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# ASSOCIATION OF ROUTINE BIOCHEMISTRY, HEMATOLOGICAL INDICES, AND ELECTROLYTES WITH CHRONIC KIDNEY DISEASE: A CASE-CONTROL STUDY

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**Abstract**

*The present study aimed to evaluate standard laboratory biomarkers in patients with chronic kidney disease (CKD) and determine how they associate with disease status. It was hypothesized that some biomarkers from serum electrolytes (Potassium), liver function tests (Alkaline Phosphate), complete blood counts (HB, WBC, monocytes, eosinophils), and renal function tests (RFTs) would be significantly associated with chronic kidney disease (CKD). Case-Control research design was employed. The sample included 120 participants comprising 60 diagnosed CKD patients and 60 Healthy controls including both males and females with CKD with age ranging from 5 to 60 years. Purposive sampling was used to recruit the sample. Serum creatinine, blood urea nitrogen (BUN), glomerular filtration rate (eGFR), hemoglobin, leukocyte differential counts, bilirubin, alkaline phosphatase, albumin, sodium, potassium, and chloride biomarker profiles was evaluated on the basis of data obtained from hospital laboratory records.. The findings revealed significant associations between CKD and serum creatinine, BUN, serum urea, eGFR, potassium, hemoglobin, white blood cell count, monocytes, eosinophils, and ALP ($p < .05$). In contrast, sodium, chloride, platelet count, MCV, lymphocytes, ALT, AST, and total bilirubin showed no significant association with CKD ($p > .05$). These findings highlight the clinical importance of routinely available laboratory biomarkers in the early detection, monitoring, and management of CKD. The study showed the significance of readily available laboratory tests as budget friendly resources to support evidence-based CKD patient care. The outcomes are capable of assisting the medical practitioners emphasize pertinent test parameters for CKD detection early on as well as early monitoring.*

## INTRODUCTION

The kidneys are important for homeostasis, controlling fluid balance, electrolyte concentrations, acid base status and excretion of metabolic waste products. Impairment of these functions may result in serious systemic complications involving multiple organ systems. CKD is a common health problem, affecting 9.1% of the world's population and is one of the most common causes of morbidity and mortality worldwide (GBD Chronic Kidney Disease Collaboration, 2020). CKD is defined by abnormalities of kidney structure or function, present for >3 months, with implications for health. The disease is divided into five stages based on the estimated glomerular filtration rate (eGFR)

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and the markers of kidney damage (KDIGO, 2012). CKD is often asymptomatic in the early stages of progression which leads to delay in diagnosis and treatment. As a result, a large number of patients present with advanced disease, when much of the kidney damage has already been done (Levey et al., 2014).

Over the past decades, the prevalence of CKD has increased significantly, owing mostly to the increasing burden of diabetes mellitus, hypertension, obesity, cardiovascular diseases and population aging (GBD Chronic Kidney Disease Collaboration, 2020).

Laboratory biomarkers are essential in the diagnosis, monitoring and management of CKD. A biomarker is a measurable biological marker that indicates normal biological processes, pathological processes or responses to therapeutic interventions (Biomarkers Definitions Working Group, 2001). Routine laboratory investigations in clinical practice such as renal function tests (RFTs), complete blood count (CBC), liver function tests (LFTs), and serum electrolyte measurements are useful to provide valuable information regarding kidney function and associated systemic complications. Assessment of these biomarkers can help in early diagnosis, determination of disease severity and monitoring of disease progression. The renal function is commonly assessed by biomarkers such as serum creatinine and the estimated glomerular filtration rate (eGFR). However, abnormalities in hematological parameters, liver function markers, and serum electrolytes have also been reported in patients with CKD (Levey et al., 2014). A systematic evaluation of routinely available laboratory biomarkers is required to identify those most strongly associated with CKD and to support evidence-based clinical decision making.

Early detection as well as effective monitoring of Chronic Kidney Disease are crucial to prevent disease progression and reduce associated complications. In the early stages, CKD is often asymptomatic and laboratory biomarkers are important tools in identifying at-risk patients and assessing disease severity (KDIGO, 2012). The importance of this study is that a wide variety of routinely used laboratory markers such as renal function tests, parameters of complete blood count, liver function markers and serum electrolytes are evaluated in patients with CKD.

