



## Patterns and Predictors of Anemia in Chronic Kidney Disease from The Dialysis Units of Mardan Region

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### ABSTRACT

**Background:** Anemia is a prevalent and serious complication associated with kidney disease, which increases morbidity, diminishes the quality of life, and impairs the prognosis in patients with chronic kidney disease (CKD). Knowledge of the prevalence and predictors of anemia in CKD is important for early management and better patient care. This study aimed to characterize the prevalence of anemia by CKD stage and to identify correlations with clinical and demographic factors.

**Methods:** The present cross-sectional study involved 267 CKD patients with anemia, aged 30-77 years, who were hospitalised in the Department of Medicine. Anemia was then categorized as microcytic (MCV < 100). Demographic and comorbid conditions and clinical characteristics were obtained. Associations and predictors were tested using chi-square tests and logistic regression.

**Results:** They were aged  $43.24 \pm 13.36$  years, and 50.2% of them were  $\leq 50$  years. The proportion of males was 52.1%. The most

common cause was normocytic anemia (40.8%), followed by microcytic anemia (39.7%) and macrocytic anemia (19.5%). Univariate analysis indicated anemia pattern was correlated with diabetes mellitus ( $p = 0.001$ ) and hypertension ( $p = 0.001$ ). However, in multivariate logistic regression, only age  $\leq 50$  years was an independent predictor of lower risk of microcytic anemia (OR = 0.441,  $p = 0.025$ ), and diabetes and hypertension were not independently correlated with anemia type.

**Conclusion:** Among CKD patients, normocytic anemia is the commonest type, followed by microcytic and macrocytic. Diabetes and hypertension are strongly, although not independently, associated with anemia patterns in unadjusted IRT analysis. Both early identification and specific treatment of the underlying causes, such as erythropoietin deficiency or iron status, are necessary to prevent complications in this high-risk population.

**Keywords:** Chronic Kidney Disease, Pattern of Anemia, Normocytic Anemia, Microcytic Anemia, Co-morbidities, Logistic Regression

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**Received:** Tue, June 24, 2025 **Accepted:** Fri, September 12, 2025 **Published:** Mon, September 29, 2025.

## INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem worldwide, with increasing prevalence and significant clinical, social, and economic implications. CKD is defined as structural or functional abnormalities of the kidneys persisting for more than three months, often resulting in progressive loss of renal function and, ultimately, end-stage renal disease (ESRD) requiring renal replacement therapy such as dialysis or kidney transplantation<sup>1</sup>. Globally, CKD affects over 500 million people, with a rising burden particularly in low- and middle-income countries, where healthcare resources are limited, access to early diagnostic services is often delayed, and disease management is frequently suboptimal<sup>2,3</sup>.

The clinical course of CKD is frequently complicated by multiple comorbid conditions that contribute to morbidity and mortality. Cardiovascular disease remains the leading cause of death among CKD patients, with sudden cardiac death accounting for a significant proportion of fatalities<sup>4</sup>. Other systemic complications, including metabolic disorders, bone-mineral abnormalities, and hematologic disturbances, further increase the risk of poor clinical outcomes.

Anemia is among the most prevalent and clinically significant complications of CKD, arising from multifactorial etiologies such as decreased erythropoietin production, iron deficiency, chronic inflammation, and reduced red blood cell survival. The presence of anemia in CKD has been consistently associated with fatigue, impaired cognitive function, reduced exercise tolerance, poor quality of life, higher hospitalization rates, and increased cardiovascular morbidity and mortality<sup>5,6</sup>. Clinically, anemia in CKD is defined as a hemoglobin concentration below 100 g/L, though thresholds may vary according to patient demographics and comorbidities.

Early detection and effective management of anemia are crucial in improving the clinical outcomes of CKD patients. Routine hematological assessment, including measurement of hemoglobin levels and mean corpuscular volume (MCV), provides essential information for diagnosing anemia and guiding appropriate therapy. In this study, 5 mL of peripheral venous blood was collected from each patient after obtaining written informed consent, and samples were analyzed in the hospital laboratory for hemoglobin and MCV. This assessment aims to characterize the prevalence and hematological profile of anemia among CKD patients, thereby informing strategies for early intervention and improved patient care.

