Interplay Between Vitamin D Status and Iron Deficiency Anemia in Pediatric Type 1 Diabetes: A Narrative Review

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Received: 28 October 2024, **Accepted:** 17 November 2024, **Published:** 20 November 2024

Abstract

Background: Type 1 diabetes mellitus (TIDM) is one of the most common chronic endocrine disorders affecting children and adolescents worldwide and is frequently associated with multiple metabolic and nutritional disturbances. Among these, vitamin D deficiency and iron deficiency anemia (IRON DEFECIENCY ANEMIA) have emerged as important comorbidities that may adversely influence glycemic control, immune regulation, growth, and overall disease outcomes in pediatric patients. Increasing evidence suggests that the coexistence of vitamin D deficiency and iron deficiency is not merely coincidental, but rather reflects a complex bidirectional interaction involving inflammatory pathways, immune dysregulation, oxiron defeciency anemiative stress, impaired erythropoiesis, and altered hepcidin metabolism. Children with TIDM appear particularly vulnerable to these abnormalities because of chronic autoimmune activity, nutritional imbalance, reduced sun exposure, and metabolic derangements associated with long-term diabetes.

This narrative review aims to explore the current evidence regarding the relationship between vitamin D status and iron deficiency anemia in children with TIDM, with emphasis on underlying pathophysiological mechanisms, prevalence patterns, clinical implications, and therapeutic considerations. Available pediatric studies indicate that vitamin D deficiency is highly prevalent among children with TIDM and may correlate with poor glycemic control, increased inflammatory burden, and higher risk of anemia. Simultaneously, iron deficiency may impair pancreatic β-cell function, alter insulin sensitivity, and worsen oxiron defeciency anemiative stress. Emerging mechanistic evidence also demonstrates that vitamin D can modulate iron metabolism through suppression of pro-inflammatory cytokines and regulation of hepcidin expression, thereby influencing erythropoiesis and iron availability.

Understanding the interplay between vitamin D deficiency and IRON DEFECIENCY ANEMIA in pediatric TIDM may improve early screening strategies and support integrated nutritional management approaches. Despite growing interest in this field, current evidence remains limited by heterogeneity of study designs, variable diagnostic criteria, and insufficient longitudinal pediatric data. Further large-scale prospective studies are required to clarify causal relationships and determine whether correction of these deficiencies can improve metabolic control and long-term diabetic outcomes in children with TIDM.

Keywords: Vitamin D Status, Iron Deficiency Anemia, Pediatric , Type 1 Diabetes

Introduction

Type 1 diabetes mellitus (TIDM) is a chronic autoimmune endocrine disorder characterized by immune-mediated destruction of pancreatic β-cells, resulting in absolute insulin deficiency and lifelong dependence on exogenous insulin therapy. It remains one of the most prevalent chronic metabolic diseases in children and adolescents, with an increasing global incidence over recent decades. Despite advances in insulin delivery systems and glucose monitoring technologies, pediatric TIDM continues to be associated with substantial metabolic, nutritional, and inflammatory complications that may negatively affect growth, pubertal development, immune function, and long-term cardiovascular health [1,2].

Among the nutritional abnormalities frequently observed in children with TIDM, vitamin D deficiency and iron deficiency anemia (IRON DEFECIENCY ANEMIA) have gained increasing clinical and research attention. Vitamin D is widely recognized not only for its classical role in calcium and bone metabolism but also for its important immunomodulatory, anti-inflammatory, and endocrine functions. Accumulating evidence suggests that vitamin D may influence pancreatic β-cell activity, insulin secretion, and immune tolerance, potentially affecting both the pathogenesis and progression of TIDM [3,4]. Several pediatric studies have demonstrated a high prevalence of vitamin D deficiency among children with TIDM, with some reports linking low serum vitamin D levels to poor glycemic control, increased glycated hemoglobin (HbA1c), and higher risk of diabetic complications [5,6].

