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Article

Correlation of Serum Creatinine, Urea, and Hemoglobin Level in Chronic Kidney Disease

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ABSTRACT

Background: Chronic kidney disease (CKD) is a global health concern characterized by progressive renal function decline and is commonly associated with anemia. Although creatinine and urea are established biomarkers of CKD, their correlation with hemoglobin levels remains underexplored in local populations, limiting early detection of anemia in clinical practice. **Objective**: This study aimed to assess the correlation between serum creatinine, urea, and hemoglobin levels in patients with CKD, and to determine the extent to which anemia is associated with disease severity. **Methods**: A cross-sectional correlational study was conducted among 170 confirmed CKD patients aged ≥18 years at Chaudhry Muhammad Akram Teaching and Research Hospital, Lahore, Pakistan, from October 2024 to March 2025. Participants with acute renal failure, recent blood transfusion, or unrelated hematologic disorders were excluded. Blood samples were analyzed for serum creatinine, urea, hemoglobin, and eGFR using standardized protocols with Mindray analyzers. Ethical approval was obtained in compliance with the Declaration of Helsinki. Pearson correlation analysis was performed using SPSS version 25.0. **Results**: A moderate to strong inverse correlation was found between hemoglobin and both serum creatinine ($r = -0.626$, $p < 0.001$) and urea ($r = -0.499$, $p < 0.001$). A strong positive correlation existed between creatinine and urea ($r = 0.719$, $p < 0.001$). Hemoglobin levels also declined with advancing CKD stage ($R^2 = 0.528$) and were positively associated with eGFR ($r = 0.780$, $p < 0.001$), highlighting the clinical linkage between renal impairment and anemia severity. **Conclusion**: Anemia in CKD patients is significantly associated with elevated serum creatinine and urea, and declining eGFR. These correlations support routine monitoring of renal and hematologic parameters to enable early detection and management of anemia, thereby improving patient outcomes.

Keywords: Chronic Kidney Disease, Anemia, Serum Creatinine, Blood Urea Nitrogen, Glomerular Filtration Rate, Hemoglobin, Correlation Studies

INTRODUCTION

Chronic kidney disease (CKD) represents a persistent, progressive loss of renal function, marked by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2 sustained over a period of at least three months (1). Globally, CKD affects approximately 10% of the adult population and continues to rise as a significant contributor to morbidity and mortality (1,3). The disease progression disrupts various physiological functions, particularly the renal excretory and endocrine roles, leading to serious systemic complications.

One of the most prominent and early-detected laboratory manifestations of CKD is the rise in serum creatinine and urea, which serve as indicators of declining kidney function (4,5). Concurrently, anemia frequently emerges as a co-morbid condition, primarily attributed to decreased erythropoietin production due to renal impairment (15). This triad—elevated creatinine, elevated urea, and reduced hemoglobin—forms a critical cluster of interrelated parameters that reflect the clinical trajectory of CKD.

Several studies have demonstrated the predictive value of serum creatinine and urea in identifying early renal dysfunction. These markers are routinely used in both diagnosis and monitoring due to their sensitivity to changes in renal clearance mechanisms (6,10). Elevated creatinine originates from the breakdown of muscle creatine and reflects diminished glomerular filtration, whereas elevated urea, a byproduct of protein metabolism, indicates reduced renal excretion capacity (11,13). As kidney function declines, these waste products accumulate in the bloodstream, exacerbating metabolic derangements and contributing to uremic symptoms (20). However, while both markers are indicative of CKD severity, their direct correlation

with hemoglobin levels has been underexplored in regional populations, especially within Pakistani clinical settings.

Anemia in CKD, though multifactorial, primarily arises from inadequate erythropoietin synthesis due to nephron loss, compounded by iron deficiency, chronic inflammation, and reduced red blood cell lifespan (22,23). Its prevalence escalates with advancing CKD stages and is closely tied to increased risk of cardiovascular events, hospitalization, and mortality (18,25). Despite the recognition of anemia as a key clinical issue, the extent to which it correlates with routinely monitored renal biomarkers like serum creatinine and urea remains inadequately characterized, particularly in developing nations where delayed diagnosis and under-treatment are common (14,16). Thus, assessing these interrelationships can improve understanding of disease pathophysiology and guide clinicians in anticipating anemia risk based on renal profile trends.

