



# Analysis of Red Cell Parameters in Patients with Anemia in Chronic Kidney Disease

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## ABSTRACT

Chronic kidney disease is one of the most dreaded diseases having a huge prevalence. Anemia is one of the most important complications of the disease process particularly in patients undergoing hemodialysis having a significant effect on quality of life and cardiovascular manifestations. Our study is on determining iron deficiency through iron studies and red cell parameters in various stages of CKD.

## METHODS

Hundred cases of Chronic Kidney disease were randomly selected for the study done between November 2020 and December 2022. According to the proforma, thorough history and physical examination done, data collection is done.

## RESULTS

Most common presenting symptom of anemia is easy fatigability (62%), followed by pedal edema (49%), facial puffiness (31%), dyspnea (19%) and decreased urine output (18%). 70% of them are diabetics, 52% are hypertensive and 21% have both the comorbidities. Majority of the patients (56%) are in Stage 5 of CKD, followed by 32% in Stage 4, 8% in Stage 3 and 4% in Stage 2. Mean Creatinine values are  $4.69 \pm 2.01$  mg/dl. Mean Hemoglobin values is  $8.23 \pm 1.33$  gm/dl When severity of anemia is compared with stage of renal failure, there is a positive statistical co-relation, severe anemia is more commonly seen in Stage 5 of CKD ( $p = 0.03$ ). 71% of the patients show normocytic normochromic picture on peripheral smear while 27% show microcytic hypochromic picture and 2% show macrocytic hypochromic picture.

Mean values of various red cell parameters are, RBC count is  $2.4395 \pm 0.79 \times 10^6$  cells/microliter, PCV of  $25.12 \pm 0.07\%$ , MCV value is  $76.15 \pm 8.15$  fl, MCH value is  $26.83 \pm 2.11$  pg/cell, MCHC value is  $31.73 \pm 8.15$  gm/dl, RDW value is  $18\% \pm 3\%$ . There is a positive co relation when compared to various stages of Chronic Kidney Disease. Mean values of various serum iron studies

are, Serum Ferritin is  $31.91 \pm 11.97$  mcg/dl, Serum Iron is  $57.22 \pm 91.5$  mcg/dl, TIBC is  $312.5 \pm 16.56$  mcg/dl, Transferrin Saturation is  $18\% \pm 3\%$ ,

## CONCLUSION

Anemia worsens as the stage of Chronic Kidney Disease progresses along with the red cell parameters indicating iron deficiency indirectly. Serum iron studies also show an iron deficiency requiring the need for iron supplementation.

## I. INTRODUCTION

Chronic Kidney Disease is a significant non-communicable disease having a high prevalence in India. The disease process involves permanent and irreversible destruction on nephrons thereby leading to a reduction in its number and thereby its excretory capacity. There are a number of endocrine and metabolic complications leading to increased morbidity and mortality.

Anemia is one of the most common complications of Chronic Kidney Disease. Its incidence increases as the disease process worsens, the End Stage Renal Disease having affected the maximum. A number of different mechanisms have been put forward to explain the pathophysiology of the underlying condition.

Anemia has a significant morbidity in patients with Chronic Kidney Disease including reduced exercise tolerance, increased cardiovascular events and reduced quality of life. Iron deficiency is one of the most important reversible causes of anemia especially in patients undergoing hemodialysis; hence Red cell parameters and iron studies form an important part of the diagnostic workup of anemia in Chronic Kidney Disease.

KDIGO defines anemia in a CKD patient when the Hemoglobin (Hb) values are less than 13 mg/dl in a male and 12 mg/dl in a female patient (1). These values are similar to the definition of anemia given by the World Health Organization (WHO). Studies have shown Hb values decrease proportionately with a fall in eGFR levels, most of them showing a decline below  $75 \text{ ml/min/1.73 m}^2$  in men and  $50 \text{ ml/min/1.73 m}^2$  in women. (2) Hb values drop



significantly in Stage 5 of the disease (3). Although anemia develops independent of progression of CKD, diabetic patients tend to form a greater proportion of anemic cases and CKD due to Polycystic Kidney disease have higher Hb values (1)(4).

There is decreased rate of production of RBC from the normal bone marrow and decreased life span of RBC, the former mechanism being more significant than the latter. The bone marrow responds to this reduction but is inadequate. The response to hypoxia is seen in anemic conditions.

