cellular degradation requires strict metabolic control before full tissue necrosis occurs.

Ischemia and Peripheral Arterial Disease (PAD)

Both macrovascular and microvascular complications combine to push the distal extremities into a state of physiological starvation. Peripheral Arterial Disease is a devastating independent risk factor which accelerates tissue death and severely delays wound healing. The atherosclerotic plaque buildup and microvascular narrowing create a hypoxic environment where normal cellular metabolism is impossible. Furthermore, nutritional status is a key determinant of outcomes in gangrene

pathology; when patients are lacking in sufficient vascular perfusion, the delivery of essential macronutrients to the wound bed is severed. In gangrene pathology, severe nutritional impairment and sarcopenia are strongly associated with adverse clinical outcomes and mortality [**7**]. Aggressive systemic nutritional therapy is an absolute prerequisite to prevent major amputations in these starved, ischemic limbs [**3**].

Neuropathic Degradation and Metformin Trap

Diabetic peripheral neuropathy is the primary driver of foot ulceration in nearly 60 percent of cases. This neuropathy causes a severe loss of protective sensation, leaving the foot vulnerable to undetected mechanical trauma. However, this neurological degradation is often worsened by the very pharmacological interventions used to treat the underlying diabetes. Long-term metformin therapy is strongly associated with severe Vitamin B12 malabsorption; recent comprehensive reviews show this disruption occurs via interference with calcium-dependent membrane activity and detrimental alterations in gut microbiota [**6**]. Metformin reduces the uptake of Vitamin B12, leading to a dangerous systemic depletion which manifests in a significant percentage of patients, with studies showing a deficiency prevalence of over 28 percent in long-term users [**5**]. Because Vitamin B12 is essential for supporting myelin sheaths and ensuring effective nerve impulse transmission, its depletion leads to progressive demyelination and irreversible axonal damage. The clinical data is unequivocal: diabetic patients suffering from Vitamin B12 deficiency face a 3.1 times higher risk of developing foot ulcers compared to those with best micronutrient levels [**8**]. By treating hyperglycemia with high-dose metformin while not monitoring serum B12 levels, practitioners inadvertently accelerate the neuropathic decay which leads directly to ulceration.

The Immunocompromised Microenvironment

The transition of a superficial Grade 1 ulcer into limb-threatening gangrene is largely driven by a systemic breakdown of the host immune response, a failure heavily worsened by specific micronutrient deficiencies. Adequate Vitamin C is biologically imperative for innate immunity, in easing the neutrophil oxidative burst required for early bacterial clearance [**4, 9**]. Concurrently, zinc depletion compromises nearly all stages of wound healing and diminishes the population of mature B-cells, further crippling the localized immune defense [**4**]. This immunocompromised state is highly prevalent in the diabetic population; clinical cohorts prove that 73 percent of DFU patients show suboptimal Vitamin C levels, and nearly 27 percent suffer from zinc deficiency [**10**]. When this immunocompromised state goes unrecognized, localized infections rapidly invade deep subcutaneous and bone tissues. Because an estimated 85 percent of diabetes-related amputations could be prevented with early detection and comprehensive management [**4**], integrating aggressive nutritional fortification into primary wound care is critical to stalling this systemic collapse.

METHODOLOGY

Review Design and Protocol

This study was designed as a comprehensive clinical and narrative review aimed at assessing the pathophysiological impact of Medical Nutrition Therapy (MNT) in the prevention and treatment of Diabetic Foot Ulcers (DFU). Given the highly fragmented nature of global nutritional research, the review protocol was designed to synthesize existing cross-sectional cohorts, retrospective analyses and targeted clinical intervention trials. This mixed-methods approach aligns with established methodological protocols seen in recent high-impact nutritional meta-analyses [**1, 4**]. The overarching protocol was specifically calibrated to find systemic nutritional deficits, with strict emphasis on documenting hypermetabolism and specific micronutrient depletions across varying stages of ulcer severity.

