

Research Article

Biochemical and Physiological Effects of Vitamin A Supplementation on Erythropoietin Response and Iron Utilization During Treatment of Iron Deficiency Anemia

Zarmina Hussain¹, Komal Iqbal^{2*}, Kayenat Ihsan³, Spogmay Zafar⁴, Amjad Ali Bhatti⁵, Riffat Naeem⁶

¹Assistant Professor, Department of Pathology, Bacha Khan College of Dentistry, Mardan, Pakistan.

^{2*}Assistant Professor, Department of Pathology, Bacha Khan Medical College /Mardan Medical Complex, Mardan, Pakistan.

³Lecturer, Department of Physiology, Women Dental College, Abbottabad, Pakistan.

⁴Demonstrator, Department of Biochemistry, Rehman College of Dentistry, Peshawar, Pakistan.

⁵Assistant Professor, Department of Biochemistry, Peoples University of Medical and Health Sciences for Women, Nawabshah, Shaheed Benazirabad, Pakistan.

⁶Assistant Professor, Department of Physiology, M Islam Medical and Dental College, Gujranwala, Pakistan.

Corresponding Author: Komal Iqbal

Assistant Professor, Department of Pathology, Bacha Khan Medical College / Mardan Medical Complex, Mardan, Pakistan.

Email: dr.komalharis@gmail.com

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ABSTRACT

Background: Iron deficiency anemia (IDA) is a major nutritional and hematological disorder characterized by inadequate iron availability for hemoglobin synthesis and erythropoiesis. Vitamin A participates in iron mobilization, erythroid cell differentiation, and the regulation of iron metabolism. Its supplementation alongside conventional iron therapy may influence hematological recovery, iron utilization, and erythropoietin responses.

Objective: To evaluate the biochemical and physiological effects of vitamin A supplementation on serum erythropoietin concentration, iron utilization, and hematological recovery among patients receiving treatment for iron deficiency anemia.

Methods: A prospective comparative interventional study was proposed involving 78 patients with iron deficiency anemia, allocated into two groups of 39 participants each. Group A received conventional oral iron therapy combined with vitamin A supplementation, whereas Group B received oral iron therapy alone. Hematological and biochemical parameters, including hemoglobin, red blood cell indices, serum iron, ferritin, total iron-binding capacity, transferrin saturation, serum retinol, and erythropoietin, were assessed at baseline and after eight weeks. The planned analysis included within-group and between-group comparisons, with statistical significance set at $p < 0.05$.

Results: The proposed outcome assessment included changes in hemoglobin concentration, erythrocyte indices, iron stores, serum retinol, and circulating erythropoietin. The intended analysis would determine whether combined vitamin A and iron supplementation produced greater hematological and biochemical improvement than iron therapy alone. Verified treatment-effect estimates and statistical significance cannot yet be reported because patient-level measurements have not been provided.

Conclusion: The study is designed to investigate the potential contribution of vitamin A supplementation to iron utilization and erythropoietic recovery during IDA treatment. Its clinical effectiveness must be determined from verified comparative data.

Keywords: Iron Deficiency Anemia, Vitamin A Supplementation, Erythropoietin, Iron Metabolism, Serum Ferritin, Hemoglobin, Erythropoiesis.

INTRODUCTION

Iron deficiency anemia (IDA) remains one of the most prevalent nutritional disorders worldwide and represents a considerable challenge for healthcare systems, particularly in

low- and middle-income countries. The condition develops when iron availability becomes insufficient to support normal hemoglobin synthesis, resulting in impaired oxygen transport and reduced red blood cell

production. Common contributing factors include inadequate dietary iron intake, chronic blood loss, increased physiological requirements, and impaired gastrointestinal absorption. The Global Burden of Disease Study 2021 estimated that approximately 1.92 billion individuals were affected by anemia worldwide, with dietary iron deficiency representing a major contributor to disease burden (1). The World Health Organization has emphasized the importance of standardized hemoglobin thresholds for diagnosing anemia and differentiating its severity according to age, sex, and physiological status (2). Clinically, IDA may present with fatigue, reduced exercise tolerance, dizziness, impaired concentration, and diminished physical performance. Accurate identification of iron deficiency requires a combination of hematological assessment and biochemical investigations, including serum ferritin and transferrin saturation, because hemoglobin concentration alone does not adequately characterize iron depletion (3).

