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Original Article

Evaluation of Iron Status in Non-dialysis Chronic Kidney Disease Patients

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Abstract

Background: Iron deficiency is very common in non-dialysis chronic kidney disease (CKD) patients. It plays a significant role in the causation of anemia. Both the absolute and functional iron deficiency are associated with increased cardiovascular hospitalization and overall mortality in these group of patients.

Objectives: This study was conducted to evaluate the iron status in non-dialysis CKD patients.

Methods: This cross-sectional study was carried out in the Department of Biochemistry, Dhaka medical college, Dhaka from the period of July 2018 to June 2019. In this study, thirty non-dialysis CKD patients were taken from the Department of Nephrology, Dhaka Medical College Hospital, Dhaka. For better assessment another age and sex matched thirty healthy individuals were also taken. Hemoglobin, serum creatinine, iron, total iron binding capacity (TIBC), transferrin saturation (TSAT) and ferritin levels of all participants were measured and all values were analyzed statistically.

Results: Mean age of the non-dialysis CKD patients was 48.07 ± 12.42 years in this study. All of them were anemic with hemoglobin concentration <11gm/dl. 44% of them had iron deficiency and absolute iron deficiency was predominant which was 27% of the CKD patients. Hypertension was the most common etiology of CKD followed by diabetes mellitus. Serum creatinine and ferritin level were significantly raised in non-dialysis CKD patients than the control group while hemoglobin, serum iron and TSAT were significantly low in non-dialysis CKD patients. Hemoglobin level was negatively correlated with serum creatinine in CKD patients which was significant.

Conclusion: Iron deficiency is common in non-dialysis CKD patients where absolute iron deficiency is predominant. Early evaluation of iron deficiency should be done in every CKD patient.

Key words: non-dialysis CKD, anemia, iron deficiency, TSAT.

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Introduction

Anemia is a relatively earlier but clinically most significant consequence of chronic kidney disease (CKD). Persistent anemia is associated with high mortality, frequent hospitalization and adverse cardiac events in CKD patients. It is also responsible for poor renal outcome and rapid progression of CKD itself.[1,2] Level of anemia is also associated with quality of life in CKD patients.[3] The prevalence of anemia is higher in the advanced stages of CKD. In the United States the prevalence of CKD increases from 8.4% at stage 1 to 53.4% at stage 5.[4] The overall prevalence of anemia in CKD patients in different countries were found between 45% & 58.5%. [5,6]

The mechanism of anemia in CKD patients is multifactorial. Anemia is mostly attributed to the decrease of erythropoietin production resulting in decreased production of red blood cell that accompanies the declining GFR. Other causes include chronic blood loss, reduced life span of RBC, nutritional deficiencies of iron, folate and vitamin B12, chronic inflammation with increased hepcidin levels.[7,8]

Iron deficiency occupies a larger percentage of anemia in CKD patients. Iron deficiency may be two types in these patients: absolute or functional iron deficiency. In absolute iron deficiency there is decreased iron store in the body and in functional iron deficiency there is inadequate availability of iron despite adequate iron stores.[9] Though high transferrin saturation is associated with lower

mortality and kidney disease progression but both absolute and functional iron deficiency are associated with increased cardiovascular hospitalization and overall mortality.[10] Absolute iron deficiency may be caused by frequent blood sampling, low grade gastrointestinal bleeding or decreased iron absorption. There is also nutritional deficiency because of dietary restrictions. Functional iron deficiency is caused largely by the use of erythropoiesis stimulating agent which stimulates red blood cell production sometimes beyond the ability of the body to supply iron.[11] Other factors of functional iron deficiency include chronic inflammation, impaired tissue responsiveness to erythropoietin that can inhibit iron transport.[12]

Iron deficiency leads to decreased production of hemoglobin causing microcytic hypochromic anemia. Iron deficiency is accompanied by reduced serum iron & transferrin saturation (TSAT) and also increased serum total iron binding capacity (TIBC).[13]

Data regarding iron status in non-dialysis CKD patients is very limited in our country hence this study was done to evaluate the iron status among non-dialysis CKD patients.

Materials & Methods

This cross-sectional study was carried out in the Department of Biochemistry, Dhaka medical college, Dhaka from the period of January 2019 to June 2019. In this study, thirty diagnosed non-dialysis CKD patients were selected by purposive sampling technique from the Department of Nephrology, Dhaka Medical College Hospital, Dhaka.

CKD patients who didn't receive any dialysis and more than 18 years of age were included in this study. Patients on dialysis, hematinic, erythropoietin and blood transfusion in the last three months were excluded. Patients with history of recent severe hemorrhage or known hematological disorder were also excluded. For better assessment another thirty healthy individual above 18 years of age were selected.

