Original Article

Serum total iron-binding capacity and iron status in patients with non–dialysis-dependent chronic kidney disease: A cross-sectional study in Vietnam

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Background and Objectives: We performed this study to evaluate serum iron and ferritin concentrations, serum total iron-binding capacity (TIBC), and proportion of overall iron deficiency among patients with non–dialysis-dependent chronic kidney disease (ND-CKD). **Methods and Study Design:** A hospital-based cross-sectional observational study was conducted on 175 adult patients with stage 3–5 chronic kidney disease (CKD) by using 51 healthy age–sex-matched Vietnamese adults as the control group. We next examined the prevalence of anemia and determined the serum iron and ferritin concentrations and TIBC. Anemia in CKD was defined as hemoglobin levels <13 g/dL in men and <12 g/dL in women. Transferrin saturation (TSAT, %) was calculated as (serum iron x 100)/TIBC. Functional iron deficiency was defined as serum ferritin >100 ng/mL and TSAT <20%, and absolute iron deficiency was defined as serum ferritin <100 ng/mL and TSAT <20%. Overall iron deficiency was defined as the presence of either absolute or functional iron deficiency. **Results:** Anemia prevalence in our study was approximately 88.6% with a mean hemoglobin concentration of 9.71±2.26 g/dL. The median serum TIBC was lower in the CKD group (50.4 μmol/L) than in the control group (66.0 μmol/L; $p<0.001$). The proportion of overall iron deficiency was 44.0%. TIBC had a diagnostic value for overall iron deficiency (area under the ROC curve=0.81; $p<0.001$). **Conclusions:** Anemia and iron deficiency are common in Vietnamese patients with ND-CKD. TIBC had diagnostic value for overall iron deficiency.

Key Words: anemia, CKD, ferritin, TIBC, transferrin saturation

INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem globally, and end-stage renal disease (ESRD) is conventionally considered the most serious outcome of CKD.[1] Anemia is a very common complication of CKD and is results from interference with erythropoietin production. However, iron and vitamin deficiencies, blood loss, reduced erythrocyte lifespan, chronic inflammation, and uremic milieu are also the contributing factors for anemia in patients with CKD.[2] Published data suggest that anemia is an independent risk factor for cardiovascular morbidity and mortality.[3] A major cause of anemia in CKD is the reduction in erythropoietin production due to kidney damage. However, dysregulated iron homeostasis has a central role in the development of anemia in CKD and is a major contributor toward resistance to erythropoiesis-stimulating agent-based (ESA) treatments.[4] Absolute or functional iron deficiency is present in 25%–38% of patients with CKD-related anemia.[5] Serum ferritin and transferrin saturation (TSAT) are the most common tests used for diagnosing iron deficiency anemia. TSAT, calculated using free iron as a proportion of the total iron-binding capacity (TIBC), assesses the blood iron content.[6] Absolute iron deficiency is defined by low iron stores and low blood iron content, whereas functional iron deficiency is defined by high iron stores and low blood iron content. In this condition, the iron stores cannot be used. A transferrin deficiency with normal iron content has never been studied independently but may also affect both iron

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use and hemoglobin (Hb) level. Serum iron and ferritin levels and TIBC may facilitate the identification of iron disorders in CKD-related anemia.[7] In Vietnam, data on anemia prevalence, serum iron and ferritin concentration, and TIBC in pre-dialysis patients with chronic renal failure previously diagnosed as having CKD remain scant.

METHODS

We conducted this hospital-based cross-sectional study on 175 adult patients with CKD who attended the Department of Nephrology and Hemodialysis, Military Hospital 103, Vietnam Military Medical University, Ha Noi, Vietnam. The study was conducted as study design shown in Figure 1. This study was approved by the Ethical Committee of the Vietnam Military Medical University (No.2521/QĐ/HVQY). All male and female patients were aged ≥16 years diagnosed as having stage 3–5 CKD who had received no renal replacement therapy. We excluded all patients who were receiving renal replacement therapy (hemodialysis, peritoneal dialysis, or kidney transplant); had received parenteral iron therapy within the preceding 6 months; had received EPO therapy in the preceding 2 weeks; demonstrated evidence of active bleeding or active infection; had received blood transfusions within the previous 6 months; had previously been diagnosed as having anemia, except iron deficiency anemia, with non-renal causes; and exhibited pre-diagnostic comorbidities, such as malignancy, end-stage liver disease, and collagen vascular disease (systemic lupus erythematosus and rheumatoid arthritis). Furthermore, 51 age-and-sex–matched healthy adults were included to determine serum iron and ferritin levels and TIBC in the general adult Vietnamese population.

