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(RESEARCH ARTICLE)

# Correlation between serum hepcidin level and stages of chronic kidney disease: A cross sectional study

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## Abstract

**Introduction**: Chronic Kidney Disease (CKD) has been associated with significant mortality and morbidity. Despite significant numbers of cases, biomarkers related to iron status and development of anaemia in these patients has not been looked upon extensively. Few biomarkers have been studied, one of which is serum hepcidin levels. We aimed to estimate the serum hepcidin levels in patients with CKD and its correlation with its successive stages.

**Materials and Methods:** The study design was cross-sectional observational study. 51 patients of CKD KDIGO stage II to V were included and patients of obstructive uropathy or malignancy or transplant recipient were excluded from the study. The aim of the study was to evaluate the association between serum hepcidin levels and Stages of CKD in terms of eGFR.

**Results**: The mean serum hepcidin levels which were found in Stage II, III, IV and V of CKD patients was 65.48, 116.03, 136.61 and 160.37 ng/ml respectively. There was a strong negative correlation between eGFR and serum hepcidin level, and this correlation was statistically significant ($r = -1.0$, $p = <0.001$). The Krushkal-Wallis Test also provided p value of <0.001 when stages of CKD and serum hepcidin levels were correlated.

**Conclusion:** There was significant positive correlation of serum hepcidin with the stages of CKD ($P < 0.001$) and the levels of serum hepcidin were found to be significantly higher as the stage increased. Thus, serum hepcidin may be used as a marker of iron metabolism, prognosis and progress of disease in the CKD patients.

**Keywords:** Hepcidin; Chronic Kidney Disease; HIF-PH (Hypoxia-Inducible Factor-Prolyl Hydroxylase); Iron; Anemia

**Key Messages :** Serum hepcidin level has significant positive correlation with progression of CKD stage (P<0.001) and significant negative correlation with eGFR (P<0.001). It may be used as an important prognostic marker in different stages of CKD.

## 1. Introduction

The estimated global prevalence of CKD is 11% including patients from stage 3 to stage 5 and 13% for patients with CKD stage 1 to stage 5.[1] In India 1 in 5 adults is found to have CKD. Diabetes is the single largest contributor to the CKD/ESKD burden in India, accounting for one-third of the patients with CKD, while other etiologies such as hypertension (13%), glomerulonephritis (14%), and undetermined causes (16%).[2]

Anaemia is very commonly associated with CKD. It causes poorer outcomes in the CKD patients. It compromises quality of life and increases utilization of health care resources. Anaemia also increases risk of cardiovascular adverse events,

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risk of progression of the disease and increase all cause mortality. The therapeutic modalities for the anaemia are oral or intravenous iron supplementation, blood transfusion and intravenous blood transfusion agents. All these modalities increase the risk of cardiovascular accidents.[1] Even excessive use of erythropoietin stimulating agents (ESA) also does not improve the quality of life. On the contrary it increases the risk of development of cardiovascular mortatily.[3]

There is progressive decline in the response to the ESA in CKD patients. hepcidin is hypothesised to be the principle mediator behind this progressive decline in the response to the ESA.[4]

The principle role of the hepcidin is to prevent release of iron from the cellular basolateral surface, be it intestinal epithelium or iron storing hepatocytes. Hepcidin achieve this by blocking a protein called Ferroportin. It is a protein ubiquitously present on any iron storing cell. It is required for the release of the cellular iron into the circulation. So inhibition of this protein by increasing concentration of hepcidin creates a relative state of iron deficiency. In any inflammatory condition hepcidin increases as it is an acute phase reactant. So hepcidin is the key molecule behind the pathogenesis of the anaemia of any chronic disease.[5]

Anaemia in CKD is not solely contributed by increased level of hepcidin. There are various factors which interplay among themselves to give rise to the anaemia in the CKD. Decreased production of erythropoietin, effect of uremic toxins on the Erythroid progenitor, uraemia induced coagulopathy are some of the few mechanism by which anaemia develops in CKD but the progressive ESA refractory anaemia is hypothesised to be mainly caused by the increased hepcidin concentration in the blood.[6]

