e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 900-905

Original Research Article

Evaluation of Hematological, Biochemical Parameters and Hepcidin Levels in Chronic Kidney Disease Non-Dialysis Dependent Patients

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Received: 01-03-2026 / Revised: 15-04-2026 / Accepted: 21-05-2026
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Conflict of interest: Nil

Abstract

Background: Chronic Kidney Disease (CKD) is associated with progressive impairment of renal function and disturbances in iron metabolism. Hepcidin, a key regulator of iron homeostasis, has emerged as an important biomarker in CKD-related anemia and inflammation.

Aim: To evaluate serum hepcidin levels and their association with ferritin, serum creatinine, and blood urea among non-dialysis dependent CKD patients.

Methodology: A cross-sectional study was conducted on 150 CKD patients categorized into Stage 3, Stage 4, and Stage 5 CKD. Serum hepcidin, ferritin, creatinine, a blood urea was measured and compared across CKD stages. Correlation between ferritin and hepcidin was assessed.

Results: Serum hepcidin increased significantly from Stage 3 (52.71±8.52 ng/ml) to Stage 5 CKD (74.88±12.22 ng/ml) (p<0.001). Serum ferritin also showed a significant increase from 242.04±171.30 ng/dl in Stage 3 to 446.16±414.84 ng/dl in Stage 5 (p<0.001). Blood urea and serum creatinine demonstrated progressive elevation with advancing CKD stages (p<0.001). A significant positive correlation was observed between ferritin and hepcidin in Stage 3 (r=0.36, p=0.05), Stage 4 (r=0.66, p<0.001), and Stage 5 CKD (r=0.45, p=0.001).

Conclusion: Serum hepcidin, ferritin, serum creatinine, and blood urea increase significantly with worsening CKD. Hepcidin shows a positive association with ferritin, suggesting its role in altered iron metabolism and inflammation in CKD patients.

Keywords: Chronic Kidney Disease, Hepcidin, Ferritin, Serum Creatinine, Blood Urea, Iron Metabolism.

DOI: 10.25258/ijcpr.18.6.146

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Introduction

Chronic Kidney Disease (CKD) is a major global public health concern characterized by progressive and irreversible deterioration of renal function. It affects millions of individuals worldwide and is associated with significant morbidity, mortality, and healthcare burden. The diagnosis and progression of CKD are commonly assessed using renal function markers such as serum creatinine and blood urea, which reflect the glomerular filtration capacity of the kidneys. As kidney function declines, retention of nitrogenous waste products leads to elevated serum creatinine and blood urea concentrations, serving as important indicators of disease severity. [1,2]

Anemia is one of the most common complications of CKD and contributes substantially to reduced quality of life and increased cardiovascular risk. Although erythropoietin deficiency has long been considered the primary cause of anemia in CKD, disturbances in iron metabolism are now recognized as equally important contributors. Iron homeostasis is tightly regulated by hepcidin, a 25-amino acid peptide hormone synthesized predominantly by hepatocytes. [3,4] Hepcidin regulates systemic iron balance by binding to ferroportin, the principal cellular iron exporter, resulting in its internalization and degradation. This process decreases intestinal iron absorption and restricts iron release from macrophages and hepatic stores, thereby reducing circulating iron availability.

In patients with CKD, hepcidin levels are frequently elevated due to reduced renal clearance and chronic inflammation. Increased hepcidin concentrations contribute to functional iron deficiency by limiting iron mobilization despite adequate or increased body iron stores. Consequently, iron becomes sequestered within

reticuloendothelial cells, impairing erythropoiesis and exacerbating anemia. Serum ferritin is the most widely used biochemical marker of body iron stores. Ferritin is an intracellular iron-storage protein that releases iron in a controlled manner according to physiological requirements. In CKD patients, serum ferritin levels may be elevated not only because of increased iron stores but also as an acute-phase reactant in response to chronic inflammation. Hepcidin-mediated iron sequestration further promotes ferritin synthesis and release, making the relationship between serum ferritin and hepcidin particularly important in understanding iron metabolism abnormalities in CKD. [5,6]

Assessment of renal function using serum creatinine and blood urea remains fundamental in the evaluation and staging of CKD. [7] Progressive renal impairment leads to accumulation of these metabolites and is often accompanied by worsening disturbances in iron regulation. Emerging evidence suggests that increasing renal dysfunction may influence hepcidin metabolism, resulting in elevated circulating hepcidin levels and altered ferritin concentrations. [8]

Therefore, evaluating the association between serum hepcidin, ferritin, serum creatinine, and blood urea may provide valuable insights into the interplay between iron homeostasis and renal dysfunction in CKD patients. Understanding these relationships could improve the assessment of anemia and iron status, thereby contributing to better clinical management and therapeutic decision-making in patients with chronic kidney disease.

