ONLINE FIRST

ORIGINAL ARTICLE

Early Screening of Chronic Kidney Disease (CKD) Among the Patients of Punjab, Pakistan

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doi: 10.22442/jlumhs.2025.01360

ABSTRACT

OBJECTIVE: To explore the early detection of chronic kidney disease (CKD) through primary care physicians (PCPs) and laboratory testing.

METHODS: A case-control study involving 200 participants with diabetes, hypertension, cardiovascular disease, arthritis, and chronic glomerulonephritis was conducted at Nishtar and Ibn-e-Sina Hospital, Multan, Pakistan, from November 2023 to May 2024. Participants' medical histories were documented, creatinine was assessed using the rate-Jaffe method, and estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equation. Laboratory tests included electrolyte levels, complete blood count (CBC), differential leukocyte count (DLC), and erythrocyte sedimentation rate (ESR). Statistical analysis was performed using one-way ANOVA via the computer software GraphPad Prism.

RESULTS: Of 200 participants, 113 were identified as CKD patients, 17 as acute kidney injury (AKI), and 70 as healthy controls. The eGFR values were significantly reduced in AKI (5.53mL/min/1.73 m ±2.71) and CKD (17.9mL/min/1.73m²±15.5) patients, where the creatinine level increased dramatically in AKI (11.69mg/dl± 4.71) and CKD (7.46 mg/dl±4.54) patients compared to their controls. Hemoglobin and platelets were decreased in CKD and AKI patients, while the total leukocyte count range increased in AKI patients, compared to controls. ESR was significantly increased in patients with CKD (49mm/hr±14.9) and AKI (65mm/hr±13) compared to the control group. The range of lymphocytes decreases in CKD patients, compared to controls.

CONCLUSION: The study underscores the importance of PCPs and laboratory tests aligning with Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for early and timely detection of CKD.

KEYWORDS: CKD, Kidney, Identification, PCPs, AKI, Disease.

INTRODUCTION

Chronic kidney disease (CKD) is a leading cause of death on a global scale[1]. The CKD is increasingly recognized as a global health issue, yet its management, causes, and prevalence in low- and middle-income countries remain poorly understood, impacting morbidity and mortality[2]. CKD is characterized by the gradual loss (over time) of kidney function, while acute kidney injury (AKI) is a rapid decline in kidney function[3]. In Pakistan, the prevalence of CKD is between 12.5 to 31.2%.[2] An estimated glomerular filtration rate (eGFR) of <15 ml/min/1.73 m^2 is indicative of end-stage renal disease (ESRD), which is diagnosed when CKD advances to the point that life cannot be sustained without renal replacement therapy[1]. The weight of medication, education level, age, gender, treatment costs, medical procedures, unemployment, lack of social support, inaccessibility of caretakers, and dietary restrictions are some of the factors that contribute to ESRD patients' poor quality of life[2].

The early detection, prevention, and prompt treatment of CKD is within the realm of family physicians or primary care physicians (PCPs)[4]. They provide continuous, comprehensive care that delays or even prevents the need for specialized nephrology care. In Pakistan, primary healthcare practices for CKD align with Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, which emphasize early detection, risk factor management, and appropriate referral[5]. Monogenic diseases significantly contribute to CKD, causing 70% of pediatric and 10–15% adult ESRD[6].

The PCPs recommend several laboratory tests for detecting kidney disease, including eGFR, creatinine, electrolytes, complete blood count (CBC), differential leukocyte count (DLC), and erythrocyte sedimentation rate (ESR). A kidney's structural, functional abnormalities or a reduced eGFR of <60 ml/min/1.73 m^2 for longer than three months are basic criteria for CKD identification[1]. These reasonably priced laboratory tests are used to identify kidney issues early in underdeveloped areas, particularly rural areas where people frequently rely on PCPs[4]. A very few earlier studies are available that demonstrate their impact on the identification of CKD. Moosazadeh M 2023[7], reported that a raised peripheral leukocyte count indicates greater systemic inflammation, which may lead to renal illness. Similarly, previous studies[8,9], reported that the decreased level of hemoglobin adversely affects CKD.