The increase in hepcidin concentration is not only related to the chronic inflammatory state of the CKD. The decrease in eGFR also hypothesised to an important factor in the increasing concentration of hepcidin because hepcidin is mainly cleared off from the circulation via glomerular filtrate.[7] There is a need of further explorations and studies to establish this hypothesis because the establishment of significant negative correlation between serum hepcidin level and eGFR have very significant therapeutic and prognostic implication in future. There are already available drugs in the phase III trial targeting this hepcidin-Ferroportin axis to improve iron availability and quality of life in the CKD patients. They achieve this via Hypoxia-Inducible Factor-Prolyl Hydroxylase (HIF-PH) inhibitors. These HIF-PF inhibitors are also shown to act via reducing levels of hepcidin levels in the CKD patients.[8] Thus this study is designed to fulfil this goal i.e. to explore whether there exist a significant correlation between serum hepcidin level and eGFR.

## 2. Materials and methods

### 2.1. Study Design

This is a hospital based crossed sectional study

### 2.2. Setting

The study was conducted in the Department of Medicine and Department of Nephrology, VMMC and Safdarjung Hospital, New Delhi.

After the approval by ethics committee, written informed consent was taken from respective patients or relatives of the diagnosed patients of CKD. A total of 51 patients of CKD were subjected to detailed history and systemic examination including a detailed abdominal examination which was recorded in the study proforma.

### 2.3. Study Details

Detailed history was taken. Structured questionnaires were administered and physical examinations were done. The baseline clinical characteristics analyzed in each group was the age, gender, hypertension, diabetes mellitus, smoking status, personal and family history, iron profile and various other blood parameters like CBC, LFT, KFT and serum hepcidin levels. These assessments were done at the time of admission to decide the stage of CKD and other comorbidities. Serum hepcidin was done within 24hrs of admission.

### 2.4. Aim of the study

The aim of this study is to correlate between serum hepcidin level and stages of CKD.

### 2.5. Inclusion criteria

All patients fulfilling diagnostic criteria for CKD and within KDIGO stage II to V; Age above 18 years.

### 2.6. Exclusion criteria

CKD due to any obstructive uropathy; Patients with malignancy; Kidney transplant recipient and those who are on dialysis.

### 2.7. Sample Size

For tests of association using bi-variate correlations, a moderate correlation between serum hepcidin level and stages of CKD in terms of eGFR was considered meaningful. To detect a moderate negative correlation (r = -0.40), a sample of 51 analyzable subjects provided 80% power to discover that the correlation is significantly different from there being no correlation (i.e. that the correlation would be zero) at the 0.05 level

### 2.8. Statistical Analysis

Descriptive statistics was analyzed with SPSS version 21.0 software. Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. The Pearson's chi-square test or the chi-square test of association was used to determine if there is a relationship between two categorical variables.

Spearman/Pearson correlation was used between serum hepcidin level and stage of CKD in terms of eGFR. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

## 3. Results

Our study was performed on the patients of CKD and various other parameters which influenced the risk and poor outcomes in the CKD patients. The patient population evaluated was from the patient pool who visited the Safdarjung hospital. The mean age of our study population was 49.92 years. 3.9% of the participants had age between 21-30 Years. 70.6% of the participants were male and 29.4% were female. The demographic profile of our study is enlisted in Table 1.

**Table 1** Demographic profile

| **Age/Gender** | **Mean ± SD \|\| Median (IQR) \|\| Min-Max \|\| Frequency (%)** |
|---|---|
| Age (Years) | 49.92 ± 11.54 \|\| 52.00 (39.00-60.00) \|\| 22.00 - 69.00 |
| Age | |
| 21-30 Years | 2 (3.9%) |
| 31-40 Years | 12 (23.5%) |
| 41-50 Years | 11 (21.6%) |
| 51-60 Years | 14 (27.5%) |
| 61-70 Years | 12 (23.5%) |
| Gender | |
| Male | 36 (70.6%) |
| Female | 15 (29.4%) |

