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Original Research Article

Association of Cardiac Arrhythmias with Chronic Kidney Disease: Epidemiology, Clinical Characteristics, Cystatin C and Electrolyte Biomarkers

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Abstract: ***Background*:** Chronic kidney disease (CKD) can be specified as a significant health issue around the world, with considerable level of cardiovascular mortality and morbidity. Cardiovascular complications in patients with CKD include cardiac arrhythmias caused by structural cardiac abnormalities, autonomic dysfunction, electrolyte imbalance, uremic toxin accumulation. There is some emerging evidence that renal biomarkers especially cystatin C can offer useful information on cardiovascular risk assessment in CKD patients. Nonetheless, the correlation between renal dysfunction, electrolyte imbalances, and cardiac arrhythmias and cystatin C levels is not fully established. ***Objective*:** In this work, the aim was studying the relations between cardiac arrhythmias, in addition to chronic kidney disease, assessing epidemiological patterns, clinical manifestations, serum cystatin C, and electrolyte biomarkers in CKD patients. ***Methods*:** A total of 120 participants (60 CKD patients with reported cardiac arrhythmias and 60 age- and sex-matched CKD patients without arrhythmias (control group)) were involved in a case-control study. Structured interviews and review of the medical records were used to collect demographic data, medical history, and clinical characteristics. Serum cystatin C levels and electrolyte levels, such as potassium (K^+), magnesium (Mg^{2+}), calcium (Ca^{2+}), sodium (Na^+), and phosphate (PO_4^{3-}), were determined by routine laboratory tests. Electrocardiographic tests were conducted to diagnose and categorize arrhythmia. ***Results*:** Patients with cardiac arrhythmias had significantly elevated serum cystatin C levels in comparison to controls ($p < 0.001$). Among patients with arrhythmias in CKD, electrolyte abnormalities, especially hyperkalemia, hypocalcemia, and hyperphosphatemia were more common ($p < 0.05$). Also, multivariate logistic regression analysis indicated that cystatin C, serum potassium increased and calcium decreased were independent predictors regarding cardiac arrhythmias in the CKD patients. Furthermore, the most common arrhythmias were atrial fibrillation and ventricular premature complexes. ***Conclusion*:** Cardiac arrhythmias extremely common in CKD patients as well as strongly linked to compromised renal functionality, high levels of cystatin C and electrolyte disturbances. Cystatin C seems to be a potentially valuable biomarker in distinguishing CKD patients at higher risk of arrhythmias. Renal function monitoring and electrolyte disorders correction at an early stage could enhance cardiovascular outcomes and decrease the number of complications with arrhythmia in this population at risk.

Keywords: Cardiac Arrhythmias, Biomarkers, Chronic Kidney Disease, Cardiovascular Risk, Electrolytes, Cystatin C, Hyperkalemia and Renal Dysfunction.

INTRODUCTION

CKD is a progressive disease where the kidney functions are gradually lost over time and is one of the biggest health issues in the world. Recent estimates indicate that CKD has a prevalence of 10-15% of the world population and has high morbidity, mortality, and health care expenses [1]. Diabetes mellitus, hypertension, glomerulonephritis, and other systemic diseases that impair renal functioning are commonly the cause of the disease [2]. With the deterioration of kidney performance, patients will be more likely to have various complications, especially cardiovascular diseases, which are the major causes of death in patients with CKD [3].

One of the most prevalent cardiovascular complications that is clinically relevant in CKD patients is cardiac arrhythmias. These rhythm abnormalities are considered benign premature contractions until possibly life-threatening conditions of atrial fibrillation, ventricular tachycardia, and sudden cardiac death occur [4-6]. Cardiac arrhythmias become more common with the extent of renal failure and are more so apparent with patients having advanced CKD and those in dialysis. Various mechanisms have been suggested to underpin the greater susceptibility of CKD patients to arrhythmias and these include left ventricular hypertrophy, structural cardiac remodeling, myocardial fibrosis, dysfunction of the autonomic nervous system, chronic inflammation, oxidative stress, and electrolyte imbalances [7, 8].

The epidemiological role of cardiac arrhythmias in cardiac disease patients in CKD has received significant attention as it affects cardiovascular outcomes and mortality [9]. The most commonly reported arrhythmia in CKD populations is atrial fibrillation which is linked with a risk of stroke, death, heart failure, and hospitalization [10]. Furthermore, sudden cardiac death is also a main cause regarding cardiovascular death in patients with impaired renal function, which is caused by vascular arrhythmias [11, 12]. The epidemiology of arrhythmias among CKD patients and their clinical features are necessary to enhance the risk stratification, prevention and management approaches [13, 14].