The study evaluates kidney disease via PCPs and physician-recommended laboratory tests, addressing the lack of local data on early CKD identification in Pakistan. Findings will inform targeted interventions and support programs aimed at enhancing patient management and improving their quality of life.

METHODOLOGY

Study Design

A case-control study was conducted among 200 participants in the Nephrology Outpatient Department of Nishtar and Ibn-e-Sina Hospital, Multan, Pakistan, from November 2023 to May 2024. Each participant provided informed consent, as outlined in the Declaration of Helsinki.

Diagnostic evaluation proforma

Diagnostic evaluation proformas for kidney disease were designed, incorporating demographic data such as age, gender, height, weight, and body mass index. Some evaluating questionnaires (Yes/No) were also included in this proforma, such as history of (H/O) ischemic heart disease, diabetes, hypertension, smoking, and family history of CKD. The proforma also included screening and laboratory tests, such as heart rate, blood pressure, blood sugar, hepatitis B virus and hepatitis C virus screening, complete blood count (CBC), differential Leukocyte Count (DLC), erythrocyte sedimentation rate (ESR), serum creatinine levels, and eGFR for CKD diagnosis. Before conducting the study, these diagnostic evaluation Performa's were distributed to 200 selected participants. The study included patients with diabetes, hypertension, cardiovascular disease, arthritis, and chronic glomerulonephritis, while excluding those with cancer, uterine fibroids, steroid therapy, systemic lupus erythematosus, rheumatoid arthritis, acute infections, septic shock, hypotension, and COVID-19, based on the inclusion and exclusion criteria.

Diagnostic Evaluation by Laboratory Testing

For diagnosis, height (m^2), weight (kg), body mass index (kg/m^2), body temperature (°C), heart rate (beats per minute), and blood pressure (mmHg) were measured using typical instruments. For further evaluation, blood samples were collected. Serum creatinine was assayed using the rate-Jaffe reaction on the Siemens ADVIA 18 analyzer, with calibrators supplied by the manufacturer (Standard Reference Material 967). After estimated creatinine values, eGFR[10], was measured manually and automatically using the Modification of Diet in Renal Disease (MDRD) equation through a customized Laboratory Information System machine. For further laboratory testing, levels of electrolytes Na^+ and K^+ were measured using commercially available diagnostic kits[11]. The CELL-DYN Emerald 22 Hematology Analyzer was used to estimate CBC parameters, including white blood cells (WBCs) and platelets. Hemoglobin content was measured by the cyanmethemoglobin method as described by Dibbasey M et al.[12] ESR was measured using the automated ESR STAT™ analyzer, as defined by Alqershi KA 2020[13]. The DLC test was measured manually using a hemocytometer, as described by Tishkowski K 2020[14].

Data Analysis

CKD patients were separated from AKI based on several characteristics, such as period (at least 3 months), urine color, pH, granular sediment, previous history of patients, level of electrolytes, eGFR, and creatinine level, as described by Behera BP 2020[16]. The mean and standard deviations of collected data were analyzed in Microsoft Excel. One-way analysis of variance (ANOVA) and the Tukey multiple comparison test were used to statistically analyze the data using GraphPad Prism (https://www.graphpad.com/). In statistical significance testing, "ns" denotes a non-significant result where the p-value is greater than 0.05 ($p > 0.05$). On the other hand, asterisks (*) indicate increasing levels of statistical significance, with * representing $p \leq 0.05$.

RESULTS

The study involved 200 participants, comprising 83 (63.8%) male and 47 (36.2%) female kidney disease patients, and 42 (60%) male and 28 (40%) female healthy controls. The mean age of kidney disease patients was 45 years ± 15, while the healthy control group had a mean age of 42 years ± 14. Weight averages were 57 kg ± 15 for kidney disease patients and 58.5 kg ± 13 for controls. The smoking prevalence was high among patients, with 79 (60.7%) being smokers compared to only 10 (14.3%) in the control group. Ischemic heart disease was present in 93 (71.54%) kidney disease patients, while 22 (31.43%) controls were affected. A family history of diseases was reported by 64 (49%) kidney disease patients and 34 (48%) controls. Hypertension was absent in the controls, with 73 (56%) kidney disease patients affected, and Type II diabetes mellitus was found in 41 (32%) kidney disease patients, whereas none were found in the controls. Hepatitis B and C were detected in small subsets of patients with kidney disease, while none were found in healthy controls (**Figure I**). Overall, the study examined a range of demographic parameters and their distribution among patients with kidney disease and healthy controls.