Search Strategy and Information Sources

A systematic and exhaustive literature search was executed across the five major electronic databases: PubMed Central (PMC), ScienceDirect, Oxford Academic Database, MDPI and the Wiley Online Library. To support high clinical relevance, the search was restricted to peer-reviewed articles published in the English language. The search strategy used a highly specific combination of Medical Subject Headings (MeSH) and free-text keywords, connected via Boolean operators (AND, OR). The primary search strings included combinations of "Diabetic Foot Ulcer" OR "DFU" OR "Gangrene Pathogenesis" combined with "Medical Nutrition Therapy" OR "Nutritional Screening". Secondary searches targeted specific metabolic pathways using terms such as "Vitamin B12 Deficiency", "Metformin Induced Malabsorption", "Serum Albumin" and "Vitamin D Deficiency". Furthermore, a manual backward citation search was conducted on the reference lists of all found high-impact articles to capture any critical epidemiological cohorts missed by the first database algorithms.

Inclusion and Exclusion Criteria (The PICO Framework)

To ensure maximum clinical applicability and strict control for selection bias, the study selection was governed by a rigorous Population, Intervention, Comparator and Outcomes (PICO) framework.

Population

The review included adult patients (aged 20 to 79 years) formally diagnosed with Type 2 Diabetes Mellitus for a minimum duration of five years, presenting with active diabetic foot complications.

Intervention and Exposure

Eligible studies must have documented patient exposure to specific nutritional deficiencies (quantified via Mini Nutritional Assessment scores, Body Mass Index or targeted biochemical markers) or recorded specific interventions using calories, protein or micronutrient-fortified clinical supplements.

Comparator

Control groups consisted of diabetic patients supporting best nutritional status, patients on standard glycemic control diets devoid of targeted Medical Nutrition Therapy, or baseline intra-patient measurements recorded prior to nutritional intervention.

Outcomes

The primary clinical endpoints required for inclusion were a quantifiable association between nutritional status and ulcer severity, measured via standardized tools such as the Wagner Ulcer Classification System [**11**], wound healing trajectories (measured by surface area reduction), and the preservation of lean body mass.

Exclusion Criteria To support strict relevance to human pathology, studies based exclusively on pre-clinical animal models or in vitro tissue cultures were discarded. Furthermore, the synthesis excluded clinical studies that focused entirely on surgical debridement, vascular bypass or mechanical offloading without including a quantitative arm for nutritional and metabolic assessment. Non-peer-reviewed case reports were also excluded to prevent anecdotal bias.

Quality Assessment and Risk of Bias

To ensure the integrity of the synthesized argument, all selected studies underwent a rigorous quality and bias assessment. Cross-sectional and observational cohorts were scrutinized for selection bias to guarantee that the sampled patient populations accurately represented standard diabetic demographics rather than statistically rare anomalies. Randomized trials and nutritional supplementation studies were strictly evaluated for confounding variables. Research was excluded if the original investigators did not account for chronic renal failure, concurrent pharmacological factors (specifically Metformin dosage), or baseline glycemic control (HbA1c levels). Furthermore, studies not defining exact statistical parameters, such as p-values and confidence intervals for their nutritional data, were eliminated to prevent the inclusion of nutritionally insignificant or fabricated results.

Data Extraction Protocol

Data extraction was executed systematically to isolate the exact drivers of metabolic collapse. For every included study, critical clinical parameters were extracted and categorized. Anthropometric measurements included baseline weight, Body Mass Index, reported unintentional weight loss and clinical markers of hypermetabolism. Biochemical data focused heavily on the extraction of serum albumin and prealbumin to assess visceral protein status. Concurrently, Hemoglobin A1c was extracted to gauge the biochemical stability of glucose control, alongside specific serum micronutrient levels, specifically Vitamin B12 and Vitamin D. Finally, clinical endpoints were recorded, capturing exact ulcer progression rates, localized infection rates and specific risk multipliers for lower limb amputation.

Synthesis and Translation Strategy

Due to the vast heterogeneity in global dietary baseline metrics and the methodological differences between observational correlations and specific intervention trials, conducting a traditional statistical meta-analysis was precluded. Instead, a rigorous narrative synthesis was performed. Quantitative data, including Chi-Square correlations and specific risk ratios, were interpreted conceptually and mapped directly to clinical pathology. This data was grouped into three primary pathophysiological domains: systemic protein depletion, micronutrient deficiencies accelerating peripheral neuropathy, and metabolic factors impairing microvascular oxygenation. This structured synthesis provides the evidence base needed to mandate a new, standardized Medical Nutrition Therapy protocol for high-risk DFU patients, aligning with the multidisciplinary urgencies outlined by global diabetic foot guidelines [**4**].

