



Original Article

Evaluation of Hematological profile in Chronic Kidney Disease patients in a Tertiary Care Center, Kanchipuram: A Cross Sectional Study

Authors

Saumya¹, V. Eswari^{2*}

¹Post Graduate Pathology, Meenakshi Medical College and Research Institute, Kanchipuram, Tamil Nadu - 631552, India

²Professor and Head of Dept, Meenakshi Medical College and Research Institute, Tamil Nadu-631552, India

*Corresponding Author

V. Eswari

Email: dreswarimd@gmail.com

Abstract

Introduction: Anemia is a very common complication of chronic kidney disease (CKD) and is associated with a poor cardiac health, cognitive function and an overall quality of life. We aimed to assess the various hematological changes in patients with chronic kidney disease and to assess the correlation between hemoglobin and serum creatinine.

Methodology: The study was conducted for a period of one year during which 60 patients with a diagnosis of CKD, and having a serum creatinine value higher than 1.5 mg/dl were included in our study using a predesigned semi-structured questionnaire, we recorded clinical and laboratory related information of the patients. The patients were classified into stages of CKD using eGFR (Estimated Glomerular Filtration Rate). Spearman's correlation coefficient was calculated to look for correlation between hemoglobin and serum creatinine.

Results: Majority of the patients (n=34) had serum creatinine between 5.1 and 10 mg/dl and half of all patients had hemoglobin level between 7.1 and 10 mg/dl. Iron Overload was seen in 42 patients, and majority of the patients were in CKD stage 4 and 5. Decreased mean serum iron, transferrin and total iron binding capacity was seen in remaining patients.

Conclusion: Prompt identification and correction of anemia in patients with CKD is recommended. Further detailed studies are required to support the results of our study.

Keywords: Chronic kidney disease, Anemia, Creatinine.

Introduction

Chronic Kidney Disease is an alarming public health problem. Hematological parameters are commonly deranged in CKD and the effect enhances with the progress in the stage of CKD. Hematological and biochemical parameters are rarely investigated in great detail in CKD patients

in our nation due to less access and unavailability of tertiary care hospitals and high cost of hematological and biochemical parameters. CKD is a disease of bad prognosis and it involves expensive screening, diagnostic and therapeutic procedures. Anemia was first linked to chronic kidney disease (CKD) many years ago.¹ CKD is

defined as either kidney damage or a glomerular filtration rate (GFR) less than 60 ml/minute/1.73 m² for three or more months.² The latest criteria include kidney damage for ≥ 3 months, as defined by structural or functional abnormality of the kidney, with or without decreased glomerular filtration rate, manifested by either pathological abnormality, markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests.³ Stages of kidney damage has been stratified by both estimated GFR and the degree of albuminuria in order to predict the risk of progression of CKD.

The exact prevalence of CKD in India is unknown due to lack of large nationwide studies and has only been estimated by smaller regional studies with poor quality of data. Although incompletely understood, anemia in CKD is a multifactorial process due to relative erythropoietin deficiency, uremic-induced inhibitors of erythropoiesis, shortened erythrocyte survival, and poor iron homeostasis⁴. It is also associated with reduced quality of life and increased cardiovascular disease, hospitalizations, cognitive impairment, and mortality. Chronic kidney disease has been divided into 5 stages based on the GFR. (National Kidney Foundation-Kidney Disease Outcomes Quality 2006) Anemia usually appears at GFR below 60 mL/min or stage 3.⁵

Previous studies have shown that untreated anemia may have a negative impact on cardiac health, cognitive function, functional capacity and an overall quality of life among patients with chronic kidney disease.⁶ Furthermore, correction of anemia has been shown to improve cardiac function, cognitive function, quality of life, and physical activity. Despite knowing the benefits of correcting anemia in CKD, incomplete/suboptimal management of anemia among patients with chronic kidney disease has been seen in clinical practice.⁷ In light of this, we aimed in the present study to assess the various hematological changes in patients with chronic kidney disease and to assess the correlation between hemoglobin and serum creatinine.