When patients were diagnosed as having CKD, all variables—such as its etiology and risk factors—were considered. Subsequently, patients received counseling on dietary changes (reducing salt, reducing protein, increasing energy intake, and supplementing kidney protein) and on treatment (treatment etiology and risk factor treatment) and were scheduled reappointments.

Written informed consent and the study hospital's ethics committee's clearance were obtained before the recruitment of the participants to the study. Laboratory investigation included complete blood count, high-sensitivity C-reactive protein (hs-CRP) level test, kidney function test, liver function test, plasma glucose, and HbA1c. Diagnosis and staging of CKD were performed as per the National Kidney Foundation (NKF)/Kidney Disease Outcome Quality Initiative (KDOQI) 2002 classification criteria,8 and the estimated glomerular filtration rate (eGFR) was calculated using a 4-variable modification of diet in the renal diseases equation. Anemia in CKD was defined as Hb <13 g/dL in men and <12 g/dL in women as per Kidney Disease: Improving Global Outcomes 2012 clinical practice guidelines.[9] Blood samples were collected with venipuncture. Serum was obtained by centrifuging the blood at 3000 rpm for 10 min after clot formation and then stored at −80°C. Blood was collected in iron-free tubes for iron studies. C-reactive protein was estimated quantitatively using solid-phase ultrasensitive enzyme immunoassay. This test is based on the two-site sandwich enzyme immunoassay principle. The expected upper limit for hs-CRP using the provided kit in healthy individuals is 1.0 mg/L.

Serum iron profiles consist of free iron, ferritin, and TIBC, in which TIBC was estimated using a Diagnosis-Related Group TIBC (bioactive) enzyme-linked immunosorbent assay kit using the principle of competitive binding. Normal of iron and ferritin concentration and TIBC in the Vietnamese population are unknown; therefore, we also used 51 Vietnamese healthy adults to estimate the aforementioned normal values.

TSAT (%) was calculated as (serum iron × 100)/TIBC. We determined low iron tests as the percentage of individuals with serum ferritin level <100 ng/mL or TSAT <20% at different levels of kidney function. These levels

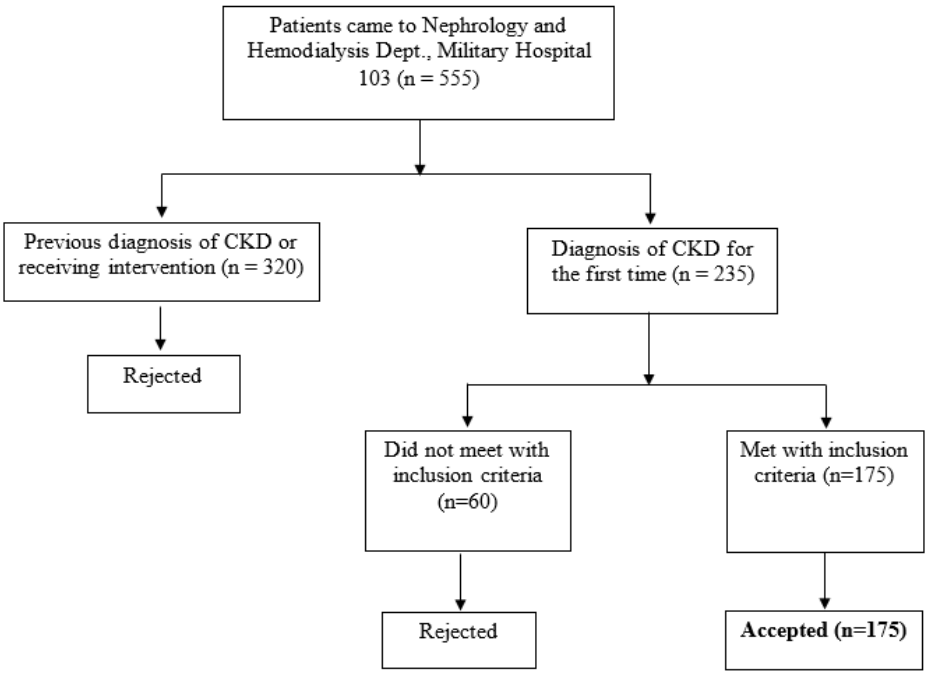

Figure 1. Study design

of ferritin and TSAT were chosen because they are the recommended levels for patients with non–dialysis-dependent CKD (ND-CKD) according to the NKF's KDOQI anemia guidelines.10 Functional iron deficiency was defined by serum ferritin level >100 ng/mL and TSAT <20%, whereas absolute iron deficiency was defined by serum ferritin level <100 ng/mL and TSAT <20%.10 Overall, iron deficiency was defined as the presence of either absolute or functional iron efficiency.