In CKD, kidneys undergo fibrosis, during this process there is transdifferentiation of fibroblasts into myofibroblasts, thus losing their ability to produce normal EPO response to hypoxia.

Risk of hemorrhage and mortality is more in CKD patients compared to normal study population, highest incidence in patients undergoing hemodialysis. Causes include:

(a) Peptic Ulcer Disease, Gastritis and Duodenitis:(b) Angiodysplasia(c) Systemic vasculitis

Around 5-6 mg/day of iron is lost in patients undergoing hemodialysis compared to normal individuals. This is not adequately compensated by oral absorption either, due to underlying inflammation due to upregulation of Hcpidin.

CKD produces a normocytic anemia and hence the PCV values are usually within the normal range.

## II. METHODOLOGY

### SOURCE OF DATA

In the current study, 100 cases diagnosed of Chronic Kidney Disease admitted to AJ Institute of Medical Sciences between December 2020 and December 2022 were considered. They were selected based on Simple Random Sampling method. Patients were diagnosed and staged according to CKD-EPI equation.

### METHODS OF COLLECTION OF DATA

#### (1) INCLUSION CRITERIA

- A. Patients above the age of 18.
- B. Definition of Chronic Kidney Disease according to KDOQI and KDIGO guidelines that CKD is defined by the presence of kidney damage or decreased kidney function for three or more months, irrespective of the cause. Glomerular filtration rate (GFR)  $<60$  mL/min/1.73 m<sup>2</sup>. Kidney damage, as defined by structural abnormalities or functional abnormalities other than decreased GFR (5).
- C. Patients enrolled in the study were required to have been clinically stable for 3 months preceding study entry, with no clinically

significant cardiovascular, neurologic, pulmonary, endocrine, genitourinary, or renal system disease that was not well controlled.

- D. Definition of Anemia according to National Health and Nutrition Examination Survey (NHANES) hemoglobin [Hb]  $<12$  g/dL in men and  $<11$  g/dL in women. The National Kidney Foundation's kidney dialysis outcome quality initiative recommends a workup for anemia in patients with CKD if hemoglobin level less than 11 gm/dl in premenopausal women and pre pubertal patients and when the hemoglobin less than 12 gm/dl in adult men and postmenopausal women. The world health organization defines anemia as a hemoglobin concentration lower than 13 gm/dl in men and postmenopausal women and lower than 12 gm/dl in other women.

#### (2) EXCLUSION CRITERIA

- A. Received dialysis within the past 2 months.
- B. Received treatment with Epoetin Alfa (including clinical study of Epoetin Alfa or any investigational forms of erythropoietin therapy)
- C. Received iron supplementation within the past 3 months.
- D. Received cytotoxic drug therapy within the past 3 months
- E. Known diagnosis of human immunodeficiency virus, vitamin B12 or folate deficiency, hemolytic anemia, active gastrointestinal bleeding.
- F. Current treatment with drugs known to be nephrotoxic (i.e. aminoglycosides).

## III. RESULTS

Among 100 patients with CKD, maximum incidence of 34 (34%) seen in age group of 51 to 60 years. Patients in the group are from 34 to 80 years. Mean age group of the patients is  $56.15 \pm 10.32$  years, 56% are male and 44% are female. Male: Female ratio is 1.27:1, most common presenting symptom is easy fatigability (62%), followed by pedal edema (49%), facial puffiness (31%), dyspnea (19%) and decreased urine output (18%), 70% of them are diabetics, 52% are hypertensive and 21% have both the comorbidities, majority of the patients (56%) are in Stage 5 of CKD, followed by 32% in Stage 4, 8% in Stage 3 and 4% in Stage 2. Mean Creatinine values are  $4.69 \pm 2.01$  mg/dl. Mean eGFR values are  $18.84 \pm 13.53$  mL/min/1.73 m<sup>2</sup>. Mean Hemoglobin values is  $8.23 \pm 1.33$  gm/dl, within a range of 4.9



gm/dl to 11.9 gm/dl. 48% of these patients have severe anemia, 43% have moderate anemia and 9% have mild anemia.

Among 48 patients with severe anemia (<8 gm/dl), 31 patients (64.58%) are in Stage 5 of CKD, 14 patients (29.17%) in Stage 4, 2 patients (4.17%) in Stage 3 and 1 patient (2.08%) in Stage 2 CKD.