**Table 2** Association between eGFR (mL/min/1.73m$^2$) and Parameters

| **Parameters** | **eGFR (mL/min/1.73m$^2$)** | **p value** |
|---|---|---|
| Hemoglobin (g/dL)*** | Correlation Coefficient (rho) = 0.99 | <0.001[1] |
| TLC (/mm$^3$) | Correlation Coefficient (rho) = -0.18 | 0.218[1] |
| Platelet Count (x10$^3$/mm$^3$)*** | Correlation Coefficient (rho) = -0.46 | <0.001[1] |
| RBS (mg/ dL) | Correlation Coefficient (rho) = -0.16 | 0.256[1] |
| S. Sodium (mEq/L) | Correlation Coefficient (rho) = 0.1 | 0.505[1] |
| S. Potassium (mEq/L)*** | Correlation Coefficient (rho) = -0.34 | 0.014[1] |
| S. Calcium (mg/dL)*** | Correlation Coefficient (rho) = 0.99 | <0.001[1] |
| PO4 (mg/dL)*** | Correlation Coefficient (rho) = -1 | <0.001[1] |
| Blood Urea (mg/dL)*** | Correlation Coefficient (rho) = -0.98 | <0.001[1] |
| S. Creatinine (g/dL)*** | Correlation Coefficient (rho) = -0.97 | <0.001[1] |
| Total Bilirubin (mg/dL)*** | Correlation Coefficient (rho) = 0.42 | 0.002[1] |
| Direct Bilirubin (mg/dL)*** | Correlation Coefficient (rho) = 0.37 | 0.008[1] |
| Indirect Bilirubin (mg/dL)*** | Correlation Coefficient (rho) = 0.4 | 0.004[1] |
| SGOT (U/L) | Correlation Coefficient (rho) = -0.27 | 0.057[1] |
| SGPT (U/L)*** | Correlation Coefficient (rho) = -0.68 | <0.001[1] |
| ALP (U/L)*** | Correlation Coefficient (rho) = -0.31 | 0.024[1] |
| Total Protein (g/dL) | Correlation Coefficient (rho) = 0.14 | 0.325[1] |
| S. Albumin (g/dL)*** | Correlation Coefficient (rho) = -0.32 | 0.021[1] |
| USG Grade*** | | <0.001[2] |
| Grade 1 MRD | 77.18 ± 0 | |
| Grade 2 MRD | 59.00 ± 11.28 | |
| Grade 3 MRD | 30.90 ± 6.66 | |
| Grade 4 MRD | 8.40 ± 5.08 | |
| Urine CS (No Growth) | 24.31 ± 21.02 | - |
| Urine R/M: Protein*** | | <0.001[2] |
| Nil | - | |
| 1+ | 63.09 ± 11.20 | |
| 2+ | 22.63 ± 11.58 | |
| 3+ | 4.31 ± 0.92 | |
| Urine R/M: Glucose | | 0.149[2] |
| Nil | 25.74 ± 21.45 | |
| 1+ | 12.98 ± 10.59 | |
| 2+ | 3.52 ± 0 | |
| 3+ | - | |
| S. Iron (µg/dL)*** | Correlation Coefficient (rho) = 1 | <0.001[1] |

| | | |
|---|---|---|
| S. Ferritin (ng/mL)*** | Correlation Coefficient (rho) = -1 | <0.001[1] |
| TIBC (µg/dL)*** | Correlation Coefficient (rho) = -0.97 | <0.001[1] |
| Hepcidin (ng/dL)*** | Correlation Coefficient (rho) = -1 | <0.001[1] |
| CKD Stage*** | | <0.001[2] |
| 1 | - | |
| 2 | 68.21 ± 6.98 | |
| 3 | 40.41 ± 5.66 | |
| 4 | 22.09 ± 6.18 | |
| 5 | 5.66 ± 2.10 | |