Written informed consent was taken from all the participants after explaining the objectives of the study, risks and benefits involved. Institutional ethical clearance was taken prior to the study. Demographic and clinical data were collected from the participants by structured questionnaire. Samples were collected with aseptic precaution from each subject in the morning. Serum was separated and analyzed in the same day. All the required investigation findings were recorded in a predesigned data collection sheet. Transferrin saturation was calculated by the following equation [TSAT = (serum iron ÷TIBC) x 100] and expressed as a percentage.

Data analysis:

All the data were analyzed statistically by using SPSS software for windows (version 22). Continuous variables were presented as means ± standard deviations and categorical variables were presented as numbers (percentages). Student's t test and chi square test were used to compare between groups. Pearson's correlation was used for the correlation test. All p value significance was defined as $p < 0.05$ at the level of 95% confidence interval.

Results

Data from thirty diagnosed cases of non-dialysis CKD and thirty control subjects were analyzed. All the data are summarized below:

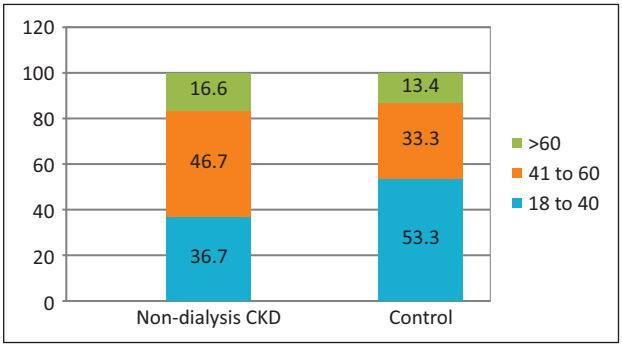

Figure 1: Distribution of respondents according to age group.

Table 1: Comparison of age distribution between two groups

Age Group	Group		Significance
	Non-dialysis CKD Frequency (%)	Control Frequency (%)	
18 to 40 years	11 (36.7%)	16 (53.3%)	Exact value=1.726 DF=2 p=.419
41 to 60 years	14 (46.7%)	10 (33.3%)	
>60 years	5 (16.6%)	4 (13.4%)	
Total	30 (100%)	30 (100%)	
All ages (Mean ± SD)	48.07±12.42	45.27±10.63	P=0.352

There was no significant age difference between non-dialysis CKD patients and control subjects. Majority of the CKD patients belonged to 41 to 60 years age group (46.7%).

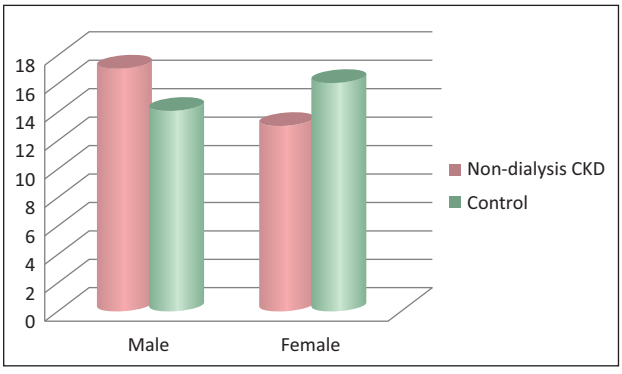

Figure 2: Distribution of respondents according to gender.

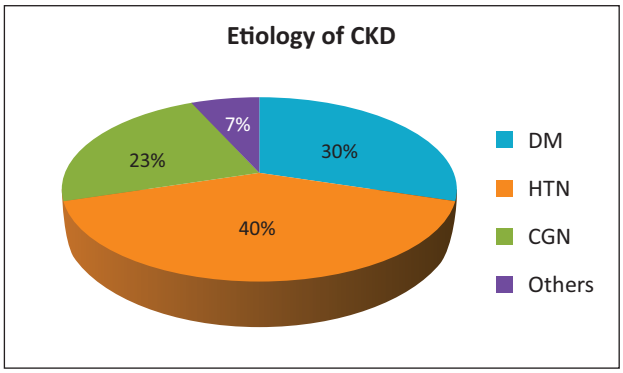

Figure 3: Pie chart showing etiology of the CKD.

The most frequent causes of CKD were hypertension (40%). Other frequently found causes were diabetes mellitus and chronic glomerulonephritis.

Table 2: Comparison of clinical & biochemical parameters between groups.

Parameter	Group		Significance (p value)
	Non-dialysis CKD (Mean±SD)	Control (Mean±SD)	
SBP (mm Hg)	149.67±13.06	121.33±10.25	<0.00
DBP (mm Hg)	91.33 ± 6.81	76.33±8.19	1< 0.00
S creatinine (mg/dl)	3.68±1.48	0.84±0.15	1< 0.00
Hemoglobin (g/dl)	9.29±0.98	12.73±0.97	1< 0.001

The clinical and biochemical parameters are shown in table 2. The systolic and diastolic blood pressure were higher in non-dialysis CKD patients than control subjects. The mean serum creatinine level was also higher in non-dialysis CKD group compared to control. The hemoglobin level was markedly decreased in non-dialysis CKD patients which was <11 gm/dl in all cases. All the differences were statistically significant.

