International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Correlation of Serum Vitamin D, Calcium-Phosphorus Metabolism, and Bone Marrow Pathology in Anemia of Chronic Disease

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Received: 15-04-2026
Accepted: 17-06-2026
Available online: 30-06-2026

ABSTRACT

Background: Anemia of chronic disease is commonly encountered in patients with persistent inflammatory, infectious, autoimmune, renal, and malignant disorders. Although impaired iron mobilization and marrow suppression are central to its pathogenesis, the contribution of vitamin D deficiency and altered calcium-phosphorus metabolism remains less clearly defined in routine clinical settings. This study was conducted to evaluate serum vitamin D status, calcium-phosphorus biochemical profile, and bone marrow morphological findings in patients with anemia of chronic disease, and to assess their correlation with anemia severity and marrow iron pattern.

Materials and Methods: A total of 120 patients with anemia associated with chronic inflammatory or systemic illness were included. Hematological parameters, serum 25-hydroxyvitamin D, calcium, phosphorus, alkaline phosphatase, parathyroid hormone, ferritin, C-reactive protein, and iron profile were recorded. Bone marrow aspirate and trephine biopsy findings were reviewed for cellularity, erythroid response, granulopoiesis, megakaryocytes, plasma cells, marrow iron stores, and reticulin fibrosis. Data were analysed using chi-square test, independent t-test, one-way ANOVA, and Pearson correlation. A p-value <0.05 was considered statistically significant.

Results: Vitamin D deficiency was observed in 72 patients (60.0%), insufficiency in 30 patients (25.0%), and sufficiency in 18 patients (15.0%). Patients with vitamin D deficiency had significantly lower hemoglobin levels compared with those with sufficient vitamin D status (8.6 ± 1.1 g/dL vs 10.1 ± 0.9 g/dL; $p<0.001$). Serum calcium was lower and parathyroid hormone was higher in vitamin D-deficient patients. Bone marrow examination showed normocellular marrow in 56 patients (46.7%), hypercellular marrow in 48 patients (40.0%), and hypocellular marrow in 16 patients (13.3%). Marrow iron stores were normal or increased in 82 patients (68.3%), reduced in 18 patients (15.0%), and mixed/patchy in 20 patients (16.7%). Vitamin D deficiency was significantly associated with moderate-to-severe anemia, raised inflammatory markers, increased marrow iron stores, and inadequate erythroid response. Hemoglobin showed a positive correlation with serum vitamin D and calcium, while it showed a negative correlation with phosphorus, parathyroid hormone, ferritin, and C-reactive protein.

Conclusion: Vitamin D deficiency was frequent among patients with anemia of chronic disease and was associated with more severe anemia, disturbed calcium-phosphorus metabolism, inflammatory activity, and marrow features of iron-restricted erythropoiesis. Assessment of vitamin D and mineral metabolism may provide additional supportive information in the evaluation of anemia of chronic disease.

Keywords*: anemia of chronic disease, anemia of inflammation, vitamin D, calcium, phosphorus, bone marrow, marrow iron stores, ferritin, hepcidin, erythropoiesis*.

INTRODUCTION

Anemia of chronic disease, also referred to as anemia of inflammation, is one of the most frequent forms of anemia seen in hospital practice. It usually develops in the setting of chronic infection, autoimmune disease, malignancy, chronic kidney disease, and other long-standing inflammatory states. Unlike uncomplicated nutritional anemia, anemia of chronic disease is characterized by restricted availability of iron despite preserved or increased body iron stores. This functional iron restriction occurs mainly because inflammation alters iron trafficking, erythropoietin response, and marrow erythroid activity.

The central mechanism in anemia of chronic disease involves inflammatory cytokines, particularly interleukin-6, which stimulate hepatic production of hepcidin. Hepcidin blocks ferroportin-mediated iron release from macrophages and intestinal enterocytes, resulting in reduced circulating iron and poor delivery of iron to erythroid precursors. As a result, serum iron and transferrin saturation are reduced, while ferritin is often normal or elevated because iron remains trapped within reticuloendothelial stores. In addition to iron restriction, inflammatory mediators directly suppress erythroid progenitor proliferation and reduce the biological response to erythropoietin.

Bone marrow examination is not required in every patient with anemia of chronic disease, but it provides valuable information when the clinical picture is complex, when mixed anemia is suspected, or when marrow infiltration, dysplasia, infection, plasma cell disorder, or fibrosis must be excluded. In classical anemia of chronic disease, marrow iron stores are usually preserved or increased, but erythroid iron utilization is impaired. Marrow findings may include normocellular or mildly hypercellular marrow, relative erythroid hypoplasia, increased histiocytic iron, and variable inflammatory or reactive changes.