***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon-Mann-Whitney U Test

**Table 3** Comparison of the 5 Subgroups of the Variable CKD Stage in Terms of hepcidin

| **Hepcidin (ng/ml)** | **CKD Stage** | | | | | **Kruskal Wallis Test** | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | χ2 | p value |
| Mean (SD) | (NA) | 65.48 (21.01) | 116.03 (7.21) | 136.61 (9.71) | 160.37 (3.61) | 45.102 | <0.001 |
| Pairwise Comparison of Subcategories of CKD Stage | | | | | | Adjusted P Value | |
| 2 - 3 | | | | | | 0.916 | |
| 2 - 4 | | | | | | 0.029 | |
| 3 - 4 | | | | | | 0.235 | |
| 2 - 5 | | | | | | <0.001 | |
| 3 - 5 | | | | | | <0.001 | |
| 4 - 5 | | | | | | 0.002 | |

Post-Hoc pairwise tests for Kruskal-Wallis test performed using Dunn Test method with Sidak correction.

The various biochemical parameters are also analysed and their trend is followed with respect to the eGFR and stages of CKD. The Table 2 summarises the results.

The following variables were significantly associated ($p<0.05$) with the variable eGFR (mL/min/1.73m$^2$): hemoglobin (g/dL), platelet count (x10$^3$/mm$^3$), S. potassium (mEq/L), S. calcium (mg/dL), S. phosphate (mg/dL), blood urea (mg/dL), S. creatinine (g/dL), total bilirubin (mg/dL), direct bilirubin (mg/dL), indirect bilirubin (mg/dL), SGPT (U/L), ALP (U/L), S. albumin (g/dL), urine R/M: protein, S. iron (µg/dL), S. ferritin (ng/mL), TIBC (µg/dL), hepcidin (ng/dL), CKD stage.

Fig.1 depicts the correlation between eGFR (mL/min/1.73m$^2$) and hepcidin (ng/mL). Individual points represent individual cases. The blue trend line represents the general trend of correlation between the two variables. The shaded grey area represents the 95% confidence interval of this trend line. Non-parametric tests (Spearman Correlation) were used to explore the correlation between the two variables, as at least one of the variables was not normally distributed. There was a very strong negative correlation between eGFR (mL/min/1.73m$^2$) and hepcidin (ng/ml), and this correlation was statistically significant (rho = -1, p = <0.001).For every 1 unit increase in eGFR (mL/min/1.73m$^2$), the hepcidin (ng/ml) decreases by 1.47 units. Conversely, for every 1 unit increase in hepcidin (ng/ml), the eGFR (mL/min/1.73m$^2$) decreases by 0.66 units.The variable hepcidin (ng/ml) was not normally distributed in the 5 subgroups of the variable CKD Stage. Thus, non-parametric tests (Kruskal Wallis Test) were used to make group comparisons. There was a significant difference between the 5 groups in terms of hepcidin (ng/ml) ($\chi2 = 45.102$, p = <0.001), with the mean hepcidin (ng/ml) being highest in the CKD Stage 5. Strength of Association (Kendall's Tau) = 0.85 (Large Effect Size). This is also depicted in the figure 2 and 3.