**Literature Review**

| Author(s) | Year | Method / Design | Main Results / Findings |
|---|---|---|---|
| Ogolla et al. | 2025 | Retrospective study; 120 CKD patients | Lower hemoglobin and lymphocyte counts, higher red cell distribution width (RDW), and higher neutrophil-to-lymphocyte ratio (NLR) were independent predictors of CKD progression. |
| Tahir et al. | 2025 | Cross-sectional study; 412 patients with CKD stages 3–5 | Hemoglobin, hematocrit, red blood cell counts, and platelet levels decreased as CKD advanced. RDW and anemia prevalence increased with disease severity. |
| Shaheen et al. | 2025 | Observational study; 100 male and female CKD patients | Serum creatinine, serum urea, and urinary albuminuria increased with CKD progression. Urinary albuminuria showed a strong positive correlation with disease progression. |

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| Author(s) | Year | Method / Design | Main Results / Findings |
|---|---|---|---|
| Lin et al. | 2025 | Longitudinal cohort study; 2,978 patients with incident pre-dialysis CKD | Long-term electrolyte patterns involving increased potassium and phosphorus and decreased sodium and calcium were associated with a greater risk of dialysis initiation and faster eGFR decline. |
| Gupta et al. | 2024 | Review of CKD biomarkers, particularly in older adults | Traditional markers such as serum creatinine and urinary protein have diagnostic limitations. Cystatin C, KIM-1, and NGAL may improve early detection and assessment of CKD progression. |
| Xu et al. | 2024 | Observational study; 451 individuals across CKD stages | Increased IL-6 and blood urea nitrogen (BUN), alongside decreased hemoglobin, were associated with CKD progression. Combined assessment of inflammatory, hematological, and renal biomarkers may improve monitoring. |
| Lopez-Giacoman and Madero | 2015 | Literature review of conventional and emerging kidney biomarkers | Cystatin C and combined creatinine–cystatin C equations can improve GFR estimation. Albuminuria helps predict renal impairment and cardiovascular risk, while KIM-1 and NGAL may detect tubular injury earlier. |
| Majoni et al. | 2020 | Cohort study; 547 Indigenous Australian adults | Lower serum albumin and hemoglobin were associated with faster eGFR decline. GGT, ALP, and bilirubin were also associated with renal outcomes, suggesting potential value for routine blood tests in risk assessment. |
| Wu et al. | 2022 | Proteomic observational study of chronic hemodialysis patients | IL-8 independently predicted mortality. TIM-1 and CCL20 were associated with adverse mortality and cardiovascular outcomes, supporting the potential value of multiple protein biomarkers. |
| Dopierała et al. | 2025 | Review of emerging biomarkers in kidney replacement therapy | Pentraxin-3, IL-6, TNF-alpha, and trimethylamine-N-oxide (TMAO) may improve assessment of inflammation, metabolic disturbances, cardiovascular |

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| Author(s) | Year | Method / Design | Main Results / Findings |
|---|---|---|---|
| | | | complications, and mortality risk in dialysis patients. |
| Ren et al. | 2025 | Large-scale proteomic analysis using two cohort studies and machine learning | Multi-protein models predicted mortality more accurately than individual biomarkers. Proteins associated with vascular dysfunction, fibrosis, and immune activation were important predictors of adverse outcomes. |
| Valls et al. | 2026 | Biomarker prediction study following ischemic acute kidney injury in surgical patients | Fibroblast growth factor-23 (FGF-23) increased early after ischemic kidney injury and showed potential for predicting kidney injury before changes in serum creatinine. Its role in dialysis-related cardiovascular risk warrants further evaluation. |
| Zhang et al. | 2025 | Study of high-flux hemodialysis and online hemodiafiltration in older patients | Elevated IL-6, TNF-alpha, and CRP were associated with inflammation, protein-energy wasting, and increased mortality risk. Inflammatory biomarker monitoring may help guide dialysis and nutritional management. |
| Sapna et al. | 2025 | Review/discussion of emerging structural and tubular injury biomarkers | KIM-1 and NGAL may detect tubular injury earlier than creatinine. Monitoring these biomarkers could help identify loss of residual kidney function and guide nephroprotective interventions in dialysis patients. |
| Cossettini et al. | 2024 | Urinary proteomics study using mass spectrometry | Reduced urinary uromodulin and epidermal growth factor (EGF) were associated with declining eGFR, increased proteinuria, and kidney injury. These biomarkers may help assess tubular damage and fibrosis. |
| Tolou-Ghamari | 2025 | Review of 101 peer-reviewed articles | Reliance on serum creatinine and estimated GFR may inadequately assess kidney injury in dialysis patients. The review advocated combining injury, inflammation, fibrosis, and metabolic biomarkers for improved monitoring. |

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**Rationale of the Current Study**

