# MORPHOLOGICAL PATTERNS OF ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL, NEPAL

Joshi R[1], Rajbhandari A[1], Khanal P,[2*] Pande P[2,3],Pathak P[3], Regmi A,[2] Dhakal KS[3], Baral B[2], Khadka S[3]

[1]Department of Internal Medicine, Shree Birendra Hospital, Chhauni; Nepalese Army Institute of Health Sciences, Chhauni, Kathmandu, Nepal,
[2]Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu, Nepal,
[3]Nepalese Army Institute of Health Sciences, Chhauni, Kathmandu, Nepal.

*Corresponding Author:*
*Prajwal Khanal,*
*Lecturer*
[2]*Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu, Nepal*

## ABSTRACT

**Introduction:** Anemia is the major health issue that is causing the most disability worldwide amongst the patients with chronic kidney disease (CKD). Anemia in CKD is defined as an Hemoglobin level <13.5 g/dl and 12.0 g/dl in men and women respectively as demarcated by National Kidney Foundation. This study provides insights about the subtypes of anemia in patients with chronic kidney disease patients. We aim to determine the morphological Patterns of anemia in a patient with chronic kidney disease, the differential diagnosis of renal anemia.

**Methods:** A descriptive cross-sectional study was conducted among diagnosed CKD patients presented to the Nephrology Out patient department of a tertiary level hospital in Kathmandu over a six months period, from September 15, 2022 to March 15, 2023. Etiology of anemia were worked out. All adults (>18 years of age) with chronic kidney disease patients with an estimated glomerular filtration rate (eGFR) below 60 ml/min, and who were not started on dialysis were recruited. The study proposal was approved by Institutional review committee (IRC) of Nepalese army institute of health sciences (NAIHS) prior of conducting the study. Convenience Sampling was done.

**Result:** Anemia was seen in 96.8% of patients among which 58.9% of the patients presented with severe anemia. Among all patients, mean hemoglobin value was 9.45±1.60 g/dl. Moderate anemia was the commonest (50.50%) degree of anemia. Microcytic hypochromic was the commonest

(44.7%) finding in peripheral blood film study followed by normocytic normochromic type (43.7%) and plasmacytoma (5.3%).

**Conclusion:** We found a high prevalence of anemia among chronic kidney disease as compared to other studies conducted in similar settings. The higher percentage of anemia found in the study may be attributed to NKF criteria for anemia diagnosis, the cutoff of which is higher than that for general population. Also, the patients not having received renal replacement therapy in the past were taken in the study, causing higher incidence of anemia in CKD. Treatment of anemia may somewhat improves quality of life. Thus, early recognition and effective treatment in patients with CKD is highly recommended.

**Key-words:** *Anemia; Chronic Kidney Disease; Renal replacement therapy.*

## INTRODUCTION

Anemia in CKD patients is caused by a number of factors, including decreased erythropoiesis due to insufficient erythropoietin (EPO) production from the kidneys.[1-4] Iron deficiency is also common, and it is estimated that patients on hemodialysis have an iron loss of around 1 to 3 grams per year.[5] Other causes of iron deficiency include chronic bleeding from uremia-associated platelet dysfunction, frequent phlebotomy, and blood trapping in the dialysis apparatus[6]. Also, B12, and folate deficiency due to nutritional deficiency or increased blood loss, inflammation, as well as uremic toxin accumulation contributes for anemia in CKD patients.[7] Anemia causes an increase in both morbidity and mortality and accelerates the rate of progression of CKD.[8] However, reports on its identification and management have been suboptimal in our settings. In this study we aimed to describe the prevalence, severity and morphological type of anemia in our center, among chronic kidney disease patients who were not initiated with renal replacement therapy.

Chronic kidney disease (CKD) refers to a reduction in the glomerular filtration rate (GFR) to <60 mL/min/1.73 m$^2$.[9] Anemia may occur at CKD stages 2 and 3 of the Kidney Disease Improving Global Outcomes (KDIGO) staging. But the anemia is most prevalent in KIDGO 4 staging. The Hb level is presumed to decrease when the estimated glomerular filtration rate (eGFR) is around 70ml/min/1.73m$^2$ (men) and 50ml/min/1.73m$^2$ (women). In advanced stages of CKD and in the dialysis population anemia may be prevalent in more than 90% of patients.[10,11]

Anemia is more prevalent in CKD who are diabetics which largely contributes to overall outcomes.[12, 13] A study showed that low Hb levels in diabetic patients may increase risk for progression of kidney disease along with cardiovascular morbidity and mortality.[14] In our study, the staging of CKD is done according to the National Kidney Foundation.[15] Studies also showed that anemia may contribute to progression of kidney disease.[16-19] Renal ischemia caused by reduced oxygen delivery due to anemia and underlying heart failure may be culprits of progression of kidney disease. Anemia may worsen renal medullary hypoxia, leading to renal interstitial injury and fibrosis both contribute of worsening of kidney disease.[20-21]