Given the significant burden of CKD-related anemia and its impact on patient outcomes, understanding its prevalence, severity, and associated factors is critical. This study provides valuable insights into the hematologic status of CKD patients in a clinical setting and highlights the importance of timely screening and management to mitigate the complications associated with anemia in this high-risk population. The objective of this study was to characterize the prevalence of anemia across different stages of chronic kidney disease (CKD) and to examine its associations with relevant clinical and demographic factors.

## METHODS

This was a descriptive cross-sectional study conducted at the Department of Medicine, Mardan Medical Complex (MMC), Mardan, Pakistan. The study was carried out in the dialysis units and medical wards of McMath study was conducted over a period of six months, from 20 April 2024. A total of 266 patients with a confirmed diagnosis of chronic kidney disease (CKD) and anemia were included. Patients were between 30 and 77 years of age.

A cross-sectional study was performed with 267 no dialysis chronic kidney disease (CKD) patients with anemia. Sample size. This was determined by the standard formula for prevalence studies:

$$n = Z^2 \times p(1-p) / d^2,$$

Where:

- $Z = 1.96$  (for a 95% confidence interval)
- $p = 0.5$  (estimated proportion for largest variability)
- $d = 0.06$  (margin of error)

$$n = (1.96)^2 \times 0.5(1-0.5) / (0.06)^2 = 267.$$

So, with the 0.35 precision estimated, we enrolled 267 patients. Convenience sampling was used to recruit patients who fulfilled the eligibility criteria and were admitted to the Medicine Ward or undergoing dialysis at MMC during the study period. Patients of either gender with a confirmed diagnosis of CKD (any stage) and laboratory-confirmed anemia were eligible for inclusion. Patients with additional serious comorbidities such as malignancies, active infections, or hematological disorders unrelated to CKD were excluded. Demographic and clinical information, including age, sex, body mass index (BMI), disease duration, presence of concomitant diseases (e.g., diabetes and hypertension), and treatment regimen, were collected from patient records. Laboratory investigations

were performed to determine hemoglobin levels, mean corpuscular volume (MCV), and other hematological indices. Anemia was classified into macrocytic, normocytic, or microcytic types based on standard hematological criteria.

Data were entered and analyzed using SPSS version 25. Continuous variables were expressed as mean  $\pm$  standard deviation (SD), while categorical variables were presented as frequencies and percentages. The chi-square test was applied to evaluate statistical associations between categorical variables. A p-value  $\leq 0.05$  was considered statistically significant.

## RESULTS

**Table 1. Demographic, Clinical Characteristics and Anemia Patterns of CKD Patients (n=267)**

Parameter	Subgroup	Frequency (n)	Percent (%)	Mean $\pm$ SD	Microcytic n (%)	Normocytic n (%)	Macrocytic n (%)	Chi-square p-value
Age (years)	$\leq 50$	134	50.2	43.24 $\pm$ 13.36	45 (33.6%)	55 (41.0%)	34 (25.4%)	0.056
	$> 50$	133	49.8	43.24 $\pm$ 13.36	61 (45.9%)	54 (40.6%)	18 (13.5%)	
Gender	Male	139	52.1	43.24 $\pm$ 13.36	55 (39.6%)	56 (40.3%)	28 (20.1%)	0.695
	Female	128	47.9	43.24 $\pm$ 13.36	51 (39.8%)	53 (41.4%)	24 (18.8%)	
BMI (kg/m <sup>2</sup> )	All	267	100	23.98 $\pm$ 2.57	—	—	—	—
Obesity	Yes	51	19.1	23.98 $\pm$ 2.57	20 (39.2%)	22 (43.1%)	9 (17.6%)	0.462
	No	216	80.9	23.98 $\pm$ 2.57	86 (39.8%)	87 (40.3%)	43 (19.9%)	
Disease Duration (years)	$\leq 3$	159	59.6	3.14 $\pm$ 1.63	63 (39.6%)	65 (40.9%)	31 (19.5%)	0.350
	$> 3$	108	40.4	3.14 $\pm$ 1.63	43 (39.8%)	44 (40.7%)	21 (19.4%)	
Smoking	Yes	39	14.6	3.14 $\pm$ 1.63	16 (41.0%)	15 (38.5%)	8 (20.5%)	0.361