Material and Methodology

This hospital-based cross-sectional analytical study was conducted in the Department of Biochemistry in collaboration with the Department of Nephrology of RNT Medical College & MB Hospital, Udaipur, and Rajasthan, India. The study was carried out after obtaining approval from the Institutional Ethics Committee and written informed consent from all participants.

A total of 150 patients who diagnosed as a CKD and attending at Nephrology OPD of our Institute were included in the study,

Inclusive Criteria for CKD: Patients>18 years with presence of following for >3 months:

- Albuminuria
- Electrolytes abnormalities.
- Urine sediment abnormalities.
- History of kidney transplantation.
- Decreased GFR: GFR <60ml/min/1.73m^2.

Exclusive Criteria:

- Patients on Renal replacement therapy (Haemodialysis, peritoneal dialysis and Kidney transplant), Iron therapy, EPO therapy.
- Patients with any kind of blood disorders.
- Patients taking any kind of supplements.

In this study, area, socioeconomic status and dietary habits and tobacco smoking habit of the enrolled participants will be noted.

Sample Collection: Patients that are coming to Nephrology department of MB Hospital, Udaipur will be enrolled. Informed consent will be taken from each patient.10 ml blood will be drawn through vein puncture. For routine biochemical parameters blood will be collected in plain vials For haematological parameters blood will be collected in EDTA vials. Samples will be incubated & centrifuge at 3000 rpm for15 minutes after clot formation. Precautions will be taken to avoid hemolysis of sample.

The separated serum was used for estimation of biochemical parameters.

Biochemical Analysis: Serum Hepcidin: Serum hepcidin concentration was measured using a commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kit according to the manufacturer's instructions. Results were expressed in ng/ml.

Serum Ferritin: Serum ferritin was estimated by Chemiluminescent Immunoassay (CLIA). Ferritin levels were expressed in ng/dl and used as an indicator of body iron stores.

Serum Creatinine: Serum creatinine was measured using the modified Jaffe's kinetic method on an automated biochemistry analyzer. Results were expressed in mg/dL.

Blood Urea: Blood urea concentration was determined by the enzymatic urease method using an automated clinical chemistry analyzer. Results were expressed in mg/dL.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 26.0. Continuous variables were expressed as mean ± standard deviation (SD). Comparison between groups was performed using Student's independent t-test. Correlation between serum hepcidin and serum ferritin, serum creatinine, and blood urea was assessed using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Results

CKD is most prevalent in middle-aged adults (48–62 years), with a sharp decline in the elderly (78+ years). (Table 1)

Table 1: Demographic and Clinical Distribution

Age Group	No. of CKD Patients	Percentage
18–32	34	22.67%
33–47	39	26%
48–62	51	34%
63–77	23	15.33%
78–92	3	2%
Total	150	

Table 2: Sex Distribution and CKD Stages

Sex	Stage 3	Stage 4	Stage 5	P-Value
Male (n=88)	23	30	35	0.005
Female (n=62)	6	36	20	

Male patients predominate in stages 3 and 5, while females form the majority in stage 4. The distribution is statistically significant.

Table 3: Marital Status and Stages of CKD

Marital Status	Stage 3	Stage 4	Stage 5	P-Value
Married	**20**	**59**	**46**	**0.0483**
Unmarried	**9**	**7**	**9**	

Married individuals form the vast majority of the patient pool across all stages, showing a statistically significant demographic association.

Table 3: Area and Stages of CKD

Area	Stage 3	Stage 4	Stage 5	P-Value
Rural	17	44	34	0.723
Urban	12	22	21	

More patients reside in rural areas, but geographical location is not significantly associated with the severity of the CKD stage.

Table 4: Alcohol and Stages of CKD

Alcohol	Stage 3	Stage 4	Stage 5	P-Value
Alcohol	15	49	38	0.0933
Non-Alcohol	14	17	17	

Alcohol consumers heavily outnumber non-consumers in later stages, though the overall association stops just short of statistical significance.