Chronic Kidney Disease is one of the most common and challenging non-communicable diseases worldwide, affecting an estimated 9.1% of the global population (GBD Chronic Kidney Disease Collaboration, 2020). Early-stage chronic kidney disease (CKD) is most often undiagnosed and underreported as early stages are asymptomatic. This delay in diagnosis stems from a public health concern. CKD has a high level of morbidity and mortality due to its irreversible progression to end-stage renal disease (Levey et al., 2014). Therefore, the early detection and diagnosis of CKD is essential. This can be achieved through routine laboratory testing. Kidney function testing has clearly evolved beyond serum creatinine and estimated glomerular filtration rate (eGFR), as there are limitations of both of these tests. Factors such as age, sex, and muscle mass, as well as hydration and diet, contribute to variances in creatinine and eGFR. Furthermore, serum creatinine does not increase until there is a loss of approximately 50% of nephron function (Lopez-Giacoman & Madero, 2015). It is essential to assess the impact of CKD on the entire body. Declining kidney function reduces the synthesis of erythropoietin, resulting in anemia which is normocytic and normochromic. This condition is progressive with the decrease in glomerular filtration rate (Tahir et al., 2025). Uremia is also correlated with a chronic inflammatory condition of low-grade intensity which also alters the white blood cell profile and reduces the function of bone marrow.

This shift raises the levels of neutrophils and reduces lymphocytes, both of which predict the progression of CKD and its poorer prognoses (Ogolla et al., 2025). CKD-Mineral Bone Disorder and protein-energy wasting also affect liver function markers such as alkaline phosphatase and albumin, along with electrolyte disturbances of low sodium, elevated potassium, and low chloride, which demonstrate the progressive deterioration in renal function (Majoni et al., 2020). These different systemic problems are usually picked up by routine laboratory investigations, however they are seldom considered together or assessed with regards to their relationship to CKD. Additionally, there is a dearth of clinical evidence generated in Pakistan. Most of the studies on CKD biomarkers and their investigations are from high income countries with healthcare systems which may be unrelated to Pakistan. Due to the high prevalence of uncontrolled diabetes and hypertension, their dietary habits, genetic make up, the poor availability of modern diagnostic tests and other social factors, Pakistan has a clinically different setting (KDIGO, 2012). In the absence of evidence from local hospitals, the international studies which are often irrelevant to Pakistan have to be relied on. The aim of this study is to analyze laboratory investigations from the patients with CKD from multiple hospitals in Pakistan. The rationale for emphasizing routinely available tests versus some of the newer biomarkers is both practical and scientific.

More sensitive and specific biomarkers may target specific tissues; however, their use in Pakistan and other resource-constrained countries is hampered by costs, the absence of built-in standard tests, and lack laboratory facilities (Gupta et al., 2024). Conversely, renal function tests, complete blood counts, liver function tests, and serum electrolytes are readily accessible, low-cost, and almost universally ordered for all patients that are admitted to the hospital. There is an opportunity to prove the utility of these tests. If a limited number of routine tests are able to reliably identify CKD and its associated patterns and therefore its complications, this knowledge can significantly improve the clinical practice in lower- and middle-income countries. This study seeks to answer ordinary clinical questions in diagnosing CKD earlier and comprehensively beyond the routine creatinine clearance test. This includes a shift in thinking of CKD to a multi-organ system approach with an understanding of the reach and significance of blood, liver, and electrolyte disturbances. There has been an absence of locally relevant information from Pakistani hospitals.

**Objectives of the Present Study**

The following objectives were formulated for the present study

- This study's goals are to evaluate a wide variety of standard laboratory biomarkers between CKD

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positive patients and healthy controls, such as RFTs, CBCs, LFTs, and serum electrolytes, and to implement the Chi-square test to access the statistically significance nature of each biomarker's association with CKD.

- To collect data from one hundred and twenty hospital patients, classify biomarkers that are either significantly or non-significantly associated with CKD status.

**Hypothesis**

The following hypotheses were formulated

- There will be a significant and non-significant association between the standard laboratory parameters (renal function tests, complete blood count parameters, liver function markers, and serum electrolytes) and Chronic Kidney Disease
- Serum creatinine, BUN, and eGFR are renal function markers that are predicted to establish a statistically significant association with chronic kidney disease.
- There will be a non-significant association between CKD and serum electrolytes (sodium, and chloride), indicating the individuals sample renal electrolyte regulating function is disrupted.

**Methodology**

**Study Design**

The present study utilized a case-control research design. "A case-control study is a type of observational study commonly used to look at factors associated with diseases or outcomes. The study starts with a group of cases (individuals with the outcome of interest) and a group of controls (individuals without the outcome), and then examines previous exposures to determine whether they are associated with the outcome." (Tenny,
Kerndt, & Hoffman, 2023).

**Sample and Sampling Strategy**

The sample for the current study comprises children and adults. The obtained sample was 120 participants (N = 120), comprising 60 diagnosed CKD patients (Cases) and 60 healthy individuals without CKD (Controls). For the present study, Purposive sampling was used to recruit data for the present study. Purposive sampling is a non-probability sampling technique in which researchers intentionally select participants who are most knowledgeable about or experienced with the phenomenon being studied, so that they can provide rich and relevant information (Palinkas et al., 2015).