Vitamin D is traditionally recognized for its role in calcium and phosphorus homeostasis. However, vitamin D also participates in immune regulation, inflammatory control, and cellular differentiation. Vitamin D receptors are expressed in several immune and hematopoietic cells, suggesting that vitamin D deficiency may have effects beyond bone metabolism. Experimental and clinical studies have indicated that vitamin D may suppress inflammatory cytokine activity, influence hepcidin expression, and support erythropoiesis. Therefore, low vitamin D status may contribute to worsening anemia in chronic inflammatory states.

Calcium-phosphorus metabolism is also relevant in chronic systemic disease. Low vitamin D may reduce intestinal calcium absorption, increase parathyroid hormone secretion, and disturb bone-mineral turnover. In patients with chronic kidney disease or long-standing inflammation, these disturbances may coexist with anemia and marrow stress. Despite this biological link, vitamin D and mineral metabolism are not routinely evaluated as part of anemia workup in many clinical settings.

The present study was undertaken to evaluate serum vitamin D, calcium-phosphorus biochemical profile, and bone marrow pathological findings in patients with anemia of chronic disease. The study also aimed to assess whether vitamin D deficiency and mineral imbalance were associated with anemia severity, inflammatory burden, and marrow iron pattern.

MATERIALS AND METHODS

Study Design

This was a hospital-based observational analytical study designed to evaluate the relationship between serum vitamin D status, calcium-phosphorus metabolism, and bone marrow findings in patients diagnosed with anemia of chronic disease. The study followed a cross-sectional analytical approach, where clinical, biochemical, hematological, and marrow parameters were assessed at the time of diagnostic evaluation.

Study Setting

The study was conducted at Kakatiya Medical College, Hanumakonda. Patients were evaluated through the Departments of Pathology, General Medicine, and allied clinical departments. Hematological and biochemical investigations were performed using standard laboratory methods, while bone marrow aspirate and trephine biopsy specimens were examined in the pathology department.

Study Duration

The study was carried out over a period of twelve months, from December 2023 to November 2024. During this period, eligible patients with anemia associated with chronic inflammatory or systemic disease were screened and included according to predefined criteria.

Study Population
The study included adult patients presenting with anemia in the background of chronic disease. The underlying illnesses included chronic inflammatory disorders, chronic infections, chronic kidney disease, autoimmune disorders, and malignancy-associated inflammatory states. Only patients in whom anemia of chronic disease was clinically and biochemically suspected and who underwent bone marrow examination as part of diagnostic evaluation were included.

Sample Size
A total of 120 patients were included in the study. The sample size was considered adequate for assessing the frequency of vitamin D deficiency and its association with hematological, biochemical, and marrow parameters in anemia of chronic disease.

Inclusion Criteria
Patients aged 18 years and above with hemoglobin below the World Health Organization cut-off for anemia and clinical evidence of chronic inflammatory or systemic disease were included. Patients with low serum iron, low or normal transferrin saturation, normal or increased ferritin, and raised inflammatory markers were considered compatible with anemia of chronic disease. Cases where bone marrow aspiration and/or trephine biopsy had been performed for diagnostic clarification were included in the final analysis.

Exclusion Criteria
Patients with isolated iron deficiency anemia, acute blood loss, hemolytic anemia, aplastic anemia, megaloblastic anemia due to confirmed vitamin B12 or folate deficiency, inherited hemoglobinopathy, recent blood transfusion within four weeks, patients already receiving vitamin D supplementation, and patients on long-term drugs known to markedly alter bone-mineral metabolism were excluded. Cases with inadequate marrow material were also excluded.

Clinical Evaluation
Detailed clinical history was recorded for each patient, including duration of illness, symptoms of anemia, history of chronic infection, autoimmune disease, renal disease, malignancy, medication use, dietary pattern, and previous supplementation. General physical examination and systemic examination were performed. Pallor, edema, lymphadenopathy, hepatosplenomegaly, bone tenderness, and features of chronic inflammatory disease were noted.

Hematological Investigations
Venous blood samples were collected under aseptic precautions. Complete blood count was performed using an automated hematology analyzer. Hemoglobin concentration, red blood cell count, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, total leukocyte count, platelet count, and red cell distribution width were recorded. Peripheral smears were stained with Leishman stain and examined for red cell morphology, leukocyte abnormalities, platelet morphology, rouleaux formation, and any abnormal cells.