Previous investigations have acknowledged the association between anemia and CKD progression but often lacked comprehensive statistical correlation with creatinine and urea levels. Studies have hinted at these associations but did not quantify the strength of relationships or control for confounding variables like CKD stage and eGFR (12,17). Additionally, much of the existing literature focuses on advanced CKD or dialysis patients, with limited cross-sectional insights across all stages of disease. By filling this gap, a focused analysis of the correlation between hemoglobin, creatinine, and urea can yield valuable clinical implications, enabling early interventions for anemia management in CKD patients. This is particularly relevant in resource-limited healthcare systems where access to erythropoiesis-stimulating agents or dialysis is constrained.

Given this background, the current study aims to evaluate the correlation between serum creatinine, serum urea, and hemoglobin levels in patients with chronic kidney disease. It seeks to determine whether these parameters are statistically and clinically interlinked, thereby supporting the use of renal biomarkers to predict anemia in CKD. The study also considers the influence of CKD staging and eGFR on hemoglobin status to further refine anemia risk stratification. The central hypothesis is that hemoglobin levels demonstrate a significant inverse relationship with both creatinine and urea levels in CKD patients, and that these associations can serve as reliable indicators for disease monitoring and therapeutic decision-making.

MATERIALS AND METHODS

This cross-sectional correlational study was conducted at the Pathology Department of Chaudhry Muhammad Akram Teaching and Research Hospital, Lahore, Pakistan, over a six-month period from October 2024 to March 2025. A total of 170 participants diagnosed with chronic kidney disease (CKD) were enrolled using a random sampling technique. Eligibility was restricted to individuals aged 18 years or older with a confirmed diagnosis of CKD at any stage.

Patients with acute renal failure, hematological disorders unrelated to CKD, active malignancy, or recent blood transfusions were excluded to minimize confounding factors. All participants provided written informed consent prior to enrollment, and the study adhered to the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional ethical review board. Participant confidentiality was maintained by anonymizing all personal identifiers and securing access to data.

Blood samples were collected using standard phlebotomy protocols. Hemoglobin levels were assessed using whole blood collected in EDTA tubes and analyzed on the Mindray BC-5000 automated hematology analyzer. Serum creatinine and urea levels were measured from blood samples collected in yellow-top serum separator tubes and processed using the Mindray BS-240 biochemistry analyzer. Estimated glomerular filtration rate (eGFR) was calculated using serum creatinine values according to standard clinical formulas. The primary outcome was the correlation between hemoglobin and serum creatinine levels. Secondary outcomes included the correlations of hemoglobin with serum urea, eGFR, and CKD stage. All laboratory tests followed standard operating procedures to ensure result reliability and reproducibility.

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY). Descriptive statistics such as frequencies and percentages were used to summarize categorical variables including gender and CKD stages. Continuous variables like age, hemoglobin, creatinine, and urea levels were expressed as means and standard deviations. Pearson correlation coefficient (r) was used to evaluate the relationships among hemoglobin, creatinine, urea, and eGFR. The statistical significance threshold was set at $p < 0.05$ for all analyses. All p-values reported were two-tailed. Missing data were minimal and handled using pairwise deletion. No imputation or adjustment for confounding variables was required due to the direct correlational nature of the analysis.

RESULTS

A total of 170 patients diagnosed with chronic kidney disease (CKD) were enrolled in the study, with a male predominance (n = 102, 60%) compared to females (n = 68, 40%). Participant ages ranged from 24 to 93 years, with the 51–60-year age group being the most affected, followed by those aged 41–50 and 61–70 years. CKD staging revealed that the majority of patients were in Stage 3, followed by Stages 4 and 2, with fewer participants in Stages 1 and 5.

A statistically significant moderate inverse correlation was observed between serum creatinine and hemoglobin (Hb) levels ($r = -0.626$, $p < 0.001$). This negative relationship implies that as creatinine levels increase, Hb levels decline, suggesting a worsening of anemia with declining renal function. The coefficient of determination ($R^2 = 0.361$) indicates that approximately 36.1% of the variance in hemoglobin levels is explained by changes in serum creatinine, underscoring a moderately strong predictive association. A moderate negative correlation was identified between serum urea and Hb levels ($r = -0.499$, $p < 0.001$). The R^2 value of 0.195 suggests that 19.5% of the variability in hemoglobin levels can be attributed to urea levels, indicating that although urea is significantly associated with anemia in CKD, other factors also contribute substantially.