**Inclusion criteria for Cases**

- Patients aged from 5 to 60 years
- Diagnosed cases of CKD (Stages 1–5).
- Both male and female patients.

**Inclusion criteria for Controls**

- Healthy individuals aged 5-60 years
- No history of CKD
- Both male and female patients

**Exclusion Criteria**

- Patients with acute kidney injury (AKI).
- Pregnant women.
- Patients with severe infections, malignancies, or other chronic inflammatory diseases.
- Patients unwilling to participate.

**Clinical Setting**

The study was conducted at Sheikh Zaid Hospital, Jinnah Hospital Lahore. The target population consisted of patients diagnosed with Chronic Kidney. The target population (Cases) consisted of patients diagnosed with Chronic Kidney Disease recruited from both the Outpatient department (OPD) and the Inpatient Wards. However, controls had been selected from healthy staff members as well as individuals who visited the hospital for regular examinations.

**Data Collection Tools**

Collection of data was based on Hospital laboratory reports. The laboratory tests used as sources of data were:

- RFT Reports
- CBC Reports
- LFT Reports
- Serum Electrolyte Reports

**Operational Definitions**

**Chronic Kidney Disease (CKD)**

It is a chronic condition characterized by renal damage or reduction in kidney functioning (eGFR < 60 mL/min/1.73 $m^2$) that persist for more than

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three months, regardless of underlying cause (KDIGO, 2012).

**Biomarker**

A measurable biological indicator found in blood or other fluids that indicate normal physiological functioning, disease states, or responses of treatment (Biomarkers Definitions Working Group, 2001).

**eGFR**

An estimated value of kidney filtration capacity, calculated from serum creatinine, age, and sex using the CKD-EPI or MDRD equation (Levey et al., 2009).

**Data collection procedure**

- First, the research title was selected and discussed with the supervisor
- After that, it was approved by the committee
- Then, Laboratory reports of CKD patients and healthy controls were reviewed
- Analysis was done By using Statistical package for Social Sciences(SPSS)

**Data Analysis**

The statistical analysis was performed to evaluate the distribution of different biomarkers among CKD patients. Descriptive statistics were used to summarize the distribution patterns of the analyzed biomarkers. Furthermore, Chi-square goodness-of-fit test was used to analyze whether the observed frequencies of biomarker categories (High, Low, Normal) are different significantly from the expected distribution.

**Ethical Considerations**

- Before data collection, formal permission was obtained from the hospital administration and the authorities of the hospital to conduct the study.
- Confidentiality and anonymity of the patients were strictly maintained throughout the study.
- names or contact details were kept anonymous and confidential, and all collected data was used only for the research purposes.
- The data was only accessible only to the researcher to ensure the privacy of the participants.

**Results**

**Statistical Analysis**

Biomarkers evaluation included renal function tests (serum creatinine, blood urea nitrogen, serum urea concentration, and eGFR), serum electrolytes (sodium, potassium, and chloride), complete blood count parameters (hemoglobin, WBC, platelet count, MCV, lymphocytes, monocytes, and eosinophils), and liver function tests (ALT, AST, ALP, and total bilirubin). The Chi-Square test was employed to assess the statistical significance of the association between each biomarker and CKD status (positive vs. negative), and each biomarker was labeled as Normal or Abnormal based on accepted clinical reference ranges. The level of statistical significance was characterized as a p-value of below 0.05.

**Renal Function Biomarkers**

The results revealed a highly significant association ($p<0.001$) among the abnormal creatinine levels in the blood of 51 (85.0%) of the 60 CKD-positive patients in contrast to only 10 (16.7%) of the healthy controls. Similarly, 52 (86.7%) of patients having CKD showed abnormal serum BUN versus 10 (16.7%) of controls ($p<0.001$). In contrast to 26 (43.3%) of healthy control subjects, 51 (85.0%) of CKD patients exhibited abnormal serum urea concentrations, that further attained statistical significance ($p<0.001$). Compared to only 10 (16.7%) of healthy control subjects, 52 (86.7%) of CKD-positive patients exhibited abnormal eGFR values, that imply poor kidney filtration efficiency ($p<0.001$).

Compared with only 10 (16.7%) of healthy control subjects, 52 (86.7%) of CKD-positive patients exhibited abnormal eGFR values, suggesting indicated reduced kidney filtration capacity ($p<0.001$). These outcomes support the established effectiveness of serum creatinine, BUN, urea, and eGFR as key biochemical parameters for CKD determination by revealing that these deviations are strongly and strongly correlated with a diagnosis of CKD.

