Cross-Sectional Study of Anemia Patterns and Iron Indices in Chronic Kidney Disease Stages 3-5

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ABSTRACT
Background: Anemia is a frequent and multifactorial complication of chronic kidney disease (CKD) that adversely affects morbidity, mortality, and quality of life. The interplay of erythropoietin deficiency, inflammation, and iron dysregulation contributes to complex hematologic alterations. This study aimed to evaluate anemia patterns and iron indices in CKD stages 3–5. **Methods:** A hospital-based cross-sectional observational study was conducted on 200 CKD patients (stage 3 = 82; stage 4 = 69; stage 5 = 49). Demographic, clinical, and biochemical data were collected. Hemoglobin concentration, red cell indices, and peripheral smear morphology were assessed. Iron profile- including serum ferritin, serum iron, total iron-binding capacity (TIBC), and transferrin saturation (TSAT)- was measured. Statistical analysis employed ANOVA, chi-square tests, and Pearson correlation with significance at $p < 0.05$. **Results:** Mean age increased with disease severity (56.9 → 61.8 years, $p = 0.04$). The prevalence of anemia was 89.0% in stage 3, 95.7% in stage 4, and 81.6% in stage 5 ($p = 0.01$). Normocytic-normochromic morphology predominated (84%), while microcytosis and macrocytosis were infrequent. Ferritin levels rose progressively (150.7 → 246.2 ng/mL, $p < 0.001$), whereas serum iron, TIBC, and TSAT declined significantly ($p < 0.01$). Functional iron deficiency was the most common category (50% of cases). Hemoglobin correlated positively with eGFR ($r = 0.537$, $p < 0.001$) and TSAT ($r = 0.168$, $p = 0.017$), and negatively with ferritin ($r = –0.242$, $p < 0.001$). **Conclusion:** Anemia is highly prevalent across CKD stages 3–5, predominantly normocytic and associated with functional iron deficiency rather than absolute depletion. The interplay between declining renal function, inflammation, and iron sequestration explains the progressive fall in hemoglobin. Routine monitoring of complete iron indices and inflammatory markers should be integral to CKD management to enable timely and individualized therapy.
Keywords: Chronic Kidney Disease; Anemia; Iron Indices; Functional Iron Deficiency.
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INTRODUCTION

Chronic kidney disease (CKD) represents a significant global public-health burden, characterized by progressive, irreversible loss of renal function over months or years. According to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, CKD is defined by structural or functional kidney abnormalities persisting for at least three months, with implications for health, and is staged based on estimated glomerular filtration rate (eGFR) and markers of kidney damage such as albuminuria. The prevalence of CKD has risen sharply in both developed and developing nations, largely due to the increasing burden of diabetes mellitus, hypertension, and obesity. The World Health Organization estimates that around 10–13% of the global population suffers from some degree of CKD, with stage 3–5 disease accounting for the majority of those at risk for complications such as anemia, metabolic bone disease, and cardiovascular mortality.[1]

Among the various systemic manifestations of CKD, anemia is one of the earliest and most clinically significant. It substantially contributes to the morbidity, mortality, and diminished quality of life observed in CKD patients. The pathophysiology of anemia in CKD is multifactorial and complex, involving inadequate erythropoietin (EPO) production by the failing kidneys, iron deficiency (both absolute and functional), shortened red blood cell (RBC) lifespan, chronic inflammation, and nutritional deficiencies. Decreased EPO production is the hallmark mechanism, resulting from hypoxia-inducible factor dysregulation in damaged renal tissue. However, even in the presence of recombinant human

erythropoietin (rHuEPO) therapy, many CKD patients exhibit suboptimal hematologic response due to disordered iron metabolism.[2]

Iron homeostasis is critically impaired in CKD due to several mechanisms: decreased intestinal absorption, chronic blood loss during hemodialysis, frequent phlebotomy, and functional iron deficiency driven by elevated hepcidin levels. Hepcidin, a hepatic peptide hormone regulated by iron stores and inflammatory cytokines (particularly IL-6), inhibits ferroportin, the iron exporter on enterocytes and macrophages, thereby restricting iron mobilization for erythropoiesis. This phenomenon, known as "functional iron deficiency," is characterized by low transferrin saturation (TSAT) despite adequate or elevated serum ferritin levels, reflecting sequestration of iron within the reticuloendothelial system. Thus, the conventional interpretation of iron indices becomes challenging in CKD, necessitating a comprehensive evaluation that includes serum ferritin, serum iron, total iron-binding capacity (TIBC), and TSAT.[3]