Methodology

Study Design and Setting

We designed a cross-sectional study in the Department of Pathology (Clinical Pathology) on the CKD patients. Blood samples were received from the Department of Nephrology. For a period of 1 year from June 1, 2016 till May 1, 2017. All the patients with a diagnosis of chronic kidney disease, admitted in our hospital were included in the study. After fulfillment of the inclusion criteria informed and written consent was obtained from all the patients and their bystanders.

Inclusion criteria

We included patients who were at least 18 years of age, had a serum creatinine value higher than 1.5 mg/dl within the past 12 months, were clinically stable for three preceding months, had no clinically significant cardiovascular, pulmonary, endocrine, genitourinary, bleeding disorders or renal system disease. Patients who met the inclusion criteria consecutively were approached for enrolment in the study.

Exclusion Criteria

Patients were excluded if they had received within the past three months erythropoietic therapy, iron supplementation, or cytotoxic drug therapy. Patients were also excluded if they had a known diagnosis of human immunodeficiency virus, vitamin B12 or folate deficiency, hemolytic anemia, active gastrointestinal bleeding, or current treatment with drugs known to be nephrotoxic (i.e. aminoglycosides).

Data Collection and Data Analysis

We took and recorded clinical history of the enrolled patients from their medical records registers in a pretested semi-structured questionnaire/ proforma. Laboratory investigations, was also abstracted from the medical records register with the help of senior technicians. Information abstracted from the chart included age, gender, presenting complaints, past medical history and physical examination findings. Laboratory data gathered from the chart included serum creatinine, serum urea, serum electrolytes, hemoglobin, hematocrit, total leucocyte count, platelet count,

serum iron, total iron-binding capacity, serum ferritin and serum transferrin.

CKD stages were defined based on eGFR level by using the Cockcroft –Gault Formula:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times (\text{weight in Kg})}{72 \times \text{serum creatinine}}$$

Stages of CKD	
CKD Stages	Description (eGFR ml/min/1.73m ²)
Stage-1	Normal eGFR(>90) With Other Evidence of kidney damage*.
Stage-2	eGFR 60-89 With Other Evidence of kidney damage*.
Stage-3	eGFR 30-59
Stage-4	eGFR 15-29
Stage-5	eGFR <15

Absolute iron deficiency was diagnosed in those with serum ferritin values less than 100 mg/L and low transferrin saturation (<20%). while functional iron deficiency was diagnosed with normal serum ferritin (100 to 300 mg/L) These definitions of iron deficiency has been applied in studies previously.^{8,9} Patient was diagnosed with iron overload if serum ferritin was higher than 500ng/ml.¹⁰

Results

We included 60 patients in the study,of which 60% were males (n== 36) and 40% females (n=24)and 41 to 55 years was the most common age group (Table 1). Decreased urinary output was the commonly reported presenting complaint of the patients 40% (n=21) followed by nausea and vomiting 11% (n=7), fatigue 31% (n=19), swellings seen in 8% (n =5) and breathlessness seen in 8% (n=5) (Table 2). On examination, pallor was the most common sign observed in the patients (Table 3).Pallor was seen in 63%(n =38) pedal edema 20% (n= 12) crepitation 20% (n =5) and ascites 8% (n=5) Hypertension was the most common etiology among the study patients seen in 50% of patients (n=30).Diabetes Mellitus was seen in 8% patients(n =11) (Table 4). Less common etiological conditions were chronic glomerulonephritis 10% patients (n =6),

obstructive nephropathy was seen in 3% patients (n =2)and polycystic kidney disease was seen in 3% patients (n= 2) .Loss of corticomedullary junction was the most common finding on ultrasonographic examination seen in 36%of patients (n=22),bright echogenicity was noted in33% of patients,(n=20) decreased kidney size was noted in 26% of patients,(n=16) hydronephrosis in 3% of patients (n=2)(Table 5). Majority of the patients had serum creatinine between 5.1 and 10 mg/dl (Table 6). Serum sodium between 136 and 145 mEq/l was seen in 60%(n=36)patients and serum potassium between 3.5 and 5.5 mEq/l was seen in 65% (n=39)(Table 7). Half of all patients had hemoglobin level between 7.1 and 10 mg/dl (Table 8), 49 had total leucocyte count between 4000 and 12000 per cu mm (Table 9) and 35 patients had platelet count above 1.5 lakh per ml (Table 10). Normocytic normochromic anemia was the most common morphological type of anemia (Table 11). Chronic Kidney Disease was staged based on Glomerular Filtration Rate and majority of them were in stage 5.(Table 12).Mean serum iron was 69.8 mcg/dl, mean ferritin 285.4 ng/ml, mean total iron binding capacity 309.4 mcg/dl and mean serum transferrin was 192.4 ng/dl (Table 13). 6 patients had functional deficiency of iron,6 had an absolute deficiency of iron and 42 patients were iron overload (table 14)

