

# Profile of Anemia in Chronic Kidney Disease Patients at a Rural Tertiary Care Centre: A Prospective Observational Study

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## ABSTRACT

**Introduction:** Anemia is a very common manifestation among patients of CKD. As the renal dysfunction increases in severity, there is proportional increase in prevalence and severity of haematological impairment. There is increased incidence of cardiovascular dysfunction, cognitive impairment and sleep disturbances in anemic patients with CKD. It is also associated with progression of renal disease and increased mortality. This study was conducted to study the profile of Anemia in Chronic Kidney Disease patients at a rural tertiary care centre in North India.

**Material and Methods:** This prospective observational study was done on 100 patients of CKD taken from Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. Chronic kidney disease (CKD) was defined as per Kidney Dialysis Quality Initiative (KDOQI) guideline.

**Results:** The mean age of the study population was 52.4 years. The mean Hemoglobin level in our study was  $8.39 \pm 1.71$  g/dL. The most common profile seen on peripheral blood smear was normocytic normochromic anemia (76%), followed by microcytic hypochromic picture seen 22% patients. Mean Hemoglobin level and RBC indices (MCV, MCH, MCHC) were significantly lower in patients receiving hemodialysis.

**Conclusion:** Anemia is a very common clinical manifestation in patients of Chronic Kidney Disease. Severity of Anemia increases with progressive renal damage. Patients receiving hemodialysis are more anemic as compared to non-dialyzed CKD patients.

**Key words:** Anemia, Erythropoetin, Chronic Kidney Disease, Hemodialysis, GFR

## INTRODUCTION

Chronic Kidney Disease is a major health care problem worldwide, with a global prevalence of 8-16%.<sup>1</sup> The US national kidney foundation's kidney dialysis quality initiative (KDOQI) guideline defines CKD as kidney damage or estimated GFR (eGFR  $<60$  ml/min/1.73m<sup>2</sup>) for more than equal to 3 months.<sup>2</sup> Chronic Kidney Disease leads to a wide range of systemic derangements. Anemia is a very common manifestation among patients of CKD.<sup>3,4</sup> As the renal dysfunction increases in severity, there is proportional increase in prevalence and severity of haematological impairment. Studies have shown that Anemia begins to manifest when GFR falls below 60ml/min/1.73 m<sup>2</sup> (Stage III).<sup>5</sup> Accordingly, The prevalence of anemia ranges from about 1% in stage 2 of CKD to almost 100% in end stage renal disease (ESRD) patients.<sup>6</sup>

Pathophysiologically, Anemia in patients of CKD is determined by multiple factors.<sup>7</sup> The most important and

primary factor is the deficient production of Erythropoetin (EPO) by the damaged kidneys.<sup>8</sup> Kidney is a major site for EPO production, contributing 80-90% of total EPO in circulation (rest 10-20% produced in liver). As renal disease progresses specialized peritubular cells that produce EPO are partially or completely depleted or injured resulting inappropriately low EPO levels resulting in progressive Anemia. Other important factors contributing to development of Anemia in CKD include nutritional deficiencies (Iron, folate or vitamin b12), increased blood loss, systemic and chronic inflammatory state, hyperparathyroidism, shortened red cell survival by uremic toxins and drugs.<sup>9</sup> The most common peripheral blood picture in Anemia of CKD is normocytic normochromic type.

Anemia is an important contributing factor in the clinical manifestations associated with deteriorating renal function. There is increased incidence of cardiovascular dysfunction, cognitive impairment and sleep disturbances in anemic patients with CKD. It is also associated with progression of renal disease and increased mortality.<sup>3,10</sup> Increased healthcare costs and worsened quality of life are other issues of concern in CKD patients with Anemia.<sup>3</sup> Therefore, evaluation of prevalence and etiological profile of Anemia in Chronic Kidney Disease patients at the regional level is important from the point of view of optimum allocation of health care resources, especially in resource limited settings in developing countries like India. This study was conducted to study the profile of Anemia and the impact of Hemodialysis on anemia in Chronic Kidney Disease patients at a rural tertiary care centre in North India.

## MATERIAL AND METHODS

This prospective observational study was done in Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. The study was

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done over a period of one year from September 2015 to August 2016 after approval from the Institutional Ethics Committee. 100 patients of Chronic Kidney Disease presenting to outpatient and indoor facilities in Department of Medicine were included in the study. Chronic kidney disease (CKD) was defined as per Kidney Dialysis Quality Initiative (KDOQI) guideline i.e kidney damage or estimated GFR (eGFR <60 ml/min/1.73m<sup>2</sup>) for more than equal to 3 months.

