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Original Research Article

Study of Hematological and Biochemical Markers Including Hepcidin in Chronic Kidney Disease Non-Dialysis-Dependent Patients

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Abstract

Background: Chronic Kidney Disease (CKD) is a progressive systemic disorder associated with widespread hematological and biochemical derangements. Anemia is an early, debilitating complication predominantly driven by reduced erythropoietin (EPO) synthesis, chronic inflammation, and defective iron homeostatic mechanisms. Serum hepcidin has recently emerged as a key regulatory hormone implicated in functional iron deficiency during CKD progression.

Aim: A Study aim is to analyze the clinical significance of specific hematopoietic markers (Erythropoietin and Hepcidin), liver aminotransferases (SGPT/ALT and SGOT/AST), and renal function markers (Serum Creatinine) in non-dialysis dependent (NDD) CKD patients, evaluating their cross-correlations across progressive disease stages.

Methodology: A cross-sectional observational clinical study evaluated 150 non-dialysis dependent CKD patients aged over 18 years. Laboratory assessments quantified serum erythropoietin, hepcidin (via ELISA), and serum glutamate pyruvate transaminase (SGPT/ALT), and serum glutamic oxaloacetic transaminase (SGOT/AST), and serum creatinine levels across stages 3, 4, and 5. Statistical cross-correlations were calculated to establish the systemic pathophysiological relationships.

Results: Serum creatinine and serum hepcidin levels increased progressively and significantly with advancing stages of renal dysfunction. In contrast, serum erythropoietin levels exhibited a continuous decline as kidney disease progressed. Changes in liver aminotransferases (SGOT and SGPT) were relatively minor and did not show a direct association with serum hepcidin levels. However, SGOT levels demonstrated a noticeable reduction from baseline with increasing severity of renal impairment.

Conclusion: As chronic kidney disease (CKD) progresses to more advanced stages, serum creatinine and hepcidin levels rise concurrently. The negative relationship between declining erythropoietin production and increasing hepcidin concentrations underscores the complex mechanisms contributing to anemia in non-dialysis-dependent CKD (NDD-CKD). Regular assessment of these biomarkers can provide valuable clinical insight for the early management of systemic complications prior to the initiation of dialysis.

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Introduction

Chronic Kidney Disease (CKD) represents a substantial and growing global public health threat characterized by irreversible structural and functional renal damage. It is formally diagnosed when the estimated glomerular filtration rate (eGFR) falls below 60 mL/min/1.73m2for a sustained period exceeding 3 months. The progressive nature of the syndrome induces multiple metabolic and hematological complications that severely escalate cardiovascular morbidity and mortality. [1,2] Anemia typically manifests during CKD Stage 3 and worsens dramatically through Stage 5. [3]While primary etiology is traditionally ascribed to the failure of interstitial fibroblasts to secrete adequate erythropoietin (EPO), absolute or functional iron deficiencies present a substantial secondary hurdle. Iron kinetics in the human body are tightly dictated by hepcidin, a 25-amino acid peptide hormone generated primarily by hepatocytes. Hepcidin works by binding to and inducing the internalization and degradation of ferroportin, the

exclusive cellular iron export channel. In CKD, declining glomerular clearance paired with persistent subclinical inflammation triggers pathologically elevated hepcidin levels. This sequesters functional iron stores inside macrophages and hepatocytes, starving active erythropoiesis. [4,5] At the same time, serum creatinine remains the primary biochemical marker used to assess and stage the decline in kidney filtration function. In addition to changes in filtration, interactions between the liver and kidneys can influence various metabolic processes within the hepatorenal axis. Liver enzymes, including serum glutamate pyruvate transaminase (SGPT/ALT) and serum glutamic oxaloacetic transaminase (SGOT/AST), often show subtle changes in patients with uremia. [6,7]These alterations are generally marked by a gradual reduction in aminotransferase activity as chronic kidney disease progresses.

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 Erythropoietin: Serum Erythropoietin was estimated by Enzyme-Linked Immunosorbent Assay (ELISA) kit. Erythropoietin levels were expressed in mIU/mL.

