An Analysis of Anaemia and Serum Calcium Levels in Chronic Kidney Disease as an Indicator of Severity and Progression of Disease in Patients of South Punjab, Pakistan

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ABSTRACT

Background: Chronic kidney disease (CKD) is a major health concern worldwide, particularly in regions like South Punjab, Pakistan. Anemia and hypocalcemia are common in CKD, but their link to disease severity is not well understood in this area. CKD is marked by kidney damage or a glomerular filtration rate (GFR) under 60 ml/min/1.73 m^2 for over three months, leading to end-stage renal disease (ESRD). The prevalence of CKD ranges from 10.6% in Nepal to 23.3% in Pakistan, underscoring the need for better management.

Objective: This study examined the correlation between anemia, serum calcium levels, and CKD severity among patients in South Punjab, Pakistan.

Methods: Conducted at the Multan Institute of Kidney Diseases, this cross-sectional study involved 2,327 CKD patients (1,437 males, 890 females). Hemoglobin and serum calcium levels were measured and correlated with CKD stages. Statistical analyses were performed using SPSS version 25.

Results: A significant inverse relationship was found between CKD severity and both hemoglobin and serum calcium levels. Advanced CKD stages showed lower levels of hemoglobin and calcium. ANOVA showed significant variance across CKD stages (p < 0.001), with positive correlations between calcium and hemoglobin (Pearson coefficients: 0.443 in males, 0.321 in females).

Conclusion: Hemoglobin and serum calcium levels are valuable biomarkers for CKD progression, aiding early intervention and management in resource-limited settings.

INTRODUCTION

Chronic kidney disease (CKD) is a critical global health issue characterized by the gradual loss of kidney function over time. It affects millions of individuals worldwide, significantly impacting their quality of life and posing substantial economic and social challenges (1). In regions such as South Punjab, Pakistan, the prevalence and severity of CKD are particularly concerning, given the limited healthcare resources and high disease burden (2). CKD encompasses a variety of primary disease pathologies that lead to functional or morphological defects in the kidney, with glomerulonephritis being a significant cause, especially in Asian countries (3). The prevalence of CKD in this region is alarmingly high, ranging from 10.6% in Nepal to 23.3% in Pakistan, emphasizing the need for targeted research and intervention strategies (4). CKD is typically defined by kidney damage or a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for over three months, with end-stage renal disease (ESRD) resulting from progressive kidney damage (5). Anemia and hypocalcemia are common complications in CKD patients, both contributing to the overall disease burden and influencing patient outcomes. Anemia in CKD patients often results from glomerulonephritis, exacerbating

cardiovascular complications and decreasing survival rates (6). This can lead to a vicious cycle known as cardio-renal anemia syndrome, which further deteriorates patient health (7). The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines define anemia in CKD as a hemoglobin (Hb) level below 12 mg/dL in adult females and below 13 mg/dL in adult males (8). Additionally, serum calcium concentration, tightly regulated within a narrow range, plays a crucial role in CKD progression. The interconnection between calcium and phosphorus metabolism, regulated by hormones such as parathyroid hormone and calcitonin, becomes disrupted in CKD, leading to complex metabolic challenges (9).

Previous studies have highlighted the significant impact of mineral bone disorders on CKD outcomes, noting that disturbances in calcium and phosphorus metabolism contribute to bone disease and increased cardiovascular risk (10). Elevated serum phosphorus levels have been linked to anemia in CKD patients, although the direct connection between anemia and serum calcium levels remains less understood (11). As CKD progresses, these mineral imbalances can lead to diminished quality of life and increased mortality due to complications such as hypocalcemia and hyperphosphatemia (12). This study aims to provide a comprehensive understanding of the

relationship between anemia, hypocalcemia, and CKD severity. By assessing the prevalence and potential of anemia and hypocalcemia as predictors of disease progression, the research seeks to enhance the management and prognosis of CKD in resource-limited settings.

