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Original Article

The Impact of Chronic Kidney Disease on Iron Metabolism and Hemoglobin Parameter in Patients with and without Diabetes Mellitus

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Abstract

Chronic kidney disease (CKD) is one of the most common public health concerns around the world with numerous adverse outcomes such as cardiovascular disease (CVD), end stage renal disease (ESRD) and premature death. The progression of the CKD leads to an increase in the development of hematological alterations, such as low hemoglobin levels and iron deficiency. Diabetes mellitus is the most common cause of CKD, leading to ESRD and therefore, is also the most common cause of renal anemia. The aim of this study was to find out the influence of Iron Metabolism and Hemoglobin parameter among CKD patients with and without diabetes mellitus by determining iron profile and hemoglobin level. This cross-sectional analytical study was carried out in the department of Nephrology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka over a period of one year July 2022 to June 2023. A total of 100 CKD patients were included in this study as respondents and divided them in to two halves; 50 CKD patients with DM were selected as group- I and other 50 CKD patients without DM as group II. After taking written informed consents, data were taken from patients by using a structured questionnaire. Data was analyzed by Statistical Package for Social Sciences (SPSS), version- 26. In this study serum iron was found significantly lower in group- I (Mean±SD: 6.16±2.36) than group- II (Mean±SD: 12.73±7.36), which was statistically significant. Group- I also represents 56% absolute iron deficiency, 18% functional iron deficiency and 26% normal iron status, Group- II represents 18% absolute iron deficiency, 38% functional iron deficiency and 44% normal iron status respectively. These differences between two groups were statistically significant (p value: <0.001.). Hb level as mean±SD was, 8.5±1.83 in group- I and 12.89±2.54 in group- II respectively and statistically differences were significant. Among the study subjects, frequency of anemia was higher in group- I. In correlation analysis, variables of all study subjects with eGFR showed significant positive correlation with serum iron and Hb level. This study showed that serum iron and Hb level were significantly lower in diabetic chronic kidney disease patients than non-diabetic CKD patients. The findings also revealed that absolute iron deficiency was more common in diabetic CKD patients.

Key words: *Chronic kidney disease, diabetes mellitus, serum iron, hemoglobin*

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INTRODUCTION

Chronic kidney disease (CKD) has been identified as a major public health issue worldwide with increasing prevalence & mortality.[1] the national kidney foundation defines CKD as damage or a glomerular filtration rate (GFR) of less than 60ml/min/1.73 m^2 of body surface area for longer 3 months.[2] the prevalence of CKD was 22.48% in Bangladeshi population.[3] Diabetes mellitus (DM) contributes to a major cause of CKD & end stage renal disease (ESRD). DM affects more than 422 million people worldwide, with 40% of those affected developing CKD.[4] A recent systematic review found that overall prevalence of CKD among type 2 diabetic patients in Bangladesh is 21.3%.[1]

The progression of CKD to ESRD, as well as development of other complications related to impaired renal function, are the most common consequences of CKD. Anaemia is

the most common complication of CKD. Anaemia due to iron deficiency is a typical consequence of CKD.[5] Both absolute and functional iron deficiency affects CKD patients. Low transferrin saturation (TAST) <20% combined with low serum ferritin < 100 is diagnostic of absolute iron deficiency in CKD patients. Functional iron deficiency is diagnosed by a low transferrin saturation (TAST) <20% paired with a normal or high serum ferritin level (≥ 100). The decline in erythropoietin production and dysregulated iron homeostasis plays a key role in the development of anaemia in CKD.[6] The most common test for diagnosis of iron deficiency anaemia is serum iron and serum ferritin.[6]

Approximately 40% of patients with type 2 Diabetes mellitus develop CKD which causes albuminuria, reduced glomerular filtration rate or both.[7] Dysregulation of iron homeostasis is also a crucial cause in the development of anaemia in CKD with type 2 diabetic patients.[8]

Anaemia is a common consequence in people with CKD. A gradual and progressive decline of hemoglobin level is noted when renal function deteriorates, and as the estimated glomerular filtration rate falls, its prevalence grows.[9] The World Health Organization (WHO) defines renal anaemia when hemoglobin level < 13 gm/dl in men and < 12 gm/dl in women, is an important complication of CKD. Idris et al. studied when CKD patients with type 2 DM were compared to those without type 2 DM, the prevalence of anaemia was shown to be higher.[10] Many factors have been proposed as contributing to the anemia etiology in the patients. In case of diabetic neuropathy, erythropoietin insufficiency can be caused by efferent sympathetic denervation of the kidney.[11] Chronic inflammatory reaction resulting in functional iron shortage and erythropoietin loss due to non-selective urinary protein loss.[5] In addition, anemia has also been found to be a significant independent factor for progression of CKD to ESRD in type 2 diabetic patients.[10]

However, a direct comparison between diabetic and non-diabetic CKD patients with regards to anemia has not done yet in Bangladesh. So, the aim of this study is to compare iron profile and Hb level among CKD patients from stages (3-5) with or without type 2 DM.