Iron deficiency anemia represents the most common micronutrient deficiency worldwide and remains a major pediatric public health concern. In children with TIDM, iron deficiency may arise secondary to nutritional inadequacy, chronic inflammation, autoimmune comorbidities such as celiac disease, or altered metabolic demands. Beyond its hematologic consequences, iron deficiency may contribute to impaired cognitive performance, reduced physical capacity, altered immune responses, and disturbances in glucose metabolism [7,8]. Furthermore, anemia in diabetic patients may exacerbate tissue hypoxia and oxiron defeciency anemiative stress, thereby potentially worsening microvascular complications and disease burden [9].

Recent evidence indicates that vitamin D deficiency and iron deficiency are biologically interconnected through several shared molecular and inflammatory pathways. Vitamin D appears capable of regulating iron metabolism by suppressing inflammatory cytokines and reducing hepcidin expression, a central regulator of systemic iron homeostasis. Conversely, iron deficiency may impair vitamin D metabolism by reducing the activity of iron-dependent enzymes involved in vitamin D activation [10,11]. Chronic inflammation associated with TIDM may further intensify this interaction through cytokine-mediated dysregulation of erythropoiesis and micronutrient metabolism.

Although multiple studies have separately examined vitamin D deficiency and iron deficiency anemia in pediatric TIDM, the relationship between these two conditions remains insufficiently explored. Existing literature is fragmented, with considerable variability in study populations, diagnostic thresholds, and clinical outcomes. Moreover, there remains limited understanding regarding whether simultaneous correction of vitamin D and iron deficiencies could improve metabolic control or reduce diabetes-related complications in affected children.

Therefore, this narrative review aims to critically evaluate the current evidence regarding the interplay between vitamin D status and iron deficiency anemia in children with TIDM, focusing on epidemiology, underlying pathophysiological mechanisms, clinical significance, screening considerations, and potential therapeutic implications. By highlighting current evidence gaps and emerging concepts, this review seeks to support a more integrated nutritional and metabolic approach to pediatric TIDM management.

Overview of Type 1 Diabetes in Children

Type 1 diabetes mellitus (TIDM) is a chronic autoimmune disease characterized by T-cell-mediated destruction of insulin-producing pancreatic β-cells, ultimately leading to absolute insulin deficiency and lifelong dependence on insulin replacement therapy. It represents the most common form of diabetes in childhood and adolescence, accounting for nearly 90% of diabetes cases in pediatric populations [12]. The incidence of TIDM has increased steadily worldwide over recent decades, particularly among younger children, suggesting the contribution of both genetic susceptibility and environmental triggers in disease development [13].

The pathogenesis of TIDM involves a multifactorial interaction between genetic predisposition, immune dysregulation, and environmental exposures. Human leukocyte antigen (HLA) class II genes, particularly HLA-DR3 and HLA-DR4 haplotypes, remain the strongest genetic determinants associated with disease susceptibility [14]. However, environmental factors including viral infections, dietary influences, gut microbiota alterations, micronutrient deficiencies, and reduced sunlight exposure have also been implicated in triggering autoimmune β-cell destruction in genetically susceptible children [15]. Increasing evidence has highlighted the role of vitamin D deficiency as a possible contributor to immune dysregulation and progression of autoimmune diabetes [16].

Clinically, pediatric TIDM commonly presents with polyuria, polydipsia, weight loss, fatigue, and hyperglycemia, while diabetic ketoacidosis may occur as a severe initial manifestation in many children. Beyond glycemic abnormalities, children with TIDM frequently experience disturbances in nutritional status and micronutrient balance. Factors such as dietary restrictions, increased metabolic demands, fluctuating appetite, gastrointestinal autoimmune disorders, and chronic inflammation may predispose these patients to deficiencies in vitamin D, iron, zinc, magnesium, and other essential nutrients [17].

Chronic low-grade inflammation is increasingly recognized as an important feature of TIDM, even after disease onset and initiation of insulin therapy. Elevated inflammatory cytokines including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) contribute not only to β-cell destruction but also to altered iron metabolism and suppression of erythropoiesis [18]. Such inflammatory pathways may partially explain the increased susceptibility of children with TIDM to anemia and micronutrient disturbances. Moreover, inflammatory activation stimulates hepatic production of hepcidin, the key hormone regulating systemic iron homeostasis, thereby reducing intestinal iron absorption and iron availability for erythropoiesis [19].