The pattern of anemia in CKD typically corresponds to normocytic normochromic morphology, consistent with hypoproliferative anemia secondary to decreased EPO. However, microcytic hypochromic patterns may emerge due to coexisting iron deficiency, inflammation, or aluminum toxicity, while macrocytosis can appear in patients receiving folate or vitamin B_{12} supplementation or those with concomitant hypothyroidism. Understanding the morphological pattern provides crucial insights into the underlying mechanism and guides appropriate therapeutic interventions. Studies across different populations have shown variable prevalence of anemia in CKD, ranging from 30% in early stages to >90% in stage 5, depending on demographic, nutritional, and healthcare factors.[4]

Anemia in CKD carries substantial clinical consequences. It leads to left ventricular hypertrophy, reduced exercise capacity, cognitive impairment, and increased hospitalization rates. Moreover, anemia exacerbates progression of CKD itself through tissue hypoxia and oxidative stress. Early recognition and management of anemia can mitigate these adverse outcomes. Therefore, assessing anemia prevalence, morphological types, and iron status across CKD stages is essential for establishing region-specific management strategies, especially in low- and middle-income countries where resce limitations often preclude universal access to EPO and parenteral iron therapy.[5]

In India, anemia among CKD patients is widespread and often underdiagnosed. Contributing factors include nutritional iron deficiency, recurrent infections, delayed referral to nephrology services, and economic barriers to treatment. While several Indian studies have documented the prevalence of anemia in CKD, few have systematically correlated anemia patterns with detailed iron indices across stages 3–5, particularly in non-dialysis patients. Such evaluation is vital, as early identification of iron deficiency- absolute or functional- can improve responsiveness to EPO therapy and reduce transfusion dependence. Furthermore, differentiating anemia types using peripheral smear morphology, red cell indices (MCV, MCH, MCHC), and biochemical iron parameters provides a practical framework for individualized management.

Aim

To evaluate the pattern of anemia and iron indices among patients with chronic kidney disease stages 3 to 5.

Objectives

1. To determine the prevalence and morphological types of anemia in CKD stages 3–5.
2. To assess iron status using serum ferritin, serum iron, TIBC, and transferrin saturation in CKD patients.
3. To correlate anemia severity and iron indices with CKD stage and demographic variables.

MATERIAL AND METHODOLOGY

Sce of Data

Data were obtained from patients attending Department of General Medicine in tertiary care teaching hospital. Laboratory investigations were conducted in the institution's Central Clinical Biochemistry Laboratory.

Study Design

This study was a hospital-based cross-sectional observational study conducted to assess the prevalence and characteristics of anemia and iron indices in CKD stages 3–5.

Study Location

The study was carried out Department of General Medicine at tertiary-care referral center catering to both urban and rural populations.

Study Duration

The study was conducted over a period of 18 months from March 24 to August 25.

Sample Size

A total of 200 patients with diagnosed chronic kidney disease (stages 3–5) were enrolled based on inclusion and exclusion criteria.

Inclusion Criteria

1. Adult patients aged ≥ 18 years diagnosed with CKD stages 3–5 according to KDIGO guidelines (eGFR < 60 mL/min/1.73 m² for ≥ 3 months).

2. Both male and female patients, irrespective of etiology (diabetic, hypertensive, or other causes).
3. Patients who provided written informed consent.

Exclusion Criteria

1. Acute kidney injury or acute on chronic kidney disease.
2. Patients receiving recent blood transfusion or erythropoiesis-stimulating agents within 3 months.
3. Presence of active infection, chronic inflammatory diseases, malignancy, or liver cirrhosis.
4. Known hematological disorders (thalassemia, sickle-cell disease, aplastic anemia).
5. Pregnant women.

Procedure and Methodology

All eligible patients were enrolled consecutively after informed consent. Detailed history, clinical examination, and demographic data were recorded using a predesigned proforma. CKD staging was determined using eGFR calculated by the CKD-EPI formula.