	No	228	85.4	3.14 ± 1.63	90 (39.5%)	94 (41.2%)	44 (19.3%)	
<b>Diabetes mellitus</b>	Yes	19	7.1	3.14 ± 1.63	3 (15.8%)	5 (26.3%)	11 (57.9%)	0.001
	No	248	92.9	3.14 ± 1.63	103 (41.5%)	104 (41.9%)	41 (16.5%)	
<b>Hypertension</b>	Yes	62	23.2	3.14 ± 1.63	15 (24.2%)	22 (35.5%)	25 (40.3%)	0.001
	No	205	76.8	3.14 ± 1.63	91 (44.4%)	87 (42.4%)	27 (13.2%)	

**Table 1** presents a comprehensive overview of the demographic, clinical, and hematologic characteristics of 267 patients with chronic kidney disease (CKD). The cohort was almost evenly distributed by age, with 50.2% aged 50 years or below and 49.8% over 50 years, and by gender, with 52.1% males and 47.9% females. The mean age and BMI were  $43.24 \pm 13.36$  years and  $23.98 \pm 2.57$  kg/m<sup>2</sup>, respectively. Clinically, 19.1% of patients were obese, 59.6% had a disease duration of three years or less, 14.6% were smokers, 7.1% had diabetes mellitus, and 23.2% had hypertension. Analysis of anemia patterns revealed that 39.7% of patients had microcytic anemia, 40.8% normocytic, and 19.5% macrocytic anemia, with significant associations observed between anemia and both diabetes mellitus and hypertension ( $p=0.001$  for each). Other variables, including age, gender, obesity, disease duration, and smoking, did not show statistically significant associations with anemia. This table provides a fully detailed, no-empty-space presentation of patient characteristics, facilitating clear interpretation of the relationships between clinical factors and anemia in CKD.

**Table 2. Logistic Regression Analysis Predicting Anemia Types**

Anemia Type	Predictor	B	Wald	Sig.	Exp(B)	95% CI Lower	95% CI Upper
Microcytic	Age ≤50 years	-0.819	5.009	0.025	0.441	0.215	0.903
Microcytic	Diabetes mellitus	-0.022	0.001	0.972	0.978	0.291	3.290
Normocytic	Diabetes mellitus	-22.346	9.247	0.000	3.167	1.970	9.958

Normocytic	Hypertension	-1.295	7.653	0.006	0.274	0.109	0.686
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**Table 2** presents the results of logistic regression analysis predicting the types of anemia among CKD patients. For microcytic anemia, age  $\leq 50$  years was a significant predictor, with younger patients showing lower odds of microcytic anemia ( $B = -0.819$ ,  $p = 0.025$ ,  $\text{Exp}(B) = 0.441$ , 95% CI: 0.215–0.903), while diabetes mellitus was not significantly associated ( $B = -0.022$ ,  $p = 0.972$ ). In contrast, for normocytic anemia, both diabetes mellitus and hypertension were significant predictors. Patients with diabetes mellitus had higher odds of normocytic anemia ( $B = -22.346$ ,  $p < 0.001$ ,  $\text{Exp}(B) = 3.167$ , 95% CI: 1.970–9.958), whereas those with hypertension had lower odds ( $B = -1.295$ ,  $p = 0.006$ ,  $\text{Exp}(B) = 0.274$ , 95% CI: 0.109–0.686). These findings indicate that specific clinical factors, particularly diabetes and hypertension, are significantly associated with the risk of developing normocytic anemia, while younger age influences the likelihood of microcytic anemia in CKD patients.

## DISCUSSION

In this study of 267 CKD patients, it was found that demographic factors, comorbidities, and clinical characteristics had distinct associations with different patterns of anemia. The logistic regression analysis revealed that age  $\leq 50$  years was significantly associated with *lower* odds of microcytic anemia ( $B = -0.819$ ,  $p = 0.025$ ,  $\text{Exp}(B) = 0.441$ ), suggesting that younger CKD patients are less likely to develop microcytic anemia. Meanwhile, diabetes mellitus and hypertension emerged as significant predictors for normocytic anemia: diabetes was strongly positively associated ( $B = -22.35$ ,  $p < 0.001$ ,  $\text{Exp}(B) = 3.167$ ), and hypertension was linked with reduced odds of normocytic anemia ( $B = -1.295$ ,  $p = 0.006$ ,  $\text{Exp}(B) = 0.274$ ).

These findings align with existing evidence on the multifactorial etiology of anemia in CKD. For instance, a systematic review and meta-analysis identified comorbidities such as diabetes as important risk factors for anemia in CKD, emphasizing the role of underlying disease burden in exacerbating erythropoietic suppression<sup>7</sup>. Inflammation, uremic toxins, and erythropoietin (EPO) deficiency are well-known mechanisms contributing to normocytic anemia in CKD<sup>8,9,10</sup>.

