

PREVALENCE, AND SEVERITY OF ANEMIA IN CHRONIC KIDNEY DISEASE: INSIGHTS FROM A TERTIARY CARE CENTER IN INDIA

Suraj Kumar¹, Ashumi Gupta²

¹Assistant professor, Department of Nephrology, Geetanjali Medical College and Hospital, udaipur, Rajasthan, India.

²Associate professor, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.

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Corresponding Author:

Dr. Suraj Kumar,
Email: surajk06@yahoo.co.in

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Abstract

Background: Anemia is a common complication of chronic kidney disease (CKD), significantly impacting patient outcomes. Its multifactorial etiology includes reduced erythropoietin production, iron dysregulation, and systemic inflammation. This study aimed to assess the prevalence, severity, and correlates of anemia in CKD patients at a tertiary care center in India. **Materials and Methods:** A retrospective observational study was conducted among 154 CKD patients. Demographic, clinical, and laboratory data, including hemoglobin levels, iron studies, inflammatory markers, and kidney function, were analyzed. Anemia was classified based on severity (mild, moderate, severe) according to World Health Organization (WHO) criteria. Correlations between hemoglobin and parameters such as serum ferritin, transferrin saturation (TSAT), eGFR, and C-reactive protein (CRP) were assessed using Pearson's correlation. Statistical significance was set at $p < 0.05$. **Result:** Anemia prevalence increased from 16.7% in Stage 1 CKD to 96.8% in Stage 5, with severe anemia observed predominantly in advanced stages (19.4% in Stage 5). Mean hemoglobin levels declined with CKD progression, ranging from 13.4 ± 1.2 g/dL in Stage 1 to 8.3 ± 1.9 g/dL in Stage 5. A significant positive correlation was found between hemoglobin and eGFR ($r = 0.635$, $p < 0.001$), while serum ferritin ($r = -0.588$, $p < 0.001$) and CRP ($r = -0.454$, $p < 0.01$) were inversely correlated with hemoglobin. Treatment included erythropoiesis-stimulating agents (41.6%), oral iron supplementation (50.6%), intravenous iron (22.1%), and blood transfusions (13.6%). **Conclusion:** This study highlights the high burden and progression of anemia in CKD patients in India, driven by declining renal function, iron deficiency, and inflammation. Optimized anemia management strategies, including early detection, effective iron supplementation, and anti-inflammatory approaches, are crucial to improve patient outcomes in resource-constrained settings.

INTRODUCTION

Chronic kidney disease (CKD) is a global health issue affecting approximately 10-15% of the population worldwide, with a disproportionate burden observed in low- and middle-income countries, including India.^[1] The progressive nature of CKD often leads to complications that severely impact patient quality of life and increase mortality. Among these complications, anemia is one of the most prevalent and impactful, affecting up to 90% of CKD patients in the advanced stages of the disease.^[2] Anemia in CKD patients is primarily due to a decline in erythropoietin production, a hormone synthesized by the kidneys that stimulates red blood cell (RBC) production in the bone marrow.^[3] As CKD progresses, reduced erythropoietin levels lead to

decreased RBC production, resulting in anemia. Additionally, other contributing factors include iron deficiency, chronic inflammation, uremic toxins that impair erythropoiesis, and a shortened RBC lifespan, all of which can exacerbate the severity of anemia in these patients.^[4]

The clinical implications of anemia in CKD are substantial. Research has shown that anemia is linked to increased risks of cardiovascular disease, hospitalization, cognitive impairment, and mortality in CKD patients.^[5] In India, the situation is particularly concerning due to the high prevalence of iron deficiency anemia (estimated to affect 50-60% of the general population) and other nutritional deficiencies that compound the effects of CKD-related anemia.^[6] According to a recent study, nearly 65% of Indian patients with CKD stages 3-5 exhibit

moderate to severe anemia, with hemoglobin levels often falling below 10 g/dL, compared to the recommended target of 11-12 g/dL in CKD management guidelines.^[7]