In our study it was found that there is no correlation between hemoglobin and serum creatinine. And also statistically there is no significant difference. Figure 1 describes the scatter plot between hemoglobin and serum creatinine (Pearson’s correlation = -0.20, p value = 0.11).

Table 1 Age and gender distribution of patients

Age distribution	N	
Less than 25 years	2	
25-40 years	13	
41-55 years	24	
56-70 years	21	
More than 70 years	0	
Mean age ± standard deviation (years)	48.45±13.49	
Gender distribution	N	%
Males	36	60%
Females	24	40%

Table 2 Frequency distribution of Symptoms

Symptoms	N	%
Decreased Urinary Output	24	40%
Nausea and Vomiting	7	11%
Fatigue	19	31%
Swelling	5	8%
Breathlessness	5	8%

Table 3 Frequency distribution of signs in the patients

Signs	N	%
Pallor	38	63%
Pedal edema	12	20%
Ascites	5	8%
Crepitation	5	8%

Table 4 Distribution of cases according to their etiology

Etiology	N	%
Diabetes mellitus	11	18%
Hypertension	30	50%
Chronic Glomerulonephritis	6	10%
Polycystic kidney disease	2	3%
Undiagnosed	9	15%
Obstructive Nephropathy	2	3%

Table 5 Frequency distribution of Ultrasonographic findings

Ultrasonography findings	N	%
Loss of corticomedullary junction	22	36%
Bright echogenicity	20	33%
Decreased kidney size	16	26%
Hydronephrosis	2	3%

Table 6 Distribution of cases according to Serum Creatinine and Urea Levels

Serum Creatinine (mg/dl)	N	%
1.5-5	9	15%
5.1-10.0	34	56%
10.1-15	8	13%
More than 15.1	9	15%

Serum urea (mg/dl)	N	%
14-25	7	11%
26-50	7	11%
51-75	2	3%
76-100	7	11%
More than 100	37	61%

Table 7 Frequency distribution of electrolyte levels of the patients.

Serum sodium (mEq/l)	N	%
Less than 135	6	10%
136-145	36	60%
More than 145	18	30%
Serum potassium(mEq/l)	N	%
Less than 3.5	17	28%
3.5-5.5	39	65%
More than 5.5	4	6%

Table 8 Frequency distribution of hemoglobin levels

Hemoglobin (mg/dl)	N	%
Less than 5	5	8%
5.1-7	17	28%
7.1-10	30	50%
More than 10.1	8	13%

Table 9 Frequency distribution of total leucocyte counts

Total leucocyte count (per cumm)	N	%
Less than 4000	5	8%
4001-12,000	49	81%
More than 10,000	6	10%

Table 10 Frequency distribution of platelets levels

Platelet count (lakh per ml)	N	%
Less than 1	4	6%
1-1.5	2	3%
1.6-2	18	30%
More than 2	17	28%

Table 11 Frequency distribution of cases according to the type of anemia

Type of anemia	N	%
Normocytic normochromic	27	45%
Microcytic hypochromic	16	26%
Macrocytic	6	10%
Dimorphic	11	18%

Table 12 Frequency distribution of cases according to the stage of chronic kidney disease

Chronic kidney disease stage (based on eGFR)	N	%
Stage 1	3	5%
Stage 2	6	6%
Stage 3	5	8%
Stage 4	4	6%
Stage 5	42	70%

