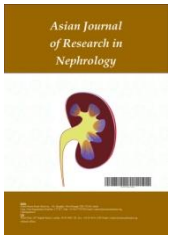

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# Evaluation of Iron Profile Status in Different Stages of Chronic Kidney Diseases (CKD)

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** Iron deficiency is common in Nepal due to low socioeconomic reason in pre-dialysis chronic kidney disease (CKD) patients than in the hemodialysis population. Little is known about the iron indices in CKD patients in Nepal.
**Aim:** The aim of this study was to evaluate the iron status among anemic pre-dialysis patients with different stages of CKD.
**Patients and Methods:** We used a cross-sectional study design to assess serum iron, ferritin, transferrin saturation (TSAT), and haemoglobin concentration in 70 pre-dialysis CKD patients with anaemia who came to our outpatient nephrology clinic. CKD was defined as a glomerular filtration rate less than 60 ml/min/1.73 m2 for 3 months or more, while anemia was defined as a hemoglobin concentration (Hb) less than 11 g/dl.
**Results:** The mean age of the study participants was 52.5 ± 13.2 years and 40 (57.1%) of the patients were males. The most common causes of CKD were diabetic nephropathy (45%) and hypertension (34%). The mean serum iron and mean TSAT were 95 ± 34.9 µg/dl and 28.9% ±

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13.8%, respectively.
**Conclusions:** Anemia due to iron deficiency is a hallmark of different stages of CKD patients, mostly moderate in severity with serum creatinine level > 3.0 g/dl. Hemoglobin and other iron profile aggravates with progressive loss of kidney functions.

*Keywords: Chronic kidney disease (CKD); iron profile; anemia.*

## 1. INTRODUCTION

"Anemia is an important and prevalent complication of chronic kidney disease (CKD) and causes increased morbidity and mortality" [1], "and end-stage renal disease (ESRD) is considered as a most serious outcome" [2]. of In anemia decrease of hemoglobin (Hb) levels is also established and in up to 68% of CKD patients with having a hemoglobin concentration (Hb) less than 11 g/dl at the time of starting dialysis [3,4]. "Recently, it has been appreciated that anemia begins to develop early in the course of CKD, and the prevalence of anemia in stage 3–5 CKD was 12.0%" [5]. "The causes of anemia in CKD is depends on number of factor such as with the decreased production of erythropoietin by the failing kidneys as one of the important cause and is the main determinant of anemia in stage 4-5 of CKD, apart from that chronic blood loss, reduced intestinal absorption, inflammation, infection, reduced red blood cells (RBC) survival, hyperparathyroidism, bone marrow depression, folate, iron and vitamin B12 deficiencies also contribute to the development of anemia in CKD" [6,7]. "Anemia due to iron deficiency is very common in patients with chronic kidney disease. One of important reason for iron deficiency may be due to poor dietary intake or sometimes occult bleeding, or an imbalance between the actual iron supply and iron requirements of the erythroid marrow. Other contributing factors for anemia in CKD include the presence of uremic inhibitors such as inflammatory cytokines, parathyroid hormone" [8].

Iron an important constituent of hemoglobin (Hgb) when deficiency of iron occurs it leads to impaired Hgb production [9,10]. Homeostasis of normal iron is maintained by compensating daily loss by absorption of dietary iron through duodenum [11]. "Number of evidence suggest that diabetes and hypertension to be the major causes of kidney disease worldwide" [12,13].

Therefore, the aim of this study was to determine iron profile levels among anemic pre-dialysis CKD patients attending the out-patient nephrology clinic at the Birat Medical College Teaching Hospital Tankisinuwari, Morang, Nepal.

## 2. PATIENTS AND METHODS

A total of 120 consecutively presenting pre-dialysis CKD patients attending renal outpatient were screened and 70 (seventy) adults above 17 years age, of either sex, diagnosed with CKD (pre-dialysis) were randomly selected as cases and 50 (fifty) healthy persons as controls. Patients providing informed consent and patients with documented chronic kidney disease were included in the study. The study was carried out between October 2021 and May 2022. All participating patients gave written informed consent. About 10 ml of blood was obtained from each patient for the determination of hemoglobin concentration, RBC indices, reticulocyte count as well as white blood cell count. Serum creatinine, serum ferritin, serum total iron, and unsaturated iron binding capacity were also determined by fully automated analyzer. "CKD was defined as the presence of markers of kidney damage and/or eGFR of <60 mL/min/1.73 m2 for at least three months" [14].