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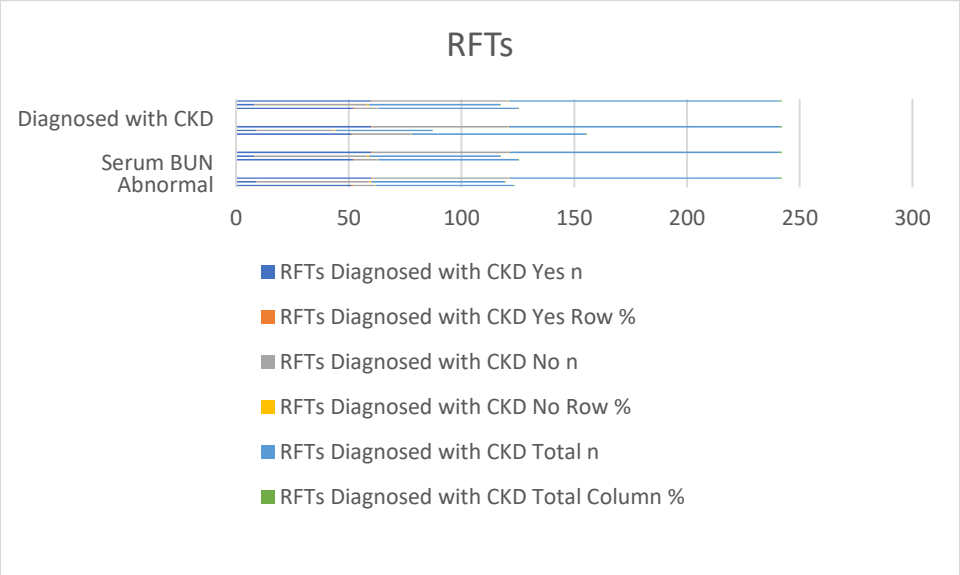



**Table 1 and Figure 1 demonstrate the distribution of renal function biomarkers in both groups.**

**Electrolyte Biomarkers**

The association among electrolyte abnormalities & CKD status appeared unclear. With 39 (65.0%) of CKD-positive patients showing abnormally elevated potassium levels compared to 10 (16.7%) of healthy control subjects ($p<0.001$), potassium revealed the strongest and only statistically significant electrolyte association with CKD. This outcome aligns with the previously reported role of reduced renal potassium excretion in chronic renal disease (CKD), leading to hyperkalemia as the disease progresses. Sodium abnormalities were observed in 10 (16.7%) of healthy controls versus 20 (33.3%) of CKD-positive patients; however, this difference failed to reach statistical significance ($p=0.058$), suggesting that sodium regulation may be partially maintained in the population under study. In the same way, 27 (45.0%) of CKD patients exhibited abnormal chloride values compared to 18 (30.0%) of controls; nevertheless, this distinction wasn't of statistical significance ($p=0.131$).

While sodium and chloride deviations, while more prevalent in CKD patients, did not demonstrate statistically significant associations in the sample we used, these findings demonstrate that potassium derangement is significantly associated with CKD diagnosis.

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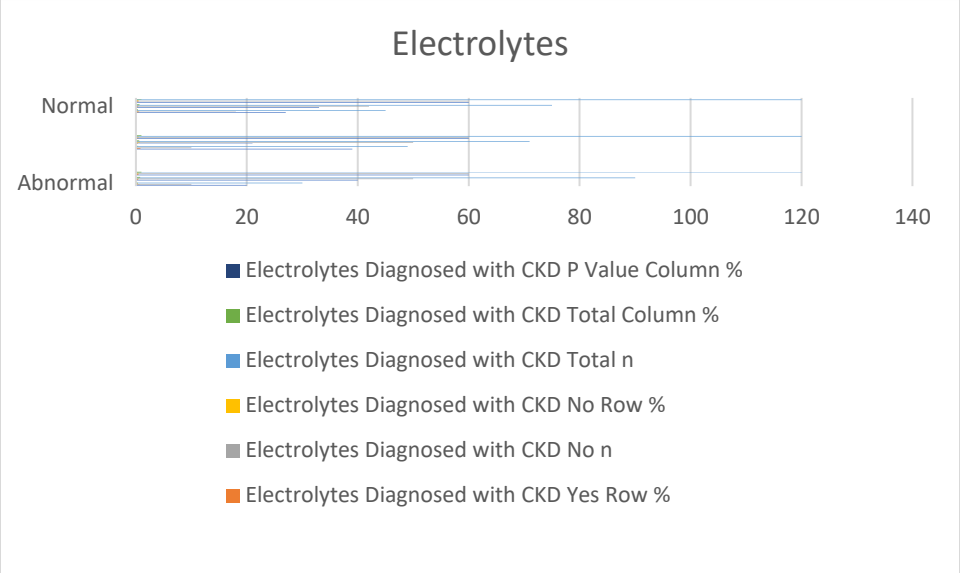