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

SGPT and SGOT: SGPT and SGOT was measured using the IFCC Kinetic method on an automated biochemistry analyzer.

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

The study population predominantly consisted of males (58.7%). The majority of CKD patients belonged to the 48–62 years age group, indicating higher disease burden among middle-aged and elderly individuals.

Table 1: Demographic Characteristics of CKD Patients (n=150)

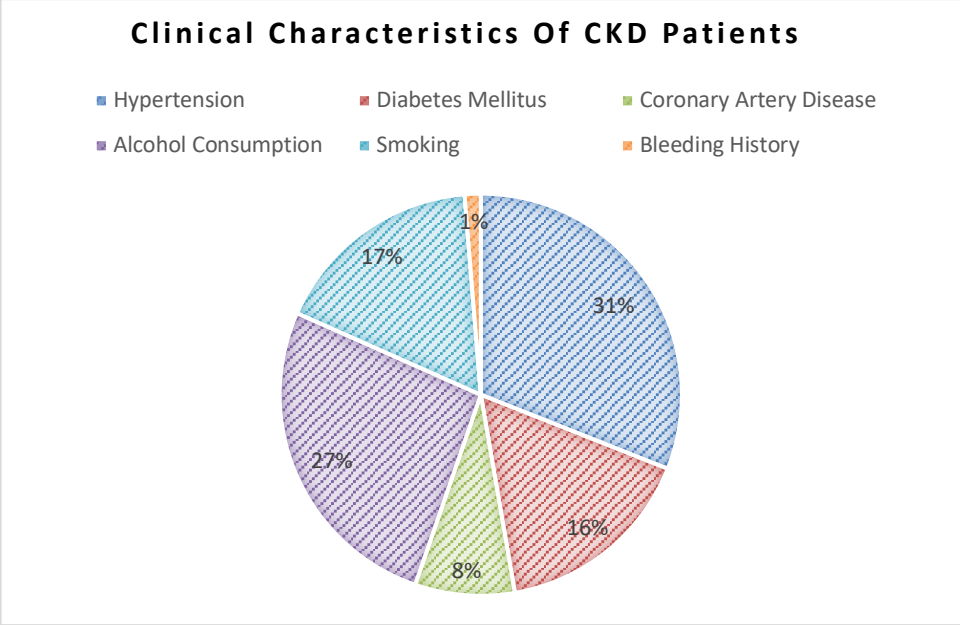
Variable	Category	Number (%)
Sex	Male	88 (58.7%)
	Female	62 (41.3%)
Age Group	18–32 years	34 (22.7%)
	33–47 years	39 (26.0%)
	48–62 years	51 (34.0%)

	≥63 years	26 (17.3%)

Table 2: Clinical Characteristics of CKD Patients

Clinical Variable	No (%)
Hypertension	120 (80.0%)
Diabetes Mellitus	63 (42.0%)
Coronary Artery Disease	31 (20.7%)
Alcohol Consumption	102 (68.0%)
Smoking	66 (44.0%)
Bleeding History	5 (3.3%)

Hypertension was the most common comorbidity, affecting 80% of patients, followed by diabetes mellitus. These findings support the established role of hypertension and diabetes in CKD progression.



Graph 1: Showing Clinical Characteristics of CKD Patients

Table 3: Distribution of Patients According to CKD Stage

CKD Stage	Number (%)
Stage 3	29 (19.3%)
Stage 4	66 (44.0%)
Stage 5	55 (36.7%)

Most patients belonged to Stage 4 CKD, followed by Stage 5, indicating that a large proportion presented with advanced renal dysfunction.

Table 4: 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 5: 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 6: 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 7: Serum Creatinine across CKD Stages

CKD Stage	Mean ± SD (mg/dL)	P-value
Stage 3	2.13 ± 0.32	
Stage 4	3.10 ± 0.78	
Stage 5	6.58 ± 3.64*	<0.001

Serum creatinine increased significantly with advancing CKD stage, reflecting progressive deterioration of renal function.