### 2.1 Statistical Analysis

Comparison between means was carried out using the student's t-test while comparison between percentages was carried out using chi square test. One-way Analysis of variance (ANOVA) and Kruskal–Wallis tests were used to compare participants' parameters across the stages of CKD. The level of statistical significance was set at a P value less than 0.05.

### 2.2 Definition of Terms

TSAT was calculated using the formula (TSAT) = Serum Iron/TIBC × 100[15]
Where TIBC (µg/dL) = iron level + UIBC and serum iron.

CKD was defined as the presence of markers of kidney damage and/or eGFR of 90 mL/min/1.73 m2 and/or persistent proteinuria;

Stage 2, eGFR of 60–89 mL/min/1.73 $m^2$ and/or persistent proteinuria;
Stage 3, eGFR of 30–59 mL/min/1.73 $m^2$;
Stage 4, eGFR of 15– 29 mL/min/1.73 $m^2$; and
Stage 5, eGFR <15ml/min/1.73 $m^2$[16]

## 3. RESULTS

70 diagnosed cases of pre-dialyzed chronic kidney disease patients were included in the study and 50 healthy persons as controls. Majority (48.5%) of the participants belonged to 41 to 60 year age group and mostly belongs to male category (Fig. 1).

The mean age of CKD patients and controls in males were 54.8±12.9 and 56.4±13.8 respectively, while there were 50.8±11.6 and 52.9±12.7 mean age of CKD and controls in female patients respectively. The difference was not statistically significant (*P* = 0.44 in male and 0.34 in case of female). Out of 70 CKD patients ten (14.3%) were in Stage 1, 9(12.8%) in Stage 2, 22 (31.4%) in Stage 3, 17 (24.2%) in Stage 4, and the remaining 12 (17.1%) were in Stage 5 (Table 1).

The etiology of CKD in the study were diabetes mellitus (45%), hypertension (34%), chronic glomerulonephritis (14%), chronic pyelonephritis (4%) and polycystic kidney disease (3%) (Fig. 2).

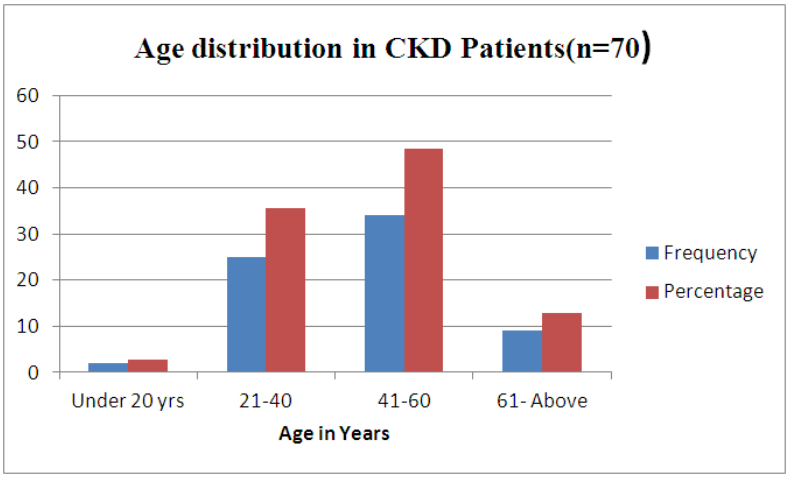


**Fig. 1 Age distribution in CKD patients (n=70)**

**Table 1. Characteristics of the study population**

| Gender | CKD patients (Mean±SD) | Control (Mean±SD) | p-value |
|---|---|---|---|
| Male | 54.8±12.9 | 56.4±13.8 | 0.44 |
| Female | 50.8±11.6 | 52.9±12.7 | 0.34 |
| Stages of CKD | n (%) | | |
| 1 | 10(14.3) | | |
| 2 | 9(12.8) | | |
| 3 | 22(31.4) | | |
| 4 | 17(24.2) | | |
| 5 | 12(17.1) | | |