Among 43 patients with moderate anemia (8-10 gm/dl), 22 patients (51.16%) are in Stage 5 of CKD, 16 patients (37.21%) in Stage 4, 4 patients (9.30%) in Stage 3, 1 patient (2.33%) in Stage 2 CKD.

Among 9 patients with mild anemia (>10 gm/dl), 3 patients (33.33%) in Stage 5 of CKD, 2 patients (22.22%) in each of Stage 4, 3 and 2 of CKD.

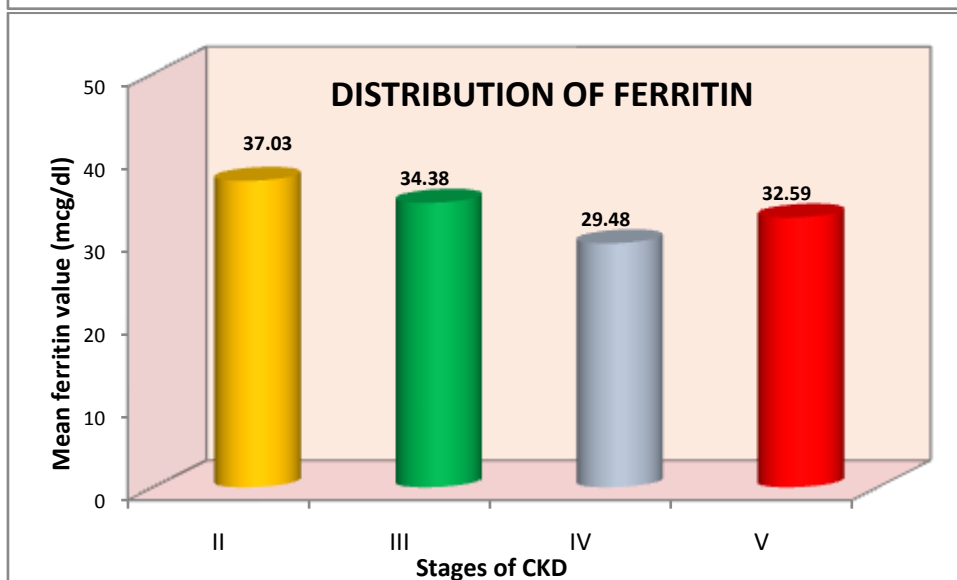
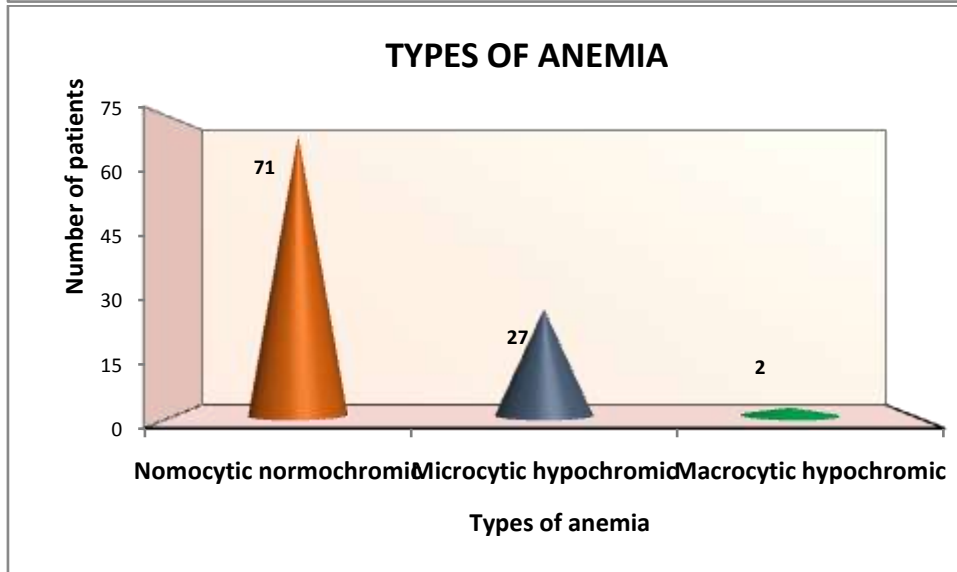
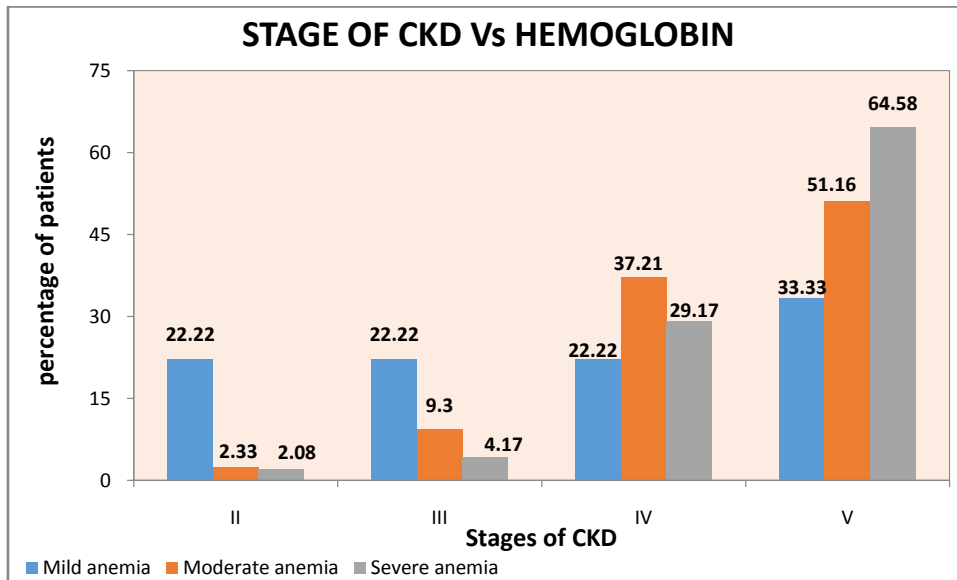
When severity of anemia is compared with stage of renal failure, there is a positive statistical co-relation, severe anemia is more commonly seen in Stage 5 of CKD ( $p=0.03$ ), 71% of the patients show normocytic normochromic picture on peripheral smear while 27% show microcytic hypochromic picture and 2% show macrocytic hypochromic picture, Mean RBC count is  $2.4395 \pm 0.79 \times 10^6$  cells/microliter, within a range of 1.25 to  $4.16 \times 10^6$  cells/microliter. 78% of patients have counts less than  $3 \times 10^6$  cells/microliter, among them 50 patients (64.10%) in Stage V, 25 patients (32.05%) in Stage IV, 3 patients (3.84%) in Stage III while none in Stage II. 22% have counts more than  $3 \times 10^6$  cells/microliter, among them 7 patients (31.81%) in Stage IV, followed by 6 patients (27.27%) in Stage V, 5 patients (22.72%) in Stage III and 4 patients (18.18%) in Stage II. There is a positive co-relation when RBC count is compared with the stage of CKD ( $p=0.0000091$ ), Study patients have a mean PCV of  $25.12 \pm 0.07\%$  in range of 11.56% to 42.56%. 75% of the patients have PCV value less than 30% among them, 50 patients (66.66%) in Stage V, 24 patients (32%) in Stage IV, 1 patient (1.33%) in Stage III and none in Stage II. 25% of patients have values more than 30% among them 8 patients (32%) in Stage IV, 7 patients (28%) in Stage III, 6 patients (24%) in Stage V and 4 patients (16%) in Stage II. There is a positive co-relation when PCV values is compared with the stage of CKD ( $p=0.0000001$ ), Mean MCV value is  $76.15 \pm 8.15$  fl in range of 64.13 fl to 106.49 fl. 77% of the patients have MCV values less than 80 fl, among them 53 patients (68.83%) are in Stage V followed by 23 patients (29.87%) in Stage IV, 1 patient (1.29%) in Stage III and none in