Table 8: Serum Hepcidin across CKD Stages

CKD Stage	Mean ± SD (ng/mL)	P-value
Stage 3	52.71 ± 8.52	
Stage 4	60.16 ± 11.09	
Stage 5	74.88 ± 12.22	<0.001

Serum hepcidin levels increased significantly with CKD progression, suggesting impaired renal clearance and increased inflammatory activity in advanced disease.

Table 9: Serum Erythropoietin across CKD Stages

CKD Stage	Mean ± SD (mIU/mL)	P-value
Stage 3	19.31 ± 7.11	
Stage 4	16.57 ± 6.67	
Stage 5	7.72 ± 3.42	<0.001

A significant decline in erythropoietin levels was observed with worsening CKD stage, indicating progressive loss of renal endocrine function.

Table 10: SGOT (AST) Across CKD Stages

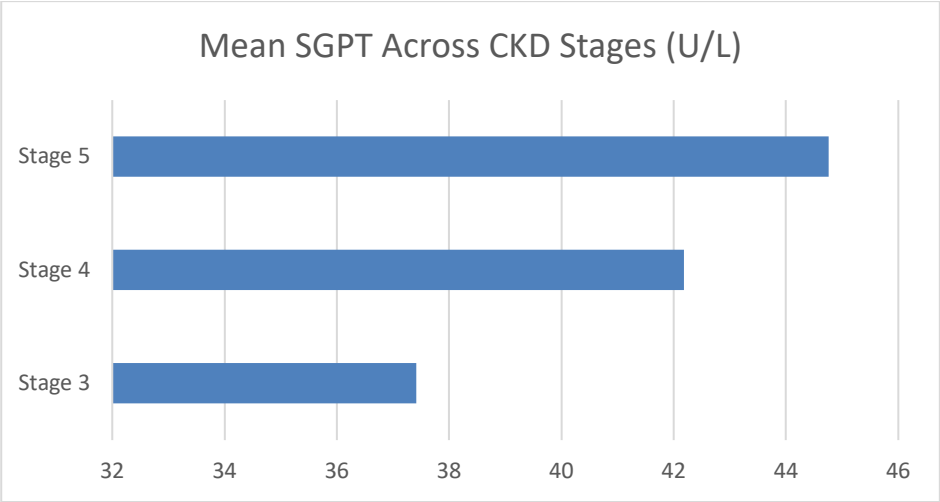
CKD Stage	Mean ± SD (U/L)	P-value
Stage 3	44.03 ± 45.40	
Stage 4	48.41 ± 84.74	
Stage 5	45.42 ± 88.16	0.963

SGOT levels showed no significant variation among CKD stages, suggesting minimal influence of CKD progression on AST levels.

Table 11: SGPT (ALT) Across CKD Stages

CKD Stage	Mean ± SD (U/L)	P-value
Stage 3	37.42 ± 38.22	
Stage 4	42.18 ± 78.64	
Stage 5	44.76 ± 89.16	0.917

No statistically significant difference in SGPT levels was observed across CKD stages.



Graph 2: Mean SGPT across CKD Stages (U/L)

Table 12: Correlation of Hepcidin with Erythropoietin and Creatinine

Parameter	Correlation with Hepcidin	Interpretation
Erythropoietin	Negative	Increasing hepcidin is associated with declining EPO production
Serum Creatinine	Positive	Higher hepcidin levels occur with worsening renal dysfunction

Elevated hepcidin appears to be associated with reduced erythropoietin synthesis and deteriorating renal function.

Table 13: Correlation of Hepcidin with Liver Enzymes

Parameter	Stage 3 (r)	Stage 4 (r)	Stage 5 (r)	P-value
AST	-0.12	-0.12	+0.09	NS
ALT	-0.02	-0.14	+0.01	NS

(NS = Not Significant)

Hepcidin demonstrated weak and statistically non-significant correlations with AST and ALT in all CKD stages, suggesting that liver enzyme variations do not substantially influence circulating hepcidin levels in CKD patients.