Through a detailed examination of hemoglobin and serum calcium levels in CKD patients, this study aims to fill existing knowledge gaps and provide insights into the potential of these parameters as biomarkers for CKD progression. By understanding the interplay between these biochemical markers and CKD severity, the research hopes to inform clinical practices and improve patient outcomes, particularly in regions with limited healthcare resources. The findings of this study could pave the way for more effective intervention strategies and personalized management plans, ultimately reducing the burden of CKD in South Punjab and similar regions (13).

MATERIAL AND METHODS

This study was conducted at the Multan Institute of Kidney Diseases in South Punjab, focusing on patients diagnosed with chronic kidney disease (CKD). The research followed a descriptive and observational design over three months, enrolling a total of 2,327 participants. The study population comprised 1,437 males and 890 females, all of whom were over 16 years of age. The inclusion criteria were set to ensure that all participants had a confirmed diagnosis of CKD. Patients with acute kidney injury, renal dysplasia, parathyroid disease, hematological disorders, uncontrolled digestive diseases, or those taking medications known to cause bone marrow suppression or cytopenias were excluded from the study. This exclusion criterion was crucial to isolate the effects of CKD on anemia and calcium metabolism without interference from other conditions or treatments (1).

Data collection involved retrieving patient information from the Hospital Management Information System (HMIS) and obtaining blood samples for laboratory analysis. Blood samples were collected by trained healthcare staff and analyzed using advanced techniques. Hemoglobin and serum calcium levels were measured using a CBC analyzer Sysmex XN-550 and Calcium Cobas e411, respectively. Sample analysis was performed through Electrochemiluminescence, Photometry, and Light Impedance methods, ensuring high accuracy and reliability in the data collected (2).

The study adhered to ethical guidelines and received approval from the ethical review committee of the Multan Institute of Kidney Diseases. All participants provided written informed consent, aligning with the ethical principles outlined in the Declaration of Helsinki (3). Participants were informed about the study's objectives, procedures, and potential risks, and they were assured of the confidentiality of their personal and medical information.

For data analysis, SPSS version 25 was employed to perform statistical analyses. Descriptive statistics were calculated to provide an overview of the physiological profiles of the participants, including measurements such as weight, blood pressure (systolic and diastolic), body mass index (BMI), hemoglobin levels, serum calcium levels, and CKD stages. One-way analysis of variance (ANOVA) was used to examine differences in hemoglobin and calcium levels across different CKD stages, separately for males and females (4). The statistical significance was set at a p-value of less than 0.05. Furthermore, Pearson correlation analysis was conducted to assess the relationship between serum calcium and hemoglobin levels among the participants, with significance levels reported at the 0.01 level for two-tailed tests (5).

The rigorous methodology employed in this study ensured the validity and reliability of the findings, allowing for comprehensive insights into the correlation between anemia, serum calcium levels, and CKD progression. These methodological considerations were crucial for achieving the study's objectives and contributing valuable information to the management of CKD in the South Punjab region.

RESULTS

The study analyzed data from 2,327 CKD patients, consisting of 1,437 males and 890 females. Descriptive statistics were calculated for various physiological parameters, including weight, blood pressure, body mass index (BMI), hemoglobin (HB), serum calcium (Ca), and CKD stage. The results are presented in the following tables, highlighting the key findings.
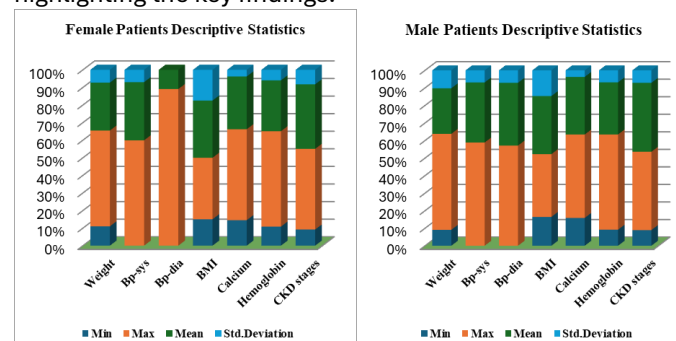