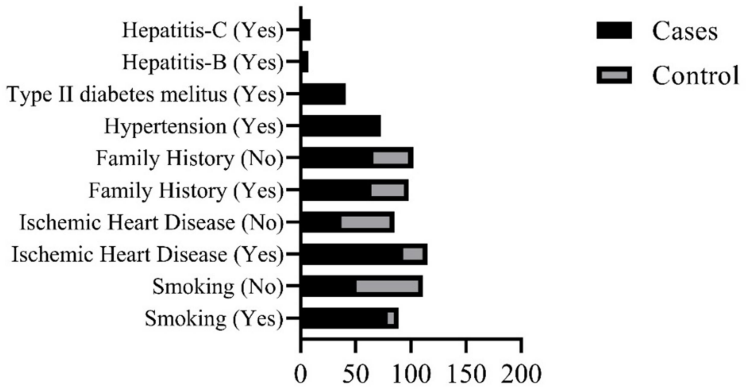

Figure I: Distribution of cases (kidney disease patients) and control (normal participants) based on smoking habits, ischemic heart disease, family disease history, hypertension, Type II diabetes, and viral infections.

The results of the current study found eGFR value was significantly ($p < 0.0001$) reduced in AKI (5.53 mL/min/1.73 m^2 ± 2.71) and CKD (17.9 mL/min/1.73 m^2 ±15.5) patients compared to control (74.08 mL/min/1.73 m^2 ±19.5) (**Figure IIb**). Where's creatinine level significantly ($p < 0.0001$) increases in AKI (11.69 mg/dl ± 4.71) and CKD (7.46 mg/dl ± 4.54) patients compared to control (0.99 mg/dl ± 0.17) (**Figure IIc**). Therefore, it is concluded that eGFR and creatinine are reliable indicators for the diagnosis of CKD. CKD patients were separated from AKI based on several characteristics, such as eGFR and creatinine values. Results showed 113 (56%) patients with CKD, 17 (8.5%) with AKI, and 70 (35%) healthy controls from a total of 200 participants (**Figure IIa**).

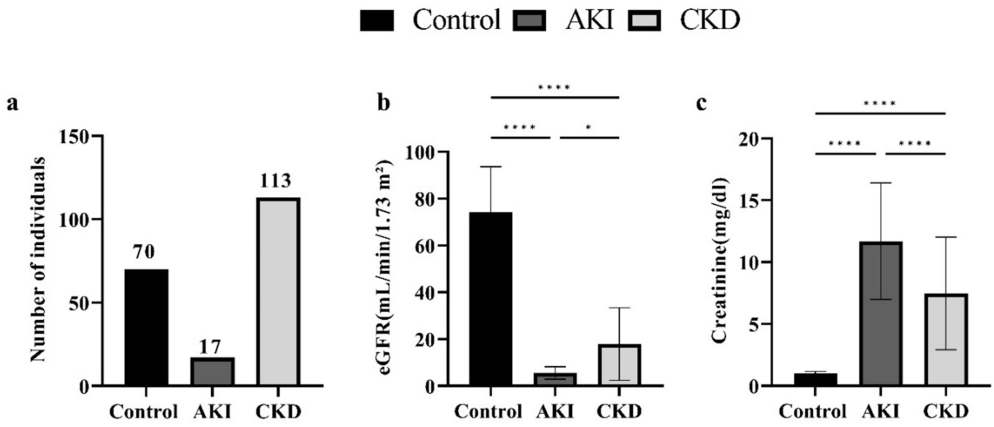

Figure II: Total number of individuals (a) eGFR (b) and creatinine (c) values among healthy control, AKI and CKD patients. One-way ANOVA and Tukey test were used to assess data; "ns" denotes non-significant, asterisks (*) indicate statistical significance.