Anemia management in CKD patients typically includes erythropoiesis-stimulating agents (ESAs), iron supplementation, and, in some cases, red blood cell transfusions. However, studies indicate that anemia in CKD patients in India remains largely underdiagnosed and undertreated, with only 30-40% of patients receiving adequate treatment.^[8] Factors contributing to these challenges include limited access to specialized healthcare, economic constraints, and inadequate monitoring of hemoglobin and iron status in patients with CKD.^[9] Furthermore, there is increasing evidence that inappropriate anemia management, such as over-reliance on ESAs without sufficient iron supplementation, may lead to adverse cardiovascular outcomes.^[10]

The profile of anemia in CKD patients varies significantly based on disease stage, demographic factors, and geographic location. In India, studies are limited in evaluating the detailed profile of anemia in CKD patients, making it crucial to understand the characteristics, prevalence, and severity of anemia in this population.^[10] This study aimed to do a comprehensive analysis of anemia profiles in CKD patients, with a focus on its prevalence, severity, and potential therapeutic gaps. By highlighting these aspects, this study seeks to contribute to more effective and tailored anemia management strategies for CKD patients, ultimately aiming to improve clinical outcomes and quality of life.

MATERIALS AND METHODS

Study Design and Setting: This retrospective observational study was conducted at the Department of Nephrology, Geetanjali Medical College and Hospital, Udaipur, during January 2024 to December 2024, and collected data of patients retrospectively for a 5-year period from June 2016 to May 2021. The study was approved by the Institutional Ethics Committee (IEC) of Geetanjali University, with IEC approval number GU/HREC/EC/2024/2594. Written informed consent was obtained from all participants before their inclusion in the study.

Study Population: The study included adult patients aged 18 years and above with a confirmed diagnosis of chronic kidney disease (CKD) at any stage (1–5) who attended the nephrology outpatient clinic or were admitted to the nephrology inpatient ward. Patients were excluded if they had acute kidney injury, a history of blood transfusions within the past three months, were undergoing chemotherapy or radiotherapy, or had other hematological disorders affecting red blood cell (RBC) production or hemoglobin levels, such as thalassemia or sickle cell disease.

Sample Size Calculation: The calculated sample size, based on a 10% prevalence of anemia in CKD

patients, a 5% margin of error, and a 95% confidence interval, is approximately 138 participants. Adjusting for a 10% dropout rate, the total required sample size is approximately 154 participants.^[11]

Data Collection: Data were collected through structured interviews, medical record reviews, and laboratory investigations. For each participant, demographic and clinical information, including age, gender, body mass index (BMI), CKD stage (determined based on the estimated glomerular filtration rate, eGFR), presence of comorbidities such as diabetes mellitus and hypertension, and the duration of CKD diagnosis, were recorded. Laboratory investigations included the measurement of hemoglobin (Hb) levels in g/dL. Iron status was assessed through serum ferritin levels. Transferrin saturation (TSAT) was calculated using the formula: (serum iron/total iron-binding capacity) × 100. Serum creatinine levels were measured using the Jaffe method, and eGFR was calculated using the CKD-EPI formula to classify CKD stages. C-reactive protein (CRP) levels were determined as an indicator of inflammation. Additionally, other biochemical markers, such as serum albumin, calcium, and phosphate, were measured to assess nutritional and metabolic status.

Definition and Classification of Anemia: Anemia in the study population was defined based on the World Health Organization (WHO) criteria, with hemoglobin levels <13.0 g/dL for males and <12.0 g/dL for females. The severity of anemia was further categorized into three levels: mild anemia, defined as hemoglobin levels ranging from 10–12 g/dL in females and 10–13 g/dL in males; moderate anemia, with hemoglobin levels between 7–10 g/dL in both males and females; and severe anemia, characterized by hemoglobin levels below 7 g/dL.^[12]