CLINICAL REVIEW

The Biochemical Triad: Systemic Micronutrient Depletion

The progression of injury is profoundly affected by an internal biochemical imbalance that severely restricts tissue regeneration. Meta-analyses of diabetic foot ulcer cohorts have found that circulating levels of key micronutrients are profoundly diminished, with a pooled mean Vitamin D level of 15.55 ng/ml and an average Vitamin C concentration of 4.99 µmol/L [**10**]. Prospective cohorts find that suboptimal Vitamin C negatively affects 73 percent of diabetic foot ulcer patients, while clinical zinc deficiency is prevalent among 27 percent [**11**]. The etiology of non-healing wounds is strongly correlated with severe Vitamin D deficiency [**6**] and profound trace element reduction, severely impairing antioxidant functions when compared to healthy controls [**12**]. Primary randomized controlled trials showing the clinical benefit of mineral supplementation found that co-supplementation of magnesium and vitamin E significantly improved ulcer size and lipid concentrations [**13**], while 250 mg of magnesium oxide daily reduced ulcer dimensions and HbA1c levels [**14**]. Targeted zinc sulfate therapy significantly lowered ulcer length, width and depth after 12-week intervention [**9**]. Trace elements are

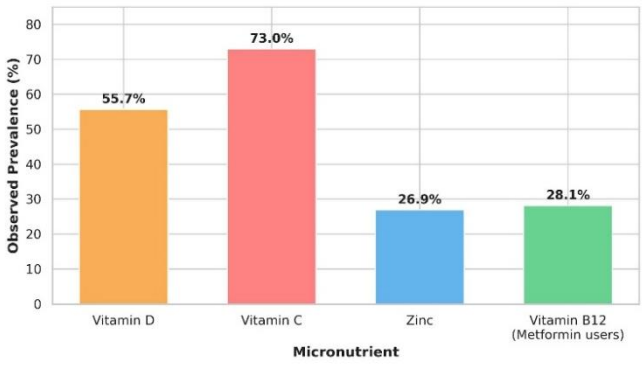


Figure 1: Prevalence of micronutrient deficiencies in diabetic foot ulcers.

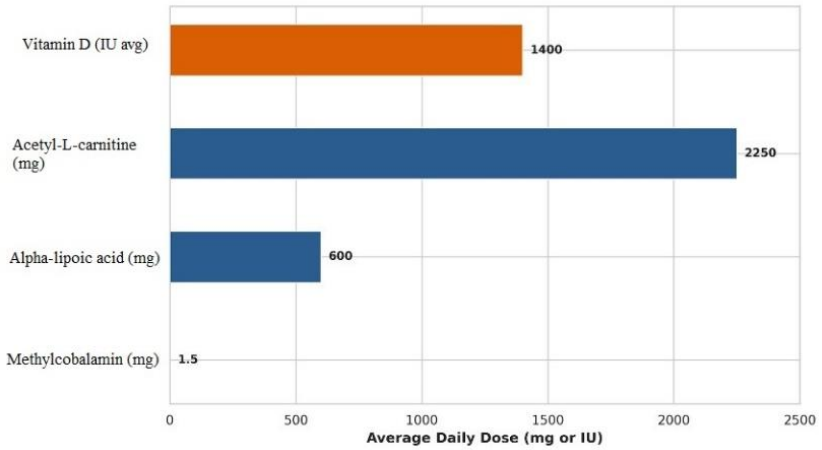


Figure 2: Comparative daily dosing of therapeutic agents for neuropathy.

Table 1: Prevalence and clinical impact of micronutrient deficiencies in DFU.

Micronutrient	Observed Prevalence in DFU	Primary Clinical Impact	Primary Source
Vitamin D	55.7% prevalence of deficiency	Impairs macrophage immune response and early bacterial clearance	Pena et al. [**11**]
Vitamin C	73% suboptimal levels	Terminates fibroblast collagen synthesis and tensile strength	Pena et al. [**11**], Anderson [**15**]
Zinc	26.9% deficiency	Deals tissue repair phases and diminish mature B-cells	Pena et al. [**11**]
Vitamin B12	28.1% deficiency in long-term Metformin users	Accelerates peripheral demyelination and axonal damage	Qureshi et al. [**5**]

Table 2: Targeted pharmaco-nutritional interventions for neuropathy and microvascular preservation.