Statistical analysis

Baseline characteristics were assessed with standard descriptive statistics. eGFR was examined both on a continuous scale and categorically by using NKF's stage system. Categorical variables were presented as numbers and percentages (%), whereas continuous variables were presented as mean ± standard deviation and median with interquartile range (as applicable). The independent t test and Mann–Whitney test (for nonparametric data) were used to compare quantitative variables between two groups. Qualitative variables were compared using chi-square test and Fisher's exact test. To examine the trend for each parameter across the CKD stages, the Jonckheere–Terpstra trend test and the Cochran–Armitage test were used. Multivariable adjusted regression analysis was performed to identify the predictors of iron deficiency. Receiver operating characteristic (ROC) curves were plotted and the areas under the ROC curve (AUC) were calculated to predict overall iron deficiency in the study group.

The data were entered in an MS EXCEL spreadsheet, and analysis was performed using Statistical Package for Social Sciences (version 21.0; International Business Machine), with $p < 0.05$ considered statistically significant.

RESULTS

The mean age of 175 enrolled patients was 53.2±17.3 years, in which 69.1% of patients (n=121) were male. Approximately 91.4% (n=160) of patients in our study were hypertensive. All the patients in our study had been diagnosed as having CKD for the first time. Of the causes identified in the patients, chronic glomerulonephritis was the most common (46.9%, n=82), followed by hypertensive kidney disease (17.1%, n=30), diabetic nephropathy (13.1%, n=23), chronic pyelonephritis (12.0%, n=21), gout (6.9%, n=12), and polycystic kidney disease (4.0%, n=7). Causes were determined based on clinical and biochemical parameters and not on renal biopsy. The stage-wise clinical and laboratory profiles of patients in the study are as per Table 1. Of the study population, 17.7% (n=31), 20.0% (n=35), and 62.3% (n=109) were categorized as stage 3, 4, and 5 CKD, respectively. Median eGFR was 10.81 mL/min/1.73 m^2. Serum albumin level decreased, and serum hs-CRP level increased significantly as CKD progressed through stages 3–5 (p-trend<0.01). The prevalence of anemia was 88.6%, with a significant increase in the percentage of anemic patients observed as kidney function declined (p<0.001). The percentages of patients with mild, moderate, and severe anemia were approximately 14.8%, 60.0%, and 25.5%, respectively, with the percentage of patients exhibiting moderate and severe anemia increasing as renal function decreased. The mean Hb concentration of our study population was 9.71±2.26 g/dL. The morphological classes of anemia in our patients were hypochromic-microcytic anemia (12.3%), normochromic–normocytic anemia (86.5%), and macrocytic anemia (1.3%).

On comparing the mean values for the iron profiles of 175 patients with CKD and 51 healthy people as controls, we found that the median values for serum iron levels and TIBC in the study group (175 patients) at baseline were 11.8 and 50.4 µmol/L, respectively, and these values were significantly lower than those for the apparently healthy individuals (16 and 66 µmol/L, respectively, p<0.001). By contrast, the median value for the serum ferritin levels was significantly higher in the study group (259 ng/mL) than in the control group (160 ng/mL, p<0.001). The proportion of overall iron deficiency in the study group was 44%, which was mostly functional iron deficiency (37.1%). However, up to 25.7% of the patients exhibited iron overload. The overall proportion of iron deficiency was significantly higher in the study group than in the control group (44% vs 23.5%, p=0.008; Table 2).

As presented in Table 3, the percentage of patients with overall iron deficiency increases with the progression of CKD stages (for stages 3, 4, and 5, they were 22.6%, 42.9%, and 50.5%, respectively; p=0.022).

As seen from the results in Table 4, TIBC exhibited a weak negative correlation with serum creatinine (r=−0.19, p=0.01), a weak positive correlation with Hb concentration (r=0.17, p=0.02), a weak positive correlation with serum albumin (r=0.21, p=0.005), and a weak negative correlation with hs-CRP (r=−0.25, p=0.001). The correlation equation had been established.