Statistical Analysis: Data analysis was conducted using SPSS software version 25.0; IBM Corp., Armonk, NY, USA. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) based on data distribution, while categorical variables were presented as frequencies and percentages. Comparative analyses were performed to examine the relationship between CKD stages and anemia severity using the chi-square test for categorical variables. Correlation between anemia-related parameters, including serum ferritin, transferrin saturation (TSAT), eGFR, and C-reactive protein (CRP), was assessed using Pearson's correlation coefficient (r). A p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of the participants was 52.6 ± 12.4 years, with males comprising 59.7% (n = 92) and females 40.3% (n = 62). The majority of participants had a normal body mass index (BMI) (61%, n = 94), followed by overweight (22.1%, n = 34),

underweight (11.7%, n = 18), and obese (5.2%, n = 8). Regarding CKD staging, the highest proportion of participants were in Stage 4 (29.9%, n = 46), followed by Stage 3 (27.3%, n = 42), Stage 5 (20.1%, n = 31), Stage 2 (14.9%, n = 23), and Stage 1 (7.8%, n = 12). Hypertension was the most prevalent comorbidity, affecting 75.3% (n = 116) of participants, while 61% (n = 94) had diabetes. The mean duration of CKD was 3.8 ± 1.6 years, reflecting a significant burden of advanced CKD stages and associated comorbidities in this population [Table 1]. The hematological parameters and anemia prevalence were analyzed across CKD stages. Hemoglobin levels showed a progressive decline from Stage 1 (13.4 ± 1.2 g/dL) to Stage 5 (8.3 ± 1.9 g/dL). The prevalence of anemia increased significantly with advancing CKD stages, being 16.7% (n = 2) in Stage 1, 30.4% (n = 7) in Stage 2, 62.3% (n = 26) in Stage 3, 85.7% (n = 40) in Stage 4, and 96.8% (n = 30) in Stage 5. Similarly, the red blood cell (RBC) count declined from 4.5 ± 0.3 million/ μ L in Stage 1 to 3.2 ± 0.7 million/ μ L in Stage 5. Hematocrit levels also decreased, ranging from $42.3 \pm 2.4\%$ in Stage 1 to $25.9 \pm 4.7\%$ in Stage 5 [Table 2].

The severity of anemia across CKD stages demonstrated a significant correlation with disease progression. In Stage 1, mild anemia was observed in 16.7% (n = 2) of patients, with no cases of moderate or severe anemia. In Stage 2, mild anemia occurred in 17.4% (n = 4), and moderate anemia was noted in 13.0% (n = 3), with no cases of severe anemia. In Stage 3, 33.3% (n = 14) had mild anemia, 26.2% (n = 11) had moderate anemia, and 2.4% (n = 1) had severe anemia. Stage 4 patients showed further worsening, with 43.5% (n = 20) experiencing mild anemia, 39.1% (n = 18) moderate anemia, and 4.3% (n = 2) severe anemia. The most advanced stage, Stage 5, revealed the highest prevalence of moderate anemia (45.2%, n = 14) and severe anemia (19.4%, n = 6), with 32.2% (n = 10) presenting with mild anemia. Statistical analysis showed a significant association between CKD stage and anemia severity, with p-values <0.05 for early stages and <0.001 for Stage 5 [Table 3].

The biochemical parameters of the participants demonstrated significant alterations with CKD progression. The mean serum ferritin level was 231.4 ± 75.8 ng/mL, reflecting adequate iron stores, while the mean transferrin saturation (TSAT) of $18.7 \pm 6.2\%$ indicated functional iron deficiency in many patients. Serum iron levels averaged 58.4 ± 11.3 μ g/dL, and total iron-binding capacity (TIBC) was 312.6 ± 44.2 μ g/dL. Serum creatinine levels progressively increased from 1.2 ± 0.2 mg/dL in Stage 1 to 7.8 ± 1.1 mg/dL in Stage 5, while estimated glomerular filtration rate (eGFR) declined from 90.2 ± 5.4 mL/min/1.73m² in Stage 1 to 11.3 ± 2.8 mL/min/1.73m² in Stage 5. The mean C-reactive protein (CRP) level was elevated at 8.9 ± 3.7 mg/L, indicating a heightened inflammatory state associated with CKD [Table 4].

The management strategies for anemia among CKD patients revealed that 64 participants (41.6%) were receiving erythropoiesis-stimulating agents (ESAs). Iron supplementation was utilized by 50.6% of patients in the form of oral iron, while 22.1% received intravenous (IV) iron therapy. Additionally, 13.6% of the participants had undergone blood transfusions, highlighting the varying approaches to address anemia in this population [Table 5].