Table 13 Iron profile of patients included in the study

Variable	Mean ± standard deviation
Serum iron	69.8 ± 19.42 mcg/dl
Ferritin	285.4 ± 114.7 ng/ml
Total iron binding capacity	309.4 ± 42.9 mcg/dl
Serum Transferrin	192.4 ± 55.4 ng/dl
Transferrin saturation	33.90 % ±24.19

Table 14 Frequency distribution of iron definition

Variable	N	%
Normal	6	10%
Absolute iron deficiency	6	10%
Functional iron deficiency	6	10%
Iron overload	42	70%

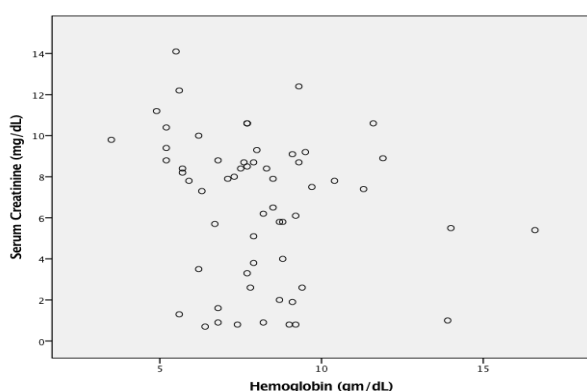


Figure 1.Correlation between hemoglobin and serum creatinine

Pearson’s correlation = -0.20, p value 0.11

Discussion

In the present study, the patients age ranged from 18 to 70 years with mean of 48.45+13.49 years. Maximum cases were found in the age group of 41 to 55 years ie 24 patients (31.67%) and lowest in <25 years (5%). This finding is comparable to the studies of Talwar et al¹¹ (2002) and Ajay k. Singh et al¹²(2013) where they found mean age of 44.6 and 45.22+ 15.2 years respectively.

Our study showed male preponderance 60% which correlate with the study of Bhattacharjee et al¹³. in 2015 with 65% males and Agarwal S.K et al¹⁴. (2005) with 56.16% males.

Most of the symptoms in the present study was decreased urinary output24%, fatigue 19%, nausea and vomiting 7%, swelling 5% and breathlessness

5 %. The finding were similar to the study of Bhattacharjee et al¹³. in 2015 with reduced urinary output the most common symptom.

Creatinine level in the present series ranged from 0.7mg/dl to 14.1mg/dl. The mean serum creatinine was 6.6 mg/dl. Bhattacharjee et al¹³. in 2015, in population based study found mean serum creatinine to be 8.85mg/dl (4.1 to 16.6mg/dl).the mean serum creatinine in the present study is comparable to the above study.

In the present study hyponatremia, hypernatremia, hyperkalemia were found in 36%, 60%, 6% cases respectively. Kovesdy et al¹⁵. found hyponatremia in 28% of cases with CKD.

In the present study anemia was present in all cases. The Hemoglobin (Hb) level ranged from 3.5 gm/dl to 16.6gm/dl with mean of 8.1+2.35 gm/dl. Majority ie 50 patients (83.33) had Hb level less than 5 to 10gm/dl . The present study was comparable to the study of Bhattacharjee et al ¹³. where the mean Hb level was 7.59+1.42gm/dl and prevalence of anemia was 94%.

In the present study majority of the cases had normocytic normochromic anemia 45% followed by microcytic hypochromic 26%, dimorphic 18%, macrocytic 10% .Bhattacharjee et al¹³. in 2015, observed normocytic normochromic anemia in 61% cases.

The present study showed thrombocytopenia in only 9% cases which is less than the study of Bhattacharjee et al¹³. in 2015, where thrombocytopenia was observed in56% cases.

In the present study leucopenia was seen in 8% cases which is similar to the study by Bhattacharjee et al¹³. 2015 with 7% leucopenia.

In the present study 70% cases had iron overload followed by 6% cases had functional iron deficiency , 6% had absolute iron deficiency , 6% had normal iron status. The cause of iron overload is cytokine mediated disturbance in the iron homeostasis which leads to increased uptake and retention of iron into macrophages

The present study revealed hypertension30% being the commonest etiology of CKD followed by diabetes mellitus 18%, chronic

glomerulonephritis 6%, obstructive nephropathy 2%, undiagnosed 9%. These findings almost correlates with the study of Bhattacharjee et al¹³ in 2015 who found diabetes mellitus 42% being the commonest etiology of CKD followed by hypertension 35%, chronic glomerulonephritis 7% and undiagnosed 12%.