MATERIALS AND METHODS

This cross-sectional analytical study was conducted in the Department of Nephrology at BIRDEM General Hospital during the period over one year. A total of 100 CKD patients from stage 3 to 5 were included in this study as study population. All of them were divided into Group- I as CKD (stage 3 to 5) patients with type 2 DM and Group II as CKD (stage 3 to 5) patients without type 2 DM. CKD patients on hemodialysis, patients of known hematological disorder, patients taking iron supplement and pregnant women were excluded. A structured questionnaire and a data sheet were designed with a view to collect data from the respondents. With all aseptic precautions venous blood was drawn for laboratory work up for estimation of fasting blood glucose, serum iron and serum ferritin. After counselling, informed written consent was taken from each patient.

STATISTICAL ANALYSIS

Statistical analyses were performed using the Statistical Program for Social Sciences (SPSS) software (version 26.0; SPSS, Inc.). Categorical variables were presented as frequencies and percentages in tables andgraphs; continuous variables were expressed as means andstandard deviation. Correlations were assessed with Pearson's coefficient correlation. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among 100 CKD patients, 50 patients included into Group- I, who were diagnosed as CKD with type 2 DM. On the other hand, Group II included 50 patients diagnosed with CKD without type 2 DM.

Table I contains the important baseline characteristics including sex, stages of CKD & duration of DM. Among the total study subjects 56 % were male & 44% were female. The majority of the respondents, about 56% were in stage 4, 27% were in stage 3 and 17% were in stage 5. 78% of the respondents were anemic and 41% had absolute iron deficiency.

Table- I: Important baseline characteristics (sex, stages of CKD, Type of iron deficiency) of overall study subjects

Characteristics		Frequency (n=100)
Sex	Male	56
	Female	44
Stage of CKD	Stage-3	27
	Stage-4	56
	Stage-5	17
Type of Iron deficiency	Normal	33
	Functional	26
	Absolute	41
Presence of anaemia	Yes	78
	No	22

Table II showed no significant difference of Mean value of serum creatinine and eGFR between 2 groups. Statistical analysis was done by independent t- test to compare among groups.

Table- II: Comparison of glycemic and renal status between 2 groups

Variables	Group I (CKD with DM) (n=50) Mean± SD	Group II (CKD without DM) (n=50) Mean± SD	p value
FBS (mmol/L)	12.24±4.98	4.71±0.67	0.000
HbA1c (%)	8.77±1.82	5.39±0.46	0.000
Serum Creatinine (mg/dl)	3.01±1.55	3.27±1.69	0.455
eGFR (ml/min/m²)	24.33±11.50	24.58±11.70	0.532

Values are expressed as the mean± SD.
= significant (p≤0.05, **p<0.01, ***p<0.001).

Table III showed that serum iron and Hb level were significantly lower in diabetic CKD group than non-diabetic CKD group. Serum ferritin was found increased in both groups. Statistical analysis was done by independent t test to compare between two groups. Values are expressed as the mean± SD.

Table- III: Comparison of serum iron, serum ferritin and Hb level between 2 groups

Variables	Group I (CKD with DM) (n=50) Mean± SD	Group II (CKD without DM) (n=50) Mean± SD	p value
Serum Iron (µmol/L)	6.16±2.36	12.73±7.36	0.000
Serum Ferritin (ng/ml)	256.47±21.47	146.17±15.32	0.015
Hb (%)	8.5±1.83	12.89±2.54	0.019

*= significant (*p≤0.05, **p<0.01, ***p<0.001).

Comparison was done by Chi-Square Test of Independence
= significant (p≤0.05, **p<0.01, ***p<0.001).

Figure I showed that 84% of the group I were anaemic and only 16% were non anaemic. Furthermore, group II showed 68% were anaemic and 32% were non anaemic. These differences between 2 groups were statistically significant.

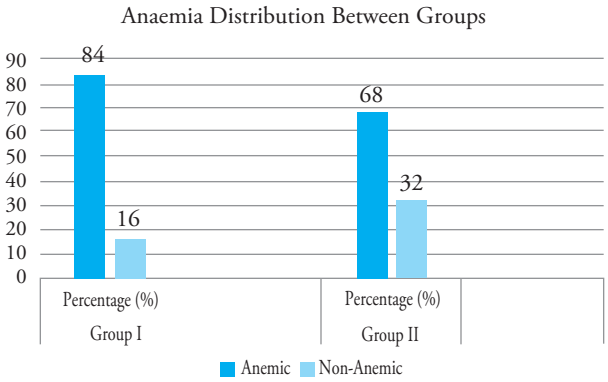

Figure- I: Frequency distribution of anaemia among the study subjects

Table IV showed group I represented 56% absolute iron deficiency, 18% functional iron deficiency and 26% showed normal iron status. And group II showed 18% absolute iron deficiency, 38% functional iron deficiency and 44% showed normal iron status. Comparison was done by Chi-Square Test of Independence

Table- IV: Frequency distribution of iron deficiency between 2 groups

Types of Iron deficiency	Group I (CKD with DM)		Group II (CKD without DM)		P-value
	F n=50	%	F n=50	%	
Normal	13	26.0	22	44.0	
Functional	9	18.0	19	33.8	0.001
Absolute	28	56.0	9	18.0	

*= significant (*p≤0.05, **p<0.01, ***p<0.001).

