Keywords:

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Serum Vitamin D as a Determinant of Hematological Profile and Anemia Severity in Adults with Iron Deficiency Anemia

Abstract

Objectives: This study set out to explore the relationship between serum 25-hydroxyvitamin D levels and hematological parameters in an adult cohort diagnosed with iron deficiency anemia (IDA). We also wanted to see if vitamin D holds onto an independent connection with hemoglobin concentrations once you filter out potential confounding variables.

Methods: We designed a cross-sectional study that tracked 500 adult patients with confirmed IDA. To make the diagnosis definitive, inclusion required low hemoglobin levels, clear microcytosis (MCV <80 fL), and serum ferritin levels dropping below 15 ng/mL. We relied on standardized laboratory techniques to map out all hematological and biochemical variables, then split the participants into groups based on their baseline vitamin D status. We used group differences, Pearson correlation coefficients, and multivariable linear regression models to make sense of the data.

Results: An overwhelming 79.6% of our participants turned out to be vitamin D deficient. The individuals in this deficient camp faced significantly lower hemoglobin levels (10.2 ± 1.4 vs 10.9 ± 1.6 g/dL; p=0.018) and a noticeable drop in MCV (72.9 ± 6.0 vs 75.8 ± 6.4 fL; p=0.027) compared to the vitamin D-sufficient group. On top of that, serum vitamin D levels showed a steady, positive correlation with both hemoglobin (r=0.31, p<0.01) and MCV (r=0.27, p=0.02). When we ran the final multivariable regression model, vitamin D stood its ground as an independent predictor of hemoglobin concentrations (β=0.248, 95% CI 0.071–0.425; p=0.004).

Conclusions: Vitamin D deficiency is incredibly widespread among adults dealing with IDA. What's more, it is directly tied to lower hemoglobin levels and more pronounced microcytosis. These insights indicate that testing vitamin D alongside regular iron panels could offer a much clearer clinical picture and pave the way for more comprehensive care plans.

Introduction

Iron deficiency anemia (IDA) is still one of the most stubborn global health challenges we face, quietly affecting more than 24% of the world's population [1,2]. It is easy to look at insufficient iron as the sole culprit, but a growing body of evidence reminds us that red blood cell production is rarely a solo act. Instead, it is a complex, multi-layered process where other micronutrients and endocrine players—including Vitamin D, Vitamin B12, and thyroid hormones—constantly shape how hematopoiesis plays out [3, 5, 6].

What makes vitamin D particularly fascinating in this context is where it shows up. Vitamin D receptors are highly concentrated on multi-lineage hematopoietic stem cells and early erythroid progenitor cells right inside the bone marrow microenvironment. Here, the active hormone works hand-in-hand with erythropoietin to drive cell division and specialization [5,18], [3,5], [19]. When circulating vitamin D levels take a hit, this local cellular support system in the marrow niche starts to struggle. The result? Erythropoietin loses its efficiency, and the structural maturation of red blood cells gets cut short [20].

When you look at past clinical studies, you see a recurring pattern: low Vitamin D levels regularly track alongside lower hemoglobin concentrations and smaller mean corpuscular volume (MCV), signaling a clear drag on red blood cell production [8]. Yet, surprisingly little research has looked database-wide or zeroed in exclusively on adults dealing with active, confirmed IDA. This is a massive oversight for regions like Iraq and neighboring Middle Eastern countries, where vitamin D deficiency is an endemic public health issue shaped by deep-rooted environmental, cultural, and lifestyle dynamics [9,14]. If we can pin down exactly how Vitamin D status alters hematological traits in this specific group, we can build sharper diagnostic strategies and ultimately offer better patient care.

From a biological standpoint, vitamin D wears several different hats when it comes to blood health. Beyond its direct role in nurturing bone marrow stem cells [3,5], it serves as a major regulator of systemic iron balance by keeping a lid on inflammatory pathways and managing the hepcidin–ferroportin axis [6,7]. Think of hepcidin, a peptide hormone generated by hepatocytes, as the body's master iron gatekeeper [16]. It binds directly to the cellular iron exporter, ferroportin, causing it to break down inside the cell [16]. When these pathways are blocked, iron gets trapped inside enterocytes and splenic macrophages [16]. This leaves the bone marrow starved of serum iron for transport, even if the body's total iron stores look fine on paper [16]. Active vitamin D (1,25–dihydroxyvitamin D3) acts as a natural brake on this shutdown. By binding to a specific response element on the hepcidin gene promoter, it turns down its expression, letting iron flow freely back into circulation through open ferroportin channels [17].