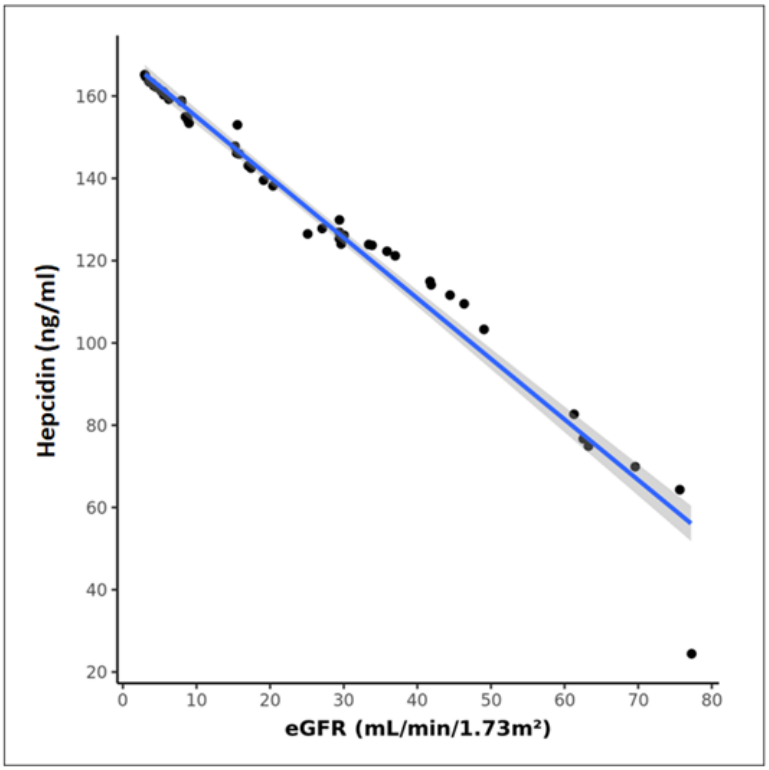


**Figure 1** Scatter plot of eGFR vs serum hepcidin

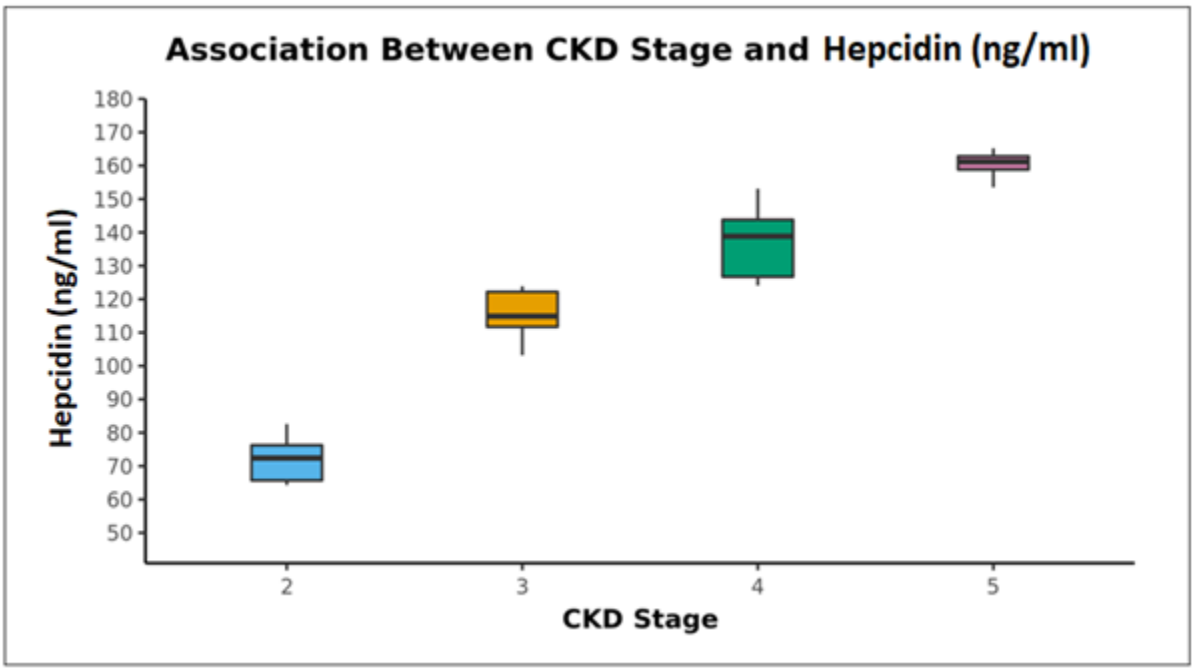


**Figure 2** Box whisker plot comparing stages of CKD in terms of serum hepcidin

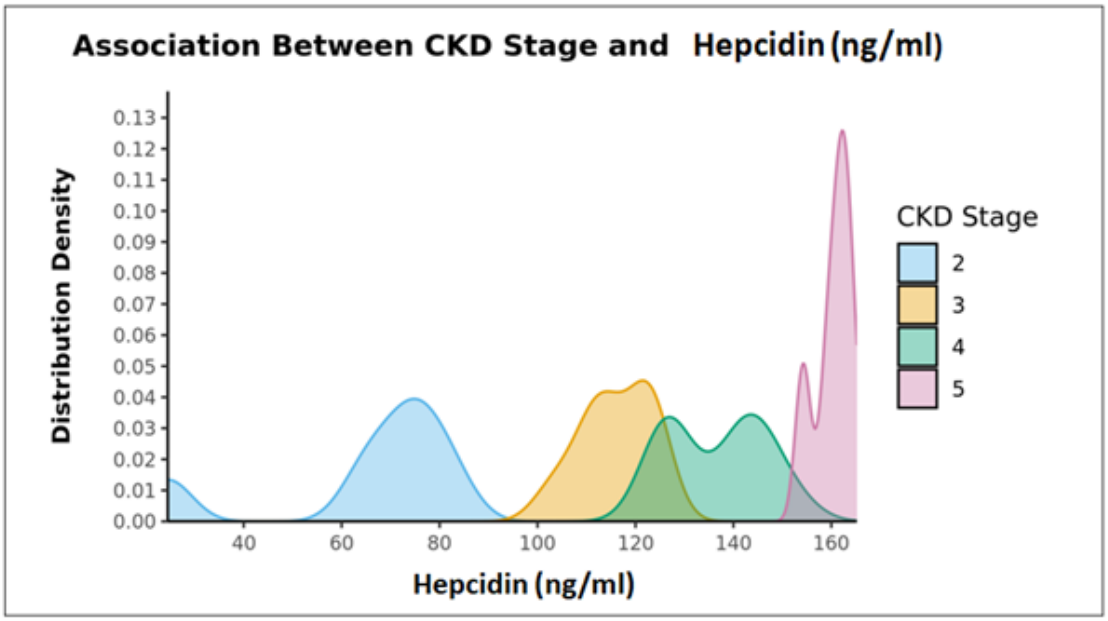


**Figure 3** Density plot comparing stages of CKD in terms of serum hepcidin

## 4. Discussion

The mean eGFR (mL/min/1.73m$^2$) in our study population was 24.31. Similar study done by Hsu C-Y and McCulloch CE found that 46% of women and 19% of men of creatinine clearance 20-30 has transferrin saturation less than 20%.[9] On the same population 40% of female and 44% of male has serum ferritin less than 100ng/ml. They also observed that 13.5 million US adults has creatinine clearance of <50. They have used anaemia definition with hb< 11gm/dl and found that burden of anaemia in CKD is around 8 lakh. The study was done in 2002 in US.

The decreasing eGFR in our study population had a significant impact on the calcium and phosphate status. The mean S. Calcium (mg/dL) was 6.53 and the mean phosphate (mg/dL) was 8.99 in our study. The calcium and phosphate had a statistically significant positive and negative correlation with the eGFR respectively. With stages of CKD increases, there was a significant association, that was found in our study. An Indian study done by Ghosh B et al. found that the prevalence of hypocalcemia in stage 4 and stage 5 CKD are 56.41% and 54.95% respectively.[10]

Similar study done by Vikrant S et al. also in India found that 70.6% patients with CKD had iPTH value above the target range.[11] Hypocalcaemia observed in 23.8% patients that were included in the study. They had taken the CKD stages 3 to 5.

Abdu A et al. studied the pattern of mineral bone disorder in CKD patients, they found that 39.5% patients had hyperphosphatemia, 46%had hypocalcaemia.[12] Their study group comprises of 81% male and 19% female. The age group ranges from 40-59yrs with the mean of 45 yrs.