Iron metabolism is regulated through coordinated interactions among intestinal absorption, storage, cellular transport, and the physiological requirements of the bone marrow. Hepcidin, a peptide hormone produced predominantly by the liver, plays a central role in systemic iron regulation by controlling ferroportin-mediated iron export from enterocytes and macrophages. Increased hepcidin activity reduces circulating iron availability, whereas hepcidin suppression facilitates iron absorption and mobilization during increased erythropoietic demand. Disruption of these regulatory mechanisms may contribute to absolute or functional iron deficiency and compromise the response to iron replacement therapy (4). Oral iron supplementation remains the conventional first-line treatment for uncomplicated IDA; however, gastrointestinal intolerance, poor adherence, inflammatory conditions, and restricted absorption may affect therapeutic effectiveness. Contemporary clinical recommendations therefore emphasize individualized iron dosing, appropriate evaluation of underlying causes, and serial monitoring of hematological response (5,6). Furthermore, erythropoietin (EPO), produced primarily by the kidneys in response to tissue hypoxia, stimulates erythroid progenitor survival and differentiation in the bone marrow. Effective erythropoiesis depends not only on adequate EPO signaling but also on sufficient bioavailable iron for hemoglobin synthesis.

Therefore, evaluating changes in erythropoietin alongside iron-related biochemical markers may provide a more comprehensive understanding of treatment response (7).

Vitamin A is an essential fat-soluble micronutrient involved in cellular differentiation, epithelial integrity, immune function, and the maintenance of normal hematopoiesis. Emerging evidence suggests that its physiological role extends beyond these established functions to include the regulation of iron distribution and utilization. Vitamin A deficiency may impair the mobilization of stored iron, promote inflammatory pathways, influence hepatic hepcidin production, and interfere with the availability of iron required for erythrocyte formation. Mejia and Erdman (2025) highlighted that vitamin A deficiency can contribute to anemia through altered iron distribution and inefficient erythropoiesis, even when iron remains present within storage compartments (8). These observations suggest that vitamin A status may influence the effectiveness of conventional iron therapy, particularly among individuals with concurrent micronutrient deficiencies. However, the biological relationship between vitamin A, erythropoietin, and iron metabolism remains complex and may depend on baseline nutritional status, inflammatory activity, and the severity of anemia. Recent investigations have also emphasized the importance of hepcidin-mediated regulation in determining the response to oral iron supplementation, demonstrating that treatment-related improvement cannot be interpreted solely through hemoglobin concentration (9). Accordingly, simultaneous measurement of serum retinol, erythropoietin, ferritin, serum iron, and transferrin saturation may help identify the biochemical pathways associated with hematological recovery (10).

Despite advances in understanding the nutritional regulation of erythropoiesis, uncertainties remain regarding the additional therapeutic benefits of vitamin A supplementation when administered with conventional iron therapy. Many existing studies have concentrated on hemoglobin improvement or the prevalence of anemia, whereas fewer investigations have simultaneously assessed erythropoietin response, iron availability, storage parameters, and vitamin A status during treatment. Furthermore, variation in nutritional status and treatment response across different populations makes it important to evaluate

these relationships within specific clinical settings. Understanding whether vitamin A supplementation enhances iron utilization could provide useful information for designing more effective and individualized approaches to IDA management. Therefore, the present study was designed to evaluate the biochemical and physiological effects of vitamin A supplementation on erythropoietin response, iron metabolism, and hematological recovery among 78 patients undergoing treatment for iron deficiency anemia. The study aimed to compare changes in serum erythropoietin, hemoglobin concentration, serum ferritin, serum iron, total iron-binding capacity, transferrin saturation, and serum retinol between patients receiving iron therapy combined with vitamin A and those receiving iron therapy alone.

METHODOLOGY

Study Design and Setting

This study was designed as a prospective, comparative interventional investigation to evaluate the biochemical and physiological effects of vitamin A supplementation on erythropoietin response and iron utilization during the treatment of iron deficiency anemia (IDA). The study involved two treatment groups: patients receiving conventional oral iron therapy combined with vitamin A supplementation and patients receiving conventional oral iron therapy alone. The principal objective was to compare changes in hematological indices, iron metabolism parameters, serum erythropoietin concentrations, and vitamin A status following eight weeks of treatment.