Discussion

Chronic kidney disease (CKD) has become a significant global public health issue and is recognized as a worldwide epidemic. It is strongly associated with an elevated risk of cardiovascular disease, vascular complications, and progression to end-stage kidney disease. The increasing prevalence of CKD poses a substantial health burden worldwide. Recent estimates indicate that nearly 119.5 million people globally are living with CKD, highlighting its growing impact on public health [8,9].

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 patients with chronic kidney disease (CKD) were studied, comprising 88 males and 62 females. The distribution of patients across CKD stages showed that males were predominantly represented in stage 5 (35 cases, 39.8%), followed by stage 4 (30 cases, 34.1%) and stage 3 (23 cases, 26.1%). In contrast, females were more frequently observed in stage 4 (36 cases, 58.1%), followed by stage 5 (20 cases, 32.3%) and stage 3 (6 cases, 9.7%).

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.

Hypertension and chronic kidney disease (CKD) commonly coexist and the interrelation between these two pathophysiological states is bidirectional. [10,11].Persistently high blood pressure (BP) can accelerate the progression of CKD and the progressive decline in the estimated glomerular filtration rate (eGFR) can conversely interfere with the achievement of adequate BP control [12].

Out of the total patients, 120 had hypertension and 30 were non-hypertensive. Among hypertensive patients, the majority were in stage 4 (55 cases, 45.8%), followed by stage 5 (45 cases, 37.5%) and stage 3 (20 cases, 16.7%). In the non- hypertensive group, the distribution was stage 4 (11 cases, 36.7%), stage 5 (10 cases, 33.3%) and stage 3 (9 cases, 30.0%). The commonest risk factor for CKD in this study was hypertension.

Out of the total CKD patients, 102 reported alcohol use and 48 were non-alcohol users. Among alcohol users, the majority were in stage 4 (49 cases, 48.0%), followed by stage 5 (38 cases, 37.3%) and stage 3 (15 cases, 14.7%). In the non-alcohol group, patients were distributed equally in stage 4 (17 cases, 35.4%) and stage 5 (17 cases, 35.4%), with fewer in stage 3 (14 cases, 29.2%).

Shankar et al. [13]. Found that chronic alcoholism is associated with CKD. Heavy alcohol consumption is consistently linked to an increased risk of CKD through mechanisms such as hypertension, oxidative stress, proteinuria, and alcohol-related liver disease, which disrupts iron metabolism and promotes systemic inflammation. Among patients with established CKD, excessive alcohol intake can accelerate disease progression, worsen blood pressure control, and contribute to malnutrition and vitamin deficiencies, while also interfering with commonly prescribed medications.

Panduranga G et al. [14]. Observed anemia in all patients with chronic kidney disease (CKD). Hemoglobin levels ranged from 4.9 g/dl to 11.4 g/dl, with a mean value of 8.7 g/dl. The majority of cases (16 patients, 50%) presented with moderate anemia.

Ruchi Khadayate et al. [15] observed that 96.8% of patients had anemia. Among them, 62.1% of stage 5 CKD patients presented with severe anemia,

while 57.1% of stage 4 CKD patients and only 3.16% of stage 3 CKD patients were anemic.

In our study, serum erythropoietin (EPO) levels were observed to decline progressively as CKD advanced from stage 3 to stage 5. This finding aligns with previous reports demonstrating that impaired renal function leads to a reduction in endogenous EPO synthesis. The primary mechanism involves the loss or dedifferentiation of peritubular fibroblast-like cells in the renal cortex, which are the principal source of EPO production [16,17]. Eschbach and Adamson first described anemia in end-stage renal disease as being largely due to insufficient EPO production, while Eckardt et al. [18] provided direct evidence of reduced EPO secretion in patients with advanced renal failure

Conclusion

As chronic kidney disease (CKD) progresses to more advanced stages, serum creatinine and hepcidin levels rise concurrently. The negative relationship between declining erythropoietin production and increasing hepcidin concentrations underscores the complex mechanisms contributing to anemia in non-dialysis-dependent CKD (NDD-CKD). Regular assessment of these biomarkers can provide valuable clinical insight for the early management of systemic complications prior to the initiation of dialysis.

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