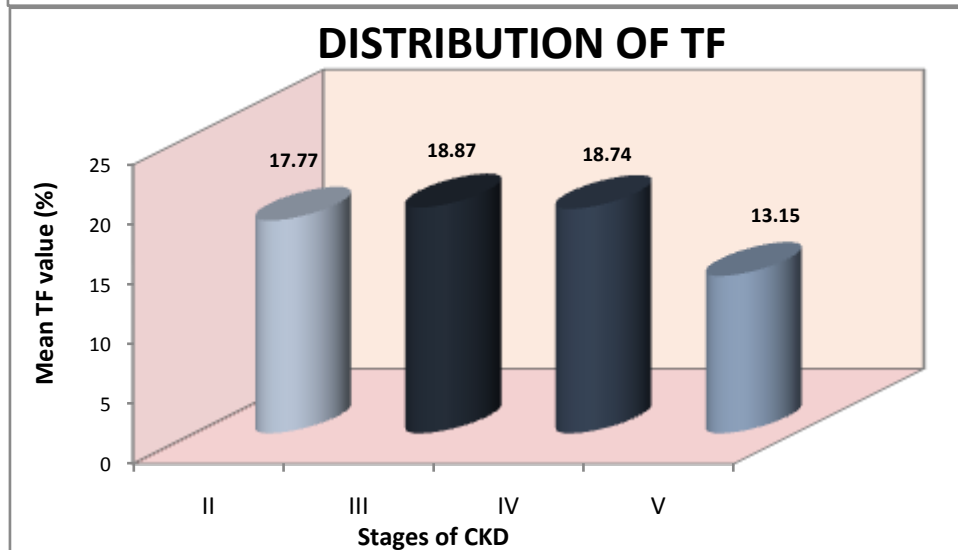
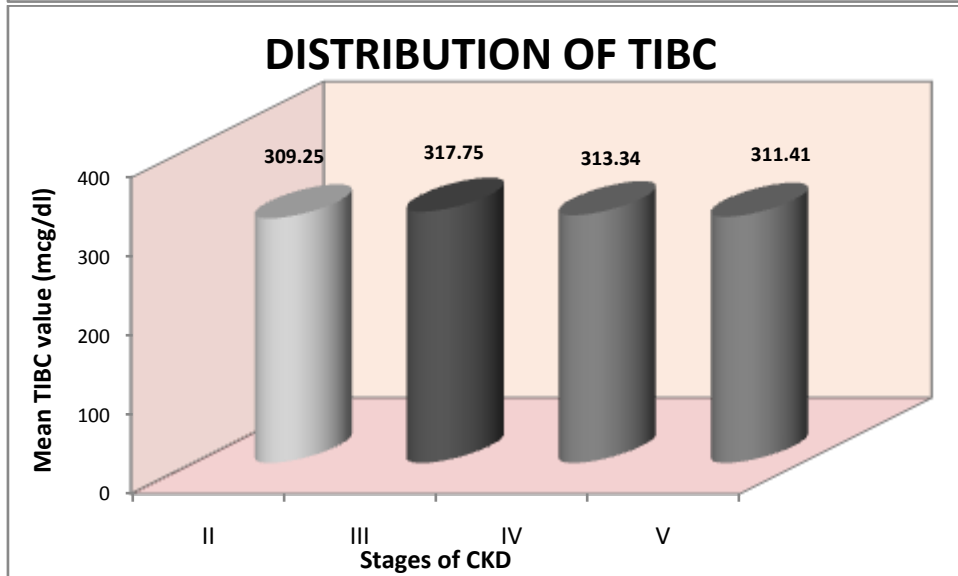
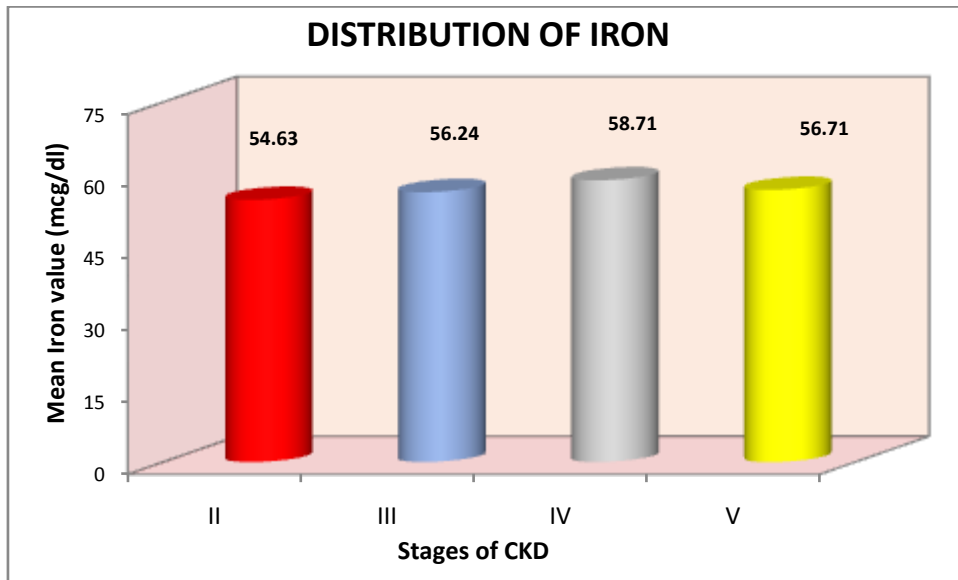
Stage II. 5% of the patients have MCV values more than 94 fl. There is a positive co-relation when MCV values is compared with the stage of CKD ( $p=0.000000001$ ), Mean MCH value is  $26.83 \pm 2.11$  pg/cell in range of 64.13 pg/cell to 106.49 pg/cell. 52% of the patients have MCV values less than 27 pg/cell, among them 34 patients (65.38%) are in Stage V followed by 17 patients (32.69%) in Stage IV, 1 patient (1.92%) in Stage III and none in Stage II. There is a positive co-relation when MCH values is compared with the stage of CKD ( $p=0.011$ ), Mean MCHC value is  $31.73 \pm 8.15$  gm/dl in range of 29.1 gm/dl to 34.8 gm/dl. 77% of the patients have MCHC values less than 32 gm/dl, among them 35 patients (66.03%) are in Stage V followed by 15 patients (28.30%) in Stage IV, 2 patients (3.77%) in Stage III and 1 patient (1.88%) in Stage II. 5% of the patients have MCHC values more than 94 fl. There is a positive co-relation when MCHC values is compared with the stage of CKD ( $p=0.098$ ), Mean RDW value is  $18\% \pm 3\%$  fl in range of 12% to 26%. 76% of the patients have RDW values more than 14, among them 43 patients (56.57%) are in Stage V followed by 24 patients (31.57%) in Stage IV, 5 patients (6.57%) in Stage III and 4 patients (5.26%) in Stage II. There is a positive co-relation when RDW values is compared with the stage of CKD ( $p=0.011$ ). Mean value of Serum Ferritin is  $31.91 \pm 11.97$  mcg/dl, values ranging from 10.5 mcg/dl to 55.6 mcg/dl. Mean values across different stages show highest in Stage II (37.03 mcg/dl), followed by Stage III (34.38 mcg/dl), Stage V (32.59 mcg/dl) and the lowest in Stage IV (29.48 mcg/dl).