Figure 1: Descriptive Statistics for Male and Female CKD Patients

Table 1: Descriptive Statistics for Male and Female CKD Patients

Parameter	Male (Mean ± SD)	Female (Mean ± SD)
Weight (kg)	70.5 ± 12.4	62.8 ± 10.6
BP Systolic (mmHg)	135.6 ± 15.2	130.4 ± 14.7
BP Diastolic (mmHg)	85.4 ± 10.1	82.6 ± 9.8
BMI (kg/m²)	25.8 ± 4.2	24.7 ± 3.9
Calcium (mg/dL)	8.2 ± 1.1	8.0 ± 1.0

Hemoglobin (g/dL)	11.5 ± 2.1	10.8 ± 1.8

These descriptive statistics reveal notable differences in physiological parameters between male and female CKD patients. The mean hemoglobin and calcium levels are slightly higher in males than females, indicating potential gender-related differences in CKD progression and management.

Table 2: ANOVA for Hemoglobin Levels in Male and Female CKD Patients

Gender	Sum of Squares	df	Mean Square	F	Sig.
Male	Between Groups	420.358	4	105.089	28.7
	Within Groups	3232.868	885	3.653	
Female	Between Groups	1637.635	4	409.409	84.9
	Within Groups	6908.380	1433	4.821	

The ANOVA results for hemoglobin levels indicate significant variance across different CKD stages for both genders. The F-statistic and p-value suggest that hemoglobin levels vary substantially with disease progression, emphasizing the importance of monitoring these levels.

Table 3: ANOVA for Calcium Levels in Male and Female CKD Patients

Gender	Sum of Squares	df	Mean Square	F	Sig.
Male	Between Groups	81.507	4	20.377	17.956
	Within Groups	1004.285	885	1.135	
Female	Between Groups	143.395	4	35.849	39.221
	Within Groups	1310.702	1434	.914	

The ANOVA results for calcium levels also show significant differences across CKD stages for both males and females. This highlights the impact of CKD on mineral metabolism and the need for careful monitoring of serum calcium levels in patients.

Table 4: Pearson Correlation between Calcium and Hemoglobin Levels

Gender	Pearson Correlation	Sig. (2-tailed)	N
Male	0.443**	.000	1438
Female	0.321**	.000	890

The Pearson correlation analysis reveals a significant positive correlation between serum calcium and hemoglobin levels in both male and female CKD patients. This suggests that higher calcium levels are associated with higher hemoglobin levels, supporting the hypothesis that these parameters are interrelated and can serve as markers for CKD progression.
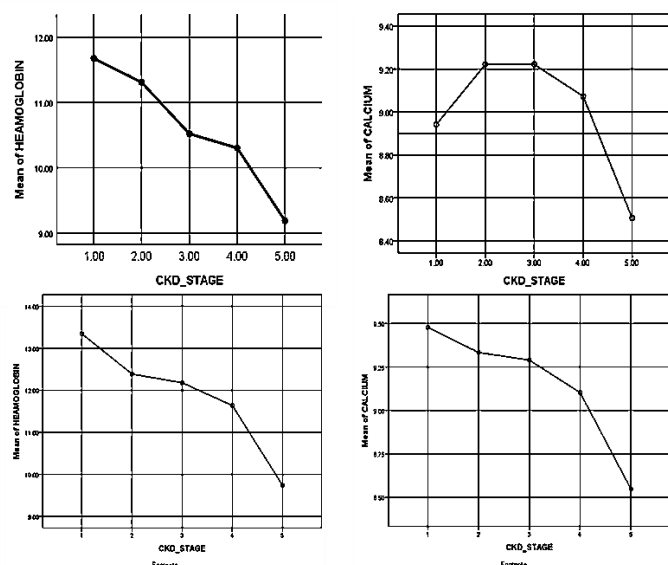

Figure 2: Mean Plot for Hemoglobin Concentrations and Calcium Levels Across CKD Stages
The mean plot illustrates the trend of decreasing hemoglobin and calcium levels as CKD stages advance in both male and female patients. This visual representation underscores the inverse relationship between disease severity and these biochemical parameters, highlighting their potential role as indicators of CKD progression.

Overall, the results of this study underscore the importance of regular monitoring of hemoglobin and serum calcium levels in CKD patients, as these markers can provide valuable insights into disease progression and help inform management strategies. The significant differences observed between genders also suggest the need for personalized treatment approaches that consider individual patient characteristics.