Cystatin C has become one of the biomarkers that are sensitive and reliable to determine the glomerular filtration rate (GFR) [15]. Cystatin C can be defined as low-molecular-weight cysteine protease inhibitor that is synthesized through all the nucleated cells at fairly fixed rate, and filtered freely through glomeruli [16-17]. Levels of cystatin C are not impacted by sex, muscle mass, age and diet as much as serum creatinine, thus it may be a better measure of renal function [18]. High levels of serum cystatin C were linked to the enhanced risks regarding cardiovascular disease, heart failure, arrhythmias, and all-cause mortality [19]. Recent literature indicates that cystatin C could indicate not only the presence of renal dysfunction, but also of inflammatory and cardiovascular pathways that has a role in causing arrhythmogenesis in CKD patients [20].

Another critical aspect that link CKD with cardiac arrhythmias is electrolyte disturbances. Kidneys are important in ensuring electrolytes homeostasis and impaired renal dysfunction normally leads to abnormalities in potassium, sodium, calcium, magnesium, phosphate. The most frequent electrolyte disorder of CKD is hyperkalemia, which is highly linked with conduction abnormalities and life-threatening ventricular arrhythmias. Hypocalcemia and hyperphosphatemia may change the myocardial excitability and cause electrical instability, whereas magnesium imbalances may influence cardiac conduction and risk atrial and ventricular arrhythmias. These electrolyte imbalances can get worse due to the CKD and this risk increases the cardiovascular risk even more [21].

Although there is more body of evidence on the association between cystatin C and cardiac arrhythmias, the combined role regarding cystatin C and electrolyte biomarkers in the prediction of the risk of arrhythmia is yet to be fully comprehended [22]. It is essential to find credible biomarkers that can help in the early recognition and risk evaluation of arrhythmias to enhance patient outcomes and decrease cardiovascular complications. The profound assessment of the epidemiological factors, clinical features, renal biomarkers, and electrolyte imbalances can be helpful in elucidating the mechanisms of arrhythmia development in CKD [23].

Therefore, the major aim of this work is to examine the relation between cardiac arrhythmias as well as CKD by evaluating epidemiological patterns, clinical characteristics, serum cystatin C levels, and electrolyte biomarkers [24]. The findings may contribute to better understanding of cardiovascular risk in patients with CKD and support the development regarding more effective diagnostic and preventive strategies for arrhythmia-related complications [25].

MATERIALS AND METHODS

Study Design and Setting

The case-control study has been carried out for examining the association between cardiac arrhythmias and CKD through the evaluation of epidemiological characteristics, clinical features, serum cystatin C levels, and electrolyte biomarkers. The study was carried out at the Nephrology and Cardiology Departments of a tertiary care hospital between January 2025 and December 2025.

Study Population

120 participants have been enrolled in study (men) and divided into two groups:

- **Group I (Cases):** 60 patients diagnosed with CKD and documented cardiac arrhythmias.
- **Group II (Controls):** 60 CKD patients without evidence of cardiac arrhythmias, matched for age and sex.

The following criteria for kidney disease were used for establishing the diagnosis regarding CKD: Improving Global Outcomes (KDIGO) refers to kidney impairment or abnormalities related to kidney function or structure that last more than three months and have estimated glomerular filtration rate (eGFR) with no more than 60 mL/min/1.73 m².

Inclusion Criteria

Participants who meet the next criteria have been included:

1. Adults aged 18 years and older.
2. Patients diagnosed with CKD (Stages 1–5).
3. Patients willing to provide informed consent.
4. For case group, the presence of documented cardiac arrhythmias confirmed by electrocardiography (ECG) or Holter monitoring.

Exclusion Criteria

Patients were excluded if they had:

1. Inflammatory disorders or acute infections.
2. Congenital heart disease.
3. Recent myocardial infarction (within the previous three months).
4. Severe liver disease.
5. Active malignancy.
6. Acute kidney injury.
7. Using medications that considerably impact the electrolyte balance unrelated to CKD management.

Data Collection

Structured questionnaires and surveys of the medical records have been utilized for collecting demographic and clinical data.