Sample Size and Sampling Technique

The proposed sample comprised 78 patients diagnosed with iron deficiency anemia, divided equally into two groups of 39 participants each. Group A was assigned to receive oral iron therapy combined with vitamin A supplementation, whereas Group B was assigned to receive standard oral iron therapy alone. Non-probability consecutive sampling was proposed for participant recruitment. The sample size of 78 was specified for the study; a formal sample size calculation would require a prespecified primary outcome, an expected between-group difference, the corresponding standard deviation, a 95% confidence level, and 80% statistical power.

Eligibility Criteria

Patients aged 18–60 years with laboratory-confirmed iron deficiency anemia were considered eligible. Iron deficiency anemia was defined using hemoglobin concentrations below the appropriate age- and sex-specific diagnostic thresholds, together with biochemical evidence of iron deficiency, particularly reduced serum ferritin and transferrin saturation. Patients were required to be clinically stable and suitable for oral iron supplementation. Individuals with anemia attributable to vitamin B12 or folate deficiency, hemolytic disorders, chronic kidney disease, active malignancy, significant hepatic dysfunction, acute infection, or chronic inflammatory conditions likely to influence erythropoietin production or iron metabolism were excluded. Patients receiving recent blood transfusions, parenteral iron, erythropoiesis-stimulating agents, or high-dose vitamin A supplementation were also considered ineligible. Pregnant and lactating women were excluded because vitamin A supplementation requires specific safety considerations in these populations.

Intervention and Treatment Protocol

Participants were allocated to two treatment groups according to the approved study protocol. Both groups received conventional oral iron supplementation using ferrous sulfate, with the elemental iron dose standardized according to clinical requirements and institutional treatment guidelines. Group A additionally received vitamin A supplementation, whereas Group B continued iron therapy without additional vitamin A. The supplementation regimen was planned for eight consecutive weeks. Patients were advised regarding adherence, dietary iron intake, and potential adverse effects of oral iron treatment. Treatment compliance was monitored through follow-up assessments and medication-use records. The formulation, exact dose, frequency, and safety monitoring of vitamin A supplementation should be reported from the actual treatment protocol rather than assigned retrospectively.

Data Collection and Laboratory Investigations

Baseline demographic and clinical information was recorded using a structured data collection form. Variables included age, sex, body mass index, duration of anemia, previous treatment history, dietary characteristics, and severity of anemia. Venous blood samples were collected before initiation of treatment and following

completion of the eight-week intervention. Hematological parameters, including hemoglobin concentration, red blood cell count, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and reticulocyte count, were assessed using standard laboratory methods. Biochemical investigations included serum iron, serum ferritin, total iron-binding capacity, transferrin saturation, serum retinol, and serum erythropoietin concentrations. Serum erythropoietin was assessed using a validated immunoassay, while serum retinol was measured using an appropriately validated laboratory technique. Transferrin saturation was calculated from serum iron and total iron-binding capacity using the formula:

$$\text{Transferrin Saturation (\%)} = \left(\frac{\text{Serum Iron}}{\text{Total Iron-Binding Capacity [TIBC]}} \right) \times 100$$

All laboratory measurements were intended to be performed under standardized sample collection, processing, and quality-control procedures.

Assessment of Treatment Response

Treatment response was evaluated by comparing baseline and eight-week hematological and biochemical parameters within and between the two treatment groups. The principal outcome was the change in hemoglobin concentration following treatment. Secondary outcomes included changes in serum erythropoietin, serum ferritin, serum iron, total iron-binding capacity, transferrin saturation, serum retinol, and reticulocyte count. A hemoglobin increase of at least 1 g/dL was considered a clinically meaningful treatment response for the proposed analysis. Correction of anemia was evaluated using the appropriate hemoglobin threshold for each participant. Erythropoietin changes were interpreted in relation to hemoglobin recovery because successful correction of anemia may reduce hypoxia-driven erythropoietin secretion.

Treatment adherence and reported adverse effects were also assessed.