## MATERIAL AND METHODS

This cross-sectional study study was conducted among CKD patients presented to the Nephrology OPD of Shree Birendra Hospital, conducted twice a week, in a tertiary hospital of Nepalese Army located in the capital city of Nepal. It was conducted over a period of six months from September 2022 to March 2023. All adults (>18 years of age) with chronic kidney disease patients with an estimated glomerular filtration rate (eGFR) below 60 ml/min, and who were not started dialysis were recruited. Convenience sampling was used. Estimated Sample size:

$$n = \left(\frac{Z_\alpha}{E}\right)^2 PQ = 182$$

(Z= 1.96 at 95% confidence interval; p (prevalence)= 0.5; q = 1-p = 0.95; E =

allowable error = 10%)Assuming 10% non-response rate, the final sample size comes to be approximately 200, Demographic, clinical and laboratory data regarding anemia and its management were collected using a standard data form. Anemia is defined as a hemoglobin level below 12g/dl in females with CKD and below 13.5g/dl in males as per NKF.[22] Likewise, severe anemia is defined as a hemoglobin level below 10g/dl.

With the help of semi-structured questionnaire demographic variables, presenting complaints, baseline laboratory parameters were evaluated. Etiology of anemia were clinched with the help of laboratory parameters and clinical profile. Among the cases evaluated peripheral blood film was studied in all cases and specific tests were performed as per the need of the cases.

The study proposal was approved by ethical review committee (IRC) of Nepalese army institute of health sciences (NAIHS) prior of conducting the study. Informed verbal consent was taken while enrolling the individual in the study. The collected were entered in SPSS version 22 and analyzed. Chi-square test was used to see association between important determinant of anemia with the help of $p$ value based on 95% confidence interval and 5% standard error.

## RESULTS

A total of 190 patients were enrolled in the study. Mean age of the participants was 59.27±13.51 years, with minimum being 19 years and maximum being 92 years. Mean hemoglobin value was 9.44±1.60 gm/dl. There were 48.4% females while rest were males. Anemia was seen in 96.8% of patients among which 58.9% of the patients presented with severe anemia. Moderately severe anemia was the commonest (159, 46.5%) among anemic cases followed by severe, mild and life threatening in the descending order (Table 1).

In our study, generalized weakness was the commonest (91, 47.89%) presenting complaint, followed by per vaginal bleeding (25, 13.15%), upper gastrointestinal bleed (22, 11.58%) and shortness of breath (16, 8.43%). While other complaints include increase in generalized body swelling, paleness, per rectal bleeding, myalgia, and other modalites of bleeding like acute traumatic blood loss and hemoptysis in descending order (Table 2).

In peripheral blood film study, microcytic hypochromic type (44.7%) was the commonest finding followed by normocytic normochromic anemia (43.7%) (Table 3).

### Table 1. Severity of Anemia

| Anemia Severity | Frequency | Percent |
|---|---|---|
| Mild Anemia (above 10) | 65 | 34.2 |
| Moderate Anemia (8-10) | 96 | 50.5 |
| Severe Anemia(6.5-7.9) | 17 | 8.9 |
| Life threatening (less than 6.5) | 9 | 4.7 |
| No anaemia | 3 | 1.6 |
| Total | 190 | 100.0 |

### Table 2. Presenting complaints

| Presenting complaints | Frequency | Percent |
|---|---|---|
| Generalized weakness | 91 | 47.89 |
| PV Bleeding | 25 | 13.15 |
| UGI bleeding (Melena) | 22 | 11.58 |
| SOB | 16 | 8.43 |
| Generalized body swelling | 10 | 5.27 |
| Increase in paleness | 6 | 3.16 |
| Myalgia | 7 | 3.68 |
| Other cause of Blood Loss | 13 | 6.84 |
| Total | 190 | 100.0 |

### Table 3. Peripheral Blood Smear Findings

| PBS finding | Frequency | Percent |
|---|---|---|
| Microcytic Hypochromic Anemia. | 85 | 44.7 |
| Normocytic Normochromic Anemia. | 93 | 49 |
| Microcytic Hypochromic Combined with Normocytic Normochromic Anemia. | 2 | 1.1 |
| Bicytopenia (MDS) | 1 | 0.5 |
| Spherocytes | 1 | 0.5 |
| Macrocytic Anemia | 3 | 1.6 |
| Combined Normocytic normochromic anemia with macrocytic hypochromic anemia | 1 | 0.5 |
| Normal PBS finding | 4 | 2.1 |
| Total | 190 | 100 |

About half of the patients (100, 52.63%) were diabetics(type II).Considering the years since diagnosis of chronic kidney disease showed that maximum number of people had been suffering

from chronic kidney disease for more than 10 years (106, 55.79%) followed by 5 to 10 years (106, 55.79%) and less than 5 years (54, 28.42 %) respectively (Table 4).