Based on the results from the ROC curve model in Figure 2, TIBC had diagnostic value for iron deficiency (AUC=0.81; p<0.001). With a cut-off value of 50.4 (µmol/L), the sensitivity was 77.9%, and the specificity was 71.4%.

The association of various clinical factors and laboratory parameters with overall iron deficiency was examined using univariate analysis (Table 5). The risk for overall iron deficiency with Hb <10 g/dL (p=0.003); serum albumin <35 g/L (p=0.006); hematocrit <30% (p = 0.01); eGFR <15 mL/min/1.73m^2 (p=0.02), and hs-CRP >1.0 mg/L (p=0.005).

DISCUSSION

In this study, the mean age of the patients in this study was similar to that reported in another study.[11] Male patients were predominant, and this resembled the results of other reports.[11,12] As presented in Table 2, the overall prevalence of anemia in patients with CKD stages 3–5 receiving no dialysis was 88.6%. A similar Chinese cohort including 2420 patients with stage 1–5 CKD with aged 18–75 years reported that 51.5% of patients had anemia, of which 1338 patients had stage 3–5 CKD.[13] A Japanese cohort study showed that 32.3% of 2930 patients with stage 3–5 CKD were diagnosed as anemic.[14] In a South Korean cohort study, 44.9% of 2198 patients with stage 1–5 CKD were diagnosed as anemic (1524 patients with stage 3–5 CKD).[15] In the United States, the prevalence of anemia in patients with CKD was 15.4% in the NHANES study and 46% in the Chronic Renal Insufficiency Cohort study.[16,17] Considering the discrepancy in

Table 1. Clinical characteristics and laboratory parameters for each chronic kidney disease stage (n=175)

Clinical characteristics and laboratory parameters	Mean±SD/ Median				*p*-trend
	Total (n=175)	CKD stage 3 (n=31)	CKD stage 4 (n=35)	CKD stage 5 (n=109)	
Ages (years)	53.2±17.3	53.5±19.1	56.9±14.5	51.9±17.7	0.34
Sex (n, %)					0.53
Female	54 (30.9%)	7 (22.6%)	12 (34.3%)	35 (32.1%)	
Male	121 (69.1%)	24 (77.4%)	23 (65.7%)	74 (67.9%)	
BMI	20.4±2.22	21.0±1.82	21.2±2.74	20.1±2.05	0.01
Hypertension (n, %)	160 (91.4%)	29 (93.5%)	30 (85.7%)	101 (92.7%)	0.39
Etiology (n, %)					0.002
CGN	82 (46.9%)	10 (32.3%)	12 (34.3%)	60 (55%)	
Hypertension	30 (17.1%)	5 (16.1%)	10 (28.6%)	15 (13.8%)	
Chronic pyelonephritis	21 (12%)	3 (9.7%)	1 (2.9%)	17 (15.6%)	
Diabetes	23 (13.1%)	8 (25.8%)	5 (14.3%)	10 (9.2%)	
Gout	12 (6.9%)	5 (16.1%)	4 (11.4%)	3 (2.8%)	
Polycystic kidney diseases	7 (4%)	0 (0%)	3 (8.6%)	4 (3.7%)	
Serum urea (mmol/L)†	24.9 (14.4–34.5)	10.5 (6.8–13.5)	15.5 (12.8–21.8)	31.1 (24.5–38.7)	<0.001
Serum creatinine (μmol/L)†	460 (241–834)	145 (123–180)	262 (220–322)	707 (521–979)	<0.001
eGFR (ml/mim/1.73 m^2)†	10.8 (6.92–21.3)	35.1 (31.4–40.3)	19.7 (15.6–23.5)	7.58 (5.53–10.3)	<0.001
Serum albumin (g/L)	35.7±5.19	38.1±5.22	36.8±4.52	34.7±5.12	0.002
hs-CRP (mg/L)	0.8 (0.5–1.9)	0.5 (0.3–0.9)	0.8 (0.6–1.7)	1.1 (0.5–2.4)	0.002
Anemia (%)	155 (88.6%)	20 (64.5%)	30 (85.7%)	105 (96.3%)	<0.001
Severity of anemia (n, %)					0.269
Mild	23 (14.8%)	5 (25%)	7 (23.3%)	11 (10.5%)	
Moderate	93 (60.0%)	11 (55%)	17 (56.7%)	65 (61.9%)	
Severe	39 (25.2%)	4 (20%)	6 (20%)	29 (27.6%)	
Morphological type (%)					
Microcytic anemia	19 (12.3%)	5 (26.3%)	4 (13.8%)	10 (9.3%)	0.215
Normocytic anemia	134 (86.5%)	14 (73.7%)	24 (82.8%)	96 (89.7%)	
Macrocytic anemia	2 (1.3%)	0 (0%)	1 (3.4%)	1 (0.9%)	
Hb (g/dL)	9.71±2.26	11.2±2.25	10.2±2.26	9.08±2.01	<0.001
Hct (%)	30.1±6.86	36.2±6.96	32.3±6.54	27.6±5.51	<0.001
RBC (T/L)	3.41±0.82	4.05±0.79	3.68±0.87	3.15±0.67	<0.001
MCV (fL)	87.1±7.18	86.7±7.66	86.8±8.70	87.3±6.54	0.873
MCH (pg)	28.4±2.84	28.1±2.97	28.47±2.92	28.5±2.81	0.758
MCHC (g/L)	324±17.7	323±17.5	328±15.1	324±18.5	0.375