At the same time, vitamin D works as a powerful anti-inflammatory agent. Both in vitro and clinical data show that it suppresses major pro-inflammatory cytokines, like interleukin-6 and tumor necrosis factor-alpha, which are notorious for triggering hepatic hepcidin production [18]. When vitamin D is missing from the picture, these underlying inflammatory signals run unchecked. This setup triggers a state of functional iron restriction, worsening the severe microcytosis that already characterizes absolute iron deficiency anemia [21].

In places like the Kurdistan Region of Iraq, a unique combination of environment and lifestyle creates a perfect storm for these nutrient deficiencies to overlap [19], [35]. It sounds like a paradox: people live in a region with abundant, year-round sunlight but still experience severe vitamin D deficiency. This happens because of local dietary patterns, a natural tendency to avoid the brutal midday heat, and traditional clothing choices that limit skin exposure to UV radiation [19]. When these two nutritional gaps hit a patient at the same time, focusing solely on standard iron tests means clinicians are missing a huge piece of the puzzle [5,6], [38]. Checking Vitamin D alongside standard iron profiles gives physicians a much deeper look at what is happening under the hood, opening the door for more integrated and genuinely effective treatment plans [5,6,7].

Materials and Methods

Study Design and Participant Selection

This cross-sectional study looked closely at 500 adult patients diagnosed with IDA. To keep our sample tightly defined, we set strict diagnostic benchmarks: low hemoglobin (Hb <12 g/dL for women, <13 g/dL for men), clear microcytosis (MCV <80 fL), and depleted iron reserves (serum ferritin <15 ng/mL).

Because we wanted to isolate the true, independent impact of vitamin D on primary IDA, we filtered out confounding variables using tight exclusion criteria during the screening phase. We excluded anyone with a known history of acute or chronic blood loss, active gastrointestinal malignancies, overt signs of acute infections, diagnosed chronic kidney disease, or underlying thyroid disorders. Additionally, to keep recent treatments from distorting baseline blood profiles, we excluded individuals who had taken regular iron supplements, received blood transfusions, or undergone vitamin D therapies within the 3 months leading up to the study.

Data Collection and Laboratory Analysis

Once we secured ethical approval, our data collection ran for a full calendar year, spanning from August 2024 to August 2025. We utilized a consecutive sampling method, screening adults who came into the laboratory for routine diagnostic workups. We kept enrollment open until we hit our target sample size of 500 eligible participants, ensuring our sub-analyses had plenty of statistical

power.

We processed all blood samples using standardized laboratory equipment. Hematological indices were analyzed using a Medonic M-Series Analyzer (Boule Diagnostics, Sweden). Biochemical markers—including serum ferritin, Vitamin D (25-hydroxyvitamin D), Vitamin B12, TSH, T3, and T4—were measured on a MAGLUMI 800 Chemiluminescence Immunoassay Analyzer (Snibe Diagnostics, China). Meanwhile, serum iron levels were tracked down via a BS-230 Analyzer (Mindray, China) [11, 12].

Even though we actively measured serum vitamin B12 and thyroid panels to rule out alternative causes of anemia during our screening phase, we intentionally kept them out of the final multivariable regression models. Our primary goal was to dissect the direct relationship between vitamin D and hematological trends in confirmed IDA. Adjusting our regression models strictly to core demographic and iron-focused metrics (age, sex, and ferritin) allowed us to keep the models clean and avoid overfitting.

We split our participants into two clinical categories based on established guidelines: Vitamin D deficient (<20 ng/mL) and sufficient (>=20 ng/mL) [13]. The baseline severity of their anemia was mapped out according to standard World Health Organization criteria [10].