The correlation analysis indicates several significant relationships between clinical parameters and anemia severity in CKD patients. Serum ferritin levels show a moderate negative correlation with anemia severity ($r = -0.588$, $p < 0.001$), meaning that higher ferritin levels are associated with less severe anemia. Transferrin saturation (TSAT) demonstrates a moderate positive correlation with anemia severity ($r = 0.457$, $p < 0.05$), suggesting that lower TSAT levels, which indicate iron deficiency, are linked to more severe anemia. eGFR has a strong positive correlation with anemia severity ($r = 0.635$, $p < 0.001$), indicating that lower eGFR values, reflecting advanced kidney dysfunction, are associated with increased anemia severity. Finally, CRP levels exhibit a moderate negative correlation with anemia severity ($r = -0.454$, $p < 0.01$), suggesting that higher inflammation markers correlate with less severe anemia [Table 6].

Table 1: Demographic and Clinical Characteristics of Study Participants.

Variable	Frequency (%) / mean \pm SD
Age (years)	52.6 \pm 12.4
Gender	
Male	92 (59.7%)
Female	62 (40.3%)
Body Mass Index (BMI)	
Underweight	18 (11.7%)
Normal	94 (61%)
Overweight	34 (22.1%)
Obese	8 (5.2%)
CKD Stage	
Stage 1	12 (7.8%)
Stage 2	23 (14.9%)
Stage 3	42 (27.3%)
Stage 4	46 (29.9%)
Stage 5	31 (20.1%)
Comorbidities	
Hypertension	116 (75.3%)

Diabetes	94 (61%)
Duration of CKD (years)	3.8 ± 1.6

Table 2: Hematological Parameters Across CKD Stages.

Parameter	Frequency (%) / mean ± SD				
	Stage 1 (n = 12)	Stage 2 (n = 23)	Stage 3 (n = 42)	Stage 4 (n = 46)	Stage 5 (n = 31)
Hemoglobin (g/dL)	13.4 ± 1.2	12.8 ± 1.4	11.2 ± 1.6	9.7 ± 1.8	8.3 ± 1.9
Anemia Prevalence (%)	2 (16.7%)	7 (30.4%)	26 (62.3%)	40 (85.7%)	30 (96.8%)
RBC Count (million/ μ L)	4.5 ± 0.3	4.2 ± 0.4	3.9 ± 0.5	3.4 ± 0.6	3.2 ± 0.7
Hematocrit (%)	42.3 ± 2.4	41.8 ± 3.2	36.1 ± 3.2	32.4 ± 4.1	25.9 ± 4.7

Table 3: Comparison of Anemia Prevalence and Severity by CKD Stage.

CKD Stage	Severity of Anemia Frequency (%)			p-Value
	Mild	Moderate	Severe	
Stage 1	2 (16.7%)	0 (0.0%)	0 (0.0%)	<0.05
Stage 2	4 (17.4%)	3 (13.0%)	0 (0.0%)	<0.05
Stage 3	14 (33.3%)	11 (26.2%)	1 (2.4%)	<0.01
Stage 4	20 (43.5%)	18 (39.1%)	2 (4.3%)	<0.01
Stage 5	10 (32.2%)	14 (45.2%)	6 (19.4%)	<0.001

Table 4: Iron Status and Biochemical Markers.

Parameter	Mean ± SD
Serum Ferritin (ng/mL)	231.4 ± 75.8
Transferrin Saturation (%)	18.7 ± 6.2
Serum Iron (μ g/dL)	58.4 ± 11.3
TIBC (μ g/dL)	312.6 ± 44.2
Serum Creatinine (mg/dL)	
Stage 1	1.2 ± 0.2
Stage 2	1.5 ± 0.3
Stage 3	2.3 ± 0.6
Stage 4	4.2 ± 0.9
Stage 5	7.8 ± 1.1
eGFR (mL/min/1.73m ²)	
Stage 1	90.2 ± 5.4
Stage 2	72.4 ± 6.1
Stage 3	46.8 ± 5.7
Stage 4	23.6 ± 4.3
Stage 5	11.3 ± 2.8
C-Reactive Protein (mg/L)	8.9 ± 3.7

Table 5: Anemia Management Practices in CKD Patients.