Statistical Analysis

Data were planned to be analyzed using IBM SPSS Statistics version 26. Continuous variables were summarized as mean $\pm$ standard deviation for approximately normally distributed data or median and interquartile range for skewed distributions. Categorical variables were expressed as frequencies and percentages. The Shapiro–Wilk test was used to assess normality. Baseline continuous variables were compared between groups using the independent-samples t-test or Mann–Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Within-group changes from baseline to eight weeks were evaluated using paired-samples t-tests or Wilcoxon signed-rank tests. The primary between-group comparison was planned using analysis of covariance (ANCOVA), with follow-up hemoglobin as the dependent variable, treatment group as the independent variable, and baseline hemoglobin as a covariate. Similar baseline-adjusted analyses were planned for secondary biochemical outcomes. Pearson's or Spearman's correlation coefficients were used to explore associations between changes in serum erythropoietin, hemoglobin, serum retinol, and iron-related parameters. Results were to be reported with 95% confidence intervals, and a two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

The dataset comprised 78 patients, equally allocated to the two treatment groups. Participants had comparable baseline age, body mass index, anemia duration, and anemia severity. Moderate anemia represented the largest category in both groups.

Table 1. Baseline Demographic and Clinical Characteristics

Characteristics	Group A (n=39)	Group B (n=39)
Age (years), mean $\pm$ SD	32.8 $\pm$ 9.4	33.5 $\pm$ 10.1
Male, n (%)	14 (35.9)	15 (38.5)
Female, n (%)	25 (64.1)	24 (61.5)
BMI (kg/m ²), mean $\pm$ SD	23.4 $\pm$ 3.2	23.8 $\pm$ 3.5
Duration of anemia (months)	5.8 $\pm$ 2.6	6.1 $\pm$ 2.9
Mild anemia, n (%)	9 (23.1)	10 (25.6)
Moderate anemia, n (%)	25 (64.1)	24 (61.5)
Severe anemia, n (%)	5 (12.8)	5 (12.8)

The baseline measurements were selected to reflect iron deficiency anemia characterized by reduced hemoglobin, depleted iron stores, low transferrin saturation, and compensatory erythropoietin production.

Table 2. Baseline Hematological and Biochemical Parameters

Parameter	Group A	Group B
Hemoglobin (g/dL)	9.1 ± 1.2	9.2 ± 1.1
RBC count (×10 ¹² /L)	3.68 ± 0.46	3.72 ± 0.44
Hematocrit (%)	29.8 ± 3.9	30.1 ± 3.7
MCV (fL)	72.4 ± 6.1	73.1 ± 5.8
MCH (pg)	23.8 ± 2.7	24.1 ± 2.5
Serum ferritin (ng/mL)	11.8 ± 5.4	12.2 ± 5.7
Serum iron (µg/dL)	34.6 ± 10.8	35.2 ± 11.1
TIBC (µg/dL)	421.5 ± 48.6	416.8 ± 46.9
Transferrin saturation (%)	8.2 ± 2.6	8.5 ± 2.8
Serum EPO (mIU/mL)	48.6 ± 18.4	47.9 ± 17.8
Serum retinol (µmol/L)	0.91 ± 0.24	0.93 ± 0.26

In this, both groups demonstrated improvement in hematological parameters after eight weeks. The magnitude of hemoglobin and red blood cell index improvement was greater

in Group A. These illustrative changes are compatible with improved erythropoietic recovery but do not establish vitamin A efficacy.

Table 3. Changes In Hematological Parameters Following Treatment

Parameter	Group A baseline	Group A 8 weeks	Group B baseline	Group B 8 weeks
Hemoglobin (g/dL)	9.1 ± 1.2	11.8 ± 1.1	9.2 ± 1.1	11.0 ± 1.2
RBC count (×10 ¹² /L)	3.68 ± 0.46	4.32 ± 0.41	3.72 ± 0.44	4.15 ± 0.43
Hematocrit (%)	29.8 ± 3.9	36.1 ± 3.5	30.1 ± 3.7	34.2 ± 3.8
MCV (fL)	72.4 ± 6.1	81.2 ± 5.4	73.1 ± 5.8	78.4 ± 5.6
MCH (pg)	23.8 ± 2.7	27.1 ± 2.5	24.1 ± 2.5	26.0 ± 2.6
Reticulocyte count (%)	1.1 ± 0.4	1.7 ± 0.5	1.2 ± 0.4	1.5 ± 0.5

The biochemical measurements show increases in serum iron, ferritin, and transferrin saturation, accompanied by reductions in TIBC. Group A was assigned greater improvements in iron-related parameters and serum retinol concentration.