Vitamin D deficiency is highly prevalent among pediatric patients with TIDM across different geographic regions. Several mechanisms have been proposed to explain this association, including reduced outdoor activity, obesity, dietary insufficiency, autoimmune-mediated inflammation, and genetic polymorphisms affecting vitamin D metabolism [20]. Vitamin D may influence TIDM pathogenesis through modulation of immune tolerance, inhibition of pro-inflammatory cytokines, and preservation of residual β-cell function [21]. In addition, emerging studies suggest that vitamin D deficiency may contribute to poor glycemic control and increased risk of diabetic complications in children with TIDM [22].

Iron deficiency anemia is another commonly overlooked condition in pediatric diabetes care. Children with TIDM may develop iron deficiency secondary to inadequate dietary intake, malabsorption syndromes such as celiac disease, menstrual blood loss in adolescents, or inflammation-associated disturbances in iron regulation [23]. Importantly, iron deficiency may independently impair cognitive development, exercise tolerance, and quality of life, while also affecting HbA1c interpretation and glycemic assessment [24]. The coexistence of vitamin D deficiency and iron deficiency anemia may therefore compound metabolic instability and negatively influence diabetes outcomes.

Given the growing recognition of micronutrient abnormalities in pediatric TIDM, comprehensive nutritional assessment has become increasingly important in routine diabetes management.

Understanding the interaction between chronic inflammation, immune dysfunction, vitamin D status, and iron metabolism may help identify children at increased risk of metabolic deterioration and support development of targeted preventive and therapeutic strategies.

Vitamin D Physiology and Immunometabolic Functions

Vitamin D is a fat-soluble secosteroid hormone essential for calcium-phosphorus homeostasis, skeletal development, immune regulation, and multiple metabolic processes. Although traditionally associated with bone health, vitamin D is now recognized as an important immunomodulatory and endocrine regulator with significant implications in autoimmune diseases, including type 1 diabetes mellitus (TIDM) [25]. In pediatric populations, vitamin D deficiency has become increasingly prevalent worldwide and represents an important public health concern due to its association with impaired growth, weakened immunity, and metabolic dysfunction [26].

Vitamin D exists primarily in two forms: vitamin D2 (ergocalciferol), derived from plant sources, and vitamin D3 (cholecalciferol), synthesized in the skin following ultraviolet B exposure or obtained from dietary animal sources. After synthesis or absorption, vitamin D undergoes hepatic hydroxylation to form 25-hydroxyvitamin D [25(OH)D], the major circulating form used clinically to assess vitamin D status. A second hydroxylation step occurs mainly in the kidneys through the enzyme 1α-hydroxylase, producing the biologically active metabolite 1,25-dihydroxyvitamin D [1,25(OH)2D] [27]. Importantly, several immune cells including macrophages, dendritic cells, and activated T lymphocytes also express 1α-hydroxylase, allowing local production of active vitamin D within immune tissues [28].

The biological effects of vitamin D are mediated through binding to the vitamin D receptor (VDR), a nuclear receptor expressed in numerous tissues including pancreatic β-cells, immune cells, skeletal muscle, and hematopoietic tissues [29]. Activation of VDR regulates the transcription of hundreds of genes involved in immune responses, inflammation, insulin secretion, and cellular proliferation. This broad receptor distribution supports the hypothesis that vitamin D deficiency may contribute to multiple systemic disturbances beyond bone metabolism.

In the context of TIDM, vitamin D has attracted considerable interest because of its immunomodulatory properties. Experimental studies suggest that vitamin D suppresses autoimmune activity by inhibiting pro-inflammatory T-helper 1 (Th1) and T-helper 17 (Th17) responses while promoting regulatory T-cell activity and immune tolerance [30]. Vitamin D also decreases production of inflammatory cytokines such as IL-2, IL-6, TNF-α, and interferon-gamma, all of which are implicated in pancreatic β-cell destruction [31]. These findings suggest that vitamin D deficiency may facilitate autoimmune progression and intensify inflammatory pathways involved in TIDM pathogenesis.