A strong positive correlation was found between serum urea and creatinine levels ($r = 0.719$, $p < 0.001$), indicating that these renal

biomarkers rise concomitantly as kidney function deteriorates. The R^2 value of 0.517 shows that over 50% of the variability in one marker can be explained by the other, confirming their strong interdependence.

Table 1. Pearson Correlation Between Serum Creatinine and Hemoglobin (Hb)

Variable	Hemoglobin (r)	Creatinine (r)	p-value	N
Hemoglobin	1.000	-0.626	<0.001	170
Creatinine	-0.626	1.000	<0.001	170

Table 2. Pearson Correlation Between Serum Urea and Hemoglobin (Hb)

Variable	Hemoglobin (r)	Urea (r)	p-value	N
Hemoglobin	1.000	-0.499	<0.001	170
Urea	-0.499	1.000	<0.001	170

Table 3. Pearson Correlation Between Serum Urea and Creatinine

Variables	Correlation Coefficient (r)	p-value	N
Urea–Creatinine	0.719	<0.001	170
Creatinine–Urea	0.719	<0.001	170

Simultaneous analysis of all three variables revealed statistically significant pairwise associations. Hemoglobin demonstrated moderate to strong negative correlations with both urea (r = -0.499) and creatinine (r = -0.626), whereas a strong positive correlation was evident between urea and creatinine (r = 0.719). All correlations were significant at $p < 0.001$.

Table 4. Correlation Matrix of Hemoglobin, Urea, and Creatinine

Variable	Hb (r)	Urea (r)	Creatinine (r)	p-value	N
Hemoglobin	1.000	-0.499	-0.626	<0.001	170
Urea	-0.499	1.000	0.719	<0.001	170
Creatinine	-0.626	0.719	1.000	<0.001	170

Hemoglobin and CKD Stage

Hemoglobin levels declined progressively across advancing CKD stages, with the lowest values observed in Stages 4 and 5. A regression analysis yielded a coefficient of determination (R^2 = 0.528), indicating that 52.8% of the variation in hemoglobin levels could be explained by CKD staging alone. This trend underscores the clinical importance of CKD staging in predicting hematologic deterioration. A strong positive correlation was observed between estimated glomerular filtration rate (eGFR) and hemoglobin levels (r = 0.780, $p < 0.001$), with an R^2 of 0.608. This implies that improved kidney function (as measured by eGFR) is associated with higher hemoglobin levels, reinforcing the pathophysiological link between renal and hematological health. Patients with eGFR values below 30 mL/min/1.73 m^2 exhibited more severe anemia (Hb < 8 g/dL), while those with preserved eGFR (above 60 mL/min/1.73 m^2) maintained near-normal hemoglobin levels.

Table 5. Pearson Correlation Between eGFR and Hemoglobin

Variable	eGFR (r)	Hemoglobin (r)	p-value	N
eGFR	1.000	0.780	<0.001	170
Hemoglobin	0.780	1.000	<0.001	170

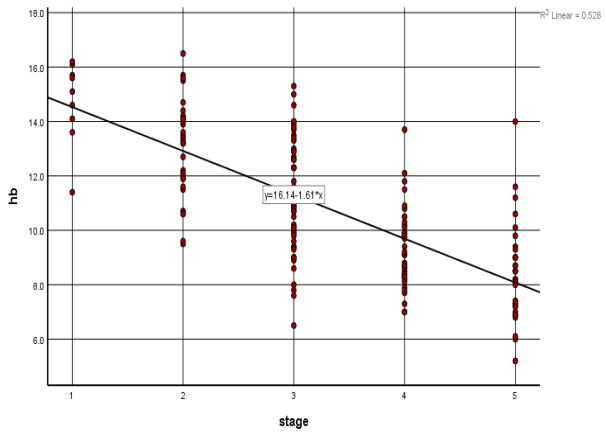

Figure 1 Relationship Between CKD Stage and Hemoglobin

All correlation results across variables—Hb, creatinine, urea, CKD stage, and eGFR—were statistically significant ($p < 0.001$), indicating high confidence in the observed relationships. While the strength of correlation varied from moderate to strong, clinical relevance remains high, particularly in identifying and monitoring anemia progression in relation to renal function decline.