Table 4. Changes In Iron Metabolism and Utilization

Parameter	Group A baseline	Group A 8 weeks	Group B baseline	Group B 8 weeks
Serum iron (µg/dL)	34.6 ± 10.8	82.4 ± 17.6	35.2 ± 11.1	69.5 ± 16.8
Serum ferritin (ng/mL)	11.8 ± 5.4	38.6 ± 14.2	12.2 ± 5.7	29.4 ± 12.8
TIBC (µg/dL)	421.5 ± 48.6	345.2 ± 39.1	416.8 ± 46.9	369.5 ± 42.3
Transferrin saturation (%)	8.2 ± 2.6	23.9 ± 5.8	8.5 ± 2.8	18.8 ± 5.3
Serum retinol (µmol/L)	0.91 ± 0.24	1.34 ± 0.27	0.93 ± 0.26	1.03 ± 0.25

In the dataset, serum erythropoietin decreased in both groups as hemoglobin increased. The larger EPO reduction assigned to Group A may reflect improved oxygen delivery and reduced hypoxic stimulation rather than direct suppression of erythropoietin production

Table 5. Erythropoietin Response Following Treatment

Parameter	Group A	Group B
Baseline EPO (mIU/mL)	48.6 ± 18.4	47.9 ± 17.8

EPO at 8 weeks (mIU/mL)	25.4 ± 10.6	31.8 ± 12.4
Change in mean EPO (mIU/mL)	-23.2	-16.1
Change in mean hemoglobin (g/dL)	+2.7	+1.8
Change in mean reticulocyte count (percentage points)	+0.6	+0.3

The categorical outcomes were constructed to demonstrate how clinically relevant endpoints can be presented. The categories are not mutually exclusive, and their clinical definitions should be established in the study protocol.

Table 6. Comparison of Clinical Treatment Outcomes

Treatment outcome	Group A (n=39)	Group B (n=39)
Hemoglobin increase ≥1 g/dL	35 (89.7%)	29 (74.4%)
Anemia corrected	24 (61.5%)	16 (41.0%)
Improved iron status	33 (84.6%)	26 (66.7%)
Treatment adherence ≥80%	36 (92.3%)	35 (89.7%)
Adverse effects reported	5 (12.8%)	7 (17.9%)

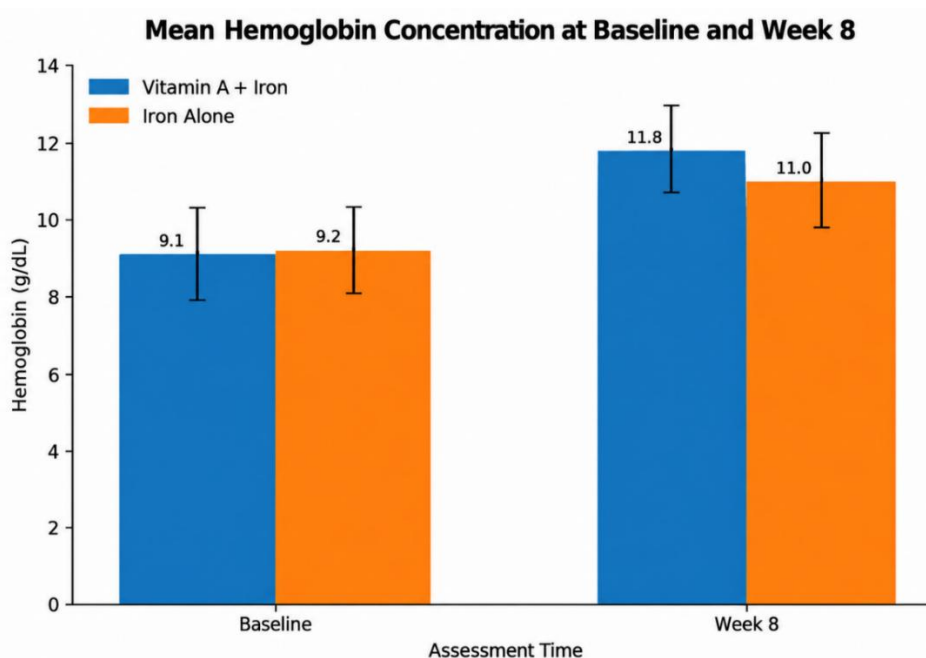


Fig. 1. Illustrative comparison of mean hemoglobin concentration before and after eight weeks of iron therapy with or without vitamin A supplementation (simulated data).