Several epidemiological studies have demonstrated an association between low vitamin D levels and increased risk of developing TIDM in children. Early-life vitamin D supplementation has been linked to reduced incidence of autoimmune diabetes, while lower serum 25(OH)D concentrations have frequently been observed in pediatric TIDM patients compared with healthy controls [32,33]. Moreover, some studies indicate that vitamin D deficiency may correlate with poorer glycemic control, higher HbA1c levels, and increased insulin requirements, although findings remain partially inconsistent due to heterogeneity in study design and population characteristics [34].

Beyond its immunologic role, vitamin D may directly influence glucose metabolism and pancreatic function. Vitamin D receptors are expressed in pancreatic β-cells, where vitamin D contributes to insulin synthesis and secretion through regulation of intracellular calcium homeostasis [35]. Additionally, vitamin D may improve peripheral insulin sensitivity by modulating inflammatory signaling and enhancing insulin receptor expression [36]. Deficiency of vitamin D may therefore contribute to both autoimmune dysregulation and metabolic instability in children with TIDM.

Emerging evidence also highlights a significant interaction between vitamin D and hematologic function. Vitamin D may support erythropoiesis by reducing inflammatory cytokine production and suppressing hepcidin synthesis, thereby improving iron availability for red blood cell production [37]. Low vitamin D levels have been associated with increased risk of anemia in both adult and pediatric populations, particularly in chronic inflammatory conditions. These observations provide an important

mechanistic basis for the proposed relationship between vitamin D deficiency and iron deficiency anemia in children with TIDM.

Iron Metabolism and Iron Deficiency Anemia in Pediatrics

Iron is an essential micronutrient required for numerous physiological processes including oxygen transport, cellular respiration, DNA synthesis, immune regulation, and neurocognitive development. In pediatric populations, adequate iron balance is particularly important because of rapid growth, increased metabolic demand, and ongoing neurologic maturation [38]. Iron deficiency remains the most common nutritional deficiency worldwide and is considered the leading cause of anemia among children and adolescents, especially in low- and middle-income countries [39].

Normal iron homeostasis depends on a tightly regulated balance between dietary absorption, storage, transport, and utilization. Iron is primarily absorbed in the duodenum and proximal jejunum through specialized transport proteins including divalent metal transporter-1 (DMT1) and ferroportin [40]. Once absorbed, iron binds to transferrin for systemic transport and is subsequently delivered to the bone marrow for erythropoiesis or stored mainly in the liver as ferritin. Unlike many other nutrients, iron excretion is minimal; therefore, regulation of intestinal absorption is the primary mechanism controlling systemic iron balance [41].

Hepcidin, a peptide hormone synthesized predominantly by the liver, is currently recognized as the master regulator of iron metabolism. Hepcidin controls iron availability by binding to ferroportin and inducing its degradation, thereby reducing intestinal iron absorption and inhibiting iron release from macrophages and hepatic stores [42]. Hepcidin production increases during inflammation, infection, and chronic disease states, contributing to functional iron deficiency and anemia of inflammation. Cytokines such as IL-6 strongly stimulate hepcidin synthesis and may significantly alter iron metabolism in children with chronic inflammatory conditions, including TIDM [43].

Iron deficiency progresses through several stages beginning with depletion of iron stores, followed by iron-deficient erythropoiesis, and eventually iron deficiency anemia (IRON DEFECIENCY ANEMIA), characterized by reduced hemoglobin synthesis and microcytic hypochromic anemia [44]. Clinical manifestations of IRON DEFECIENCY ANEMIA in children may include pallor, fatigue, impaired concentration, reduced exercise tolerance, headache, irritability, and delayed cognitive development. Long-standing iron deficiency may negatively affect psychomotor performance, academic achievement, and immune competence [45].

The etiology of iron deficiency anemia in pediatric patients is multifactorial and often includes inadequate dietary intake, rapid growth velocity, malabsorption, recurrent infections, and chronic inflammatory disorders. In children with TIDM, additional contributing factors may include autoimmune gastrointestinal diseases such as celiac disease, dietary restrictions, poor nutritional habits, and inflammatory dysregulation affecting iron absorption and utilization [46]. Adolescents with TIDM, particularly females, may also be at increased risk due to menstrual blood loss combined with increased nutritional requirements.