The mean Na^+ level was within the normal range in CKD patients (135 mmol/L ± 4.6) and healthy controls (140 mmol/L ± 3.0), but slightly reduced in AKI patients (132 mmol/L ± 7.4) compared to the normal range (135-145 mmol/L). The results of the current study show that the Na+ level was reduced in CKD compared to the control and increased compared to AKI (**Figure IIIa**). Mean of K^+ was within normal range in CKD (4.20 mmol/L ± 0.9), AKI (4.7 mmol/L ± 0.5) patients and healthy control (4.22 mmol/L ± 0.6) compared to the normal range (3.6-5.5 mmol/L). The results of the current study show that the K^+ level was slightly reduced in CKD compared to AKI and the control (**Figure IIIb**). Therefore, it is concluded that electrolyte disturbance may not be an effective tool for CKD diagnosis.

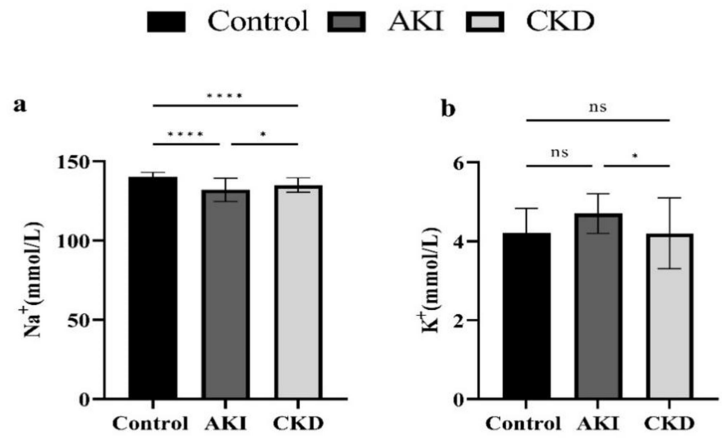

Figure III: Levels of electrolytes Na^+ (a) and K^+ (b) among AKI, CKD and healthy control participants. One-way ANOVA and Tukey test were used to assess data; "ns" denotes non-significant, asterisks (*) indicate statistical significance.

The mean of Hb was significantly ($p < 0.0001$) decreased in CKD (9.64 g/dL± 2.1), AKI (9.48 g/dL±1.99) patients compared to control (14 g/dL± 0.7) and normal range (13.5-17.5 g/dL for males and 12.0-16.0 g/dL for females) (**Figure IVa**). Mean of platelets was significantly ($p < 0.0001$) decreased in CKD (133,301±47,535), AKI patients (138,192±106674) compared to control (232,752±102900) and normal range (150,000 to 450,000µL) (**Figure IVb**). The mean of TLC was

within normal range in CKD (10,284 ±4986), healthy control (9,159±1975), and was highly increased in AKI patients (20,294 ±11059.3) compared to the normal range (4,000-11,000µL) (**Figure IVc**). It showed that a decrease in Hb and platelets can be an effective indicator for CKD diagnosis.

The results of the current study found the average range of ESR was significantly ($p < 0.0001$) increased in CKD (49 mm/hr ±14.9) and AKI (65 mm/hr±13) patients compared to healthy controls (15 ± 3.9) and the normal range (15-20 mm/hr) (**Figure IVd**). Therefore, it is concluded that an increase in ESR can be an effective indicator for diagnosing CKD. The results of the DLC found that the levels of neutrophils, eosinophils, and monocytes were within the normal range in all participants (**Figure IV**). In contrast, the percentage of lymphocytes decreased in CKD patients (17% ± 10) compared to controls (29% ± 4.5), which is outside the normal range (20-45%) (**Figure IVf**). Thus, it showed that a decrease in lymphocytes can be an effective indicator for CKD diagnosis.