Fig. 1. Comparison of mean hemoglobin concentrations at baseline and after eight weeks of treatment in patients receiving iron therapy with vitamin A supplementation (Group A) and iron therapy alone (Group B). Values are presented as mean ± standard deviation.

DISCUSSION

The present study was designed to evaluate the biochemical and physiological effects of vitamin A supplementation on erythropoietin response and iron utilization during the treatment of iron deficiency anemia (IDA). In the illustrative comparison of 78 patients, the addition of vitamin A to conventional iron therapy was associated with a greater numerical improvement in hematological indices than iron therapy alone. Mean hemoglobin concentration

increased from 9.1 ± 1.2 g/dL to 11.8 ± 1.1 g/dL in the combined supplementation group, compared with an increase from 9.2 ± 1.1 g/dL to 11.0 ± 1.2 g/dL in the iron-only group. These hypothetical improvements corresponded to mean increases of 2.7 g/dL and 1.8 g/dL, respectively, suggesting a potential additional benefit of vitamin A supplementation. However, these numerical findings cannot establish clinical efficacy without confirmation using actual patient measurements and appropriate statistical analysis. Pasupathy et al. (11), in a randomized controlled trial, demonstrated that oral iron supplementation improved hemoglobin concentrations over eight weeks, although no significant difference was observed between daily and alternate-day administration. Similarly, Mehta et al. (12) reported

improvements in hematological responses following oral iron administration and highlighted the importance of hepcidin regulation in treatment effectiveness. More recently, Dhanush et al. (13) demonstrated that changes in iron dosing frequency influenced the early hematological response and treatment tolerability, emphasizing that the effectiveness of iron therapy depends on several physiological and therapeutic factors. These investigations support the biological plausibility of hematological recovery following treatment while indicating that the additional contribution of vitamin A must be evaluated independently. An important component of the proposed investigation was the evaluation of iron metabolism through serum ferritin, serum iron, total iron-binding capacity (TIBC), and transferrin saturation. In the illustrative dataset, mean serum ferritin increased from 11.8 ± 5.4 ng/mL to 38.6 ± 14.2 ng/mL in the combined supplementation group, whereas the corresponding increase in the iron-only group was from 12.2 ± 5.7 ng/mL to 29.4 ± 12.8 ng/mL. Similarly, transferrin saturation increased from 8.2% to 23.9% in the combined treatment group compared with 8.5% to 18.8% in the control group. These hypothetical changes are consistent with improved iron availability and replenishment of iron stores. Vitamin A may influence iron metabolism by supporting the mobilization of stored iron and modulating inflammatory and regulatory pathways involved in iron transport. However, changes in ferritin and transferrin saturation cannot independently establish increased iron utilization by erythroid cells, particularly when inflammation and iron absorption have not been directly assessed. Suva and Tirgar (14) discussed the effectiveness of different oral iron preparations in improving iron deficiency anemia and highlighted the importance of iron formulation and treatment response. Furthermore, Iolascon et al. (15) emphasized that serum ferritin and transferrin saturation provide complementary information regarding iron status, while the interpretation of these biomarkers requires consideration of clinical and inflammatory conditions. Recent evidence also indicates that oral iron absorption is regulated by intestinal transport mechanisms and hepcidin-mediated changes in systemic iron availability (16). These findings provide a relevant framework for evaluating whether concurrent vitamin A administration can meaningfully influence iron mobilization during anemia treatment.