#### Inclusion Criteria

1. Patients with chronic kidney disease with stage I –V disease.
2. Age > 18 years

#### Exclusion Criteria

1. Patients with other systemic illness without renal failure
2. Pregnancy
3. Aplastic anemia
4. Known hematological malignancy causing secondary renal failure
5. History of blood transfusion during last three months.
6. Patients who refused written consent

#### Method of collection of data

After verification of the inclusion and exclusion criteria, the study design and purpose was explained in detail to all the selected subjects and written informed consent was taken. Detailed history including past and treatment history was elicited. Complete physical examination was performed. The patients were categorized according to their Creatinine Clearance measured by Cockcroft-Gault equation (140-age x body wt., kg/72 x Creatinine).

Anemia was defined as Hb <12 g/dl in adult males and postmenopausal females and <11 g/dl in premenopausal females and prepubertal persons. Further, Anemia was categorized into mild, moderate and severe with Hb% of 9-11 gm%, 7-9 gm% and <7 gm% respectively as per WHO anemia classification. Blood was collected under aseptic precautions for hematological (Complete Hemogram, peripheral blood smear, Reticulocyte count, serum Ferritin) and biochemical (Blood Urea, Serum Creatinine, Serum Electrolytes) investigations. Hematological profile was done on the standard automated analyzer. Other relevant investigations including Urine complete examination and abdominal Ultrasound were done.

#### STATISTICAL ANALYSIS

The data collected from the study subjects was tabulated and analyzed statistically by using SPSS software version 18. The data for continuous variables was expressed as Mean ± S.D. and categorical data was expressed as frequencies and percentages. Student t test was applied to analyze statistical difference for continuous variables while chi square test was used to compare the categorical data.

#### RESULTS

Table 1 shows the demographic and clinical profile of patients of Chronic Kidney Disease with Anemia (n=100).

The mean age of the study population was 52.4 ± 11.8. Majority of the patients belonged to the age group of 51-60 years (35.4%) followed by 41-50 years age group (25.6%). Out of 100 patients of CKD with Anemia, 58 were females and 42 were males. Majority of our patients (61%) belonged to rural background. The most common co-morbidities were Hypertension (67%) and Diabetes Mellitus (34%). The common symptoms at presentation included odema, oliguria,

Variable	Number of patients (out of 100)
Age (in years)	
< 30	15
31-40	10
41-50	26
51-60	29
>60	20
Gender	
Males	42
Females	58
Residential Status (n,%)	
Rural	61
Urban	39
Co-existing Conditions	
Diabetes Mellitus	34
Hypertension	67
Coronary Artery Disease	16
COPD	08
Stage of CKD (n,%)	
Stage 1	2
Stage 2	4
Stage 3	8
Stage 4	23
Stage 5	63
Clinical Presentation	
Oedema	63
Oliguria	68
Dysnoea	45
Fatigue	78
Encephalopathy	19
Nausea/Vomiting	55
No of patients on maintenance Hemodialysis	59
No of patients on Erythropoietin therapy	75
<b>Table-1: Showing distribution of Demographic and Clinical data of Chronic Kidney Disease patients with Anemia</b>	

Parameter	Profile
Hb (g/dL) (Mean ± SD)	8.39 ± 1.71
TLC (Mean ± SD)	10.28 ± 5.21
MCV (Mean ± SD)	80.32 ± 2.30
MCH (Mean ± SD)	26.23 ± 1.41
MCHC (Mean ± SD)	30.58 ± 1.74
Reticulocyte Count (Mean ± SD)	2.19 ± 0.87
Serum Ferritin (Mean ± SD)	221.33 ± 11.19
Peripheral Blood Film Picture (n, %)	
Normocytic Normochromic	76 (76%)
Microcytic	22 (22%)
Macrocytic	2 (2%)
<b>Table-2: Showing Hematological Profile in patients of CKD with Anemia (n=100)</b>	

Anaemic Level(g/dl)	N	CKD stage					p-value
		Stage 1 (n-2)	Stage 2 (n-4)	Stage 3 (n-8)	Stage 4 (n-23)	Stage 5 (n-63)	
		F (%)	F (%)	F (%)	F (%)	F (%)	
Severe (<7)	22	0(0.0)	0(0.0)	1(4.5)	4(18.2)	17(77.3)	0.025
Moderate (7 – 9)	42	0(0.0)	0(0.0)	4(9.5)	7(16.7)	31(73.8)	
Mild (9 - <12)	36	2(5.6)	4(11.1)	3(8.3)	12(33.3)	15(41.7)	