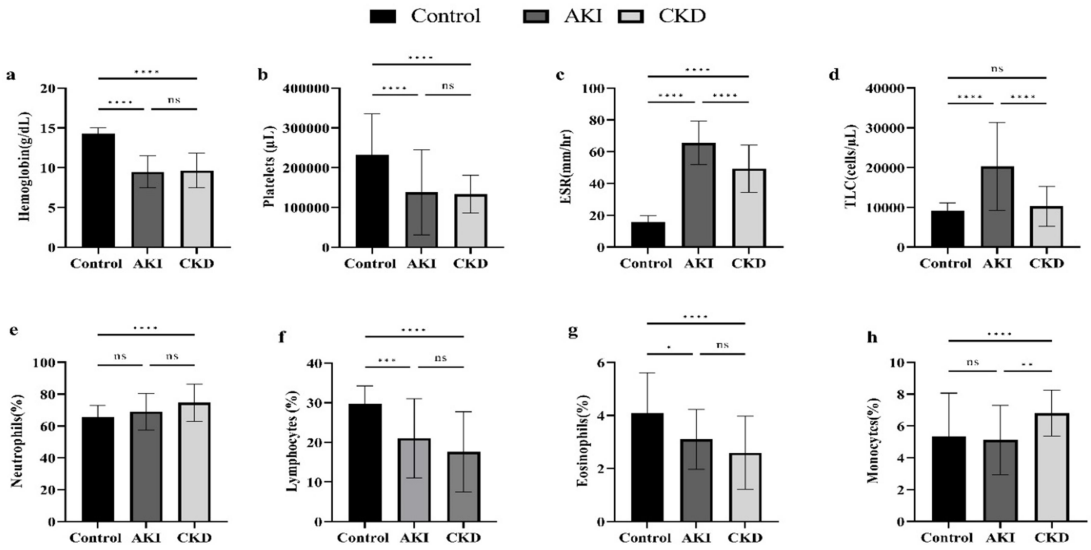

Figure IV: Hemoglobin level (a), ESR level (b), TLC level (c), platelet number (d), percentage of neutrophils (e), percentage of lymphocytes (f), percentage of eosinophils (g), percentage of monocytes (h) among AKI, CKD patients and healthy controls. One-way ANOVA and Tukey test were used to assess data; "ns" denotes non-significant, asterisks (*) indicate statistical significance.

DISCUSSION

Early screening for chronic kidney disease (CKD) is crucial for managing and preventing disease progression. Patients are referred to nephrologists upon symptom emergence, such as decreased urine output or kidney pain and complications, such as resistant hypertension, anemia, or creatinine and eGFR abnormalities. Primary care physicians (PCPs) play a key role in initial CKD screening through clinical evaluations, including medical, lifestyle, and family histories. Incorporating CKD screening into primary care facilitates ongoing monitoring, which will help reduce the health burdens on time[4,16]. In the current study, a diagnostic evaluation form was designed to assess kidney disease using detailed health information. A previous study[17] reported that age also contributes to CKD progression and found the average age of CKD patients to be 50.5 years ± 11.1. In contrast, our study found an average age of 46 ± 15 years, with 70% of patients over 40 years of age and 30% under 40 years of age. Further, in our primary diagnosis, participants were diagnosed with smoking habits, ischemic heart disease (IHD), family history of diseases, hypertension, Type II diabetes mellitus, and viral infections, including Hepatitis B and Hepatitis C. Ariyamuthu VK 2012[18], identified diabetes and hypertension are primary causes of ESRD, alongside smoking, inactivity, and dyslipidemias, affecting IHD pathophysiology in patients.