Therapeutic Agent	Primary Mechanism of Action	Clinical Evidence and Impact	Dosing Notes
Methyl cobalamin (Vit B12)	Promotes axonal transport, myelin sheath formation, and nerve repair.	RCTs demonstrate improved nerve conduction and symptom scores.	Crucial for patients on long-term Metformin. Typically, 0.5 mg orally 3x/day.
Acetyl-L-carnitine (ALC)	Provides antioxidant and cytoprotective effects, reduces synaptic glutamate.	Multicenter trials show improved nerve fiber regeneration and reduced pain.	500 to 1000 mg 3x/day. Improves targeted nerve repair.
Alpha-lipoic acid (ALA)	Reduces severe oxidative stress and enhances microvascular endothelial function.	Meta-analyses show considerable enhancement in clinical symptoms.	600 mg/day orally. Acts as a primary defense for microcirculatory integrity.
Benfotiamine (Vit B1)	Prevents advanced glycation end-product [AGE] formation.	Clinical cohorts suggest improvement in neuropathic symptoms.	Superior bioavailability compared to water-soluble Thiamine.
Vitamin D	Supports vascular endothelial function and regulates macrophage oxidative burst.	Severe deficiency [< 20 ng/mL] is correlated with deep tissue infection.	800 to 2000 IU/day. Compulsory for restoring localized immune response.
Omega-3 Fatty Acids	Provides systemic anti-inflammatory effects and improves localized perfusion.	Supports macrovascular health, cut down the risk of critical ischemia.	Administered via targeted dietary modification or supplementation.

vital as proven by Anderson, where severe Vitamin C depletion prevents fibroblast collagen synthesis, hence the proliferation phase of tissue repair **[15].**

The Impact of Protein Malnutrition and Visceral Wasting on Healing Rates

Healing Rates While micronutrient depletions stall cellular repair, the actual structural progression of tissue necrosis and gangrene is heavily dictated by protein depletion. Acute gangrene pathology sees non-surviving patients with significantly lower serum albumin concentrations than their surviving counterparts (22.9 vs. 27.4 g/L) showing that visceral protein wasting is a primary prognostic indicator of mortality [**7**]. Chronic, non-healing wounds signal a severe catabolic state that requires immediate aggressive nutritional intervention to restore lean body mass [**3**]. Furthermore, clinical trials evaluating protein energy supplementation in DFU patients show that baseline protein malnutrition severely impairs tissue repair. In a randomized control trial assessing liquid nutritional supplementation, patients suffering from baseline protein malnutrition had a drastic reduction in their six-month healing rate, dropping to 24 percent compared to a healing rate of 50 percent in an appropriately nourished patient base [**2**]. Without adequate dietary protein and amino acids, the body is unable to synthesize the structural proteins necessary to close a deep tissue wound, making all local surgical interventions ineffective.

Cross-Sectional Evidence and Multi-Factorial Risk Matrix

To set up how the systemically affecting factors contribute to local tissue death, clinical researchers have increasingly turned to cross-sectional cohorts evaluating the intersect between glycemic control, drug therapies and nutrient absorption. Landmark cross-sectional evaluations have provided the exact prevalence of Metformin-induced Vitamin B12 deficiency, with 28.1 percent of long-term users showing deficient serum cobalamin levels [**5**]. While neuropathy is a universal complication of Type 2 Diabetes, the extent of nerve damage is heavily intensified by cumulative medication dosage, exposure duration and overall glycemic stability [**6**]. The clinical outcome of this specific deficit is severe as diabetic patients suffering from Vitamin B12 deficiency have a 3.1 times higher risk of developing foot ulcers compared to those with best micronutrient levels [**8**]. These studies show that clinical management cannot rely on a single metric. An assessment of HbA1c control, renal function, daily Metformin dosage and circulating visceral protein indicators must be assessed concurrently. When a diabetic patient suffers from poor glycemic control and an unforeseen micronutrient and protein deficit, the cellular machinery responsible for microvascular repair is shut down and a manageable superficial ulcer is turned into a surgical emergency.

DISCUSSION AND CLINICAL SYNTHESIS

Stopping the Systemic Protein Catastrophe

The evidence synthesized in this review challenges the current practice of managing glycemic control. By subjecting patients with active diabetic foot ulcers to low calorie diets to bring HbA1c levels under strict parameters, healthcare professionals ignore the fact that wound healing increases the body's metabolic burden exponentially. It is well documented that the body becomes severely hypermetabolic when wounded. In the absence of enough visceral protein storage, shown by plummeting serum albumin levels, the body is forced to enter a catabolic state [**3**]. To reverse this, Medical Nutrition Therapy (MNT) must shift focus from calorie restriction to specific nutritional fortification. Clinical interventions involving protein and energy supplementation do not destabilize blood glucose levels but instead inhibit lean body mass wastage and provide the amino acids necessary to stimulate fibroblast proliferation and collagen synthesis [**2**]. Providing proper protein is a strict biological requirement to wound healing.