DISCUSSION

The findings of this study underscore the significant interrelationship between serum creatinine, urea, and hemoglobin levels in patients with chronic kidney disease (CKD), highlighting the pathophysiological interplay between renal dysfunction and hematological abnormalities. The observed moderate to strong inverse correlations between hemoglobin

and both creatinine and urea suggest that as kidney function deteriorates, the risk and severity of anemia substantially increase. These findings are consistent with prior reports indicating that anemia is a prevalent and progressive complication of CKD due to impaired erythropoietin production, persistent inflammation, and metabolic derangements (15,22). The strong positive correlation between urea and creatinine supports their conjoint elevation as reliable markers of declining renal clearance and reinforces their diagnostic utility in CKD monitoring (11,20).

These correlations align with the results of previous studies, such as those by Obeagu et al. and Naeem et al., which reported similar inverse relationships between renal biomarkers and hemoglobin, indicating that hemoglobin levels fall as urea and creatinine levels rise (7,14). Furthermore, the study corroborates findings by Sofyanita et al. and Behera, who emphasized the role of uremic toxins and impaired erythropoietin synthesis in reducing hemoglobin production in CKD patients (12,17). However, this study expands upon existing literature by simultaneously analyzing all three parameters and quantitatively demonstrating their predictive associations using coefficients of determination. Notably, the observed R^2 values indicate that over half of the variability in creatinine levels can be explained by urea, and that up to 60.8% of the variation in hemoglobin levels is accounted for by changes in eGFR, reflecting both statistical and clinical significance.

The strong positive correlation between eGFR and hemoglobin further emphasizes the role of glomerular filtration as a determinant of hematological status in CKD. This relationship underscores the mechanistic link whereby reduced renal function leads to diminished erythropoietin synthesis, thereby impairing red blood cell production and resulting in normocytic, normochromic anemia typical of CKD (22). This hormonal deficiency is often compounded by functional iron deficiency, chronic inflammation, and shortened erythrocyte survival, all of which collectively exacerbate anemia severity as kidney disease progresses (23,24). The clinical relevance of these findings lies in their implication for early screening and intervention; by closely monitoring renal biomarkers, clinicians may anticipate hematological deterioration and implement timely management strategies such as iron supplementation or erythropoiesis-stimulating agents.

While this study contributes to the growing body of evidence on CKD-related anemia, it is not without limitations. The cross-sectional design restricts the ability to infer causality, and the reliance on a single-center sample from an urban tertiary care hospital may limit generalizability to broader populations, particularly in rural or under-resourced settings. Furthermore, potential confounding factors such as nutritional status, inflammatory markers, iron indices, and concurrent medications were not controlled, which may have influenced hemoglobin levels independently of renal function. The lack of longitudinal follow-up also prevents assessment of temporal changes in hematological and renal parameters.

Despite these constraints, the study's strengths include a reasonably large sample size and the use of validated laboratory instruments and statistical methods, lending credibility to the observed associations. The uniform application of standard protocols for blood collection and analysis enhances reproducibility and reliability of the findings. Future research should consider a multicenter longitudinal design to evaluate changes in hemoglobin over time in relation to dynamic renal function metrics. Inclusion of additional variables such as serum ferritin, transferrin saturation, C-reactive protein, and erythropoietin levels would provide a more comprehensive understanding of anemia etiology in CKD. Moreover, interventional studies assessing the impact of early anemia management on CKD progression and quality of life outcomes would offer valuable clinical insights.

In conclusion, this study affirms the significant inverse associations of hemoglobin with serum creatinine and urea, and the positive correlations among urea, creatinine, and eGFR in CKD patients. These findings reinforce the integrated pathophysiology of renal and hematological systems and underscore the importance of routine hematological evaluation in CKD management. By improving recognition of these interdependencies, clinicians can enhance risk stratification, monitor disease progression more effectively, and implement timely therapeutic interventions to mitigate anemia-related complications in this high-risk population.

CONCLUSION

This study demonstrates a statistically significant inverse correlation between serum creatinine, urea, and hemoglobin levels in patients with chronic kidney disease, highlighting that as renal function declines, anemia becomes progressively more severe. The findings emphasize that serum creatinine and urea not only serve as biomarkers for renal impairment but are also closely linked with hemoglobin levels, reinforcing the clinical importance of integrated monitoring. These results have meaningful implications for early identification and management of anemia in CKD, underscoring the necessity of routine hematologic assessment alongside renal profiling to optimize patient care. From a research perspective, the study supports further investigation into the mechanistic pathways linking renal dysfunction and anemia, and encourages longitudinal studies to evaluate the impact of timely anemia management on disease outcomes and quality of life in CKD patients.

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