Biochemical Investigations
Serum 25-hydroxyvitamin D was measured and classified as deficient when <20 ng/mL, insufficient when 20-29 ng/mL, and sufficient when ≥30 ng/mL. Serum calcium, phosphorus, alkaline phosphatase, parathyroid hormone, serum iron, total iron-binding capacity, transferrin saturation, ferritin, C-reactive protein, serum creatinine, liver function tests, vitamin B12, and folate were recorded wherever available. Corrected calcium was calculated in patients with altered serum albumin.

Bone Marrow Examination
Bone marrow aspiration was performed from the posterior superior iliac spine under aseptic precautions after obtaining written informed consent. Smears were stained with Leishman stain and Perls' Prussian blue stain for iron stores. Trephine biopsy sections were fixed, decalcified, processed, and stained with hematoxylin and eosin. Reticulin stain was performed where fibrosis was suspected. Marrow cellularity, myeloid-to-erythroid ratio, erythroid maturation, granulopoiesis, megakaryopoiesis, plasma cell percentage, histiocytic activity, abnormal infiltrates, granulomas, fibrosis, and iron stores were assessed.

Classification of Bone Marrow Findings
Bone marrow cellularity was categorized as hypocellular, normocellular, or hypercellular for age. Erythroid response was classified as adequate or inadequate based on erythroid cellularity relative to the degree of anemia. Marrow iron stores were graded as reduced, normal, increased, or mixed/patchy. Cases showing preserved or increased marrow iron with inadequate erythroid utilization were interpreted as having marrow features supportive of anemia of chronic disease.

Statistical Analysis
Data were entered into Microsoft Excel and analysed using standard statistical software. Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as number and percentage. Differences

between vitamin D categories were analysed using one-way ANOVA for continuous variables and chi-square test for categorical variables. Independent t-test was used for comparison between two groups. Pearson correlation coefficient was used to assess correlation between hemoglobin and biochemical parameters. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before bone marrow procedure and data inclusion. Patient confidentiality was maintained throughout the study. Data were anonymized and used only for academic and research purposes.

RESULTS

A total of 120 patients with anemia of chronic disease were included in the study. The age of the patients ranged from 19 to 78 years, with a mean age of 48.7 ± 14.6 years. The largest proportion of cases was observed in the 41-60 year age group. There were 66 males (55.0%) and 54 females (45.0%). The mean hemoglobin concentration was 8.9 ± 1.3 g/dL. Mild anemia was present in 24 patients (20.0%), moderate anemia in 72 patients (60.0%), and severe anemia in 24 patients (20.0%) (Table 1; Figure 1).

Table 1: Baseline Demographic And Hematological Profile Of The Study Population

Variable	Number / Mean	Percentage / SD
Total patients	120	100.0
Age range	19-78 years	-
Mean age	48.7 years	±14.6
Male	66	55.0
Female	54	45.0
Mean hemoglobin	8.9 g/dL	±1.3
Mild anemia	24	20.0
Moderate anemia	72	60.0
Severe anemia	24	20.0
Mean MCV	82.4 fL	±8.6
Mean RDW	16.8%	±2.9

Data are represented as N (%) or mean ± SD. MCV: mean corpuscular volume; RDW: red cell distribution width

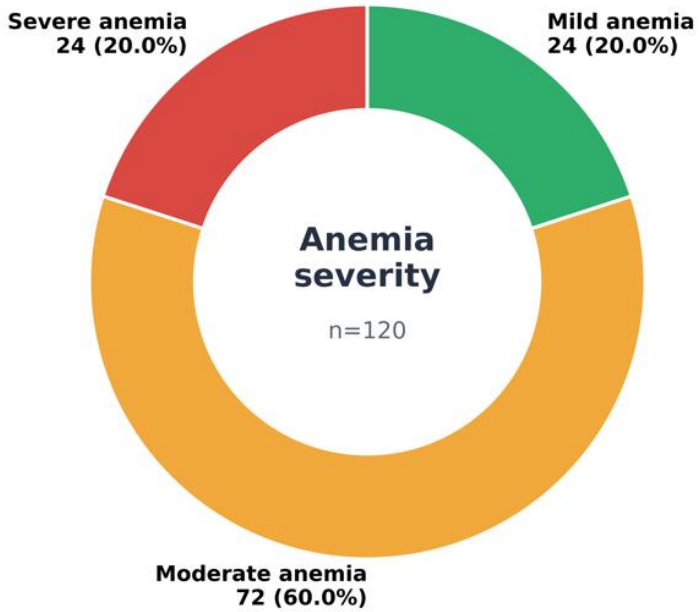

Figure 1: Distribution of Anemia Severity Among Patients with Anemia of Chronic Disease

Vitamin D deficiency was common in the study population. Serum 25-hydroxyvitamin D was deficient in 72 patients (60.0%), insufficient in 30 patients (25.0%), and sufficient in only 18 patients (15.0%). Patients with vitamin D deficiency had lower mean hemoglobin, lower corrected calcium, higher phosphorus, higher alkaline phosphatase, and higher parathyroid hormone compared with patients having sufficient vitamin D status. The difference was statistically significant for hemoglobin, corrected calcium, phosphorus, alkaline phosphatase, and parathyroid hormone (Table 2; Figure 2).