Mean value of Serum Iron is  $57.22 \pm 91.5$  mcg/dl, values ranging from 34.3 mcg/dl to 79.3 mcg/dl. Mean values across different stages show highest in Stage IV (58.71 mcg/dl), followed by Stage V (56.71 mcg/dl), Stage III (56.24 mcg/dl) and lowest in Stage II (54.63 mcg/dl).

Mean value of TIBC is  $312.5 \pm 16.56$  mcg/dl, values ranging from 285 mcg/dl to 344 mcg/dl. Mean values across different stages show highest in Stage III (317.75 mcg/dl), followed by Stage IV (313.34 mcg/dl), Stage V (311.41 mcg/dl) and lowest in Stage II (309.25 mcg/dl).

Mean value of Transferrin Saturation is  $18\% \pm 3\%$ , values ranging from 12% to 26%. Among these, 71% of the patients have values less than 20%. Mean values across different stages show lowest in Stage V (13.15%), followed by Stage II (17.77%), Stage IV (18.74%) and highest value in Stage III (18.87%).







#### IV. DISCUSSION

Most of the 100 study patients have severe anemia (48%), 43% have moderate anemia and 9% have mild anemia. The values are significantly different than the previous studies as the cut offs to classify severity of anemia is not the same as the other ones. We have used the National Cancer Institute scale to classify anemia in our study (cite). A positive co-relation is found between the number of patients with severe anemia and the stage of CKD ( $p=0.03$ ) indicating that anemia worsens with worsening eGFR similar to the co-relation found in Arun et al. On the peripheral smear, 71% of the patients in our study have normocytic normochromic, 27% have microcytic hypochromic and 2% have macrocytic picture. Our values are not comparable to those found in previous studies. Mean RBC count is  $2.4395 \pm 0.79 \times 10^6$  cells/microliter which is not comparable to counts found in previous studies. Mean PCV is  $25.12 \pm 0.07\%$  which is comparable to value found in Iyawe et al. Mean MCV value is  $76.15 \pm 8.15$  fl which is comparable to value shown in Iyawe et al. Mean MCH value is  $26.83 \pm 2.11$  pg/cell which is comparable to the value found in Talwar et al. Mean MCHC value is  $31.73 \pm 8.15$  gm/dl