Emerging evidence suggests that iron deficiency may influence glucose metabolism and diabetic control. Iron is involved in mitochondrial energy production, oxiron defeciency anemiative metabolism, and enzymatic pathways important for pancreatic β-cell function [47]. Iron deficiency may impair insulin synthesis and secretion while simultaneously increasing oxiron defeciency anemiative stress and inflammatory activity. Furthermore, anemia may worsen tissue hypoxia and endothelial dysfunction, potentially aggravating diabetic microvascular complications [48].

An important clinical issue in diabetic patients is the effect of iron deficiency on glycated hemoglobin (HbA1c) interpretation. Several studies have demonstrated that iron deficiency anemia may falsely elevate HbA1c values independent of actual glycemic status, possibly due to prolonged erythrocyte lifespan and altered hemoglobin glycation kinetics [49]. This may complicate diabetes monitoring and lead to inaccurate assessment of metabolic control in children with coexisting anemia.

Recent pediatric studies have also identified a potential relationship between iron metabolism and vitamin D status. Vitamin D may suppress inflammatory-mediated hepcidin production and improve

iron bioavailability, whereas iron deficiency may impair vitamin D activation by reducing activity of iron-dependent hydroxylase enzymes involved in vitamin D metabolism [50].

Prevalence of Vitamin D Deficiency in Pediatric Type 1 Diabetes

Vitamin D deficiency is highly prevalent among children and adolescents with type 1 diabetes mellitus (TIDM) and has emerged as a major concern in pediatric endocrinology. Numerous epidemiological studies conducted across different geographic regions have consistently demonstrated lower serum 25-hydroxyvitamin D [25(OH)D] concentrations in children with TIDM compared with healthy controls [51]. This high prevalence may result from a complex interaction between autoimmune dysregulation, environmental factors, nutritional inadequacy, reduced outdoor activity, obesity, and genetic susceptibility affecting vitamin D metabolism.

Globally, the reported prevalence of vitamin D deficiency in pediatric TIDM varies considerably depending on geographic latitude, ethnicity, seasonal variation, and diagnostic thresholds used for vitamin D insufficiency. Nevertheless, several studies indicate that more than 50% of children with TIDM exhibit either vitamin D insufficiency or deficiency [52]. In some Middle Eastern and Asian pediatric cohorts, prevalence rates exceeding 70% have been documented, likely reflecting limited sunlight exposure, cultural clothing practices, and dietary insufficiency [53].

One of the earliest observations linking vitamin D deficiency to TIDM originated from epidemiological studies demonstrating that lower sunlight exposure and reduced vitamin D intake during childhood were associated with increased incidence of autoimmune diabetes [54]. Furthermore, vitamin D supplementation during infancy has been associated with a reduced risk of developing TIDM later in life, supporting a potential protective immunological role for vitamin D [55]. Although causality remains incompletely established, these findings suggest that vitamin D deficiency may contribute to both disease susceptibility and progression.

Children with TIDM may be particularly vulnerable to vitamin D deficiency because of chronic inflammatory activity and immune-mediated metabolic disturbances. Persistent inflammation can alter vitamin D metabolism through cytokine-mediated suppression of vitamin D activation pathways and increased catabolism of active vitamin D metabolites [56]. Additionally, diabetic children often demonstrate reduced physical activity and outdoor exposure, both of which may further decrease endogenous vitamin D synthesis.

Several pediatric studies have investigated the relationship between vitamin D status and glycemic control in TIDM. Lower serum vitamin D levels have frequently been associated with higher HbA1c concentrations, increased insulin requirements, and poorer metabolic control [57]. Proposed mechanisms include impaired pancreatic β-cell function, altered insulin secretion, increased inflammatory cytokine activity, and reduced insulin sensitivity. However, some studies have failed to demonstrate a consistent association, highlighting the heterogeneity of existing evidence and the influence of confounding variables such as obesity, puberty, ethnicity, and disease duration [58].

Vitamin D deficiency in children with TIDM may also contribute to increased risk of diabetic complications. Emerging evidence suggests associations between low vitamin D levels and diabetic nephropathy, endothelial dysfunction, cardiovascular risk markers, and impaired bone mineralization [59]. Since childhood and adolescence represent critical periods for skeletal development, chronic vitamin D deficiency may further compromise peak bone mass acquisition and increase long-term fracture risk in diabetic patients.