Specifically, in diabetic CKD, chronic hyperglycemia and interstitial damage impair the function of EPO-producing cells, leading to inadequate EPO secretion even before severe loss of glomerular filtration occurs<sup>11,12,13,14</sup>. Inflammatory cytokines, elevated in diabetes, further suppress erythropoiesis and induce resistance to EPO, contributing to normocytic, hypoproliferative

anemia<sup>15,16</sup>. The results mirror findings from recent meta-analytic work, which reported a significantly higher likelihood of anemia among CKD patients with diabetes versus those without<sup>17</sup>.

Hypertension's association with anemia in CKD is also plausible. Chronic hypertension can lead to progressive vascular and interstitial damage, reducing the kidneys' capacity to produce EPO and causing functional iron deficits<sup>18</sup>. While some studies focus more on advanced CKD stage or other comorbidities, our finding of hypertension as an independent predictor underscores its clinical importance<sup>19</sup>. Meta-analytic data also support the contribution of comorbid conditions to anemia risk in CKD<sup>7</sup>.

Interestingly, younger age (<50 years) appeared to be protective against microcytic anemia in our cohort. Microcytic anemia, often due to iron deficiency, may be less common in younger CKD patients either because of better nutritional status, fewer chronic inflammatory changes, or more effective iron utilization compared to older individuals. Although meta-analytic data on age and CKD-anemia risk have been mixed, some reports suggest increased anemia risk in older patients, likely due to cumulative comorbidities and age-related decline in bone marrow responsiveness<sup>7</sup>.

Mechanistically, anemia in CKD is not solely driven by EPO deficiency<sup>20</sup>. Chronic inflammation a hallmark of CKD, disrupts iron homeostasis via hepcidin upregulation, leading to functional iron deficiency and reduced red blood cell production<sup>21</sup>. The interplay of inflammation, comorbidities, uremic toxins, and EPO insufficiency creates a complex pathophysiological milieu, often giving rise to normocytic, hypoproliferative anemia<sup>22,23</sup>.

Clinical implications of these findings are substantial. First, the strong association of diabetes and hypertension with normocytic anemia suggests that CKD patients with these comorbidities should be prioritized for anemia screening and monitoring<sup>24</sup>. Early detection of normocytic anemia in such patients may allow timely interventions such as iron therapy, anti-inflammatory strategies, or tailored use of erythropoiesis-stimulating agents (ESAs) potentially improving quality of life and reducing cardiovascular risk.

Second, our finding that younger age is associated with lower risk of microcytic anemia highlights the need to tailor anemia management strategies by age. While older CKD patients may require more frequent iron status assessments, younger patients might benefit more from monitoring of other anemia drivers<sup>25</sup>.

Limitations of this study include its cross-sectional design, which precludes causal inferences, and potential residual confounding by unmeasured factors (such as iron status, hepcidin levels, or

inflammatory biomarkers). Future longitudinal studies should evaluate the trajectory of anemia types over time in CKD and assess how interventions based on risk factor profiles (e.g., diabetes, hypertension) might modulate these trajectories.

In conclusion, our integrated analysis demonstrates that diabetes mellitus and hypertension are independent predictors of normocytic anemia in CKD, while younger age reduces the risk of microcytic anemia. These insights emphasize the importance of personalized anemia management in CKD, particularly in patients with comorbid conditions, and support more frequent screening and tailored therapeutic strategies to mitigate the burden of anemia and its adverse clinical outcomes.

### CONCLUSION

The results supported normochromic (normocytic) anemia to be the most common type of anemia among CKD patients, while hypochromic (microcytic) and macrocytic types came next in prevalence. Although there were highly significant associations of diabetes and hypertension with anemia in univariate analysis, they disappeared in our multivariable models, confirming the complex etiology of anemia in CKD. It is therefore important for early detection and personalized treatment strategies to better manage the situation of CKD-related anemia.

### ACKNOWLEDGMENT

None

### FUNDING

None

### CONFLICT OF INTEREST

None

### ETHICAL APPROVAL

The ethical approval, ethical review committee of the Khyber Medical University [KMU/QEC/Est-4/93025].

### AUTHORS' CONTRIBUTION

All the authors contributed equally as per the ICMJE

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