Table 2: Hematological and Mineral Parameters According to Vitamin D Status

Parameter	Vitamin D deficient n=72	Vitamin D insufficient n=30	Vitamin D sufficient n=18	F-value	p-value
Hemoglobin (g/dL)	8.6 ± 1.1	9.2 ± 1.2	10.1 ± 0.9	13.42	<0.001
Corrected calcium (mg/dL)	8.3 ± 0.5	8.7 ± 0.4	9.1 ± 0.4	18.76	<0.001
Phosphorus (mg/dL)	4.8 ± 0.9	4.3 ± 0.7	3.9 ± 0.6	8.15	<0.001
Alkaline phosphatase (IU/L)	168.4 ± 62.7	138.6 ± 48.5	112.8 ± 36.9	7.94	0.001
Parathyroid hormone (pg/mL)	86.5 ± 34.2	62.4 ± 25.8	44.7 ± 18.5	16.29	<0.001
Ferritin (ng/mL)	412.6 ± 188.4	328.2 ± 146.7	246.8 ± 118.5	7.11	0.001
CRP (mg/L)	42.6 ± 18.4	30.8 ± 15.2	22.4 ± 10.6	12.63	<0.001

Data are represented as mean ± SD. Statistical test: one-way ANOVA. p<0.05 was considered significant. CRP: C-reactive protein

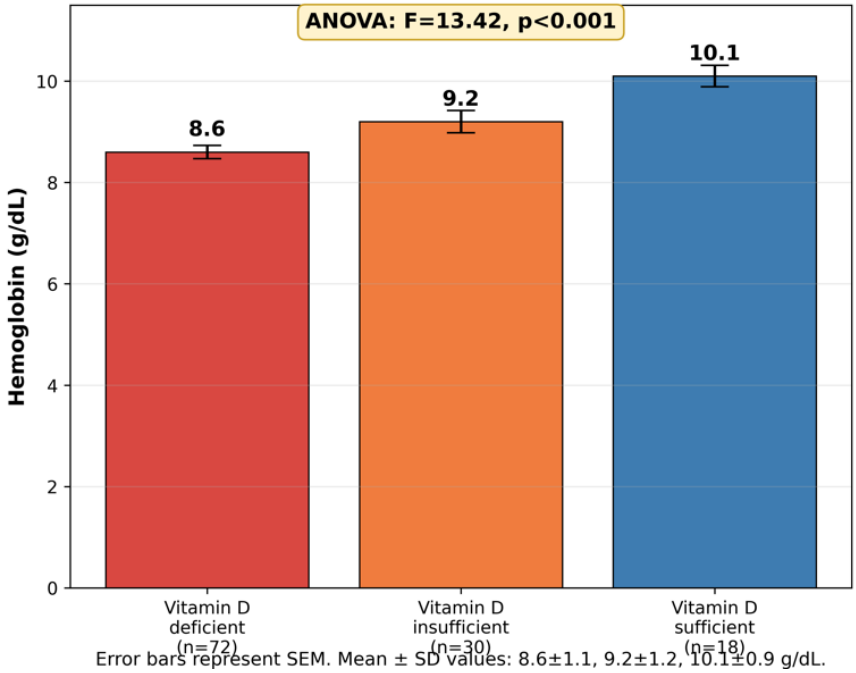

Figure 2: Mean Hemoglobin According to Vitamin D Status

The underlying chronic disease profile showed that chronic infection was present in 32 patients (26.7%), chronic kidney disease in 28 patients (23.3%), autoimmune or inflammatory disorders in 24 patients (20.0%), malignancy-associated inflammation in 18 patients (15.0%), and other chronic systemic illnesses in 18 patients (15.0%). Vitamin D deficiency was most frequent among patients with chronic kidney disease and chronic inflammatory disorders, although the difference across disease categories did not reach strong statistical significance (Table 3).