**Table 2. Biochemical parameters among control and CKD patients**

| Sr.No | Parameter | Cases n=(70) | Control n=(50) | P- value |
|---|---|---|---|---|
| **1.** | Serum iron (µg/dl) Mean±SD | 95±34.9 | 109.1±25.9 | 0.017 |
| **2.** | TIBC (µg/dl) Mean±SD | 331±68.1 | 310±43.1 | 0.05* |
| **3.** | Transferrin saturation (%) Mean±SD | 28.9±13.8 | 34.2±5.2 | 0.01 |
| **4.** | Serum Ferritin (ng/ml) | 220.12±112.78 | 150.6±64.57 | <0.0001* |
| **5.** | Serum Creatinine (mg/dl) Mean±SD | 6.9±2.8 | 1.2±0.2 | <0.0001* |
| **6.** | e GFR (mL/min/1.73 $m^2$) | 37.82±27.96 | 112.23±39.84 | <0.0001* |

**p value is significant*

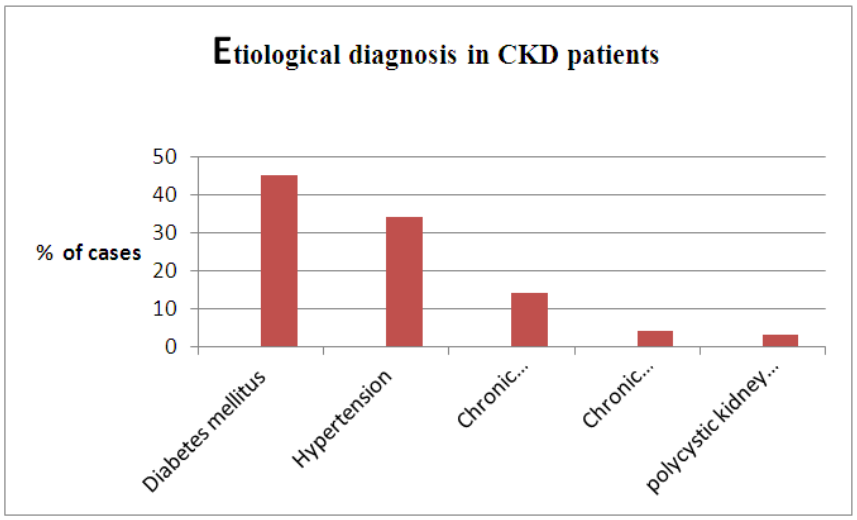


**Fig. 2 Etiological diagnosis in CKD patients (n=70)**

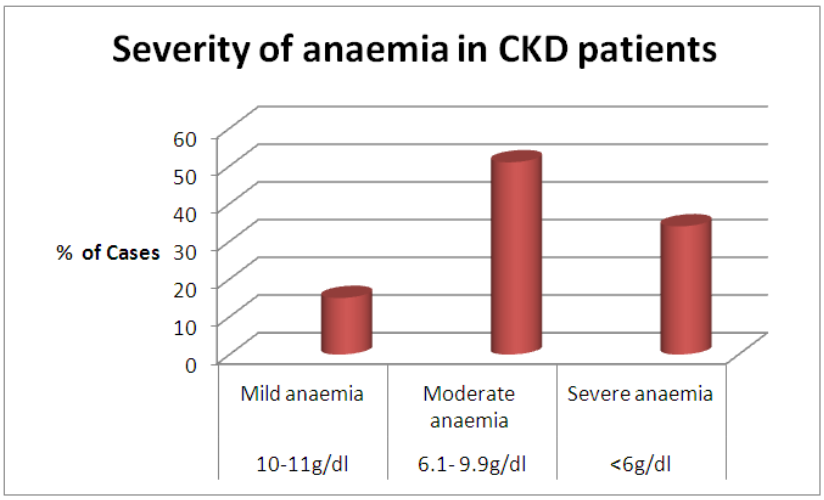


**Fig. 3. Severity of anemia in CKD patients (n=70)**

The mean serum creatinine was significantly higher in the CKD group compared to the control (6.9±2.8 vs 1.2±0.2; P <0.0001) while e GFR was significantly lower in compared to control (37.82±27.96 vs 112.23±39.84; P<0.001). The mean of serum iron (95±34.9), TIBC (331±68.1 vs 310±43.1; P<0.005) and transferrin saturation (TSAT) (28.9±13.8) in CKD patients. In the CKD group, serum iron was considerably lower than in the control group, although TIBC were significantly greater in CKD patients compared to the control group (Table 2). The ferritin level was significantly higher in the study group (220.12 ng/mL) than in the control group (150.6 ng/mL).