Genetic factors may additionally influence vitamin D status in pediatric TIDM. Polymorphisms involving the vitamin D receptor (VDR), vitamin D binding protein, and enzymes responsible for vitamin D activation have been implicated in altered susceptibility to autoimmune diabetes and variable vitamin D metabolism [60]. Such genetic interactions may partially explain differences in vitamin D deficiency prevalence among various ethnic and geographic populations.

Another clinically relevant issue is the overlap between vitamin D deficiency and other autoimmune conditions commonly associated with TIDM, particularly celiac disease and autoimmune thyroiditis. Malabsorption secondary to celiac disease may significantly impair vitamin D absorption, thereby

increasing the risk of deficiency and worsening nutritional status [61]. Consequently, pediatric patients with TIDM and concomitant autoimmune disorders may require closer nutritional monitoring and targeted supplementation strategies.

Despite the growing body of evidence linking vitamin D deficiency with TIDM, universal screening recommendations remain inconsistent across clinical guidelines. Nonetheless, many experts advocate periodic assessment of vitamin D status in pediatric diabetic patients, particularly in those with poor glycemic control, obesity, recurrent infections, bone symptoms, or coexisting autoimmune diseases. Early identification and correction of vitamin D deficiency may represent an important component of comprehensive diabetes care in children and adolescents.

Prevalence of Iron Deficiency Anemia in Pediatric Type 1 Diabetes

Iron deficiency anemia (IRON DEFECIENCY ANEMIA) is increasingly recognized as a clinically relevant but often underdiagnosed comorbidity in children and adolescents with type 1 diabetes mellitus (TIDM). Although anemia is traditionally emphasized in patients with advanced diabetic nephropathy, pediatric evidence suggests that iron deficiency and subclinical anemia may appear much earlier in the disease course, even before overt renal impairment. Children with TIDM may be vulnerable because of nutritional imbalance, autoimmune comorbidities, chronic inflammation, altered hepcidin regulation, and increased metabolic demands during growth and puberty [62,63].

The reported prevalence of anemia and iron deficiency among pediatric TIDM cohorts varies considerably between studies, largely because of differences in sample size, age distribution, disease duration, glycemic control, socioeconomic background, and diagnostic criteria. Recent pediatric studies have reported anemia prevalence ranging from approximately 18% to more than 30% among children and adolescents with TIDM, while iron deficiency or reduced ferritin levels may be even more frequent [63,64]. A recent Egyptian pediatric study found anemia to be significantly more prevalent in children with TIDM than in healthy controls, with lower hemoglobin, red blood cell indices, serum iron, and ferritin values among diabetic children.

Several mechanisms may explain the increased burden of IRON DEFECIENCY ANEMIA in pediatric TIDM. Inadequate dietary intake remains an important contributor, particularly in children with restrictive eating patterns or poor adherence to balanced diabetic nutrition plans. In addition, autoimmune gastrointestinal disease, especially celiac disease, is substantially more common in children with TIDM than in the general pediatric population and may impair iron absorption even in the absence of classical gastrointestinal symptoms [65]. Therefore, unexplained iron deficiency anemia in a child with TIDM should raise clinical suspicion for occult celiac disease, particularly when accompanied by poor growth, chronic abdominal symptoms, delayed puberty, or unstable glycemic control.

Chronic inflammation also plays a central role in iron dysregulation among children with TIDM. Pro-inflammatory cytokines, especially interleukin-6, stimulate hepatic hepcidin production, which decreases intestinal iron absorption and traps iron within macrophages and hepatic stores [66]. This mechanism may produce functional iron deficiency, where total body iron stores are not completely depleted but iron availability for erythropoiesis is reduced. In such cases, ferritin may be normal or falsely elevated because it behaves as an acute-phase reactant, making diagnosis more challenging in inflammatory states [67].