which is comparable to values found in Iyawe et al and Talwar et al. Mean RDW value is  $18\% \pm 3\%$  which is not comparable to any of the previous studies. However there is a statistically significant co-relation between the red cell parameters and the stage of CKD (RBC  $p = 0.0000091$ , PCV  $p = 0.0000001$ , MCV  $p = 0.000000003$ , MCH  $p = 0.011$ , MCHC  $p = 0.098$ , RDW  $p = 0.011$ ) all the counts in a decreasing trend as the eGFR worsens which has not been shown in any of the previous studies. These values signify iron deficiency indirectly and can be considered in a primary care setting or a center where iron studies are not available, can further guide the treatment strategy. Mean value of Serum Ferritin is  $31.91 \pm 11.97$  mcg/dl and Serum Iron is  $57.22 \pm 91.5$  mcg/dl, both of them comparable to values found in Talwar et al. Mean value of TIBC is  $312.5 \pm 16.56$  mcg/dl and Transferrin Saturation is  $18\% \pm 3\%$ , both of them are not comparable to any of the studies done previously. Values of iron studies could not be co-related with the stage of CKD as definitive cut-offs for low values could not be established. However we conclude the presence of iron deficiency in patients with anemia of renal failure and highlight the need for iron supplementation. Majority of the patients have TSAT values less than 20% indicating the need for EPO supplementation.

#### V. CONCLUSION

In our study, we conclude that anemia worsens as CKD progresses to stage V with majority of severe anemia cases seen in Stage V and IV respectively. The red cell parameters progressively decline with the worsening eGFR indirectly indicating the presence of iron deficiency. The iron studies conclude the presence of iron deficiency as the cause of anemia in CKD.

Both the red cell parameters and iron studies can guide iron supplementation and EPO therapy respectively, hence highlighting their importance in the workup of anemia in CKD patients.

#### REFERENCES

- [1]. Locatelli F, Nissenson AR, Barrett BJ, Walker RG, Wheeler DC, Eckardt KU, et al. Clinical practice guidelines for anemia in chronic kidney disease: problems and solutions. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* 2008 Nov;74(10):1237–40.
- [2]. Astor BC, Muntner P, Levin A, Eustace JA, Coresh J. Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988-1994). *Arch Intern Med.* 2002 Jun 24;162(12):1401–8.
- [3]. McClellan W, Aronoff SL, Bolton WK, Hood S, Lorber DL, Tang KL, et al. The prevalence of anemia in patients with chronic kidney disease. *Curr Med Res Opin.* 2004 Sep;20(9):1501–10.
- [4]. Pisoni RL, Bragg-Gresham JL, Young EW, Akizawa T, Asano Y, Locatelli F, et al. Anemia management and outcomes from 12 countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis Off J Natl Kidney Found.* 2004 Jul;44(1):94–111.
- [5]. Stevens PE, Levin A, Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med.* 2013 Jun 4;158(11):825–30.
- [6]. Iyawe. Hematological profile of predialysis chronic kidney disease patients in a tertiary hospital in Southern Nigeria [Internet]. [cited 2023 Jan 18]. Available from:



- <https://www.jmedtropics.org/article.asp?issn=2276-7096;year=2018;volume=20;issue=1;spage=36;epage=41;aulast=Iyawe>
- [7]. Shastry. The spectrum of red blood cell parameters in chronic kidney disease: A study of 300 cases [Internet]. [cited 2023 Jan 18]. Available from: <https://www.jahjournal.org/article.asp?issn=1658-5127;year=2019;volume=10;issue=2;spage=61;epage=66;aulast=Shastry>
- [8]. Jairam A, Das R, Aggarwal PK, Kohli HS, Gupta KL, Sakhuja V, et al. Iron status, inflammation and hepcidin in ESRD patients: The confounding role of intravenous iron therapy. *Indian J Nephrol.* 2010 Jul;20(3):125–31.
- [9]. Talwar VK, Gupta HL, Shashinarayan null. Clinicohaematological profile in chronic renal failure. *J Assoc Physicians India.* 2002 Feb;50:228–33.
- [10]. Khadayate R, Sahu P, Sahu S. Study of Hematological Profile in Chronic Renal Failure Patients on Hemodialysis in a Tertiary Care Hospital. *Int J Health Sci Res.* 2020;10(12):1–7.