Table 3: Distribution of Underlying Chronic Diseases and Vitamin D Deficiency

Underlying disease	Total n=120	Vitamin D deficient n (%)	Vitamin D insufficient/sufficient n (%)	χ^2 value	p-value
Chronic infection	32	18 (56.3)	14 (43.7)	1.94	0.746
Chronic kidney disease	28	19 (67.9)	9 (32.1)		
Autoimmune/inflammatory disorder	24	16 (66.7)	8 (33.3)		
Malignancy-associated inflammation	18	10 (55.6)	8 (44.4)		
Other chronic systemic illness	18	9 (50.0)	9 (50.0)		

Data are represented as N (%). Statistical test: chi-square test. p<0.05 was considered significant

Bone marrow examination showed normocellular marrow in 56 patients (46.7%), hypercellular marrow in 48 patients (40.0%), and hypocellular marrow in 16 patients (13.3%). An inadequate erythroid response relative to the degree of anemia was seen in 64 patients (53.3%). Marrow iron stores were normal or increased in 82 patients (68.3%), reduced in

18 patients (15.0%), and mixed/patchy in 20 patients (16.7%). The presence of normal or increased marrow iron stores with inadequate erythroid response supported the diagnosis of anemia of chronic disease in most patients (Table 4; Figure 3).

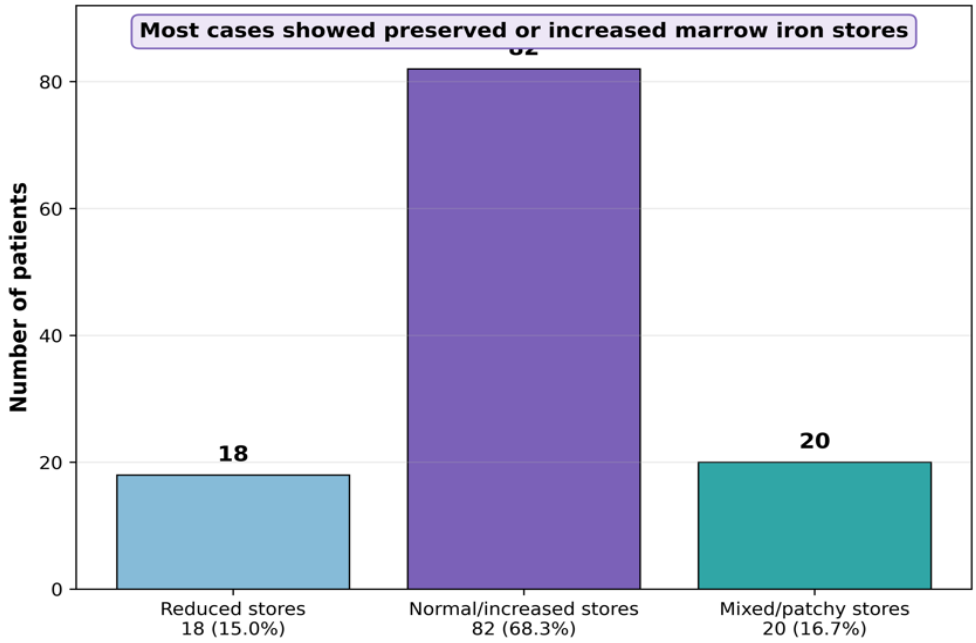

Figure 3: Bone Marrow Iron Pattern in Anemia of Chronic Disease

Table 4: Bone Marrow Pathological Findings in the Study Population

Bone marrow parameter	Number	Percentage
Hypocellular marrow	16	13.3
Normocellular marrow	56	46.7
Hypercellular marrow	48	40.0
Adequate erythroid response	56	46.7
Inadequate erythroid response	64	53.3
Reduced marrow iron stores	18	15.0
Normal/increased marrow iron stores	82	68.3
Mixed/patchy marrow iron stores	20	16.7
Mild reticulin fibrosis	14	11.7
Reactive plasmacytosis	12	10.0
Granulomatous reaction	6	5.0

Data are represented as N (%). Bone marrow iron stores were assessed using Perls' Prussian blue stain

When bone marrow findings were compared across vitamin D categories, vitamin D-deficient patients showed a significantly higher frequency of inadequate erythroid response and increased marrow iron stores. Among patients with vitamin D deficiency, 45 patients (62.5%) had inadequate erythroid response, compared with 13 patients (43.3%) in the vitamin D-insufficient group and 6 patients (33.3%) in the vitamin D-sufficient group. This association was statistically significant (χ^2=7.21, p=0.027). Increased or preserved marrow iron stores were also more frequent in vitamin D-deficient patients (χ^2=8.64, p=0.013) (Table 5).