Conclusion

In our study patients presented with classical symptoms and signs of renal failure, with normocytic normochromic anemia as the most common morphological type of anemia. Majority of the patients belonged to CKD stage 4 and 5 and a very weak correlation was found between serum creatinine and haemoglobin in our patient population. However, prompt identification and correction of anemia in patients with CKD is recommended. The results of our study needs to be supported by future multicentric interventional studies with larger sample of patients .Therefore more awareness should be created among the common public when they are diagnosed with Anemia, Hypertension and Diabetes Mellitus or all of the three. They should be screened completely to rule out CKD or any occult renal pathology. For this more number of highly equipped laboratory and specialist doctors are needed at the periphery level.

References

- Bright R. Cases and observations illustrative of renal disease accompanied with the secretion of albuminous urine. *Guy's HospRep.* 1836;1:336.
- Decreased GF. Definition and classification of CKD. *Kidney International.* 2013;3:19-62.
- Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, Zeeuw DD, Hostetter TH, Lameire N, Eknoyan G. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney international.* 2005;67(6):2089-100.
- Hsu CY. Epidemiology of anemia associated with chronic renal insufficiency. *Current opinion in nephrology and hypertension.* 2002 May 1;11(3):337-41.
- NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease. *Am J Kidney Dis* 2006;47(Suppl 4):S1
- Grützmacher P, Scheuermann E, Löw I, Bergmann M, Rauber K, Baum R, Heuser J, Schoeppe W. Correction of renal anaemia by recombinant human erythropoietin: Effects on myocardial function. In *Treatment of Renal Anemia with Recombinant Human Erythropoietin 1988* (Vol. 66, pp. 176-184). Karger Publishers.
- Obrador GT, Roberts T, Peter WL, Frazier E, Pereira BJ, Collins AJ. Trends in anemia at initiation of dialysis in the United States. *Kidney international.* 2001;60 (5):1875-84.
- Przybylowski P, Wasilewski G, Golabek K, Bachorzewska-Gajewska H, Dobrzycki S, Koc-Zorawska E, Malyszko J. Absolute and Functional Iron Deficiency Is a Common Finding in Patients With Heart Failure and After Heart Transplantation. *Transplantation Proceedings* 2016;1 (48):173-176.
- Anker SD, Colet JC, Filippatos G, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency. *N Engl J Med* 2009;361:2436e48.
- Trottier BJ, Burns LJ, DeFor TE, Cooley S, Majhail NS. Association of iron overload with allogeneic hematopoietic cell transplantation outcomes: a prospective cohort study using R2-MRI-measured liver iron content. *Blood.* 2013;122(9):1678-84.

11. Talwar VK, Gupta HL, Shashinarayan. Clinicohaematological profile in chronic renal failure. JAPI 2002; 50: 228-33.
12. Ajay k. Singh, Youssef MK Farag, Bharati V Mittal et al. Epidemiology and risk factors of chronic kidney disease in India- results from the SEEK (Screening and early Evaluation of Kidney Disease) study, BMC. Nephrology 2013; 14: 114.
13. Bhattacharjee et al. A study on haematological profile in patients of chronic renal failure with special reference to serum iron profile. J of Evidence Based Med & Hlthcare /Vol.2/Issue46/Nov,09,2015. Page 8212 - 8219.
14. Agarwal SK, Dash SC, Irshad M, Raju S, Singh R, Pandey RM. Prevalence of chronic kidney failure in adults in Delhi. India Nephrol Dial Transplant 2005; 20(8): 1638-42.
15. Kovesdy, Csaba P. Hyponatremia, hypernatremia and mortality in patients with chronic kidney disease with and without congestive heart failure- Clinical Perspective. Circulation 2013; 125. 5:677-684.
16. Guenter Weiss, M.D., Lawrence T. Goonough, M.D. Anaemia of chronic disease, N ENGL J MED 352;10 March 2005 1011-2023.