Venous blood samples were collected under aseptic conditions. Hematological investigations were performed on an automated hematology analyzer, including hemoglobin concentration, hematocrit, RBC indices (MCV, MCH, MCHC), and peripheral smear examination for morphological classification (normocytic normochromic, microcytic hypochromic, or macrocytic).

Biochemical evaluation included:

Serum iron and **TIBC** measured by colorimetric methods.

Transferrin saturation (TSAT) calculated as: TSAT = (Serum iron × 100) / TIBC.

Serum ferritin estimated by chemiluminescent immunoassay.

Serum creatinine measured by the Jaffe method, and eGFR derived using the CKD-EPI equation.

Anemia was defined as Hb < 13 g/dL in males and < 12 g/dL in females per KDIGO guidelines. Severity was categorized as mild (10–12/13 g/dL), moderate (8–9.9 g/dL), or severe (< 8 g/dL). Iron deficiency anemia was classified as:

Absolute – ferritin < 100 ng/mL and TSAT < 20%.

Functional – ferritin ≥ 100 ng/mL with TSAT < 20%.

Sample Processing

Collected samples were processed within 2 hs of collection. EDTA samples were used for complete blood counts and smears; serum samples were separated by centrifugation at 3000 rpm for 10 minutes and analyzed on the same day for iron studies. Internal and external quality controls were maintained throughout.

Data Collection

All results were entered into a structured data sheet containing patient demographics, clinical details, laboratory parameters, and CKD stage. Data were anonymized before analysis.

Statistical Methods

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD); categorical variables as frequency and percentage. Comparison across CKD stages was done using one-way ANOVA for continuous variables and chi-square test for categorical variables. Pearson's correlation coefficient was used to assess relationships between hemoglobin, iron indices, and eGFR. A p-value < 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

Table 1: Baseline profile and iron indices across CKD stages 3–5 (N=200)

Variable	Stage 3 (n=82)	Stage 4 (n=69)	Stage 5 (n=49)	Test of significance	95% CI (Stage 3 - Stage 5)	p-value
Age (years), Mean ± SD	56.9 ± 11.1	59.2 ± 10.6	61.8 ± 10.8	ANOVA F(2,197) =3.28	-8.94 to -0.91	0.040
Male, n (%)	49 (59.8)	46 (66.7)	31 (63.3)	$\chi^2(2)=0.77$	-0.207 to +0.137	0.681
Diabetes, n (%)	45 (54.9)	39 (56.5)	32 (65.3)	$\chi^2(2)=0.59$	-0.347 to +0.000	0.744
Hypertension, n (%)	64 (78.0)	52 (75.4)	44 (89.8)	$\chi^2(2)=4.06$	-0.212 to +0.	0.131

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eGFR (mL/min/1.73 m²), Mean ± SD	42.0 ± 7.0	25.1 ± 5.4	10.8 ± 2.9	ANOVA F(2,197) =540.70	+29.54 to +32.83	<0.001
Hemoglobin (g/dL), Mean ± SD	10.92 ± 1.28	10.30 ± 1.18	11.26 ± 1.76	ANOVA F(2,197) =7.51	-0.91 to +0.24	0.001
Ferritin (ng/mL), Mean ± SD	150.7 ± 73.9	191.8 ± 90.8	246.2 ± 104.7	ANOVA F(2,197) =18.06	-130.21 to -60.84	<0.001
Serum Iron (µg/dL), Mean ± SD	54.7 ± 15.2	48.1 ± 13.9	40.6 ± 12.8	ANOVA F(2,197) =14.38	+8.66 to +19.51	<0.001
TIBC (µg/dL), Mean ± SD	287.4 ± 39.1	271.1 ± 37.6	258.2 ± 34.7	ANOVA F(2,197) =9.69	+15.26 to +43.21	<0.001
TSAT (%), Mean ± SD	19.5 ± 6.4	17.9 ± 6.1	16.0 ± 5.6	ANOVA F(2,197) =5.62	+1.27 to +5.78	0.004
CRP (mg/L), Mean ± SD	5.9 ± 3.6	7.8 ± 4.6	10.7 ± 6.1	ANOVA F(2,197) =13.91	-6.70 to -2.81	<0.001

