



(RESEARCH ARTICLE)



THE IRON DEFICIENCY ANEMIA AND DEFICIENCY SERUM VITAMIN D3 STATUS IN WOMEN BODY

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ABSTRACT

Iron deficiency Anemia and hypovitaminosis D two intersecting global public challenges, mainly among premenopausal females. Generally noticed as isolated disorders, compelling biochemical and clinical literature now establishes a direct, bidirectional metabolic axis between iron status and vitamin d activation. Iron serves as a required prosthetic cofactor for the hepatic and renal cytochrome P450 hydroxylases (CYP2R1 and CYP27B1) responsible for catalyzing the converting of inactive vitamin D into its endocrinologically active form, 1,25-dihydroxyvitamin D. Concurrently, active vitamin D receptor (VDR) signaling regulates erythroblast differentiation and suppresses hepatic hepcidin expression preventing macrophage iron sequestration. This empirical study evaluated a human female group (N = 100, aged 11-50 years; Mean age: 26.88 ± 9.46 years) to assess biomarker co-occurrence and correlation. Statistical analysis via IBM SPSS Version 26.0 revealed iron deficiency (Serum Ferritin < 15 ng/mL) in 39.0% of subjects and Vitamin D deficiency (< 20 ng/mL) in 73.0% of subjects. Crucially, 82.05% (N = 32/39) of iron-deficient females exhibited concurrent Vitamin D3 deficiency. Spearman rank correlation inveterate a statistically significant positive association between serum ferritin and Vitamin D3 ($\rho = 0.243$, $p = 0.0148$). These results show that uncorrected iron deficiency blunts vitamin D hydroxylation, necessitating integrated dual-screening and co-supplementation protocols in clinical gynecology and primary care.

Keywords: Iron Deficiency; Anemia; Vitamin D3 Deficiency; Women Body.

1 INTRODUCTION

Vitamin D deficiency have impact nearly 50% of the population global. This epidemic of hypovitaminosis D can mostly be credited to daily life and ecological features such as decrease exposure the skin to sunlight, which is required for ultraviolet-B (UVB)-induced vitamin D production. White people absorb less UVB in the melanin of their skin than black people do so, need more sun exposure to produce the similar amount of vitamin D [1][2]. The high occurrence of vitamin D deficiency is a mainly important public health problem because hypovitaminosis D is an independent risk reason for total mortality happening to the common populace [3].

Recently, the concurrence of Iron Deficiency Anemia with hypovitaminosis D takes appeared as a major clinical concern [4]. The iron metabolism and erythropoiesis are affected by Vitamin D, while systemic iron is requisite for vitamin D synthesis and activation [5]. With respect to anemia, the studies have consistently informed that the levels of ferritin serum are completely related with circulating vitamin D [6] [7]. Ferritin consider a biomarker of iron stores and is reduced in topics with anemia.[8] Iron Deficiency Anemia and D deficiency stay to be worldwide public health difficulties that influenced by dietary inadequacies, cultural practices, and economic causes. In adding, dietary calcium deficiency and disorders damaging mineral absorption exacerbate both conditions [9].

1.1 Physiological Susceptibility of the Female body

In females of reproductive age (12–49 years), chronic inferior blood loss generates a persistent straining on total body iron stores. When the serum ferritin levels drop less critical edges the functional iron decrease will happened. While the hematological consequences—such as fatigue, microcytic hypochromic anemia, and reduced oxygen transport are well present, the secondary endocrine disruptions are often ignored. Exactly, systemic iron depletion impairs iron-dependent enzymatic cascades during the body, including renal enzymes and the hepatic that will responsible for activating V\itamin D [5][10].

2 THE MECHANISMS OF ACTIVATION VITAMIN D3 AND IRON

Unlike other vitamins, Vitamin D is distinctive because it can be synthesized within the skin upon exposure to solar radiation . It primarily exists as two compounds: ergocalciferol (Vitamin D2) and cholecalciferol (Vitamin D3). Whether derived from dietary intake or cutaneous synthesis, the nutrient remains inactive until it undergoes a pair of consecutive enzymatic hydroxylations to attain biological activity [2] [11].

In the liver, calciferol is first hydroxylated to 25-hydroxyvitamin D [25(OH)D] via the CYP2R1 25-hydroxylase enzyme. In the kidneys, 25(OH)D is next hydroxylated to 1,25-dihydroxyvitamin D [1,25(OH)2D] by 1-alpha hydroxylase (CYP27B1). Both CYP2R1 and CYP27B1 are heme-containing cytochrome P450 enzymes that severely depend on iron as an vital catalytic cofactor. So, severe Iron Deficiency Anemia damages the action of these hydroxylases, leading to reduced synthesis of active 1,25(OH)2D [12] [13]. Some studies noted that the iron deficiency in animal will significantly decreases circulating 1,25-dihydroxycholecalciferol levels, which confirms that the enzymatic hydroxylation of vitamin D strictly depends on maintaining sufficient iron levels [14].