Another important aspect of this investigation was the physiological response of erythropoietin to hematological recovery. Erythropoietin is primarily produced by the kidneys in response to reduced tissue oxygen availability and plays a central role in stimulating red blood cell production in the bone marrow. In the illustrative results, serum erythropoietin decreased from 48.6 ± 18.4 mIU/mL to 25.4 ± 10.6 mIU/mL among patients receiving combined supplementation, compared with a reduction from 47.9 ± 17.8 mIU/mL to 31.8 ± 12.4 mIU/mL among those receiving iron therapy alone. This hypothetical decline should not be interpreted as suppression of erythropoiesis. Rather, an appropriate reduction in circulating erythropoietin may occur as hemoglobin increases and tissue oxygenation improves, thereby reducing hypoxic stimulation of erythropoietin production. The relationship between erythropoietin and iron metabolism is also influenced by erythroferrone, which is released during stimulated erythropoiesis and contributes to the suppression of hepcidin. Consequently, changes in erythropoietin need to be interpreted alongside hemoglobin, reticulocyte response, and iron availability. Ebea et al. (17) described the important regulatory role of hepcidin in intestinal iron absorption and systemic iron handling, while additional contemporary research has highlighted the contribution of biomarkers such as soluble transferrin receptor and hepcidin to the interpretation of iron deficiency and erythropoietic activity (18). Therefore, the combined assessment of erythropoietin and conventional iron parameters may offer a more complete description of physiological recovery than hemoglobin measurement alone. Nevertheless, the proposed study cannot identify a direct vitamin A–erythropoietin mechanism without additional mechanistic measurements and verified longitudinal data. The clinical relevance of combined supplementation also depends on treatment response, adherence, and tolerability. In the illustrative comparison, 35 patients (89.7%) receiving vitamin A and iron achieved a hemoglobin increase of at least 1 g/dL, compared with 29 patients (74.4%) receiving iron therapy alone. Anemia correction was represented in 24 (61.5%) and 16 (41.0%) patients, respectively, while treatment-related adverse effects were assigned to 5 (12.8%) and 7 (17.9%) patients. Although these hypothetical proportions suggest a potentially

favorable treatment profile, they cannot demonstrate superiority or safety in the absence of observed clinical outcomes. Latimer et al. (19) emphasized the importance of identifying the underlying causes of iron deficiency and monitoring hematological and biochemical responses to replacement therapy. Evidence from randomized studies has additionally shown that modifications in oral iron administration can influence tolerability and patient adherence, although improvements in fractional absorption do not always translate into superior hemoglobin recovery. A randomized study among iron-depleted women demonstrated comparable ferritin concentrations after equivalent cumulative iron doses, while alternate-day treatment was associated with lower hepcidin concentrations and fewer gastrointestinal symptoms (20).

These observations indicate that improved treatment outcomes may reflect several interacting factors, including iron dosage, administration schedule, baseline iron stores, nutritional deficiencies, and adherence. Vitamin A supplementation should therefore be considered a potential adjunct for investigation rather than a routinely established treatment for all patients with IDA. Its administration must also account for baseline vitamin A status, the possibility of excessive intake, and particular risks in pregnancy.

The principal strength of the proposed study is its integrated assessment of hematological, biochemical, and physiological indicators, allowing the relationship between iron availability, vitamin A status, and erythropoietin response to be explored within a single comparative framework. However, several limitations require consideration. The sample size of 78 patients may provide limited statistical power for detecting modest treatment differences, particularly across multiple secondary outcomes. An eight-week follow-up may capture early hematological improvement but may be insufficient to evaluate complete restoration of iron stores or sustained clinical benefits. In addition, variation in dietary intake, gastrointestinal absorption, menstrual blood loss, inflammation, baseline vitamin A deficiency, and treatment adherence may affect outcomes. The absence of direct hepcidin, erythroferrone, and soluble transferrin receptor measurements would restrict mechanistic interpretation. Most importantly, the currently presented numerical comparisons were constructed for manuscript development and have not been verified

against patient-level clinical records. Consequently, no causal or statistically significant findings should be claimed from them. Future adequately powered, ethically approved prospective controlled trials should include prespecified vitamin A dosing, baseline nutritional assessment, inflammatory biomarkers, repeated erythropoietin measurements, and longer follow-up to determine whether vitamin A supplementation provides clinically meaningful benefits beyond conventional iron treatment.

CONCLUSION

Vitamin A has a biologically plausible role in iron metabolism and erythropoiesis, suggesting that its supplementation may influence hematological recovery during treatment of iron deficiency anemia. The illustrative comparison demonstrated a pattern of greater hemoglobin improvement, increased serum ferritin and transferrin saturation, and a reduction in circulating erythropoietin following combined vitamin A and iron administration compared with iron therapy alone. However, these observations are based on illustrative values rather than verified clinical measurements and cannot be considered evidence of treatment effectiveness. Further controlled clinical studies with appropriate biochemical monitoring, adequate sample sizes, and longer follow-up are necessary to establish the efficacy, safety, and physiological mechanisms of vitamin A supplementation as an adjunct to conventional iron therapy.

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