**Table 2 outlines the electrolyte distributions across both groups, and Figure 2 displays these.**

**Hematological Biomarkers**

37 (61.8) people with CKD showed unsatisfactory heamoglobin levels versus 10 (16.7%) controls who were healthy. The result proved statistical significance ($p<0.001$) indicating a high incidence of a condition called anaemia within CKD patients. 38 (63.3%) CKD individuals revealed abnormal WBC count in comparison to 10 (16.7%) of the control group demonstrating a significant relationship ($p<0.001$) revealing systemic autoimmune dysfunction with chronic systemic inflammation characteristic of CKD.

The most typical blood sample finding was abnormally elevated eosinophils that were detected in 48(80.0%) among CKD patients and 10(16.7%) of individuals ($p<0.001$) .

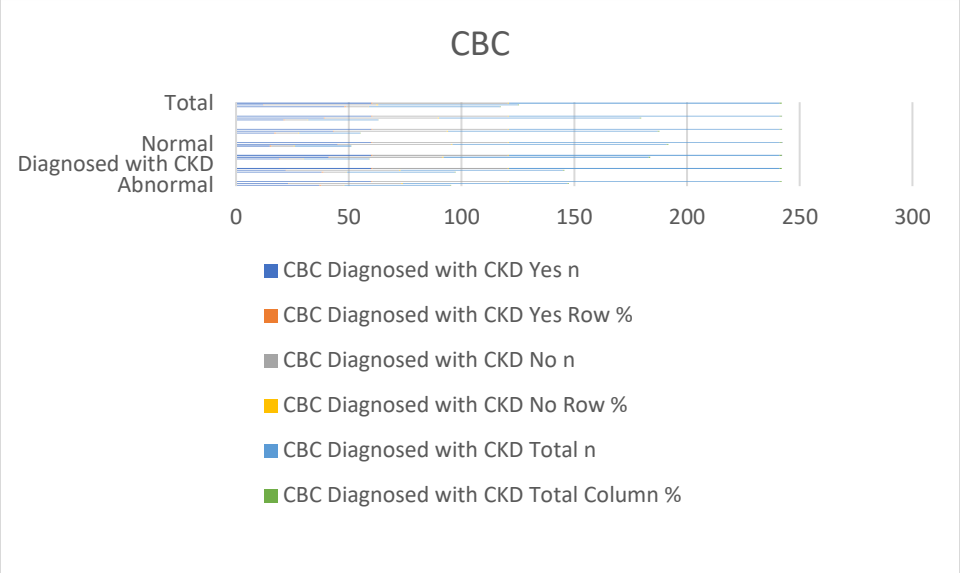
Moreover, the results showed a significant association ($p=0.037$) within monocyte irregularities with CKD individuals (21/60, 35.0%) along with healthy control group (10/60, 16.7%).

In contrast the platelet count, which had a p-value of 0.088 did not show a difference. The same was true for MCV with a p-value of 0.369 and abnormalities with a p-value of 0.190. This suggests that these parameters may not vary much between people with CKD and healthy individuals in the population.

It was found that platelet count was abnormal in 19 out of 60 CKD patients, which's 31.7% compared to 10 out of 60 healthy controls, which is 16.7%. For MCV abnormalities we saw them in 15 out of 60 CKD patients or 25.0%. In 10 out of 60 healthy controls or 16.7%. Lymphocyte abnormalities were observed in 17 out of 60 CKD patients, which's 28.3%, versus 10 out of 60 healthy controls, which is 16.7%.