Dang ZH et al. also find a similar study of mineral bone disorder in CKD patients of Tibetan population, found that hypocalcemia was present in 40% patients and hyperphosphatemia was present in 29.7% patients.[13]

The main goal of our study was to determine the correlation of the hepcidin levels with the decreasing eGFR as the stages of the CKD progressed. We found that serum hepcidin level has a significant negative correlation with the eGFR as well as a statistically significant positive association with the stages of CKD. The mean hepcidin (ng/ml) levels in the CKD Stage 2 was 65.48, in the CKD Stage 3 was 116.03, in the CKD Stage 4 was 136.61, in the CKD Stage 5 was 160.37.

An Indian study by Goyal KK et al. in children on topic of hepcidin also concluded that there is indeed a positive correlation between serum hepcidin and other inflammatory bio markers in Non Dialysed Iron and EPO naïve patients.[14] They found that hepcidin levels were highest in patients with impaired iron trafficking, followed by without any iron deficiency, followed by patients with absolute iron deficiency. Hepcidin levels were positively correlated with IL-6, TNF-

alpha, hsCRP, serum ferritin with P=0.001, 0.05, 0.03 and 0.001 respectively. Hepcidin was negatively correlated with TIBC, Hb, eGFR with p value of 0.003, 0.001, and 0.001 respectively.

Malyszko J et al. studied hepcidin, iron status and renal function in chronic renal failure.[15] They found that, in haemodialysed patients, serum hepcidin was significantly lower than controls which is strikingly opposite to our study. Mean hepcidin in control group was 239.4 and 205 in haemodialysed group. Hepcidin correlated significantly with other parameters like Total Protein (r=0.6, p<0.01), Albumin (r=0.7, p<0.001), creatinine (r=0.3, p=0.05), eGFR (r=-0.3,p<0.05). In healthy volunteers, hepcidin was related to triglyceride (r=0.3, p=0.05). A multiple regression analysis done by them showed that hepcidin was independently related to creatinine, triglyceride and residual renal function on haemodialysed patients. They also did a multiple regression analysis on kidney transplant patients, found that hepcidin was independently related to GFR only.

Many studies are also done involving patients on hemodialysis. Some of them showed similar results, while some of them contrasting. Małyszko J et al. did a study named "Is hepcidin a link between anaemia, inflammation and liver function in hemodialyzed patients?" and found hepcidin levels higher in CKD patients in hemodialysed group as compared to controls.[16] Hepcidin levels also correlated positively with TLC, Albumin, TG and negatively with Hb and Hct.

Belo Let al. did another study on "Hepcidin and diabetes are independently related with soluble transferrin receptor levels in chronic dialysis patients" and found that among diabetic patients, transferrin saturation was inversely correlated with hepcidin in Diabetic CKD patients.[17] They also found in patients on dialysis, hepcidin was significantly and positively correlated with serum iron, ferritin and CRP.

The impact of hepcidin on the iron profile is also evident in our study. We found a significant positive correlation of hepcidin with TIBC and Ferritin and significant negative correlation with the serum iron.

Rubab Z et al. found that serum hepcidin level was higher in ESRD as compared to controls.[18] The haemoglobin, Hct, serum iron, TIBC and transferrin saturation were significantly lower in ESRD. Higher hepcidin levels found in EPO non responders compared to responders (19.6 ng/ml vs 60.9 ng/ml, p=0.001).

So, there is a relation of increased levels of hepcidin in CKD and erythropoietin resistance.

## 5. Conclusion

There was significant positive correlation of serum hepcidin with the stages of CKD ($P < 0.001$) and the levels of serum hepcidin were found to be significantly higher as the stage increased. Thus, serum hepcidin may be used as a marker of iron metabolism, prognosis and progression of disease in the CKD patients. Future research is needed to investigate whether derangement in other parameters of iron profile is associated with increased progression of disease and development of EPO resistance in patients with CKD keeping in mind the newly found HIF pathway of hepcidin modulation and ongoing trials of various drugs targeting this pathway. Well planned prospective studies with serial measurements of serum hepcidin and its association with clinical deterioration could be done to elucidate its role as a prognostic marker in patients with CKD.