Table 5: Smoking Habits and CKD

Smoking	Stage 3	Stage 4	Stage 5	P-Value
Smoker	17	22	27	**0.0463**
Non-Smoker	12	44	28	

There is a statistically significant link between smoking and CKD stages, with non-smokers notably peaking in stage 4.

Table 6: Dietary Habits and CKD

Dietary	Stage 3	Stage 4	Stage 5	P-Value
Veg	13	38	30	0.515
Non-Veg	16	28	25	

Dietary preference does not significantly influence the progression or distribution of CKD stages.

Table 7: Diabetes and Stages of CKD

Diabetes Status	Stage 3	Stage 4	Stage 5	P-Value
Diabetic	8	38	17	0.002
Non-Diabetic	21	28	38	

Diabetes status is significantly associated with CKD stage progression, with diabetic frequency peaking notably in stage 4.

Table 8: Anemia and Stages of CKD

Stage	Mild Anemia	Moderate Anemia	Severe Anemia	P-Value
Stage 3	8	19	2	0.001
Stage 4	16	38	12	
Stage 5	1	37	17	

The severity of anemia worsens significantly as CKD progresses, shifting toward more moderate to severe cases in stage 5.

Table 9: Showing Results of Various Key Renal Function Parameters

Parameters	Stage 3 (Mean ± SD)	Stage 4 (Mean ± SD)	Stage 5 (Mean ± SD)	P-Value
Urea (mg/dl)	83.48 ± 12.57	100.63 ± 37.64	148.14 ± 59.83	<0.001
Creatinine (mg/dl)	2.13 ± 0.32	3.1 ± 0.78	6.58 ± 3.64	<0.001
GFR	36.11 ± 6.35	20.85 ± 4.34	10.38 ± 3.15	<0.001

As CKD progresses from stage 3 to stage 5, metabolic waste products (Urea and Creatinine) significantly accumulate, while filtering capacity (GFR) significantly declines.

Table 10: Hematological and Iron Parameters

Parameters	Stage 3 (Mean ± SD)	Stage 4 (Mean ± SD)	Stage 5 (Mean ± SD)	P-Value
TIBC (µg/dl)	287.25 ± 83.21	296.71 ± 76.75	267.8 ± 79.84	0.135
Hepcidin (ng/ml)	52.71 ± 8.52	60.16 ± 11.09	74.88 ± 12.22	<0.001
Iron (µg/dl)	65.96 ± 16.08	63.19 ± 23.70	74.67 ± 44.50	0.14
Hemoglobin (gm/dl)	9.26 ± 1.59	8.53 ± 1.67	7.5 ± 1.28	<0.001
Ferritin (ng/dl)	242.04 ± 171.30	233.08 ± 226.23	446.16 ± 414.84	<0.001

Progression of CKD causes a significant drop in hemoglobin and a significant rise in both Hepcidin and Ferritin (indicators of inflammation and iron storage). TIBC and circulating Iron show no statistically significant changes.

Table 11: Correlation between Ferritin and Hepcidin

Stage	r-value	P-Value
Stage 3	0.36	0.05
Stage 4	0.66	<0.001
Stage 5	0.45	0.001

There is a statistically significant positive correlation between iron stores (Ferritin) and iron regulation (Hepcidin) across all three measured stages of CKD. This relationship is strongest during Stage 4.

Discussion

The present study was conducted on 150 patients of chronic kidney disease attending the Department of nephrology of RNT Medical College & M.B. Hospital, Udaipur, and Rajasthan.

A total of 150 CKD patients were included in the study. The age distribution showed that the largest group was 48–62 years (51 patients, 34.0%), followed by 33–47 years (39 patients, 26.0%) and 18–32 years (34 patients, 22.7%). Fewer patients were observed in the 63–77 years age group (23 patients, 15.3%), while the 78–92 years group accounted for only 3 patients (2.0%). Thus, the majority of CKD patients belonged to the middle-aged group (33–62 years), indicating that CKD was more prevalent in this age range in the study population. Similar study In a study of 130 CKD patients, the 60–69 years age group comprised the largest share—51 patients (39.2%)—followed by 50–59 years (34 patients, 26.2%), 40–49 years (15 patients, 11.5%), and younger groups (<20 through 30–39 years) had much lower percentages (ranging from ~2% to ~6.9%). [9]