Statistical Analysis

We verified our data distribution using the Shapiro–Wilk normality test. Continuous metrics were expressed as means ± standard deviation or as medians with their corresponding interquartile ranges, depending on how the data was distributed. All statistical operations were processed through IBM SPSS v25, and we set our significance threshold strictly at a p-value <0.05.

Ethical Considerations

This study was officially reviewed and approved by the Research Ethics Committee of the Duhok Directorate General of Health under Reference No.: 30102024-9-16 (Approval date: 03 August 2024).

Results

Vitamin D deficiency was observed in 79.6% of the study population as shown in Figure 1.

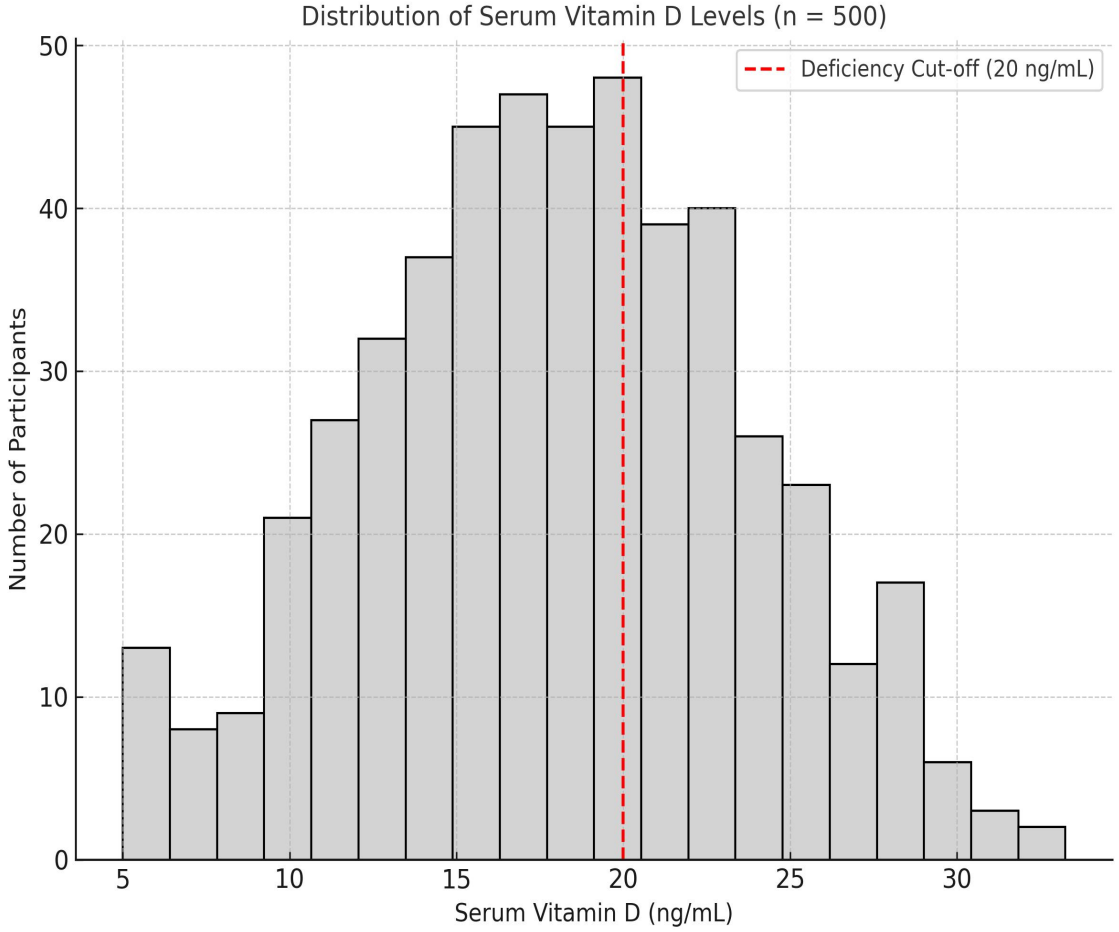

Figure 1. Distribution of Serum Vitamin D Levels(ng/ml) among IDA Participants. Histogram depicting Vitamin D distribution with deficiency threshold at 20 ng/mL.