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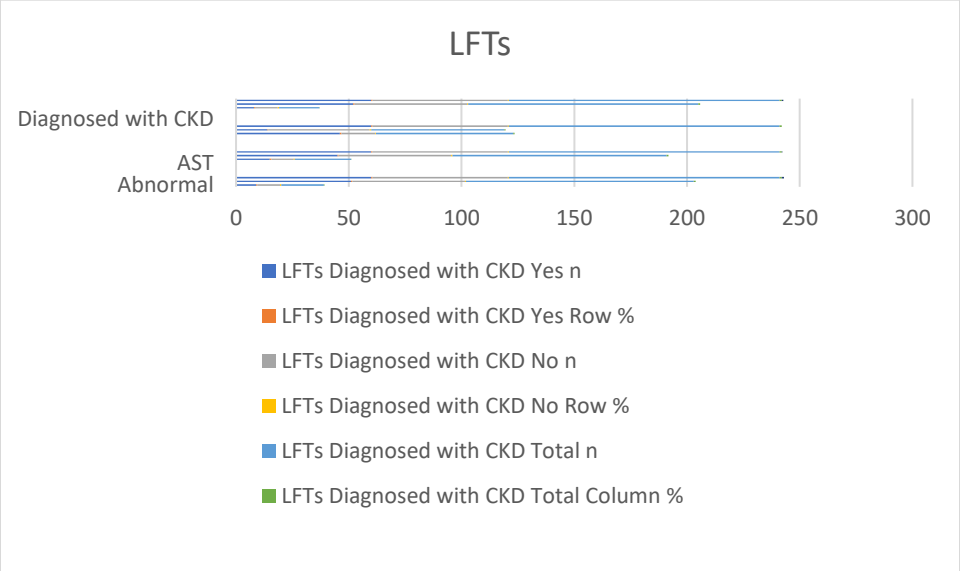
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**The full breakdown of CBC parameters, for both groups is shown in Table 3. Figure 3.**

**Liver Function Biomarkers**

Among the liver function markers only alkaline phosphatase (ALP) had a link with CKD. Out of the patients who had CKD, 46 (76.7%) had ALP levels. In contrast 15 (25.0%) of healthy individuals had abnormal ALP levels. This makes sense because we know that high ALP levels are connected to CKD-Mineral and Bone Disorder (CKD-MBD). In CKD-MBD mineral metabolism gets disrupted. This disruption leads to increased bone activity and more ALP production in the liver. On the hand ALT AST and total bilirubin did not show strong links with CKD. For ALT 9 (15.0%) of CKD patients had levels. In comparison 10 (16.7%) of individuals had abnormal ALT levels. AST was abnormal in 15 (25.0%) of CKD patients and 10 (16.7%) of individuals. Total bilirubin was abnormal, in 8 (13.3%) of CKD patients and 10 (16.7%) of individuals.




**The distribution of the liver function markers is presented in Table 4. Figure 4.**

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**Discussion**

The current research identifies changes in serum creatinine, serum urea, blood urea nitrogen (BUN), and estimated glomerular filtration rate (eGFR) in chronic kidney disease patients, suggesting the advancement of renal failure. This correlates with findings from other studies in which creatinine and BUN were identified as major biomarkers for the progression of chronic kidney disease and the onset of kidney failure (Xu et al., 2024). In the same vein, Shaheen et al. (2025) argue that monitoring both serum urea and creatinine in patients with chronic kidney disease is paramount, as their levels fluctuate in accordance with the worsening of renal function. Moreover, the observed decline in eGFR in this study coincides with the findings of Lin et al. (2021) in which there is a direct negative association between eGFR and worsening of kidney function and chronic kidney disease.

The current investigation showed major changes in serum sodium, potassium, and chloride levels among patients with chronic kidney disease (CKD). Electrolyte abnormalities are a well-known complication of CKD because of the progressive loss of glomerular and tubular function. The reported serum sodium imbalance may be due to the disturbed excretion of water, as well as the disturbed fluid regulation which are commonly reported in other patients with CKD. Similarly, along with the changes in serum sodium, the changes in serum potassium levels in the current study support the findings of Einhorn et al. (2009), who reported that hyperkalemia of CKD patients has inevitable consequences of impaired renal potassium excretion and adverse clinical outcomes. Also, chloride level fluctuations reported in our study support findings of previous studies where the disturbed chloride regulation is associated with renal function impairment and disturbances in acid-base balance (Yunos et al., 2010). According to Kovesdy (2012), changes in concentrations of sodium, potassium, and chloride are CKD markers of difficulties and deterioration.

Current Study showed that WBC are indicated as statistically significant in relation with CKD status ($p<0.001$) showing that immune system is also involved in CKD. This finding is in accordance with studies that indicate higher WBC levels represent prolonged inflammation associated with CKD. Yet the platelet count not showed a major association ($p=0.088$). This can probably be related to the evidence that platelet abnormalities is primarily qualitative not quantitative. Their findings were similar to the literature. Research in Lahore General Hospital (2023-2024) described advanced CKD stages and the concurrent increases in leukopenia and leukocytosis, and described the concurrent nature of decreased immunity and systemic inflammation and the dual nature of immune dysregulation (Akram et al., 2024).