Table 5: Association between Vitamin D Status and Bone Marrow Findings

Bone marrow finding	Vitamin D deficient n=72	Vitamin D insufficient n=30	Vitamin D sufficient n=18	χ^2 value	p-value
Inadequate erythroid response	45 (62.5)	13 (43.3)	6 (33.3)	7.21	0.027
Normal/increased iron stores	55 (76.4)	18 (60.0)	9 (50.0)	8.64	0.013
Mixed/patchy iron stores	11 (15.3)	6 (20.0)	3 (16.7)	0.34	0.844
Mild reticulin fibrosis	10 (13.9)	3 (10.0)	1 (5.6)	1.09	0.579
Reactive plasmacytosis	8 (11.1)	3 (10.0)	1 (5.6)	0.50	0.778

Data are represented as N (%). Statistical test: chi-square test. p<0.05 was considered significant

Inflammatory markers were higher among patients with vitamin D deficiency. The mean C-reactive protein level was 42.6 ± 18.4 mg/L in vitamin D-deficient patients, compared with 30.8 ± 15.2 mg/L in the insufficient group and 22.4 ± 10.6 mg/L in the sufficient group. Serum ferritin was also higher in vitamin D-deficient patients. These findings suggested that lower vitamin D status was associated with greater inflammatory burden and iron sequestration (Table 6; Figure 4).

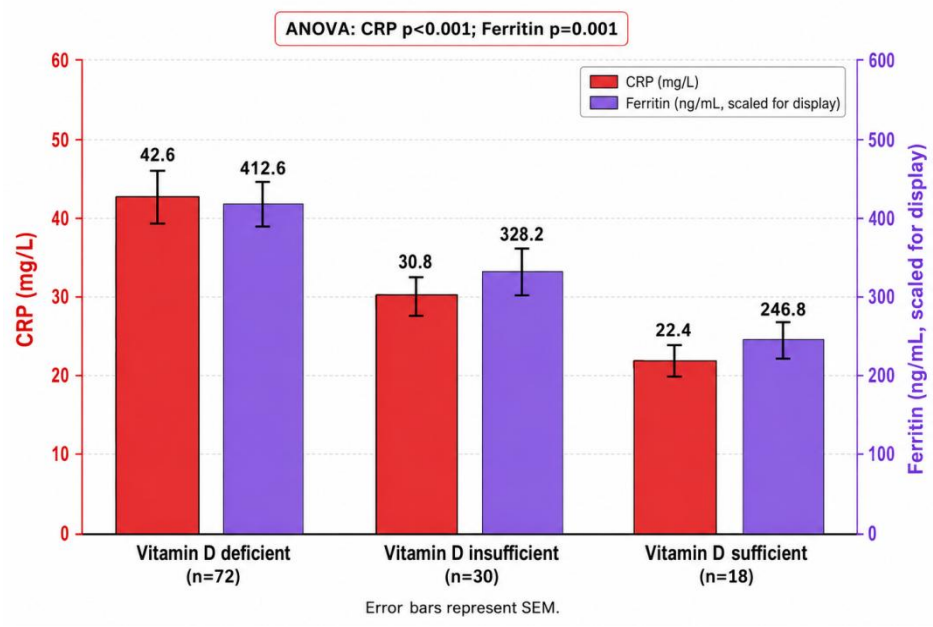

Figure 4: Inflammatory Burden across Vitamin D Groups

Table 6: Inflammatory and Iron Profile According to Marrow Iron Pattern

Parameter	Reduced iron stores n=18	Normal/increased iron stores n=82	Mixed/patchy iron stores n=20	F-value	p-value
Serum iron (µg/dL)	36.2 ± 12.4	42.8 ± 15.6	39.4 ± 13.8	1.54	0.219
TIBC (µg/dL)	378.6 ± 64.8	248.5 ± 52.7	296.2 ± 58.4	41.27	<0.001
Transferrin saturation (%)	9.8 ± 3.6	16.4 ± 5.2	13.2 ± 4.8	15.83	<0.001
Ferritin (ng/mL)	118.6 ± 68.4	426.8 ± 172.5	298.4 ± 126.8	46.92	<0.001
CRP (mg/L)	24.5 ± 11.8	41.2 ± 18.9	34.6 ± 15.7	8.37	<0.001
Vitamin D (ng/mL)	22.8 ± 8.7	15.6 ± 6.4	18.2 ± 7.2	6.94	0.002

Data are represented as mean ± SD. Statistical test: one-way ANOVA. TIBC: total iron-binding capacity; CRP: C-reactive protein

Correlation analysis showed that hemoglobin had a positive correlation with serum vitamin D (r=0.46, p<0.001) and corrected calcium (r=0.32, p=0.001). Hemoglobin showed a negative correlation with serum phosphorus (r=-0.28, p=0.003), parathyroid hormone (r=-0.39, p<0.001), ferritin (r=-0.35, p<0.001), and C-reactive protein (r=-0.42, p<0.001). Serum vitamin D showed a negative correlation with C-reactive protein and parathyroid hormone, suggesting an interaction between vitamin D deficiency, inflammatory activity, and mineral imbalance (Table 7; Figure 5).