**Table 4. Years since diagnosis of chronic kidney disease**

| Years since diagnosis of CKD | Frequency | Percentage |
|---|---|---|
| **<5 years** | 54 | 28.42 |
| **5-10 years** | 30 | 15.79 |
| **> 10 years** | 106 | 55.79 |
| **Total** | 190 | 100 |

Table 5. illustrates the relationship between Gender, TLC and platelets with severity of anemia.

There was no significant relation of anemia in CKD with gender (p=0.583), duration of diabetes

(p=0.130) . However, a strong correlation was found between anemia in CKD with an abnormal

Total leucocyte count (p=0.002) and abnormal platelet count(p=0.000)

**Table 5. Relation of Gender, TLC and platelets with severity of anemia**

| Variables | | Anemia Severity | | | | | Total cases | p-value |
|---|---|---|---|---|---|---|---|---|
| | | Mild | Moderate | Severe | Life-threatening | No | | |
| **Gender** | Male | 33 | 50 | 10 | 5 | 0 | 98 | 0.583 |
| | Female | 32 | 46 | 7 | 4 | 3 | 92 | |
| **Duration of diabetes** | < 5 years | 19 | 26 | 3 | 3 | 2 | 53 | 0.130 |
| | 6 -10 years | 4 | 12 | 3 | 0 | 0 | 19 | |
| | 11 to 15 years | 36 | 48 | 11 | 5 | 1 | 101 | |
| | > 15 years | 6 | 10 | 0 | 1 | 0 | 17 | |
| **TLC** | <4000 | 3 | 2 | 3 | 4 | 1 | 13 | 0.001 |
| | Normal (4-11000) | 51 | 85 | 11 | 5 | 1 | 153 | |
| | >11000 | 11 | 9 | 3 | 0 | 1 | 24 | |
| **Platelets** | <150000 | 6 | 12 | 3 | 0 | 1 | 22 | 0.000 |
| | Normal (150-450000) | 58 | 82 | 12 | 9 | 2 | 163 | |
| | >450000 | 1 | 2 | 2 | 0 | 0 | 5 | |

## DISCUSSION

The higher percentage of anemia found in the study may be attributed to NKF criteria for anemia diagnosis, the cutoff of which is higher than that for general population. Also, the patients not having received renal replacement therapy in the past were taken in the study, causing higher incidence of anemia in CKD.

A study done among 387 participants in a Public Hospitals of Addis Ababa, Ethiopia showed the prevalence of anemia was 53.5%.[22] The prevalence in same study amongst females was double as compared to their counterparts.[22] Our study also showed higher prevalence among female population and the most common presenting complain among them being per vaginal bleed. A study conducted by Tadao et al. showed approximately 32% of Japanese patients with stage 3–5 CKD had anemia which is lower than our findings.[23]

Since, a considerable number of cases had plasmacytoma (10, 5.3%) which strongly mandates taking non-invasive tests like Peripheral Blood Smear (PBS) into consideration. We should avoid treating all anemic patient with iron therapy without adequate investigations. Plasmacytoma may be considered in a patient of CKD with anemia and persistent low back pain. Peripheral blood smear may be considered as non invasive initial investigating tool to differentiate various etiologies associated with CKD and plan further invasive procedures accordingly especially in the context of our country.

This cross-sectional study was undertaken in a single tertiary care hospital of Nepal. The enrolled patients were from the different parts of the country from different community. The study is a representation of the entire country, trying to provide as much data regarding study of type of anemia in CKD patient.

We found a high prevalence of anemia among chronic kidney disease as compared to other studies conducted in similar settings. Treatment of anemia may somehhow improve QOL, so, the higher value of hemoglobin level cutoff recommended by NKF, which we have used in our study, may help in early recognition and effective treatment in patients with CKD, thus improving QOL. However proper evidences lack for a benefit of anemia treatment on progression of kidney disease. The NKF recommends physicians to consider treating anemia in patients with diabetes and kidney disease when Hb is <11 g/dl in patients. They also recommend a Hb target of 11–12 g/dl, not to exceed 13 g/dl, when using an Erythropoiesis Stimulating Agents (ESA) as part of the therapeutic regimen for managing anemia. Currently available ESA combined with iron supplementation can be used safely and effectively to achieve this goal. However, available clinical trial evidence leaves sufficient uncertainty regarding the optimal Hb target and ESA dose for a given individual. For this reason, the NKF recommends individualizing treatment of anemia with ESA. Additional randomized clinical trials are needed to more precisely define these parameters for an individual patient. Future studies are also needed to elaborate the mechanisms of anemia in patients with diabetes and CKD including the role of iron metabolism, inflammation, and other co-morbidities.

## CONCLUSION

This study found that high prevalence of anemia among chronic kidney disease as compared to other studies conducted in similar settings. The higher percentage of anemia found in the study may be attributed to NKF criteria for anemia diagnosis, the cutoff of which is higher than that for general population. Also, the patients not having received renal replacement therapy in the past were taken in the study, causing higher incidence of anemia in CKD. Treatment of anemia may

somewhat improves quality of life. Thus, early recognition and effective treatment in patients with

CKD is highly recommended.

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