The stage-dependent variability in WBC observed in this study is further supported by evidence showing that elevated WBC levels drive the production of pro-inflammatory cytokines, and a high WBC count combined with a low lymphocyte count is associated with poorer prognosis in CKD patients (Chen et al., 2023). Among the various pathophysiological factors related to CKD, inflammation plays a crucial role in disease initiation and progression, and the neutrophil-to-lymphocyte ratio (NLR) has been proposed as a simple and cost-effective indicator suitable for routine clinical practice in CKD management (Burlacu et al., 2023). Most notably, the consistently low lymphocyte counts across all stages in the present study point to an early and sustained impairment of adaptive immunity. This is corroborated by a PubMed-indexed study of 288 CKD patients which found that low relative lymphocyte count was independently associated with a significantly increased rate of CKD progression to end-stage renal disease, with the rate of progression nearly double in patients with low lymphocyte counts compared to those with higher counts ($p < 0.001$) (Kim & Kim, 2014)

Mossanen et al. (2022) reported that Intermediate Inflammatory Monocytes were significantly expanded in CKD patients, when compared to healthy controls. Zhang et al. (2023) also reported an elevated status of monocyte-related inflammatory activity in CKD patients. Furthermore, Kalantar-Zadeh et al. (2018) observed that higher monocyte counts were

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associated with an increased risk of mortality among CKD patients. With regard to neutrophils, the present study likewise demonstrated a statistically significant association between neutrophil levels and chronic kidney disease. Regarding eosinophils, the present study also demonstrated a statistically significant association between eosinophil levels and CKD; however, unlike monocytes and neutrophils, the available literature provides limited and less consistent evidence regarding eosinophils as independent biomarkers of CKD, and they have not been consistently recognized as primary biomarkers of CKD progression.

The findings revealed that (56.7%) of patients had elevated alkaline phosphatase (ALP) levels. This can be understood in the context of CKD-Mineral and Bone Disorder (CKD-MBD). According to research, as kidney function declines, alterations in calcium, phosphorus, and parathyroid hormone levels lead to high bone turnover which is known as renal osteodystrophy. This skeletal pathology is a well-documented cause of elevated ALP, which is released from overactive osteoblasts (Ray et al., 2015). Recent research has shown that total ALP levels increase gradually across CKD stages, driven by elevations in not only the bone but also the liver and intestinal fractions (Smout et al., 2026).

The finding that total bilirubin was high in only a small fraction of patients (13.3%) and normal in the vast majority (86.7%) is consistent with the observed non-significant overall distribution. A systematic review and meta-analysis have shown that lower serum total bilirubin levels are significantly associated with an increased risk of CKD progression (Fan et al., 2020).

## Conclusion

The findings revealed that as major clinical markers of kidney disease, each of the four kidney function variables indicated remarkably strong connections with CKD status ($p<0.001$).

An elevated level of anemia, lymphopenia, eosinophilia, leukocytosis abnormalities, and alterations to monocyte counts were identified by hematological analysis, demonstrating that CKD is associated with major immunological and hematological dysregulation. Alkaline phosphatase (ALP) is the liver function biomarker that was strongly associated with chronic kidney disease (CKD), although AST, ALT, and total bilirubin did not show statistically significant alterations. Significant non-random distributions have been identified in 10 of the 20 biomarkers that have been evaluated, indicating their potential clinical value in identifying the state of a disease.

### Limitations and Suggestions

- The study included a sample size (n = 120, 60 cases and 60 controls), which may limit the generalizability of the findings to larger populations.
- The retrospective case control design allowed assessment of associations only and could not establish causal relationships between biomarkers and CKD status.
- Data were collected retrospectively from laboratory records; therefore, some potentially important clinical information was unavailable.
- Healthy controls were selected from routine health checkup attendance at the same healthcare centers, which may not accurately reflect the general healthy population, potentially limiting the applicability of study comparisons.
- Due to a scarcity of data, it was not possible to assess advanced and emerging biomarkers such as cystatin C, NGAL, KIM-1, FGF-23, and inflammatory cytokines.
- Medication use, dietary habits, duration of disease, dialysis status, and comorbid conditions were not analyzed and may have impacted the levels of biomarkers.

### Future Implications

- Do larger, multicentric investigations to improbable generalizability and validate the results across the CKD population in Pakistan.
- To monitor the relationship between biomarker changes over time and patient survival , dialysis initiation, and CKD progression create long term cohort studies.
- Divide individuals According to their stage of chronic kidney diseases, to figure out which

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biomarkers are most diagnostically important at each stage of the disease's course.

- Combine normal indicators with new biomarkers (crystatin C, NGAL, KIM-1, FGF-23 and lL-6) to create more precise and sensitive evaluative models.
- To identify patients who are at a higher dose of experiencing adverse outcomes and rapid disease progression develop risk prediction models utilizing multi biomarker data
- Variables that were not accessible in this retrospective analysis, such as medication use, dietary habits, dialysis status, disease duration, and existing comorbidities, Future studies should include them. To facilitate personalized CKD risk evaluation and treatment suggestions, explore the integration of biomarker panels with clinical records through AI and data-driven approaches.

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