Suggested Pharmaco-nutritional Protocol

The first step to limb salvage is to restore the deficit of essential macronutrients and micronutrients. The diabetic foot is subject to microvascular and neuropathic starvation that propels its physiological decline. Standard multivitamin complexes are often ineffective against the severe oxidative stress and pharmaco-nutrient malabsorption seen in advanced Type 2 Diabetes. To prevent peripheral nerve damage and to re-establish microvascular integrity, a mandatory specific pharmaco-nutritional protocol must be implemented. This protocol directly counters the systemic inflammatory breakdown and the Metformin-induced Vitamin B12 malabsorption trap seen in clinical cohorts [**5, 6**]. Table 2 outlines the targeted interventions needed to restore local immune responses and support macrovascular health.

Breaking the Clinical Impasse

Although the biological imperative to target nutrition is overwhelming, a massive translational gap exists in clinical podiatry. The localized wound is often aggressively managed while the systemic starvation of the patient is ignored. To stop the world amputation epidemic, it is important that clinical protocols require registered dietitians to form part of primary DFU care teams. Standardized screening tools such as the Mini Nutritional Assessment (MNA) must be used in conjunction with the routine evaluation of a biochemical triad consisting of serum Albumin, Vitamin B12 and Vitamin D. These parameters must be checked as routinely as blood pressure and HbA1c [**10, 4**]. Establishing this holistic patient management model is the only evidence-based method to accelerate wound closure and prevent systemic inflammatory collapse.

LIMITATIONS AND CURRENT LITERATURE

Although the presented synthesis effectively champions the mandatory use of Medical Nutrition Therapy, it is essential to recognize the limitations of the reviewed research. First, most of the included studies are cross-sectional/outcome analyses [**10, 16**]. Although such designs are sufficient for postulating links between extreme nutrition status and Wagner Grade, they cannot formally prove temporality and isolated causation. Second, the contribution of specific micronutrients is difficult to isolate since the patients are given a combination of antibiotics, extensive surgery, and offloading. The concomitant vascular surgeries and pharma-nutritional protocols are too confounding to reliably dissect their combined impact on outcomes. Lastly, since the data analyzed comes from multiple global studies, the variations in diet between different populations may confuse the results. The next step in the research would be to organize large-scale multinational Randomized Control Trials to standardize the baseline nutrition status and delineate the independent roles of different pharmacological and nutritional interventions. A universal algorithm for the management of diabetic

foot syndrome requires comprehensive studies to define the best initial dosages and the target biomolecular processes.

CONCLUSION

The transformation of a diabetic foot ulcer into a non-healing limb gangrene is not an inevitable consequence of diabetes; instead, it is a potentially avoidable physiologic catastrophe. This review aims to highlight the crucial role of nutritional status in figuring out the outcome of a diabetic foot ulcer. The current paradigm of standard care is fundamentally flawed in its understanding of the pathophysiology of a diabetic foot ulcer. Treating the localized inflammation while ignoring the catabolic state of the organism will produce inconsistent results. A wound with concomitant infection is characterized by an abnormally high metabolic demand that, if left unaddressed, will cause cachexia due to lean body mass consumption. The review shows that the amputation risk is profoundly affected by the systemic status of the patient, particularly the levels of protein and micronutrients. Specifically, the deficiency of Vitamins D and B12 is associated with increased risks of complications, poor healing, and mortality, especially in patients treated with Metformin. On the other hand, aggressive INS is consistently beneficial by promoting lean body mass preservation and localized immunologic response without aggravating the metabolic control. Thus, the current approach of managing the local signs of a diabetic foot ulcer while leaving the systemic response to chance is unsafe. Podiatric surgeons need to upgrade their paradigm of care and provide comprehensive care to the diabetic foot ulcer patients. In particular, the MNA should be employed to evaluate the patient's overall nutritional status, and the Albumin/Vitamin B12/Vitamin D tests should be routinely ordered to assess the baseline status. It is necessary for Medical Nutrition Therapy to become the pillar of management to improve the outcomes.

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