Also, serum concentrations of vitamin D metabolites are regulated via degradative pathways (CYP24A1) and transported bound to Vitamin D Binding Protein [26]. 1,25-dihydroxyvitamin D encourages intestinal calcium and phosphorus absorption and regulates over 200 genes involved in cellular differentiation and immunity [13][15]

The relationship between iron and vitamin D is severely bilateral. Active 1,25(OH)2D3 uses a direct inhibitory influence on the transcription of the HAMP gene in hepatocytes, which encodes Hepcidin—the master controlling hormone of systemic iron metabolism. Hepcidin acts by binding to and inducing the degradation of ferroportin, the only cellular iron exporter on enterocytes and macrophages [7] [16].

When Vitamin D is deficient, unsuppressed hepcidin levels rise, causing ferroportin internalization. This tricks iron within intestinal mucosal cells and reticuloendothelial macrophages, preventing intestinal iron absorption and systemic iron recycling. Therefore, a vicious pathophysiological loop is established: Iron deficiency damages vitamin D hydroxylases, and the subsequent vitamin D deficiency raises hepcidin, further aggravating iron deficiency [17] [18].

3 THE RISK GROUPS FOR IRON AND VITAMIN D3 DEFICIENCY

The main source of vitamin D is natural sunlight exposure. Inadequate sun exposure, sunscreen use (SPF 30 reduces synthesis by>95%), dark skin pigmentation, and obesity are major causes of deficiency [19]. In clinical conditions such as uterine fibroids and chronic menorrhagia, excessive menstrual blood loss causes negative iron balance, leading to microcytic hypochromic Iron Deficiency Anemia and depleted serum ferritin stores [10]. There are association between vitamin D and gastrointestinal diseases is typically considered unidirectional with the gastrointestinal diseases which causes to hypovitaminosis D [20] [21].

Frirst, fat malabsorption syndromes (Celiac disease, Crohn's disease, surgical resection) is one of the risk groups that damage the absorption of both fat-soluble vitamin D and dietary iron . Also, hepatic enzyme-inducing accelerate the catabolism of vitamin D metabolites [22] [23] .

Second premenopausal Women and Uterine Fibroid Patients

Women experiencing heavy menstrual bleeding are at great danger for Iron Deficiency Anemia. Reduced serum ferritin directly relates with low serum vitamin D levels in this people [14][24].

Third obese Individuals

Dermal fat sequestration decreases vitamin D bioavailability [23], while chronic low-grade inflammation in obesity raises hepcidin, restricting iron absorption and predisposing to Iron Deficiency Anemia [25] [26].

4 PATHOPHYSIOLOGICAL

To imagine this complex (iron and vitamin D) , bidirectional feedback mechanism, the two figure (Figure 1,2) below [18] shows the pathophysiological cycle linking chronic menstrual blood loss, enzymatic failure, vitamin D deficiency, and hepcidin upregulation in females:

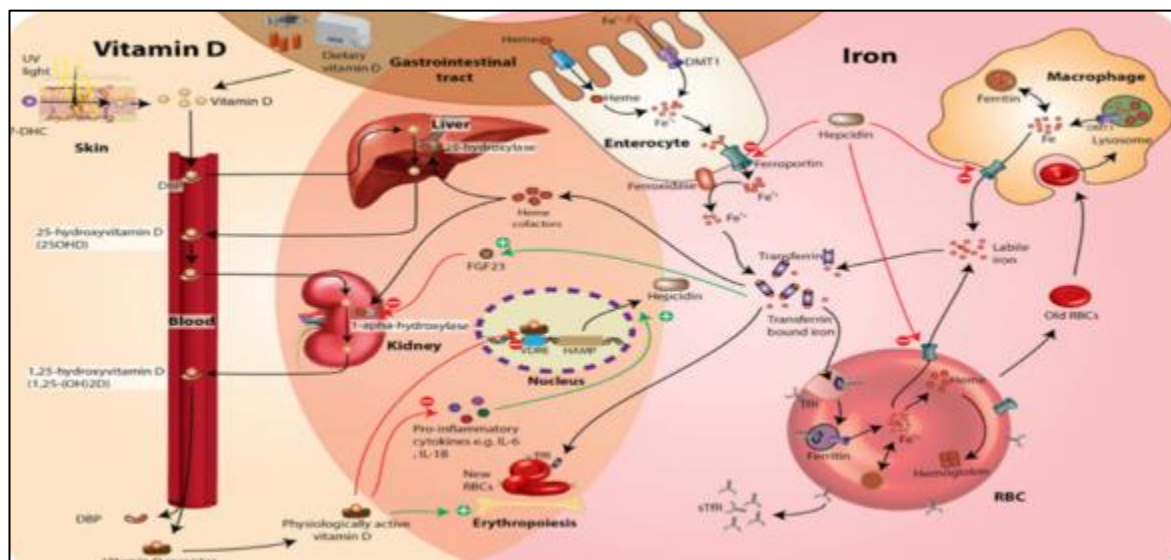


Figure 1: As summarized in this figure, data from in vitro and animal research approve that iron metabolic and vitamin D processes are closely interlinked



Source: Adapted from standard molecular hematology model [27][16].

Figure 2: (Iron deficiency impairs Vitamin D activation, elevating hepcidin and blocking iron absorption in a vicious cycle)

5 MATERIALS AND METHODS

5.1 The Study Design and Human Group

This observational irritated sectional clinical study was applied on a human female group of 100 contributors (N = 100) aged between 11 and 50 years (Mean age: 9.46 ± 26.88 years). All contributors were employed from clinical outpatient locations.

5.2 Inclusion and Rejection Standards

Inclusion standards instructed females presenting for hematological evaluations or routine wellness within adolescent and reproductive age supports. Exclusion criteria included individuals with chronic kidney disease (period 3–5), active hepatic cirrhosis, chronic inflammatory bowel disease, active malignancies, or those currently receiving parenteral iron therapy or high-dose vitamin D supplementation.

5.3 Laboratory Examines

Venous blood samples were collected subsequently an overnight fast. Serum ferritin was quantified via electrochemiluminescence immunoassay (ECLIA). Serum total 25-hydroxyvitamin D3 [25(OH)D3] was measured using chemiluminescent immunoassay (CLIA). Complete blood counts (CBC) were obtained using an automated hematology analyzer.

5.4 Statistical Study

Statistical analysis were achieved using IBM SPSS Statistics for Windows (Version 26.0). The Shapiro-Wilk test was useful to estimate the normality distribution of continuous variables. Continuous parameters were summarized as

mean $\pm$ standard deviation (SD) alongside range values, whereas group parameters were stated as counts (n) and percentages (%). To study the bivariate association between the level of ferritin and Vitamin D3, the non-parametric Spearman rank correlation coefficient (ρ) was employed. Statistical significance was established at a two-tailed p-value threshold of less than 0.05.

6 RESULTS

6.1 Demographic Overview

The studied group involved of 100 female participants spanning adolescent and premenopausal adult age groups (Range: 11 – 50 years; Mean age: 26.88 ± 9.46 years).

6.2 Prevalence of Iron Deficiency

Based on international hematological criteria (Serum Ferritin <15 ng/mL), iron deficiency was recognized in 39.0% (n = 39) of the total population. Normal iron stores (15–150 ng/mL) were observed in 59.0% (n = 59), while elevated ferritin (>150 ng/mL) was noted in 2.0% (n = 2). Mean serum ferritin across the group was 30.09 ± 32.59 ng/mL (Range: 1.5 – 200.0 ng/mL).

6.3 Prevalence of Vitamin D3 Deficiency

Serum Vitamin D3 levels revealed extensive hypovitaminosis D. Mean serum 25(OH)D3 level was 15.07 ± 12.23 ng/mL (Range: 4.0 – 73.0 ng/mL). Vitamin D deficiency (<20 ng/mL) affected 73.0% (n = 73) of the total group, with severe deficiency (<12 ng/mL) documented in 51.0% (n = 51) of participants. Vitamin D insufficiency, definite as serum concentrations reaching from 20 to 29.9 ng/mL,"

6.4 Double Deficiency Rate

Simultaneous double deficiency—defined as concurrent Serum Ferritin <15 ng/mL and Vitamin D3 <20 ng/mL—was recognized in 32.0% (n = 32) of the whole group.

6.5 High-Risk Co-occurrence in Iron-Deficient Females

Significantly, cross-tabulation of biomarker status exposed that among the 39 females diagnosed with Iron Deficiency Anemia / low ferritin, 32 individuals also afflicted by from Vitamin D3 deficiency. This explains to an overwhelming 82.05% (n = 32/39) rate of Vitamin D3 deficiency exactly within the iron-deficient sub-population.