After primary symptom identification, laboratory tests are crucial for diagnosing and staging CKD, serving as an affordable option for screening high-risk populations. To evaluate effectiveness, we performed several laboratory tests generally recommended by primary care physicians, including eGFR, creatinine, electrolytes, complete blood count, erythrocyte sedimentation rate, and differential leukocyte count. The primary lab test used serum creatinine to estimate eGFR, a key marker of kidney damage. Consistent with previous studies[19-20], our study found a significantly ($p < 0.0001$) reduced eGFR value in AKI and CKD patients, compared to healthy controls. Pandya D 2016[21], found creatinine levels were highest in the CKD group, followed by the diabetic and hypertensive groups, and the control group. Consistent with a previous study[21], our study found that creatinine levels significantly ($p < 0.0001$) increase in AKI and CKD patients compared to healthy controls. Based on these tests, CKD patients were identified and separated from AKI patients. Non-enzymatic dehydration converts creatine to creatinine, which is produced and excreted by the kidneys. Reduced kidney function affects creatinine filtration rates, making it a key indicator of renal health. Impaired kidney function leads to elevated blood serum creatinine levels due to decreased urinary excretion[22]. Behera BP 2020[16], reported that electrolyte disturbances prominently increase with advancing CKD and found the average serum electrolytes of sodium (Na+), potassium (K+), calcium are 137.31±10.05 mEq/L, 4.12±1.48 mEq/L and 1.10±0.19 mmol/L respectively in CKD patients, while our study the found average serum electrolytes of sodium, in CKD (135 mmol/L ± 4.6), AKI (132 mmol/L ± 7.4) patients and potassium, in CKD (4.20 mmol/L ± 0.90) and AKI (4.7 mmol/L ± 0.5) patients.

CKD causes notable hematological abnormalities, including decreased levels of hemoglobin (Hb), hematocrit, red blood cells (RBC), total leukocyte count (TLC), and platelet count, resulting from nephron damage[22]. Anemia is more prevalent in CKD patients (15.4%) compared to the general population (7.6%). Our study shows a significant reduction in average Hb levels in both CKD and AKI patients compared to the control group, while Xu et al.[23], found that combining CKD with chronic inflammation leads to decreased Hb levels and higher mortality rates. Van Bladel et al.[24], found that CKD patients exhibit reduced platelet counts, confirmed by flow cytometric analysis. Similarly, our study found a significant decrease in mean platelet counts ($p < 0.0001$) in patients with CKD and AKI compared to controls. Platelet dysfunction may arise from diminished dense granule content (24). Contradictory findings about TLC were noted[25], with our study indicating that TLC is within normal ranges in CKD patients but elevated in AKI patients. ESR is often used as a biomarker in immune-mediated inflammatory diseases, such as breast cancer, with elevated levels linked to pro-inflammatory cytokines, the acute-phase response, and inflammation in renal disease[26]. Consistent

with the study by Aloy-Amadi OC 2024[27], our study found that ESR was increased in CKD patients compared to the normal range. Agarwal R 2011[28] found that CKD patients have more eosinophils and granulocytes and fewer lymphocytes. In contrast, our results found that the levels of neutrophils, eosinophils, and monocytes were within normal range in all participants, while the number of lymphocytes (%) decreased in CKD patients.

To summarize, early screening of CKD through PCPs and basic laboratory tests is a vital strategy for reducing disease progression and healthcare burden. Despite its potential, early screening of CKD through PCPs and laboratory tests has several limitations. Routine tests for kidney dysfunction, such as serum creatinine and eGFR, may miss early signs, particularly in young, elderly, or malnourished patients. Therefore, improved education, training, and sensitive biomarkers are essential for effective early CKD screening.

CONCLUSION

Early screening of CKD by PCPs using basic laboratory tests can significantly enhance patient outcomes in Pakistan. The primary healthcare practices are aligning with KDIGO guidelines, which emphasize early detection, risk assessment, and timely intervention. The study highlights the vital role of PCPs in identifying kidney issues using affordable laboratory tests, especially in rural areas where sources are limited. Therefore, this study will aid in the early identification of CKD, allowing physicians to leverage enthusiasm for beneficial clinical trials effectively.

Ethical Permission: Nishtar Medical University, Multan, Pakistan, ERC letter No. 13323/NMU.
Conflict of Interest: The author states no conflict of interest.
Financial Disclosure/Grant Approval: No funding agency was involved in this research.
Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Farooq B: Conceived and designed the study, supervised data collection and finalized the manuscript.
Jaffar M: Coordinated laboratory testing, contributed to the literature review and methodology section.
Qureshi ZH: Performed statistical analysis and drafted the results section of the manuscript.
Iqbal M: Assisted in patient recruitment, data entry, and reviewed the manuscript for accuracy.
Faisal M: Helped in conducting the experiment and manuscript writing
Khan MT: Critical review of manuscript, and help in reference collection
Lodhi MS: Helped in conception, conducting experiments and data analysis

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