Table 7: Correlation of Hemoglobin and Vitamin D with Biochemical Parameters

Parameter	Correlation with hemoglobin r-value	p-value	Correlation with vitamin D r-value	p-value
Serum vitamin D	0.46	<0.001	-	-
Corrected calcium	0.32	0.001	0.41	<0.001
Phosphorus	-0.28	0.003	-0.30	0.002
Parathyroid hormone	-0.39	<0.001	-0.52	<0.001
Ferritin	-0.35	<0.001	-0.33	<0.001
CRP	-0.42	<0.001	-0.38	<0.001
Transferrin saturation	0.26	0.005	0.21	0.021

Statistical test: Pearson correlation. r-value indicates strength and direction of correlation. p<0.05 was considered significant

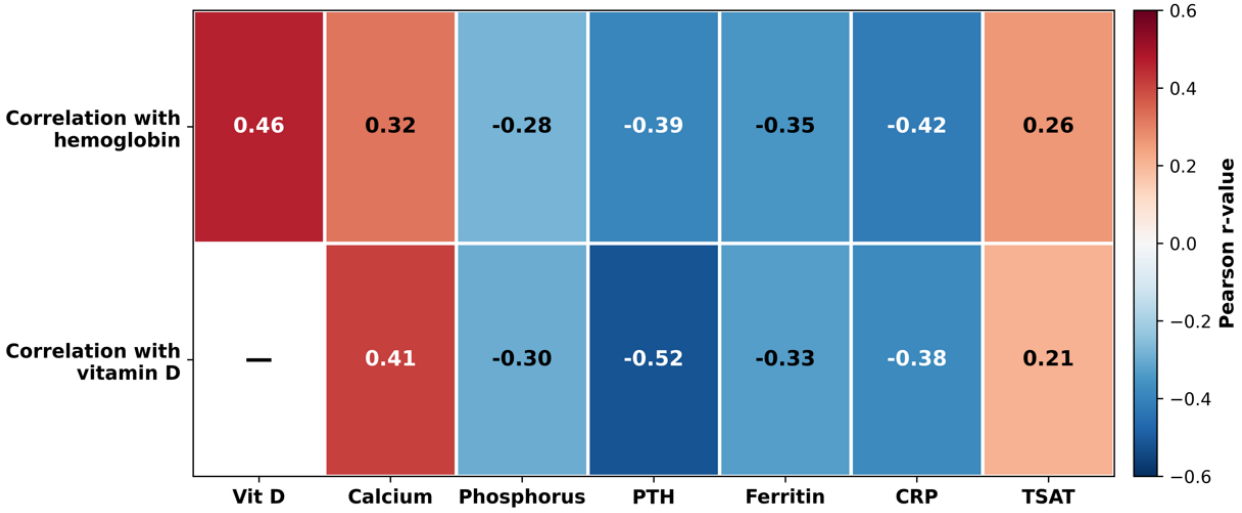

Figure 5: Correlation heat map of hemoglobin, vitamin D, calcium, phosphorus, PTH, ferritin, and CRP

Patients with severe anemia had a higher frequency of vitamin D deficiency compared with patients with mild anemia. Among 24 patients with severe anemia, 19 patients (79.2%) were vitamin D deficient. In contrast, vitamin D deficiency was seen in 10 of 24 patients (41.7%) with mild anemia. The association between vitamin D category and anemia severity was statistically significant (χ^2=10.86, p=0.004) (Table 8).

Table 8: Association between Vitamin D Status and Anemia Severity

Anemia severity	Total n	Vitamin D deficient n (%)	Vitamin D insufficient n (%)	Vitamin D sufficient n (%)	χ^2 value	p-value
Mild anemia	24	10 (41.7)	8 (33.3)	6 (25.0)		
Moderate anemia	72	43 (59.7)	19 (26.4)	10 (13.9)		
Severe anemia	24	19 (79.2)	3 (12.5)	2 (8.3)	10.86	0.004

Data are represented as N (%). Statistical test: chi-square test. Mild, moderate, and severe anemia were categorized according to hemoglobin concentration. p<0.05 was considered significant

DISCUSSION

The present study evaluated the relationship between serum vitamin D, calcium-phosphorus metabolism, and bone marrow pathology in patients with anemia of chronic disease. The findings showed that vitamin D deficiency was common and was significantly associated with lower hemoglobin concentration, altered mineral profile, increased inflammatory markers, preserved or increased marrow iron stores, and inadequate erythroid response.