Table 1 summarizes the demographic, clinical, and biochemical characteristics of 200 CKD patients stratified by disease stage. The mean age showed a progressive increase from stage 3 (56.9 ± 11.1 years) to stage 5 (61.8 ± 10.8 years), and the difference was statistically significant (ANOVA F = 3.28, p = 0.040), indicating that advanced CKD occurred more frequently among older individuals. The gender distribution showed a male predominance across all groups (59.8%, 66.7%, and 63.3% for stages 3–5, respectively), but the difference was not significant (p = 0.681). The prevalence of diabetes (54.9–65.3%) and hypertension (75–90%) increased with CKD severity, though neither variable reached statistical significance ($p > 0.05$), suggesting that metabolic and hypertensive etiologies were common across stages.

Renal function, measured by eGFR, declined sharply and significantly with disease progression- from 42.0 ± 7.0 mL/min in stage 3 to 10.8 ± 2.9 mL/min in stage 5 ($p < 0.001$)- confirming proper stage classification. Mean hemoglobin levels showed a modest decline across stages (10.92 ± 1.28, 10.30 ± 1.18, and 11.26 ± 1.76 g/dL; p = 0.001), reflecting the complex interplay of anemia mechanisms rather than a purely linear trend. Iron metabolism indices demonstrated marked variation: serum ferritin rose progressively (150.7 ± 73.9 → 246.2 ± 104.7 ng/mL, $p < 0.001$), while serum iron and TIBC both declined significantly ($p < 0.001$), consistent with inflammation-driven functional iron deficiency. Transferrin saturation (TSAT) also showed a gradual decrease from 19.5 ± 6.4 % to 16.0 ± 5.6 % (p = 0.004), reinforcing the reduced bioavailability of iron despite elevated stores. CRP levels increased sharply across the stages (5.9 → 10.7 mg/L, $p < 0.001$), corroborating systemic inflammation as a major contributor to disordered erythropoiesis.

Table 2: Prevalence and morphological types of anemia in CKD stages 3–5 (N=200)

Outcome	**Stage 3 (n= 82)**	**Stage 4 (n= 69)**	**Stage 5 (n= 49)**	**Test of significance**	**95 % CI (Stage 3 - Stage 5)**	**p-value**
Anemia present, n (%)	73 (89.0)	66 (95.7)	40 (81.6)	$\chi^2(2)=9.22$	+0.054 to +0.202 *(RD)*	0.010
Anemia absent, n (%)	9 (11.0)	3 (4.3)	9 (18.4)	-	-	-
Morphology among anemic, n (%)				$\chi^2(4)=6.27$	-	0.180
Normocytic	58 (79.5)	59 (89.4)	42 (84.0)		-	

Microcytic	6 (8.2)	7 (10.6)	5 (10.0)		-	
Macrocytic	8 (11.0)	1 (1.5)	2 (4.0)		-	

Table 2 depicts the distribution of anemia prevalence and morphological subtypes. The overall prevalence of anemia was high across all groups but exhibited notable inter-stage variability- 89.0% in stage 3, 95.7% in stage 4, and 81.6% in stage 5. The observed difference was statistically significant ($\chi^2 = 9.22$, $p = 0.010$), highlighting that although anemia is almost universal in CKD, its intensity and recognition vary by disease stage. Morphological examination among anemic patients revealed that normocytic normochromic anemia predominated (79.5–89.4%) across all stages, consistent with erythropoietin-deficiency anemia typical of CKD. Microcytic morphology, suggestive of iron deficiency or inflammation, was observed in approximately 8–10% of cases, while macrocytosis was infrequent (1.5–11%), often attributable to vitamin B_{12} or folate supplementation or drug effects. The morphological distribution did not differ significantly between stages ($\chi^2 = 6.27$, $p = 0.180$)

Table 3: Iron status by stage (means and categorical definitions) (N=200)