CKD: chronic kidney disease; BMI: body mass index; CGN: chronic glomerulonephritis; eGFR: estimated glomerular filtration rate; hs-CRP: high-sensitivity C-reactive protein; Hb: hemoglobin; HCT: hematocrit; RBC: red blood cells; MCV: mean corpuscular volume; MCH: mean corpuscular Hb; MCHC: mean corpuscular Hb concentration; SD: standard deviation.
†Data presented are median (interquartile range).

anemia prevalence, our results might have been higher than the aforementioned studies' because 175 patients in our study were diagnosed as having stage 3–5 CKD for the first time (62.3% in stage 5 CKD). The majority of the patients in our study had moderate anemia. We found that the prevalence of moderate and severe anemia increased progressively with the deteriorating of renal function. These findings reflect that anemia severity increases with declining renal function, which can be attributed to various factors associated with the development of anemia in patients with CKD, such as erythropoietin insufficiency, iron and vitamin deficiency, malnutrition, inflammation, platelet dysfunction, reduced red blood cell survival, and hemolysis.[2] Similar to the findings in other research,[11,18] we found that the mean Hb level, red blood cell count, and hematocrit level significantly decreased with the deterioration of the renal function. Most patients in our study had normochromic–normocytic anemia, comparable to the findings of other studies.[11,19]

In our study, the mean serum iron and ferritin levels and TIBC in patients with CKD were significantly different from the values for the control group. In particular, the ferritin level was significantly higher in the study group (259 ng/mL) than in the control group (160 ng/mL).

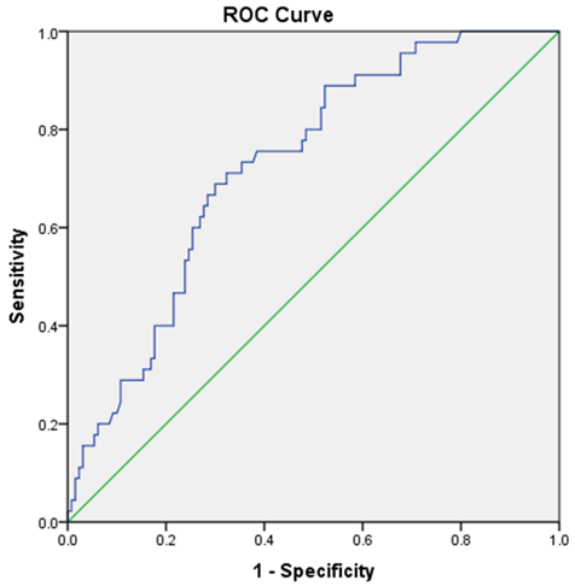

Figure 2. Diagnostic value of TIBC for overall iron deficiency (n=175). Area under the ROC curve=0.81; p<0.001; Cut-off: 50.4 (μmol/L); Sensitivity 77.9%; Specificity 71.4%.