Table 3: Comparison of the iron status between groups.

Parameter	Group		Significance (p value)
	Non-dialysis CKD (Mean±SD)	Control (Mean±SD)	
S iron (µg/dl)	79.96±29.74	104.98±25.98	<0.001
S ferritin (ng/ml)	221.23±130.04	143.273±48.12	< 0.05
TIBC (µg/dl)	332.14±78.772	313.67±53.33	0.287
TSAT (%)	0.71 ± 6.75	33.35±5.45	<0.001

Iron status in non-dialysis CKD and control group were shown in table 3. Serum iron and TSAT were significantly lower in non-dialysis CKD group as compared to the control group. There was no significant statistical difference in the mean value of TIBC.

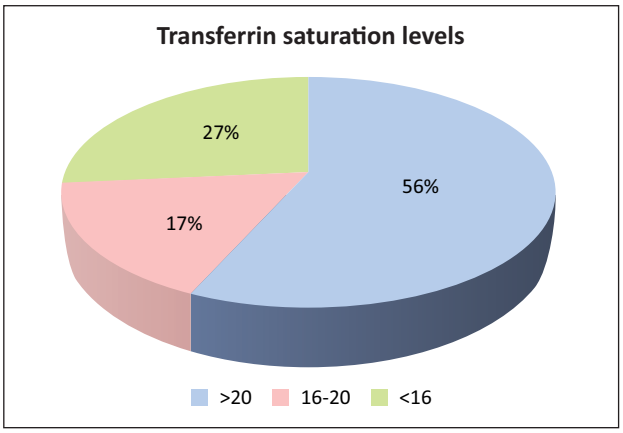

Figure 4: Pie chart showing TSAT level in non-dialysis CKD patients

Discussion

Anemia in non-dialysis CKD patients are very common which also affects the outcome of CKD. In this study all the non-dialysis CKD patients were anemic in varying degree with hemoglobin concentration <11 gm/dl. The severity of anemia in this study (9.29 ± 0.98 gm/dl) is similar to the findings from previous study by Lefebvre et al[14] comprising of more than 13 hundred pre-dialysis CKD patients with mean Hb level 9.2 gm/dl.

The primary etiology of CKD was hypertension (40%) followed by diabetes mellitus. This finding was supported by the findings of Anutrakulchai et al[15] where hypertension was found in 53% CKD patients though some other studies by Afshar et al[16] and Deori et al[17] suggest diabetes mellitus as predominant etiological factors. This difference may be due to difference in sample size. The mean systolic and diastolic blood pressure were 149 mmHg and 91 mmHg respectively which were significantly higher than control group. Hypertension (defined as SBP ≥140 mmHg or DBP ≥90 mmHg) specially SBP is significantly related to the development of kidney disease and is an independent risk factor for the rapid progression of early CKD to end stage renal disease (ESRD).[18,19]

Iron deficiency plays a vital role along with impaired erythropoietin production in causation of anemia in these patients. In this study iron deficiency was present in 44% of the patients. This is consistent with the results of study by Fishbane et al[20] Absolute iron deficiency is evidenced by TSAT <20% & serum ferritin <100 ng/ml and functional iron deficiency is defined by TSAT <20% & serum ferritin >100 ng/ml. In this study absolute iron deficiency was more common than functional iron deficiency. We found 27% non-dialysis CKD patients had absolute iron deficiency which was similar to the findings of Deori et al[17] and Lukaszyk et al[21] which were 26% and 17% respectively. However, Iyawe et al[22] reported that functional iron deficiency was more common than absolute iron deficiency.

Serum iron and transferrin saturation in non-dialysis CKD patients were found significantly low in this study comparative to the controls whereas serum ferritin level was found significantly high than the control group. Study done by Shenoy et al[23] also showed the same results except the ferritin level which was lower than control group. Very low transferrin saturation specially TSAT <10% is associated with the risk of adverse outcome in CKD patients.[24] Higher ferritin level in non-dialysis CKD patients may be due to the presence of underlying inflammation. In this study, there was no significant difference in TIBC level between two groups.

Present study found a significant negative correlation between hemoglobin and serum creatinine. However correlation of serum iron, TIBC and TSAT with serum creatinine was insignificant. Shenoy et al[23] observed significant correlation between hemoglobin and serum creatinine.

Conclusion

Anemia is a hallmark in CKD patients which have affected all the non-dialysis CKD patients in varying degree. This study showed that 44% patients had iron deficiency and absolute iron deficiency is the predominant form in non-dialysis CKD patients. Therefore, all the CKD patients must be screened for iron deficiency so that early appropriate treatment could be initiated.

Limitations:

This study was a single centered study with small sample size that cannot represent the whole population. Underlying inflammation may have affected the serum ferritin level which could not be ruled out completely.

Conflict of interest:

There is no conflict of interest.

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