## Compliance with ethical standards

### *Statement of informed consent*

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## References

[1] Hanna RM, Streja E, Kalantar K. Burden of anaemia in chronic kidney disease: Beyond erythropoietin. Adv Ther. 2021;38(1):52–75.

[2] Singh AK, Farag YMK, Mittal BV, Subramanian KK, Reddy SRK, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India - results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrol. 2013;14(1):114.

[3] Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of anaemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006;355(20):2085–98.

[4] Ueda N, Takasawa K. Impact of inflammation on ferritin, hepcidin and the management of iron deficiency anaemia in chronic kidney disease. Nutrients. 2018;10(9):1173.

[5] Wojciechowska M, Wisniewski OW, Kolodziejski P, Krauss H. Role of hepcidin in physiology and pathophysiology. Emerging experimental and clinical evidence. J Physiol Pharmacol. 2021;72(1).

[6] Portolés J, Martín L, Broseta JJ, Cases A. Anaemia in chronic kidney disease: From pathophysiology and current treatments, to future agents. Front Med (Lausanne). 2021;8:642296.

[7] Kulaksiz H, Theilig F, Bachmann S, Gehrke SG, Rost D, Janetzko A, et al. The iron-regulatory peptide hormone hepcidin: expression and cellular localization in the mammalian kidney. J Endocrinol. 2005;184(2):361–70.

[8] Del Balzo U, Signore PE, Walkinshaw G, Seeley TW, Brenner MC, Wang Q, et al. Nonclinical characterization of the hypoxia-inducible factor prolyl hydroxylase inhibitor roxadustat, a novel treatment of anaemia of chronic kidney disease. J Pharmacol Exp Ther. 2020;374(2):342–53.

[9] Hsu CY, McCulloch CE, Curhan GC. Epidemiology of anaemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey. J Am Soc Nephrol. 2002;13(2):504–10.

[10] Ghosh B, Brojen T, Banerjee S, Singh N, Singh S, Sharma OP, et al. The high prevalence of chronic kidney disease-mineral bone disorders: A hospital-based cross-sectional study. Indian J Nephrol. 2012;22(4):285–91.

[11] Vikrant S, Parashar A. Prevalence and severity of disordered mineral metabolism in patients with chronic kidney disease: A study from a tertiary care hospital in India. Indian J Endocrinol Metab. 2016;20(4):460–7.

[12] Abdu A, Abdu A, Arogundade FA. Prevalence and pattern of chronic kidney disease-mineral bone disorders among hemodialysis patients in kano, northwest nigeria. Ann Afr Med. 2019;18(4):191–5.

[13] Dang ZH, Tang C, Li GL, Luobu C, Qing D, Ma ZH, et al. Mineral and bone disorder in hemodialysis patients in the Tibetan Plateau: a multicenter cross-sectional study. Ren Fail. 2019;41(1):636–43.

[14] Goyal KK, Saha A, Sahi PK, Kaur M, Dubey NK, Goyal P, et al. Hepcidin and proinflammatory markers in children with chronic kidney disease: A case-control study. Clin Nephrol. 2018;89(5):363–70.

[15] Malyszko J, Malyszko JS, Pawlak K, Mysliwiec M. Hepcidin, iron status, and renal function in chronic renal failure, kidney transplantation, and hemodialysis. Am J Hematol. 2006;81(11):832–7.

[16] Małyszko J, Małyszko JS, Hryszko T, Pawlak K, Mysliwiec M. Is hepcidin a link between anaemia, inflammation and liver function in hemodialyzed patients? Am J Nephrol. 2005;25(6):586–90.

[17] Belo L, Rocha S, Valente MJ, Coimbra S, Catarino C, Bronze-da-Rocha E, et al. Hepcidin and diabetes are independently related with soluble transferrin receptor levels in chronic dialysis patients. Ren Fail. 2019;41(1):662–72.

[18] Rubab Z, Amin H, Abbas K, Hussain S, Ullah MI, Mohsin S. Serum hepcidin levels in patients with end-stage renal disease on hemodialysis. Saudi J Kidney Dis Transpl. 2015;26(1):19–25.