Table 2. Iron profiles in study group and control group (n=226)

Variable	Study group (n=175)	Control group (n=51)	*p*-value	OR	95%CI
Serum iron (µmol/L)	11.8 (7.7–17.3)	16.0 (12.5–19.3)	<0.001		
Ferritin (ng/mL)	259 (149–475)	160 (107–190)	<0.001	N/A	N/A
TIBC (µmol/L)	50.4 (40.0–71.0)	66.0 (57.2–72.5)	<0.001		
TSAT (%)	22.6 (13.1–33.5)	24.9 (19.0–30.1)	0.17		
Functional iron deficiency (n, %)			0.01	2.42	1.13–5.16
Yes	65 (37.1)	10 (19.6)			
No	110 (62.9)	41 (80.4)			
Absolute iron deficiency (n, %)			0.44	1.80	0.39–8.33
Yes	12 (6.9)	2 (3.9)			
No	163 (93.1)	49 (96.1)			
Overall iron deficiency* (n, %)			0.008	2.55	1.25–5.20
Yes	77 (44)	12 (23.5)			
No	98 (56)	39 (76.5)			

TIBC: total iron-binding capacity; TSAT: transferrin saturations.
*p<0.05.

Table 3. Iron profiles at various stages of CKD (n=175)

Characteristics	Percentage				*p*-trend
	Total (n=175)	CKD stage 3 (n=31)	CKD stage 4 (n=35)	CKD stage 5 (n=109)	
Functional iron deficiency (n, %)	65 (37.1)	7 (22.6)	13 (37.1)	45 (41.3)	0.16
Absolute iron deficiency (n, %)	12 (6.9)	0 (0)	2 (5.7)	10 (9.2)	0.19
Overall iron deficiency* (n, %)	77 (44)	7 (22.6)	15 (42.9)	55 (50.5)	0.02

CKD: chronic kidney disease.
*p<0.05.

Table 4. Correlation between TIBC and several paraclinical indices (n=175)

Indices	TIBC (µmol/L)		Correlation equation
	r	*p*	
Serum creatinine (µmol/L)	-0.19	0.01	TIBC = 61.5 – 0.01 x Creatinine
Hemoglobin (g/dL)	0.17	0.02	TIBC = 0.14 x Hemoglobin + 41.8
Serum albumin (g/L)	0.21	0.005	TIBC = 0.77 x Albumin + 28.2
hs-CRP (mg/L)	-0.25	0.001	TIBC = 62.4 - 5.27 x hs-CRP

hs-CRP: high-sensitivity C-reactive protein.

TIBC was lower in the study group (50.4 µmol/L) than in the control group (66.0 µmol/L). These findings were comparable to those of other studies.[20-22] The increase in ferritin levels can be explained by the nonspecific protein synthesis compensating for protein loss in advanced CKD as well as the progression of inflammation in CKD patients.

Since the KDOQI 2006 workgroup recommended targeting serum ferritin levels of more than 100 ng/mL in patients with non-dialysis ESRD, some randomized control studies showed beneficial that iron treatment had erythropoietic effects in patients with stage 3–5 CKD and ferritin levels exceeding 100 ng/mL.[10,23] Currently, the Vietnamese Nephrology Association covered the use of intravenous iron in patients with CKD and with TSAT <20.0% or ferritin <100 ng/mL, and Hb lower than 10 g/dL. In our study, 44.0% of the patients with CKD required the use of intravenous iron for the first hospitalization admission. Systemic iron balance is therefore maintained through regulation of dietary iron absorption and iron release from storage sites in the liver and reticuloendothelial macrophages.[24] Patients with CKD experienced increased iron loss due to chronic bleeding from uremia-associated platelet dysfunction, frequent phlebotomy, and blood trapping in the dialysis apparatus.[25] Data have suggested that serum hepcidin may account for the impaired dietary iron absorption and reticuloendothelial cell iron blockade present in many patients with CKD. In 2001, two groups observed independently[26,27] that hepcidin is the main hormone responsible for maintaining systemic iron homeostasis.[25] Thus, patients with CKD who are prone to true iron deficiency, and iron supplementation is part of the mainstay of anemia treatment in CKD. Intravenous iron is preferred for patients with CKD because of impaired dietary iron absorption.[10] In our study, we found some risk factors associated with overall iron deficiency in patients with CKD, including Hb <10 g/dL; serum albumin <35 g/L; hematocrit <30%; eGRF <15 mL/min/1.73m^2, and hs-CRP <1.0 mg/L. Alzaheb RA et al[28] reported that iron deficiency anemia was prevalent among female university students in the Saudi Arabian context was 12.5% and that inadequate iron intake was a risk factor related to contracting anemia. One of the most common factors influencing iron homeostasis is inflammation, which is present in CKD, especially in end-stage CKD.[29] However, we also found a relationship between