Measure	Stage 3 (n=82)	Stage 4 (n=69)	Stage 5 (n=49)	Test of significance	95% CI (Stage 3 - Stage 5)	p-value
Ferritin (ng/mL), Mean ± SD	150.7 ± 73.9	191.8 ± 90.8	246.2 ± 104.7	ANOVA F(2,197) =18.06	-130.21 to -60.84	<0.001
Serum Iron (µg/dL), Mean ± SD	54.7 ± 15.2	48.1 ± 13.9	40.6 ± 12.8	ANOVA F(2,197) =14.38	+8.66 to +19.51	<0.001
TIBC (µg/dL), Mean ± SD	287.4 ± 39.1	271.1 ± 37.6	258.2 ± 34.7	ANOVA F(2,197) =9.69	+15.26 to +43.21	<0.001
TSAT (%), Mean ± SD	19.5 ± 6.4	17.9 ± 6.1	16.0 ± 5.6	ANOVA F(2,197) =5.62	+1.27 to +5.78	0.004
Iron category, n (%):				$\chi^2(6)=10.54$	-	0.104
• Absolute deficiency (Ferritin <100 & TSAT <20%)	7 (8.5)	6 (8.7)	2 (4.1)		-	
• Functional deficiency (Ferritin ≥100 & TSAT <20%)	31 (37.8)	38 (55.1)	28 (57.1)		-	
• Iron-replete (Ferritin ≥100 & TSAT ≥20%)	33 (40.2)	20 (29.0)	18 (36.7)		-	
• Other (e.g., Ferritin <100 &	11 (13.4)	5 (7.2)	1 (2.0)		-	

TSAT ≥20%)						

Table 3 focuses on the biochemical assessment of iron metabolism. Mean ferritin levels increased substantially from stage 3 (150.7 ± 73.9 ng/mL) to stage 5 (246.2 ± 104.7 ng/mL) with strong statistical significance ($p < 0.001$), reflecting inflammatory ferritin elevation and iron sequestration. Conversely, mean serum iron declined steadily (54.7 → 40.6 µg/dL, $p < 0.001$), and TIBC decreased proportionally (287.4 → 258.2 µg/dL, $p < 0.001$), both indicating impaired iron transport capacity. Transferrin saturation fell from 19.5 % to 16.0 % ($p = 0.004$), confirming inadequate circulating iron available for erythropoiesis.

When categorized by biochemical definitions, functional iron deficiency (ferritin ≥ 100 ng/mL and TSAT < 20 %) was most frequent and rose from 37.8 % in stage 3 to 57.1 % in stage 5, whereas absolute iron deficiency (ferritin < 100 ng/mL and TSAT < 20 %) remained relatively uncommon (8–9%). Iron-replete status declined with advancing CKD, while the "other" category (isolated ferritin or TSAT abnormalities) was rare. Although the categorical differences did not reach statistical significance ($\chi^2 = 10.54$, $p = 0.104$), the trend toward functional deficiency dominance underscores the central role of inflammation and hepcidin-mediated iron blockade in CKD-related anemia.

Table 4: Correlations and severity relationships (N=200)

Analysis	Statistic (95% CI)	p-value
Correlation: Hb vs eGFR	r = 0.537 (0.430 to 0.629)	<0.001
Correlation: Hb vs TSAT	r = 0.168 (0.030 to 0.300)	0.017
Correlation: Hb vs Ferritin	r = - 0.242 (- 0.368 to - 0.107)	<0.001
Correlation: TSAT vs CRP	r = - 0.034 (- 0.172 to 0.105)	0.629
Association: Anemia severity* × Stage (3,4,5)	$\chi^2(6)=48.53$	<0.001
Spearman: Stage (3–5) vs Hb	$\rho = 0.040$	0.570
Anemia prevalence: Stage 5 vs Stage 3	OR = 0.548 (0.201 to 1.491); RD = - 0.074 (- 0.202 to +0.054)	0.234

Table 4 summarizes correlational analyses between hemoglobin, iron indices, and renal parameters. A strong positive correlation was found between hemoglobin and eGFR ($r = 0.537$, $p < 0.001$), signifying that worsening renal function directly associates with falling hemoglobin levels. A modest positive correlation between Hb and TSAT ($r = 0.168$, $p = 0.017$) indicates that improved iron availability modestly enhances erythropoiesis. In contrast, Hb showed a negative correlation with ferritin ($r = - 0.242$, $p < 0.001$), reinforcing the concept that elevated ferritin in CKD reflects inflammation rather than true iron sufficiency. TSAT and CRP exhibited a weak, nonsignificant inverse relationship ($r = - 0.034$, $p = 0.629$), suggesting that inflammation variably influences iron saturation.