DISCUSSION

The study provided important insights into the relationship between hemoglobin and serum calcium levels with the progression of chronic kidney disease (CKD) in patients from South Punjab, Pakistan. The findings demonstrated a significant inverse relationship between CKD severity and both hemoglobin and serum calcium levels, with pronounced reductions in these parameters observed in

advanced stages of the disease. This aligns with previous research that highlighted the role of anemia and mineral metabolism disorders as common complications in CKD, impacting patient outcomes and disease progression (Romagnani et al., 2017; Ati et al., 2005).

The significant variance in hemoglobin levels across different CKD stages suggests that anemia is intricately linked to kidney function decline. Anemia in CKD is primarily due to reduced erythropoietin production, which is compounded by factors such as iron deficiency and inflammation (Eckardt et al., 2009). The study confirmed that hemoglobin levels were consistently lower in patients at advanced stages of CKD, which is consistent with previous studies that identified anemia as a predictor of mortality and cardiovascular complications in CKD patients (Besarab & Levin, 2000). The positive correlation between serum calcium and hemoglobin levels further emphasized the interdependence of mineral and hematological parameters in CKD progression. This correlation indicates that disturbances in calcium homeostasis may exacerbate anemia, potentially through impaired erythropoiesis or altered erythropoietin responsiveness (Kimata et al., 2005; Oh et al., 2011).

The study's findings on serum calcium levels provided additional insights into the mineral metabolism disruptions commonly seen in CKD patients. As CKD progresses, the kidneys' ability to regulate calcium and phosphorus levels diminishes, leading to conditions such as hypocalcemia and hyperphosphatemia (Lajdova et al., 2012). These imbalances contribute to bone disease, cardiovascular events, and increased mortality in CKD patients (Kovesdy & Kalantar-Zadeh, 2008). The observed variations in serum calcium levels across CKD stages in this study align with existing literature, underscoring the need for regular monitoring and management of mineral metabolism in CKD patients (Lorenzo et al., 2010).

A notable strength of this study was its large sample size, which enhanced the statistical power and reliability of the findings. Additionally, the study's setting in South Punjab, a region with limited healthcare resources, adds value by addressing a significant knowledge gap in CKD management within resource-constrained environments. However, several limitations should be considered when interpreting the results. The study's cross-sectional design limited the ability to establish causal relationships between the observed variables. Longitudinal studies are needed to confirm these findings and explore the temporal dynamics between anemia, mineral metabolism, and CKD progression (Kumar et al., 2020). Furthermore, the study did not assess other potential confounding factors such as nutritional status, comorbidities, and medication use, which could influence hemoglobin and calcium levels.

Despite these limitations, the study's findings have important clinical implications. Regular assessment of hemoglobin and serum calcium levels in CKD patients could facilitate early detection of disease progression and guide the implementation of targeted interventions. The study supports the use of these parameters as potential biomarkers for CKD severity, which could inform personalized treatment plans tailored to individual patient needs and disease characteristics (Abo Sayed et al., 2022). Future research should focus on exploring the underlying mechanisms driving the observed associations and investigating the impact of gender-specific variations on CKD progression. Addressing these research gaps could enhance the understanding of CKD pathophysiology and contribute to the development of effective management strategies for this complex condition.

CONCLUSION

The study concluded that there is a significant inverse relationship between hemoglobin and serum calcium levels and the severity of chronic kidney disease (CKD) in patients from South Punjab, Pakistan. These findings suggest that both anemia and disturbances in mineral metabolism are critical markers of CKD progression. This study highlights the potential of using hemoglobin and serum calcium levels as biomarkers for early detection and monitoring of CKD progression, which can facilitate timely intervention and improve management strategies, particularly in resource-limited settings. By understanding these relationships, healthcare professionals can tailor treatment plans more effectively, improving patient outcomes and potentially reducing the burden of CKD in similar populations. This research underscores the importance of integrating routine assessments of these parameters into clinical practice to enhance patient care and guide therapeutic decisions.

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