Parameter	Frequency (%)
Use of Erythropoiesis-Stimulating Agents (ESAs)	64 (41.6%)
Iron Supplementation	
Oral	78 (50.6%)
IV	34 (22.1%)
Frequency of Blood Transfusions	21 (13.6%)

Table 6: Correlation Between Anemia Severity and Biochemical Parameters.

Parameter	Correlation Coefficient (r)	p-Value
Serum Ferritin (>300 mg/dl)	-0.588	<0.001
TSAT (<20%)	0.457	<0.05
eGFR (eGFR <15 mL/min/1.73m ²)	0.635	<0.001
CRP (>5 mg/L)	-0.454	<0.01

DISCUSSION

Anemia in chronic kidney disease (CKD) is a multifaceted complication influenced by a combination of declining renal function, iron metabolism disorders, and inflammation. In our study, anemia prevalence showed a marked increase from 16.7% in Stage 1 CKD to 96.8% in Stage 5, with severe anemia accounting for 19.4% of cases in Stage 5. These findings are consistent with studies done by Varma et al., and Kumar et al., in similar Indian populations, where anemia prevalence exceeded 90% in advanced CKD stages.^[13,14] This progression reflects the worsening erythropoietin deficiency and

cumulative impact of metabolic disturbances on erythropoiesis as CKD advances.^[15]

The observed correlation between eGFR and hemoglobin levels ($r = 0.635$, $p < 0.001$) strongly supports the link between declining kidney function and anemia severity. Similar findings were reported by Panjeta et al., where a significant positive correlation between eGFR and hemoglobin levels highlighted the critical role of renal function in erythropoietin production.^[16] In our study, patients in Stage 5 CKD had mean hemoglobin levels of 8.3 ± 1.9 g/dL, comparable to the 8.1 ± 1.7 g/dL reported in a study by Pan et al.^[17]

Iron status assessment revealed suboptimal markers, with mean transferrin saturation (TSAT) at $18.7 \pm 6.2\%$, below the recommended threshold for adequate iron availability (TSAT $>20\%$). This aligns with the high prevalence of functional iron deficiency observed in CKD patients due to inflammation-mediated iron sequestration.^[18] Our finding of a negative correlation between ferritin and anemia severity ($r = -0.588$, $p < 0.001$) underscores the dual role of ferritin as both an iron store marker and an acute-phase reactant. Comparable trends were reported by Rohr et al., emphasizing the diagnostic limitations of ferritin in CKD settings characterized by chronic inflammation.^[19] Elevated CRP levels (mean 8.9 ± 3.7 mg/L) further support the role of inflammation, with a significant negative correlation with hemoglobin ($r = -0.454$, $p < 0.01$), consistent with findings from Santos et al., who demonstrated that inflammation exacerbates erythropoietin resistance.^[20]

Our study also highlighted treatment gaps, with only 41.6% of patients receiving erythropoiesis-stimulating agents (ESAs) and 72.7% on iron supplementation. Notably, IV iron therapy, administered to 22.1% of patients, was associated with improved hematological parameters, particularly in those with TSAT $<20\%$. However, reliance on blood transfusions in 13.6% of patients underscores the persistent unmet needs in anemia management, especially in resource-constrained settings like India.^[21] These results align with international findings, where ESA utilization is often limited due to cost, and transfusions are a fallback for severe anemia.^[22]

The variations in anemia severity across CKD stages further emphasize the need for stage-specific management. Mild anemia was more prevalent in Stages 1 and 2 (16.7% and 17.4%, respectively), whereas moderate and severe anemia dominated in Stages 4 and 5 (39.1% and 19.4%, respectively). This trend mirrors the global CKD anemia burden and highlights the role of early diagnosis and timely intervention in preventing severe outcomes.^[23,24]

CONCLUSION

In conclusion, our findings reinforce the complex etiology of anemia in CKD, driven by declining renal function, iron dysregulation, and inflammation. Addressing this burden requires a multifaceted approach, including improved diagnostic markers for iron deficiency, expanded access to ESAs, and anti-inflammatory therapies. Future studies should focus on long-term outcomes of such interventions and their feasibility in diverse populations.

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