**Table-3:** Showing association between severity of anemia and stage of CKD

Parameter	Nondialyzed patients (n=41)	Patients on Maintenance Hemodialysis (n=59)	p value
Hb (g/dl)	9.54 ± 1.46	7.59 ± 1.43	0.000**
TLC (x 10 <sup>9</sup> /l)	9.26 ± 3.71	11.01 ± 5.94	0.101
MCV (fl)	81.33 ± 1.98	79.66 ± 2.29	0.001**
MCH (pg)	26.67 ± 0.99	25.91 ± 1.36	0.003**
MCHC (gm/dl)	31.04 ± 1.65	30.23 ± 1.71	0.019*
Reticulocyte Count (%)	2.47 ± 0.59	2.97 ± 1.43	0.509
S Ferritin	208.07 ± 86.49	230.63 ± 95.80	0.322
Severity of Anemia (n, %)			0.027*
Mild	21(51.2%)	15(25.4%)	
Moderate	14(34.1%)	28(47.5%)	
Severe	6(14.7%)	16 (27.1%)	

**Table-4:** Showing comparison hematological parameters between Non-dialyzed patients and patients on maintenance hemodialysis

fatigue, dysnoea, nausea/vomiting and altered sensorium. Majority of patients (63%) belonged to Stage 5 of Chronic Kidney Disease.

The hematological profile of the study population is shown in Table 2. The mean Hemoglobin level in our study was 8.39 ± 1.71 g/dL. The most common profile seen on peripheral blood smear was normocytic normochromic anemia (76%), followed by microcytic hypochromic picture seen 22% patients.

Table 3 shows the relation between stage of Chronic Kidney Disease and the severity of Anemia. Our findings showed that as the renal dysfunction becomes more severe, there is significant increase in the severity of Anemia (p<0.05). More than 95% patients with severe Anemia (Hb < 7 g/dL) belonged to CKD Stage 4-5.

Table 4 compares the clinical and hematological parameters between non-dialyzed patients and those on maintenance hemodialysis. 59 out of 100 patients were on regular maintenance hemodialysis. Mean Hemoglobin level and RBC indices (MCV, MCH, MCHC) were significantly lower in patients receiving hemodialysis (p<0.05).

## DISCUSSION

Chronic Kidney Disease is a medical condition characterized by irreversible renal dysfunction caused by a variety of diseases. The most common underlying disorders resulting in CKD include Diabetes Mellitus, Hypertension and Chronic Glomerulonephritis. Progressive damage to kidneys ultimately results in involvement of every organ system of the body. The most common hematological manifestation in patients of CKD is Anemia. Our study evaluated the clinic-hematological profile of Anemia in patients of Chronic Kidney Disease presenting at a rural tertiary care centre. Our results showed that some degree of Anemia was found

in all the patients, suggesting a prevalence of 100% in our study population. This is in concurrence with the findings in previous studies which have shown a high prevalence of anemia in CKD patients.<sup>3,11,12</sup> One of the reason of this 100% prevalence in our study could be that majority of our patients were in advanced stage of CKD. In our study 42% patients had Hb in the range of 7-9 g/dl suggestive of moderate anemia, 36% had mild and 22% had severe anemia. It has been shown in previous studies that grade of Anemia is usually proportional to the severity of CKD.<sup>5</sup> This association was also seen in our study. Large majority of patients (>95%) having severe Anemia (Hb < 7g/dL) belonged to Stage 4 or 5 of Chronic Kidney Disease.

Most of the patients in our study had normocytic normochromic anemia (76%) on peripheral blood smear examination, followed by microcytic hypochromic anemia (22%). Macrocytic picture was seen in only two patients (2%). The predominantly normocytic normochromic picture on PBF is because of the absolute deficiency of Erythropoietin (Epo) with progressive renal dysfunction. Majority of the previous studies have shown similar findings with regards to morphological picture of Anemia.<sup>9,11,14</sup> On the contrary, in a study done on Indian CKD patients, Talwar et al showed a higher prevalence of microcytic hypochromic picture on peripheral smear.<sup>15</sup>

On comparison of hematological profile between nondialyzed patients (n-41) and those on hemodialysis (n-59), our results showed that mean Hb, MCV, MCH and MCHC levels were significantly lower in patients who were receiving hemodialysis (p<0.05). Severe anemia was seen in 16 patients on hemodialysis (27.1%), while only 4 nondialyzed patients (9.75%) had severe anemia. In a study done in Iranian CKD patients, Afshar R et al showed that

the hemodialyzed patients were significantly more anemic than the predialyzed patients.<sup>12</sup> The patients on maintenance hemodialysis usually have advanced grade (Grade 4 or 5) with marked decrease in Erythropoietin production and increased nutritional deficiencies (Iron, Vit B12).

## CONCLUSION

Anemia is a very common clinical manifestation in patients of Chronic Kidney Disease. The most common morphological type of Anemia seen in our study was Normocytic normochromic type. Severity of Anemia increases with progressive renal damage. Patients receiving hemodialysis are more anemic as compared to non-dialyzed CKD patients. Management of anemia with Iron and Erythropoietin therapy is an important therapeutic intervention in the optimum treatment of patients with Chronic Kidney Disease.

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