Baseline demographic, hematological, and biochemical characteristics stratified by vitamin D status are presented in Table 1.

Table 1. Baseline Characteristics of the Study Population (n = 500)

Variable	Total	Vitamin D Deficient (<20 ng/mL)	Vitamin D Sufficient (≥20 ng/mL)	p-value
Age (years)	34.8 ± 10.2	35.2 ± 9.7	33.9 ± 10.9	0.27
Sex (M/F)	162/338	131/267	31/71	0.21
Hemoglobin (g/dL)	10.4 ± 1.5	10.2 ± 1.4	10.9 ± 1.6	0.018 *
MCV (fL)	73.5 ± 6.2	72.9 ± 6.0	75.8 ± 6.4	0.027 *
Ferritin (ng/mL)	10.4 (8.2–13.7)	10.2 (8.1–13.3)	11.2 (8.4–14.5)	NS

Values are presented as mean ± standard deviation or median (interquartile range) as appropriate. *p < 0.05 indicates statistical significance; NS: not significant.

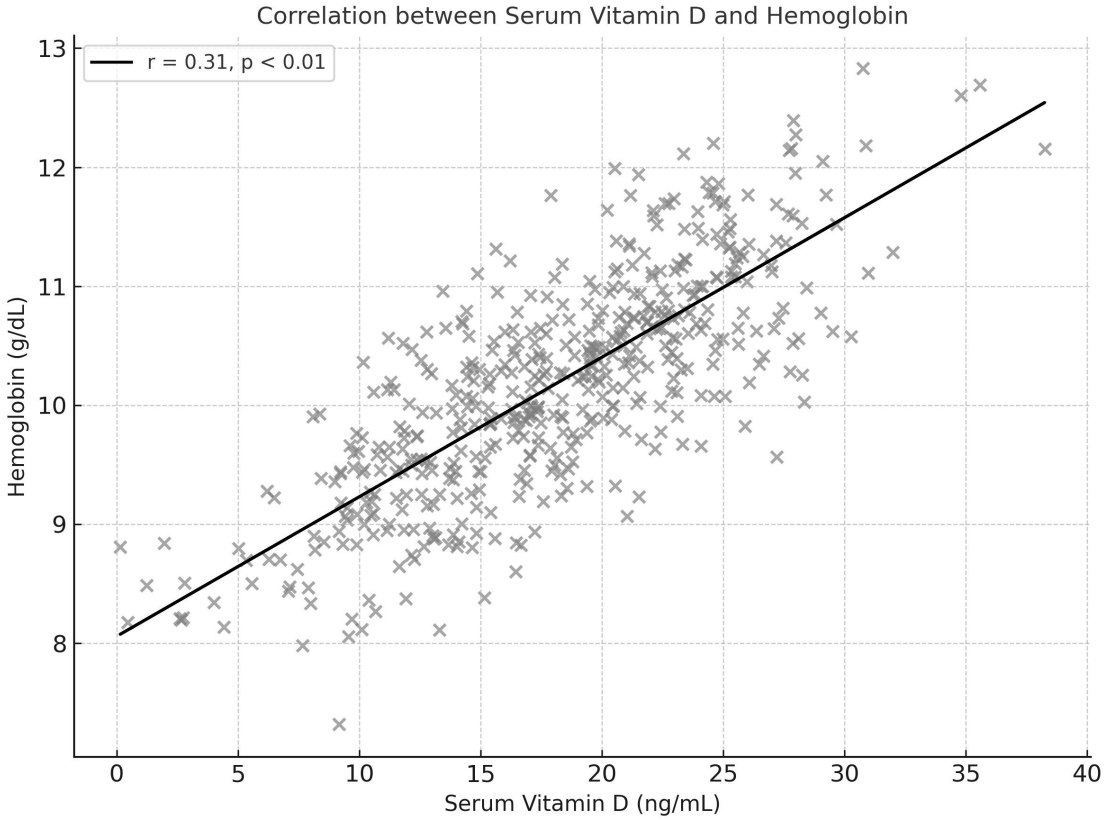

Figure 2. Correlation between Serum Vitamin D(ng/ml) and Hemoglobin(g/dl). Scatterplot with regression line showing r = 0.31, p < 0.01

Participants with vitamin D deficiency had significantly lower hemoglobin levels and reduced MCV compared with vitamin D-sufficient individuals.