Table 5. Risk factors associated with overall iron deficiency in patients with CKD (n=175)

Parameters	Overall iron deficiency		*p*-value	OR	95% CI
	n	%			
Ages (Years)			0.32	1.36	0.74–2.50
<60 (n=105)	43	41			
≥60 (n=70)	34	48.6			
Sex			0.16	0.63	0.33–1.20
Female (n=54)	28	51.9			
Male (n=121)	49	40.5			
Diabetes			0.39	1.46	0.60–3.51
Yes (n=23)	12	52.2			
No (n=152)	65	42.8			
Hemoglobin (g/dL)			0.003	2.62	1.37–5.00
<10 (n=108)	57	52.8			
≥10 (n=67)	20	29.9			
Albumin (g/L)			0.006	2.34	1.27–4.34
<35 g/l (n=73)	41	56.2			
≥35 g/l (n=102)	36	35.3			
Hematocrit (%)			0.01	2.12	1.14–3.94
<30 (n=98)	51	52			
≥30 (n=77)	26	33.8			
eGFR (mL/min/1.73m^2)			0.02	2.03	1.08–3.84
<15 (n=109)	55	50.5			
≥15 (n=66)	22	33.3			
hs-CRP (mg/L)			0.005	2.38	1.29–4.39
≤1.0 (n=98)	34	34.7			
>1.0 (n=77)	43	55.8			

TSAT: transferrin saturations; eGFR: estimated glomerular filtration rate; hs-CRP: high-sensitivity C-reactive protein.

overall iron deficiency and serum hs-CRP in the study. The proportion of overall iron deficiency increased through stage 3 CKD to stage 5 CKD. The causes of iron deficiency in patients with CKD were multifactorial. Some had true iron deficiency, characterized by a decrease in both circulating iron levels and total body iron stores. Other patients had functional iron deficiency, characterized by a decrease in circulating iron that limits erythropoiesis, which can occur even in the context of normal or adequate body iron stores. A combination of these features was also sometimes presented. Factors predisposing patients with CKD to iron deficiency included increasing blood loss, increased iron utilization from ESA therapy, impaired dietary iron absorption, and impaired iron release from body storage sites.[24,30]

When evaluating the correlation between TIBC and some para-clinical indices, we found that TIBC had a weak negative correlation with creatinine level, a weak positive correlation with Hb concentration, a weak positive correlation with serum albumin, and a weak negative correlation with hs-CRP. The correlation between TIBC and creatinine reflected the level of renal impairment as well as Hb concentration. TIBC depends on the blood's capacity to bind iron with iron-bearing proteins including transferrin. TIBC denotes the quantity of iron transported to the body. TIBC is usually lower in patients with chronic diseases, inflammation, malnutrition, or proteinuria. In patients with CKD, malnutrition is often a major problem. Malnutrition leads to hypoproteinemia, which causes decreasing TIBC as well as Hb concentration due to a lack of synthetic materials. This was consistent with the results seen in Table 1: serum albumin level was significantly decreased along with renal impairment levels ($p<0.01$). Furthermore, inflammation in patients with chronic renal failure also affected TIBC levels. The higher the hs-CRP levels were, the lower the TIBC concentration was.

Using ROC curve analysis to assess the overall iron deficiency diagnosis for TIBC, we observed that increasing TIBC had diagnostic value for overall iron deficiency with AUC=0.81; $p<0.001$. At a cut-off value of 50.4 (μmol/L), the sensitivity was 77.9%, and the specificity was 71.4% (Figure 2). This result was consistent with that from clinical practice. Overall iron deficiency is often reflected by decreasing iron and TSAT as well as increasing ferritin and TIBC concentrations.

The limitation of our study is that we conducted only a cross-sectional study, so the effectiveness of treatment and the progress of patients were not assessed.

Conclusions

In summary, the overall prevalence of anemia was approximately 88.6% in 175 Vietnamese patients with stage 3–5 CKD. In the CKD group, the mean serum iron concentration was lower; serum ferritin was higher, and serum TIBC was also lower than in the control group. In total, 44.0% of the patients exhibited overall iron deficiency. TIBC had a diagnostic value for predicting iron deficiency (AUC=0.81; $p<0.001$). The multivariable adjusted regression analysis showed that eGFR, Hb, hematocrit, serum albumin, and hs-CRP were independent risk factors for overall iron deficiency in CKD patients.

AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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