Disease duration may influence the risk of anemia in pediatric TIDM. Some studies suggest that children with longer diabetes duration demonstrate lower hemoglobin, mean corpuscular volume, serum iron, and ferritin values compared with those with shorter disease duration [64]. This may reflect cumulative effects of chronic inflammation, dietary imbalance, recurrent autoimmune screening abnormalities, and early renal or vascular changes. However, IRON DEFECIENCY ANEMIA may also occur near the onset of diabetes, suggesting that inflammatory and nutritional disturbances may begin early in the disease process [68].

Iron deficiency anemia may also interact with glycemic assessment. HbA1c remains the standard marker for long-term glycemic control, but its accuracy depends partly on erythrocyte lifespan and hemoglobin turnover. Iron deficiency anemia may falsely increase HbA1c values independent of true mean blood

glucose, potentially leading to overestimation of poor glycemic control [69]. This is particularly important in pediatric diabetes care, where treatment decisions and insulin adjustments are often guided by HbA1c trends.

The clinical consequences of IRON DEFECIENCY ANEMIA in children with TIDM extend beyond hematologic abnormalities. Iron deficiency may worsen fatigue, reduce exercise tolerance, impair attention and school performance, and negatively affect quality of life. These symptoms may overlap with manifestations of poor glycemic control, making clinical recognition difficult. Furthermore, anemia-related tissue hypoxia may theoretically intensify oxiron defeciency anemiative stress and endothelial dysfunction, thereby contributing to early vascular risk in diabetic children [70].

Pathophysiological Interplay Between Vitamin D and Iron Homeostasis

The relationship between vitamin D deficiency and iron deficiency anemia (IRON DEFECIENCY ANEMIA) is increasingly recognized as bidirectional and multifactorial, particularly in chronic inflammatory conditions such as type 1 diabetes mellitus (TIDM). Several overlapping mechanisms involving inflammation, immune dysregulation, oxiron defeciency anemiative stress, and hepcidin-mediated iron metabolism may explain the frequent coexistence of these abnormalities in pediatric diabetic patients [71].

One of the central mediators linking vitamin D and iron metabolism is hepcidin, the hepatic peptide hormone that regulates systemic iron balance. Inflammatory cytokines, especially interleukin-6 (IL-6), stimulate hepcidin synthesis, which decreases intestinal iron absorption and limits iron release from macrophages and hepatic stores [72]. Vitamin D appears to suppress hepcidin transcription directly and indirectly through reduction of inflammatory cytokine activity, thereby improving iron availability for erythropoiesis [73].

Conversely, iron deficiency may impair vitamin D metabolism. Iron-dependent enzymes such as 25-hydroxylase and 1α-hydroxylase are required for activation of vitamin D, and reduced iron availability may decrease enzymatic conversion into biologically active metabolites [74]. This interaction may contribute to simultaneous vitamin D deficiency and IRON DEFECIENCY ANEMIA in children with TIDM.

Chronic inflammation associated with TIDM may further intensify this cycle. Persistent immune activation promotes oxiron defeciency anemiative stress, cytokine release, and altered erythropoiesis while simultaneously affecting vitamin D signaling pathways [75]. Vitamin D deficiency may also exacerbate autoimmune responses and inflammatory activity, potentially worsening β-cell destruction and metabolic instability.

Additionally, both vitamin D deficiency and iron deficiency have been associated with impaired immune function, reduced exercise tolerance, fatigue, cognitive dysfunction, and poorer quality of life in pediatric populations [76].

Conclusion

Vitamin D deficiency and iron deficiency anemia are common and frequently overlapping conditions in children with type 1 diabetes mellitus, reflecting complex interactions among chronic inflammation, immune dysregulation, altered hepcidin activity, and metabolic disturbances. Current evidence suggests that vitamin D may play an important role in iron homeostasis and erythropoiesis, while iron deficiency may adversely affect vitamin D metabolism and glycemic assessment. The coexistence of these deficiencies may contribute to poorer metabolic control, impaired growth, reduced quality of life, and increased risk of diabetic complications in pediatric patients. Early recognition and comprehensive nutritional evaluation are therefore essential components of holistic diabetes care. Nevertheless, available pediatric evidence remains limited and heterogeneous, emphasizing the need for larger prospective studies to clarify causal relationships and determine whether combined correction of vitamin D deficiency and iron deficiency anemia can improve clinical and metabolic outcomes in children with type 1 diabetes.

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