Correlation analysis demonstrated a positive association between serum vitamin D levels and both hemoglobin concentration and MCV, while no significant correlation was observed with ferritin levels, as shown in Table 2.

Table 2. Correlation between Serum Vitamin D and Hematological Parameters

Parameter	r (Pearson)	p-value
Hemoglobin (g/dL)	0.31	<0.01 **
MCV (fL)	0.27	0.02 *
Ferritin (ng/mL)	0.12	0.08 (NS)

Pearson correlation coefficient (r) was used. *P < 0.05, **p < 0.01 indicate statistical significance; NS: not significant.

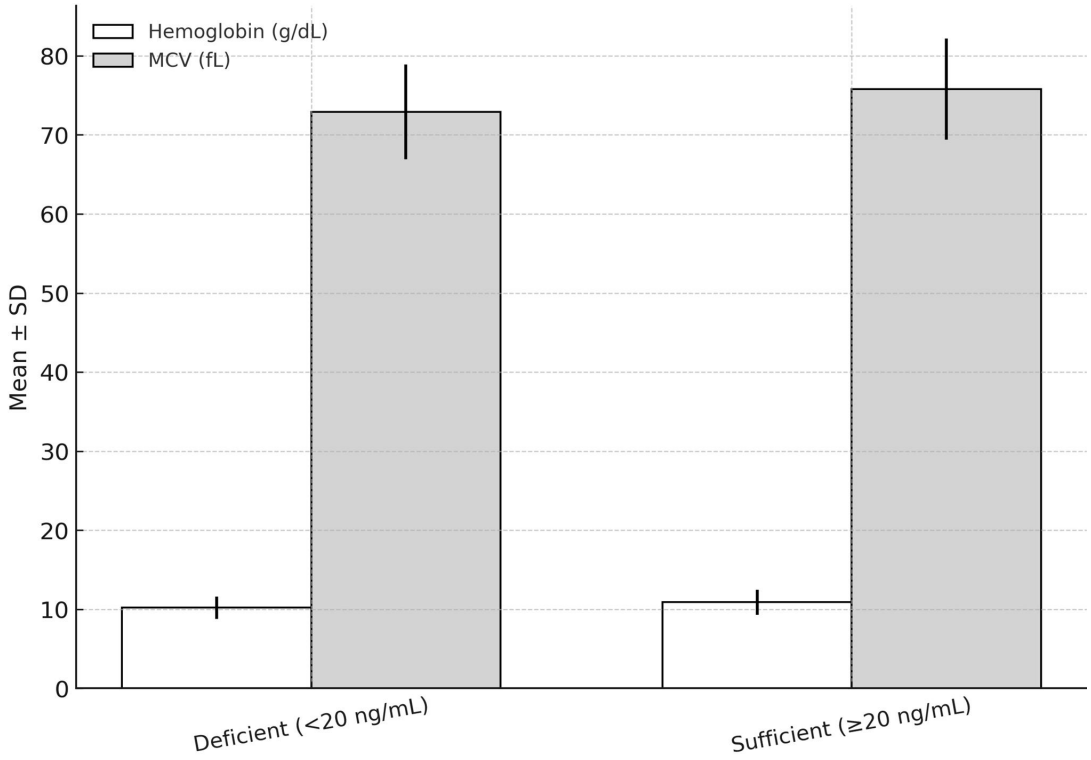

Figure 3. Mean Hemoglobin and MCV across Vitamin D Categories. Bar chart comparing deficient vs sufficient groups.

Multivariable linear regression analysis identified serum vitamin D as an independently associated with hemoglobin concentration after adjustment for ferritin, age, and sex, as shown in Table 3.