Table V represents the correlation of eGFR with serum iron, ferritin and Hb. Pearson correlation was used for statistical analysis. Here positive correlation of eGFR with serum iron and Hb level as well as eGFR showed negative correlation with serum ferritin.

Table- V: Correlation of eGFR with serum iron, ferritin, Hb

Variables	R	p-value
Iron	0.314	.041
Ferritin	-.226	.025
Hb	0.465	.000

R, Pearson correlation coefficient
= significant (p≤0.05, **p<0.01, ***p<0.001).

DISCUSSION

The hallmark of chronic kidney disease is anaemia. The majority of people with advanced CKD suffer from the complications of anaemia, which is typically caused by reduced production of erythropoietin. Over 2 million individuals globally suffer from iron deficiency[12], and iron deficiency anaemia continues to be the most common form of anaemia, with the largest incidence being seen in West Africa and South Asia.

The most common cause of chronic kidney disease is diabetes mellitus. It was recently found that anaemia occurs more commonly in CKD patients with diabetes than in those without the condition.

This current cross-sectional study was carried out over a period of one year in the Nephrology department of the BIRDEM General Hospital in Dhaka. According to inclusion criteria, the 100 study population was divided into two groups. Among them 50 were CKD with DM and another 50 subjects were non-diabetic CKD patients.

Of the study participants, 44% were female and 56% were male. The gender distribution of this study aligns with the epidemiology of chronic kidney disease, and the USRDs 2021 annual data report indicates that the incidence of ESRD was 60.6% higher for male.[13]

The iron profile and haemoglobin level of the two groups were compared in this study. The mean serum iron level in the diabetic group was significantly different from the value for the non-diabetic CKD group.

Specifically, the serum iron levels in groups I and II were 6.16 ± 2.36 and 12.73 ± 7.36, respectively, where $p < 0.001$, which was significantly low in group I. Similar result was also seen in other studies conducted by Robles NR et al., which also showed statistically significant results.[14]

A high prevalence of iron deficiency among diabetic CKD subjects was linked to our study's finding that anaemia was more common in these patients. According to the National Health and Nutrition Examination Survey Iv, up to 50% of patients with CKD stages 3-5 have either absolute or relative iron deficiency.[15]

According to this study, absolute iron deficiency was higher in the diabetic CKD group than in the non-diabetic CKD group (56 % and 18 %, respectively), while the functional iron deficiency was higher in the non-diabetic CKD group (38 % and 18 % respectively). These differences between the two groups are statistically significant.

We have found serum ferritin level increased in both groups. The mean value of serum ferritin was 256.47 ± 21.47 and 146.17±15.32 in group I and group II respectively. Other authors also found similar results in their studies.

Means serum Hb level in group I and group II were found 8.5 ± 1.83 and 12.89 ± 2.54. The results of this study demonstrate that diabetic patients with CKD stage 3-5 have Hb levels significantly lower than non-diabetic patients at the same stages of CKD. Similar results have been observed in the other studies.[15]

We have also found the frequency of anemia higher in Diabetic CKD patients which was 84% as compared with non-diabetic CKD patients which was 68%. This result is similar to other study done by M Uzma et al., 2009 which showed anemia prevalence was up to 10-fold higher among diabetic patients with CKD.[16] Thus, patients with diabetes mellitus and renal insufficiency have a higher risk of developing anemia.

In correlation analysis, hemoglobin level had significant positive correlation with e GFR. This result reflects the similar result of the study carried out by Loutradis et al., 2016.[5]

LIMITATIONS

- The sample size of the study was limited.
- All patients were collected from a single tertiary level hospital which does not reflect the whole country.
- Furthermore, underlying inflammation could not be completely ruled out in these patients which could have affected the serum ferritin level.

CONCLUSION

This study demonstrated that serum iron and hemoglobin levels were significantly lower in diabetic chronic kidney disease (CKD) patients compared to their non-diabetic counterparts. It was also observed that anemia was prevalent among CKD patients, with a higher frequency in diabetic CKD patients than in non-diabetic ones. Additionally, the findings revealed that absolute iron deficiency was more common in diabetic CKD patients, while functional iron deficiency was more prevalent in non-diabetic CKD patients. Consequently, routine screening for anemia in type 2 diabetes mellitus (T2DM) patients with CKD is recommended. This could facilitate

early treatment and enhance the overall management of CKD in T2DM patients, ultimately reducing mortality, morbidity, treatment costs, and complications associated with the condition.

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