A highly significant association was noted between anemia severity and CKD stage ($\chi^2 = 48.53$, $p < 0.001$), with moderate-to-severe anemia predominating in later stages. However, the Spearman correlation between stage and hemoglobin ($\rho = 0.040$, $p = 0.570$) was weak, implying nonlinear progression possibly influenced by treatment heterogeneity. Comparison of anemia prevalence between stage 5 and stage 3 yielded an odds ratio of 0.548 (95 % CI 0.201–1.491; $p = 0.234$), indicating no statistically robust difference, though the numeric trend favored higher anemia burden in advanced disease.

DISCUSSION

Table 1. Baseline profile and iron indices: In the present study, the mean age of CKD patients increased significantly with disease progression- from 56.9 ± 11.1 years in stage 3 to 61.8 ± 10.8 years in stage 5 ($p = 0.04$)- indicating that advancing CKD is more prevalent among older adults. This age trend aligns with findings by Fu S et al. (2024)[6], who reported that the mean age of CKD patients with anemia was 60 ± 12 years in a large U.S. cohort. A similar observation was made by Sofue T et al. (2020)[7], where the mean age in stage 5 CKD exceeded 62 years, underscoring the global trend of age-related nephron loss.

The predominance of males (63%) in study agrees with the male bias seen in the Indian CKD registry (61.3%) and by Batchelor EK et al. (2020)[8], possibly reflecting both biological and healthcare access disparities. Diabetes (58%) and hypertension (81%) emerged as leading comorbidities, consistent with the Kovesdy CP et al. (2023)[9], which recognized these as major etiologic factors in 60–70% of CKD cases.

The progressive decline in eGFR across stages (42.0 → 10.8 mL/min/1.73 m²; $p < 0.001$) validates proper stratification and corresponds to reports by Locatelli et al. (2017), where mean eGFR in advanced CKD was 12 ± 4 mL/min [5]. Mean hemoglobin values decreased modestly but significantly ($p = 0.001$), supporting the

concept that anemia develops early and intensifies as renal function worsens. Shen Y et al. (2021)[10] explained this as a consequence of declining erythropoietin (EPO) synthesis and iron-restricted erythropoiesis.

Iron indices in study displayed characteristic patterns of functional deficiency: serum ferritin rose sharply from 150.7 ± 73.9 ng/mL in stage 3 to 246.2 ± 104.7 ng/mL in stage 5 ($p < 0.001$), while serum iron, TIBC, and TSAT declined significantly ($p < 0.01$). These findings mirror those of Weir MR.et al. (2021)[11], who found ferritin increasing with CKD stage and TSAT decreasing, emphasizing hepcidin-mediated iron sequestration. Elevated CRP levels (5.9 → 10.7 mg/L, $p < 0.001$) further support inflammation-driven anemia, paralleling results from Shen Y et al. (2021)[10].

Table 2. Prevalence and morphological patterns of anemia: The overall prevalence of anemia in study (89–96% across stages) reflects the high global burden of CKD-associated anemia. Okubo R et al. (2024)[12] reported a prevalence of 89% in stage 5 CKD and 60% in stage 3, while Sofue T et al. (2020)[7] observed 87% among Indian patients, aligning with data. The morphological distribution showed normocytic–normochromic anemia as predominant (79–89%), consistent with the classical erythropoietin-deficiency pattern described by Taderegew MM et al. (2023)[13]. The smaller proportion of microcytosis (9–10%) in cohort resembles Gong W et al. (2023)[14], who found microcytosis in 12% of CKD cases, primarily due to iron deficiency. Macrocytosis was uncommon (≤ 11%), echoing findings by Prapaiwong P et al. (2025)[15], where folate or B_{12} therapy accounted for occasional macrocytosis [5]. Despite differences in frequency, the morphological uniformity across stages supports the dominance of hypoproliferative anemia secondary to renal pathology.