Table 3. Multivariable Linear Regression for Predictors of Hemoglobin

Variable	β Coefficient	95% CI	p-value
Vitamin D (ng/mL)	0.248	0.071 – 0.425	0.004 **
Ferritin (ng/mL)	0.132	–0.021 – 0.286	0.09
Age (years)	–0.062	–0.147 – 0.023	0.18
Sex (M = 1, F = 0)	0.084	–0.031 – 0.199	0.12

β: standardized regression coefficient; CI: confidence interval. *p < 0.05, **p < 0.01 indicate statistical significance.

Discussion

The most striking finding from this study is just how common Vitamin D deficiency is (79.6%) among adults with iron deficiency anemia, and how clearly it links to lower hemoglobin counts and smaller red blood cells. These numbers match up with broader epidemiological data coming out of Iraq and the Middle East, confirming that local environmental and behavioral habits frequently undermine micronutrient health and compound existing hematological struggles [19]. What we are seeing here fits right into a shifting medical perspective: vitamin D is not just for bone health anymore—it plays an active, meaningful role in how our bodies build blood.

The direct, positive ties we found between vitamin D levels, hemoglobin, and MCV hint that lacking this vitamin might actually make the structural features of anemia worse. Biologically, this makes sense. Vitamin D works on several fronts to keep red blood cells healthy: it makes cells more sensitive to erythropoietin, drives early-stage erythroblast growth within the bone marrow [3,5], and keeps hepcidin in check so iron can move freely to where it is needed [6,7]. When vitamin D levels bottom out, these pathways take a hit, creating a functional iron bottleneck and slowing down normal blood cell recovery.

Our results point in the same direction as classic findings by Perlstein et al. [4], who also mapped a clear path between low Vitamin D levels and dropping hemoglobin concentrations. This consistency across different studies strengthens the argument that vitamin D status is a key factor in how severe anemia becomes. However, while older research usually looked at broad, mixed crowds, our study focused directly on patients with confirmed, active IDA, giving us a much sharper look at this specific group. This high rate of deficiency also echoes broader reports from Iraq and neighboring Middle Eastern nations, where it remains a stubborn public health issue [9, 14].

From a practical clinical standpoint, these insights suggest that tracking vitamin D alongside standard iron panels could change how we gauge anemia severity. While iron supplements are always going

to be the foundation of treating IDA, identifying and fixing a hidden, coexisting vitamin D deficiency might help patients respond better to treatment and get their blood counts back to normal faster.

Limitations and Looking Ahead

Of course, our study has a few limitations to keep in mind. Because it is a cross-sectional study, we cannot definitively say that low Vitamin D causes lower hemoglobin—only that the two are closely intertwined. It is also a single-center study, meaning the findings might not look exactly the same in every population. On top of that, we did not measure specific systemic inflammatory markers like CRP or IL-6, nor did our design track parathyroid hormone (PTH) or ionized calcium levels. This matters because long-term vitamin D deficiency can trigger secondary hyperparathyroidism, and elevated PTH can have a direct, toxic effect on the bone marrow matrix, throwing a wrench into red blood cell production lines [20]. We also lacked precise dietary logs or direct metrics on sunlight exposure, which could have shed more light on the lifestyle factors driving these deficiencies.

Looking ahead, the logical next step is to focus on long-term, interventional trials [15]. Specifically, we need to see if adding vitamin D supplements directly boosts blood counts for IDA patients, which will help determine if vitamin D checks deserve a permanent spot in standard anemia care guidelines.

Conclusion

In summary, vitamin D deficiency turned out to be incredibly common among adults with iron deficiency anemia in this study, showing a direct, independent link to lower hemoglobin levels and smaller red blood cell sizes. These findings add to the mounting evidence that vitamin D plays a big part in how severe anemia becomes, reaching far beyond its classic roles in the human body.

In daily clinical practice, evaluating a patient's vitamin D status right alongside their standard iron panels could offer a much more complete and accurate picture. This integrated perspective is especially vital in regions where overlapping nutritional deficiencies are the norm, since these combined gaps can shift both how the illness presents and how well a patient responds to treatment. Ultimately, we need more clinical trials to confirm if fixing a vitamin D deficiency can directly speed up hematological recovery and to clarify its exact role in the future management of iron deficiency anemia.

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