6.6 Association Analysis

Spearman rank correlation analysis established a statistically significant positive association between serum ferritin and serum Vitamin D3 status (Spearman $\rho = 0.243$, p-value = 0.0148). Because $p < 0.05$, the worthless hypothesis is rejected, proving a true clinical association between iron lessening and reduced vitamin D levels.

Table 1: Clinical Parameter, Biomarker Varieties, and Classification (N =100 Female Group)

Clinical Parameter / Category	Mean $\pm$ SD / Count (n)	Percentage (%) / Range
Age (Years)	26.88 ± 9.46	11.0 – 50.0
Serum Ferritin / Iron Status (ng/mL)	30.09 ± 32.59	1.5 – 200.0
• Iron Deficiency / Depleted Stores (< 15 ng/mL)	N = 39	39.0%
• Normal Iron Stores (15 – 150 ng/mL)	N = 59	59.0%
• High Ferritin (> 150 ng/mL)	N = 2	2.0%
Serum Vitamin D3 (ng/mL)	15.07 ± 12.23	4.0 – 73.0
• Severe Vitamin D Deficiency (< 12 ng/mL)	N = 51	51.0%
• Vitamin D Deficient (12 – 19.9 ng/mL)	N = 22	22.0%
• Vitamin D Insufficient (20 – 29.9 ng/mL)	N = 15	15.0%
• Vitamin D Sufficient (≥ 30 ng/mL)	N = 12	12.0%
Double Deficiency Co-occurrence (Ferritin <15 &D3 <20)	N = 32	32.0%

Vitamin D3 Deficiency Rate in Iron-Deficient Sub-Group	N = 32 / 39	82.05%
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7 DISCUSSION

The main aim of this study was to measure the prevalence of Iron Deficiency Anemia and its link with Vitamin D3 levels amongst women of reproductive age. The statistical analysis provides healthy observed confirmation of the biochemically predicted relationship between iron levels and vitamin D grade.

Our result showed that 82.05% of iron-deficient females concurrently suffer from Vitamin D3 deficiency provides direct clinical sign associate the heme-dependent enzymatic perfect. The chronic blood loss in premenopausal females which leads to depleted serum ferritin (<15 ng/mL). As hepatic ferritin stores drain, systemic heme biosynthesis is reduced. So, the heme-containing cytochrome P450 monooxygenases exactly CYP2R1 in liver microsomes and CYP27B1 in renal tubules—experience a loss of their iron cofactor, impairing 25-hydroxylation and 1 α -hydroxylation capacity that related with D3.

Also, the positive Spearman rank association ($\rho = 0.243$, $p = 0.0148$) aligns with worldwide clinical studies. In a landmark study by Zouine et al[10]. Upon measuring iron indices together with vitamin D metabolites, reduced serum ferritin concentrations were found to be separately related to compromised 25(OH)D alteration. Similarly, animal groups showed by Seong et al. [28] noted that iron-deficient diets directly reduced circulating active 1,25(OH)2D concentrations, even in the presence of adequate dietary vitamin D.

From a clinical view, this interrelationship describes why monotherapy often fails in practice. Clinicians who recommend high-dose ergocalciferol or cholecalciferol to anemic females frequently note sluggish serum 25(OH)D recovery. Deprived of correcting underlying iron deficiency, the enzymatic machinery required to hydroxylate and utilize administered vitamin D remains blunted. Equally, uncorrected hypovitaminosis D perpetuates raised hepcidin expression, suppressing intestinal iron absorption and prolonging anemia.

8 CONCLUSIONS

- High Co-occurrence: Vitamin D3 deficiency and Iron deficiency anemia show an especially high rate of co-occurrence in females of reproductive age, with 82.05% of iron-deficient females showing concurrent Vitamin D3 deficiency.
- Statistically Significant Association: Spearman correlation analysis confirms a statistically significant positive link ($\rho = 0.243$, $p = 0.0148$) between serum ferritin and Vitamin D3 evaluation.
- Biochemical Dependency: The physiological relation is driven by the severe iron requirement of cytochrome P450 hydroxylases (CYP2R1, CYP27B1) shared with the hepcidin-suppressive effects of active vitamin D signaling.

Recommendations

- Routine Screening: Clinical practice guidelines in gynecology, hematology, and general practice should mandate simultaneous screening of the serum both ferritin and 25(OH)D in females presenting with menorrhagia, fatigue, or microcytic anemia.
- Supplementation Therapy: Patients presenting with dual deficiency should be prescribed combined therapeutic oral or intravenous iron restoration alongside Vitamin D3 supplementation to optimize enzymatic activation.
- Follow-up Monitoring: Therapeutic response should be checked by estimating both hematology (hemoglobin, ferritin) and endocrinology (25(OH)D) parameters at 8 to 12 weeks post-treatment.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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