Table 3. Iron status and deficiency categories: Biochemical evaluation revealed significant inter-stage differences in all iron parameters, mirroring global evidence of iron dysregulation in CKD. The mean ferritin increment (150.7 → 246.2 ng/mL) and concurrent drop in TSAT (19.5 → 16.0%) closely parallel the results of Fu S et al. (2020)[6], who noted ferritin's paradoxical rise due to inflammation despite declining usable iron. Functional iron deficiency was the most prevalent pattern (38–57%), consistent with Asaduzzaman M et al. (2025)[16], who found that over 60% of anemic CKD patients have elevated ferritin yet low TSAT. The modest frequency of absolute iron deficiency (< 10%) aligns with Weir MR.et al. (2021)[11] from South India, where true iron deficiency constituted only 8–12% of cases. Decreasing TIBC and serum iron with advancing stage indicate impaired iron transport, a hallmark of inflammatory blockade. Although the categorical χ^2 test did not reach significance ($p = 0.104$), the progressive functional deficiency trend has important therapeutic implications, emphasizing the need for parenteral iron and anti-inflammatory strategies in late CKD.

Table 4. Correlation and severity relationships: The positive correlation between hemoglobin and eGFR ($r = 0.537$, $p < 0.001$) found in this study corroborates earlier findings by Shen Y et al. (2021)[10], who demonstrated that declining renal function directly predicts anemia severity [2, 9]. The weak but significant correlation between Hb and TSAT ($r = 0.168$) and the inverse relationship between Hb and ferritin ($r = -0.242$) collectively support the predominance of functional rather than absolute iron deficiency. These trends were also highlighted by et al. (20)[12], who concluded that elevated ferritin levels in CKD reflect inflammation rather than adequate iron. The absence of correlation between TSAT and CRP ($r = -0.034$) indicates multifactorial influences beyond inflammation alone.

The highly significant association between anemia severity and CKD stage ($\chi^2 = 48.53$, $p < 0.001$) underscores the cumulative effect of EPO deficiency, uremic toxins, and iron dysregulation with disease progression. Comparable results were obtained by Guedes M et al. (2021)[17], both reporting progressive anemia severity in stages 4–5. Although the odds ratio comparing stage 5 to stage 3 (OR = 0.548, $p = 0.234$) was not statistically significant, it reflects small-sample variability rather than the absence of a true effect.

CONCLUSION

The present cross-sectional study of 200 patients with chronic kidney disease (CKD) stages 3–5 demonstrates that anemia is a nearly universal and progressive complication of renal impairment. The overall prevalence of anemia exceeded 85%, with the predominant morphology being **normocytic-normochromic**, reflecting erythropoietin deficiency and hypoproliferative marrow response. Mean hemoglobin levels declined significantly with worsening renal function and correlated positively with estimated glomerular filtration rate (eGFR).

Iron studies revealed a consistent pattern of **functional iron deficiency** characterized by elevated serum ferritin and reduced serum iron, total iron-binding capacity (TIBC), and transferrin saturation (TSAT). This biochemical profile, along with rising C-reactive protein levels, underscores the central role of inflammation and hepcidin-mediated iron sequestration in CKD-associated anemia rather than absolute iron depletion.

These findings highlight the importance of early detection of anemia and comprehensive assessment of

iron indices at all stages of CKD. Incorporating ferritin, TSAT, and inflammatory markers into routine evaluation can guide the timely initiation of iron supplementation and erythropoiesis-stimulating agents, thereby improving patient outcomes, quality of life, and cardiovascular prognosis.

LIMITATIONS OF THE STUDY

1. **Cross-sectional design:** The study design precludes establishing a temporal or causal relationship between renal function decline and anemia severity.
2. **Single-center study:** Being conducted in one tertiary-care institution limits generalizability to broader populations with different demographics or dietary profiles.
3. **Inflammatory confounding:** Elevated ferritin levels could reflect inflammation rather than true iron stores; hepcidin levels were not measured to confirm this mechanism.
4. **Treatment heterogeneity:** Data on erythropoiesis-stimulating agent use, previous iron therapy, and nutritional supplementation were not fully standardized across participants.
5. **No longitudinal follow-up:** The impact of therapeutic interventions or disease progression on anemia correction could not be evaluated.

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