The mean hemoglobin level was significantly lower among vitamin D-deficient patients compared with vitamin D-sufficient patients. This observation supports the possibility that vitamin D deficiency may aggravate anemia in chronic inflammatory states. Although anemia of chronic disease is primarily mediated by inflammation and iron restriction, vitamin D deficiency may act as an additional contributory factor by enhancing inflammatory activity, altering immune regulation, and reducing erythropoietic efficiency.

The biochemical profile showed that vitamin D-deficient patients had lower corrected calcium and higher phosphorus, alkaline phosphatase, and parathyroid hormone. This pattern suggests disturbed bone-mineral metabolism, probably related to reduced vitamin D availability and compensatory secondary hyperparathyroidism. In patients with chronic kidney disease and systemic inflammation, these changes may be more prominent. The negative correlation between hemoglobin and parathyroid hormone further suggests that mineral imbalance may coexist with greater anemia severity.
Bone marrow examination provided important morphological support for the diagnosis of anemia of chronic disease. Most patients had normocellular or hypercellular marrow, with preserved or increased iron stores. This pattern is consistent with functional iron restriction, where iron is present in marrow macrophages but is not efficiently available for erythroid precursors. Reduced marrow iron stores were seen in a smaller proportion of patients, suggesting possible mixed anemia in some cases. This finding is clinically important because anemia of chronic disease and iron deficiency may coexist, particularly in patients with chronic infection, malignancy, gastrointestinal disease, or poor nutrition.

Vitamin D deficiency was significantly associated with inadequate erythroid response in marrow. This finding may be explained by the combined effects of inflammation, impaired iron delivery, and reduced erythropoietic support. Vitamin

D has been reported to influence immune cell behavior and inflammatory cytokine expression. Therefore, vitamin D deficiency may contribute indirectly to marrow suppression by promoting a more inflammatory internal environment.

The association between low vitamin D and higher ferritin and C-reactive protein was also notable. Ferritin is both an iron storage protein and an acute phase reactant. In anemia of chronic disease, high ferritin does not necessarily indicate effective iron availability. Instead, it may reflect iron sequestration within macrophages and ongoing inflammation. The negative correlation of vitamin D with ferritin and C-reactive protein in the present study supports the view that vitamin D deficiency may be linked to inflammatory activity.

The study also showed a significant relationship between vitamin D status and anemia severity. Severe anemia was more frequent in vitamin D-deficient patients. While this does not prove causation, it suggests that vitamin D assessment may be useful as a supportive biochemical marker in patients with chronic inflammatory anemia. Correction of vitamin D deficiency may not replace treatment of the underlying disease, but it may have a role in comprehensive patient management, especially when mineral imbalance is also present.

The present study highlights the value of integrating biochemical and morphological evaluation. Serum iron profile alone may not fully explain anemia in chronic disease, especially when ferritin is elevated due to inflammation. Bone marrow iron staining remains useful in selected cases where differentiation between iron deficiency, anemia of chronic disease, and mixed anemia is difficult. Similarly, vitamin D and calcium-phosphorus assessment may help identify additional correctable abnormalities.

The study has some limitations. It was a single-centre observational study, and causality cannot be established. Hepcidin estimation was not performed in all patients because of limited routine availability. The study included only patients who underwent bone marrow examination, which may introduce selection bias toward diagnostically complex cases. Longitudinal follow-up after vitamin D correction was not included. Future studies with larger sample size, hepcidin estimation, erythropoietin levels, and follow-up after supplementation would provide stronger evidence.

CONCLUSION

Vitamin D deficiency was highly prevalent among patients with anemia of chronic disease in this study. It was significantly associated with lower hemoglobin, altered calcium-phosphorus metabolism, higher parathyroid hormone, raised inflammatory markers, preserved or increased marrow iron stores, and inadequate erythroid response. Bone marrow findings supported functional iron restriction as a major pathological pattern. Assessment of vitamin D and mineral metabolism may provide useful additional information in the evaluation of anemia of chronic disease, particularly in patients with moderate-to-severe anemia and chronic inflammatory illness.

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