All the cases were anemic with hemoglobin concentration (Hb) below 11g/dl and the mean hemoglobin concentration was (8.68±24.9) g/dl) compared to control (12.89±8.64). The mean Hb level in males was 8.1±2.4 g/dl and in females was 6.9±1.6 g/dl. The proportions with mild, moderate and severe anemia among CKD subjects were 15%, 51% and 34% respectively (Fig. 3).

## 4. DISCUSSION

"Iron deficiency is very common in CKD patients. Anemias cause by iron deficiency widespread in most the part of the world, mostly prevalent in the central and West Africa and South Asia including Nepal" [17]. Total serum iron (95±34.9) and the serum ferritin (220.12±112.78) in the present study were in accordance with the study by Deori

et al 2016 [18], and by Singh et al 1999[19] respectively (Table 3). Ferritin is one of the acute phase reactant and, is frequently increased in patients with different stages of CKD, irrespective of their iron stores [20,21]. Increased ferritin levels in CKD are due to systemic inflammation because ferritin synthesize in response to inflammatory cytokines [22].

The most important etiological factor was diabetes (45%) and hypertension (34%) which was almost similar to the study of William Mcclellan et al [23] (Table 4).

In our study we observed a significant decrease in hemoglobin as the CKD stage progresses, and majority of the CKD patients were anemic having hemoglobin level less than 11g/dl, the moderate degree of anemia is in 51% of CKD patients like Ashfar R et al [24,25] this statistically significant and correlated well with the different stages of CKD.

The mean hemoglobin levels among CKD cases was 8.68±2.49 while mean hemoglobin in stage 2 was 12.9 g/dl, in stage 3 was 10.2 g/dl while in stage 4 was 8.3 g/dl. Talwar et al. [26] and Singh et al. [27] observed lower hemoglobin similar to present study i.e. 7.1 g/dl and 6.93 g/dl among CKD cases. A high prevalence and strong association of anemia has been reported in all stages of CKD by Poudel et al [28].

The overall iron deficiency increased through stage 3 to stage 5 of CKD, and most of the patients in this of CKD receive erythropoietin and parenteral iron to prevent anemia and morbidities associated with anemia which may cause an iron overload in patients with functional iron deficiency. Apart from that inflammation which affects iron status is more prevalent in CKD patients, we could find out its presence in our study participants.

**Table 3. Comparison of serum iron profile in CKD**

| Sr.No | Parameter | Present study | Talwar et al 2002[26] | Singh et al 1999[27] | Jairam et al 2010[28] | Deori Et al 2016[18] |
|---|---|---|---|---|---|---|
| 1. | Serum iron (µg/dl) | 95 | 55.1 | 124.93± 123.6 | 153.4± 31.6 | 98± 37.08 |
| 2. | TIBC (µg/dl) | **331** | - | - | 476.39± 137.3 | 345.22± 75.43 |
| 3. | Serum ferritin (ng/dl) | 220 | 30.4 | 259.33± 122.05 | 331.7± 39.56 | - |
| 4. | Transferrin saturation (%) | 28.9 | - | - | - | 30.78± 14.45 |

**Table 4. Comparison of serum iron profile in CKD**

| Sr.No | Parameter | Present study | Ashfar R et al [24] | William Mcclellan et al [23] | Seuga K et al[25] |
|---|---|---|---|---|---|
| 1. | Etiological factor | Diabetes mellitus (45%), hypertension (34%), chronic glomerulonephritis (14%), and polycystic kidney disease (3%) | Diabetes 49.1%, hypertension 28.3%, glomerular disease 17.1% and polycystic kidney disease 5.6% | Diabetes 49.5%, hypertension 33.0% | - |
| 2. | Severity of Anemia | Mild, moderate and severe anemia were 15%, 51% and 34% respectively | 55% moderate and 45% mild | - | 50% moderate and 50% mild |
| 3. | Hb (g/dl) | 8.68±24.9 | 11.11±2.26 | | |

There was some limitation of our study is that sample size was small and inability to investigate the full spectrum of etiologies of anemia in observed population due to high test cost of investigations and the absence of funding for the study.

## 5. CONCLUSION

Anemia due to is iron deficiency is a hallmark of different stages of CKD patients, mostly of moderate in severity with serum creatinine levels >3.0 mg/dl. With the increasing loss of kidney function, such as a decline in eGFR and a rise in blood creatinine levels, haemoglobin and other iron profiles deteriorate.

## CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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