Similar studies Coresh J et al [10], and Viswanathan et al [11], have indicated that the prevalence of CKD is higher in older age groups with a male preponderance. The former has also reported that 11% of individuals older than 65 years have CKD. Cases in stage 5 were maximum in the 36-50 age group. The older age and the male predominance can be explained by the underlying disease entity causing CKD. Diabetes and hypertension, both of which are etiological factors of CKD are prevalent more in older age groups and male sex. Carrero JJ et al. [12] observed that chronic kidney disease (CKD) exhibits clear sex-based differences in its epidemiology and progression. Although women are more frequently diagnosed with early stages of CKD, men demonstrate a faster decline in kidney function and

a higher risk of progression to end-stage kidney disease (ESKD). This male dominance has been attributed to both biological and sociocultural factors. Testosterone has been linked to increased renal fibrosis and injury, whereas estrogen appears to exert renoprotective effects by reducing oxidative stress and glomerulosclerosis. Furthermore, men often present with more cardiovascular risk factors such as hypertension, which accelerate CKD progression. In contrast, despite slower disease progression, women with CKD may experience poorer outcomes once on dialysis, partly due to under-recognition and treatment disparities.

Liang CC et al. [13] reported that in patients with CKD who are not receiving dialysis, lower renal function is associated with an increased risk of upper gastrointestinal bleeding. The risk was particularly higher among those with a prior history of upper gastrointestinal bleeding and low serum albumin levels.

Out of the total CKD patients, 81 were vegetarians and 69 were non-vegetarians. Among vegetarians, the majority were in stage 4 (38 cases, 46.9%), followed by stage 5 (30 cases, 37.0%) and stage 3 (13 cases, 16.1%). In the non-vegetarian group, patients were distributed as stage 4 (28 cases, 40.6%), stage 5 (25 cases,36.2%), and stage 3 (16 cases, 23.2%). Overall, both dietary groups showed a similar distribution across CKD stages, with stage 4 being the most common in both.

Diabetes mellitus, particularly type 2 diabetes, is the most common cause of chronic kidney disease (CKD) worldwide and accounts for nearly 40–50% of end-stage renal disease (ESRD) cases. Persistent hyperglycemia leads to glomerular hyperfiltration, endothelial dysfunction, and podocyte injury, which gradually result in albuminuria, declining glomerular filtration rate (GFR), and renal fibrosis [14,15].

In the present study, serum urea levels increased significantly with advancing CKD stage ($p < 0.001$). The mean urea concentration was 83.48 ± 12.57 mg/dl in stage 3, 100.63 ± 37.64 mg/dl in stage 4, and 148.14 ± 59.83 mg/dl in stage 5.

This progressive rise reflects the impaired renal clearance of nitrogenous waste products as kidney function declines, a well-established biochemical hallmark of CKD. Similar findings have been reported in earlier studies, where urea levels were observed to increase progressively with CKD severity, correlating with worsening glomerular filtration rate and accumulation of metabolic waste [16,17].

These observations highlight the utility of serum urea as a supportive biochemical marker in staging and monitoring the progression of CKD.

In our study, serum creatinine levels increased significantly with advancing CKD stage ($p < 0.001$). The mean creatinine concentration was 2.13 ± 0.32 mg/dl in stage 3, 3.10 ± 0.78 mg/dl in stage 4, and 6.58 ± 3.64 mg/dl in stage 5. This progressive rise reflects declining renal clearance of creatinine as glomerular filtration rate decreases, making serum creatinine a reliable biochemical marker of renal function deterioration.

In the present study, serum ferritin levels were found to increase progressively with advancing stages of CKD. While ferritin is traditionally considered a marker of iron storage, its elevation in CKD often reflects the chronic inflammatory state rather than true iron sufficiency. Ferritin acts as an acute-phase reactant, and systemic inflammation, along with reduced renal clearance, contributes to its accumulation in later stages of CKD. Importantly, rising ferritin levels do not necessarily correlate with adequate iron availability, as concurrent increases in hepcidin restrict intestinal absorption and impair mobilization of stored iron, resulting in functional iron deficiency. Similar observations have been reported by Kalantar-Zadeh et al. [18] and Padwal MK et al. [19], who noted that elevated ferritin in CKD is strongly associated with inflammation and adverse outcomes rather than improved iron status.

Conclusion

Form this study we would Like to conclude that Serum hepcidin, ferritin, serum creatinine, and blood urea increase significantly with worsening CKD. Hepcidin shows a positive association with ferritin, suggesting its role in altered iron metabolism and inflammation in CKD patients.

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