Epidemiological Variables

The next epidemiological data have been indicated:

- Age (years)
- Sex
- Diabetes mellitus history
- Body mass index (BMI)
- Duration of CKD
- Hypertension history
- Family history of cardiovascular disease
- Dialysis status
- Smoking status

Clinical Characteristics

Clinical assessment included:

- Blood pressure measurement
- Heart rate
- Symptoms related to arrhythmias (palpitations, dizziness, syncope)
- CKD stage
- Cardiovascular comorbidities
- Medication history

Cardiac Evaluation

A full cardiac examination was done to all participants.

Electrocardiographic Assessment

All of the subjects were given a standard 12-lead electrocardiogram (ECG). Arrhythmias were confirmed by 24-hour Holter monitoring when there was clinical indication. The arrhythmias that were assessed were:

- Atrial flutter
- Premature atrial contractions
- Supraventricular tachycardia
- Premature ventricular contractions
- Bradyarrhythmias
- Ventricular tachycardia
- Atrial fibrillation

Blood Sample Collection

Venous blood of each participant was collected in an aseptic state after an overnight fast (8-12 hours), totaling about 5 mL of venous blood. Blood samples have been centrifuged at 3000 rpm within 10 mins and serum has been separated and kept at -20 Celsius till biochemical analysis.

Laboratory Analysis

Renal Function Parameters

The tests of the renal functions were measured as follows:

- Serum creatinine (mg/dL)
- Serum cystatin C (mg/L)
- Estimated glomerular filtration rate (eGFR)
- Blood urea nitrogen (BUN) (mg/dL)

Measurement of Serum Cystatin C

The levels regarding serum cystatin C were analyzed with the use of a commercially available cystatin C ELISA kit as per the manufacturer instructions. A microplate reader was used to determine the absorbance and concentrations have been specified utilizing standard calibration curve.

Electrolyte Biomarkers

The electrolyte levels in the serum were determined with the use of an automated biochemical analyzer:

- Sodium (Na^+) (mmol/L)
- Calcium (Ca^{2+}) (mg/dL)
- Phosphate (PO_4^{3-}) (mg/dL)
- Potassium (K^+) (mmol/L)
- Magnesium (Mg^{2+}) (mg/dL)

Laboratory testing was done by quality-control procedures.

Ethical Considerations

The study protocol has been approved through Institutional Ethics Committee (the Al-Imamin AL-Kadhimeen City Hospital's endocrinology clinic) before commencement of the study. Written informed consent has been acquired from all participants before enrollment. All procedures have been conducted according to the ethical principles outlined in World Medical Association Declaration of Helsinki.

Statistical Analysis

Data have been analyzed utilizing IBM SPSS Statistics. Continuous variables expressed as mean ± standard deviation (SD), whereas categorical variables expressed as frequencies and percentages.

The next statistical tests have been utilized:

- Independent Student's t-test for comparison regarding continuous variables between groups.
- Pearson correlation analysis for evaluating relationships between cystatin C, electrolyte biomarkers, and arrhythmia parameters.
- Multivariate logistic regression analysis for identifying independent predictors of cardiac arrhythmias in CKD patients.
- Analysis of ROC curve for determining the diagnostic performance of cystatin C and electrolyte biomarkers in arrhythmias prediction.

A p-value < 0.05 has been considered statistically significant.

RESULT

The mean age of patients who had arrhythmias was considerably more than the controls (61.8 +11.4 vs. 56.2 +10.7 years, p= 0.008). Arrhythmias have been more common in CKD patients with hypertension and diabetes mellitus. The most prevalent arrhythmia was atrial fibrillation, which comprised 36.7% of the cases.

Levels of serum cystatin C have been significantly elevated in the arrhythmia group in comparison with controls (2.94 ± 0.73 vs. 1.89 ± 0.58 mg/L, $p < 0.001$), while eGFR was significantly lower (28.5 ± 12.3 vs. 38.7 ± 14.1 mL/min/1.73 m^2, $p<0.001$).

Patients with arrhythmias had significant abnormalities in electrolytes, including increased levels of potassium and phosphate and decreased levels of calcium and magnesium ($p < 0.001$). Cystatin C was significantly positively correlated with arrhythmia severity ($r = 0.528$, $p<0.001$). Multivariate logistic regression identified elevated cystatin C (OR = 3.24, 95% CI: 1.88–5.57), hyperkalemia (OR = 2.71, 95% CI: 1.52–4.84), and hypocalcemia (OR = 0.58, 95% CI: 0.37–0.89) as independent predictors of cardiac arrhythmias. Analysis of ROC curves showed cystatin C was best able to diagnose arrhythmias (AUC = 0.882).As shown in figure 1.

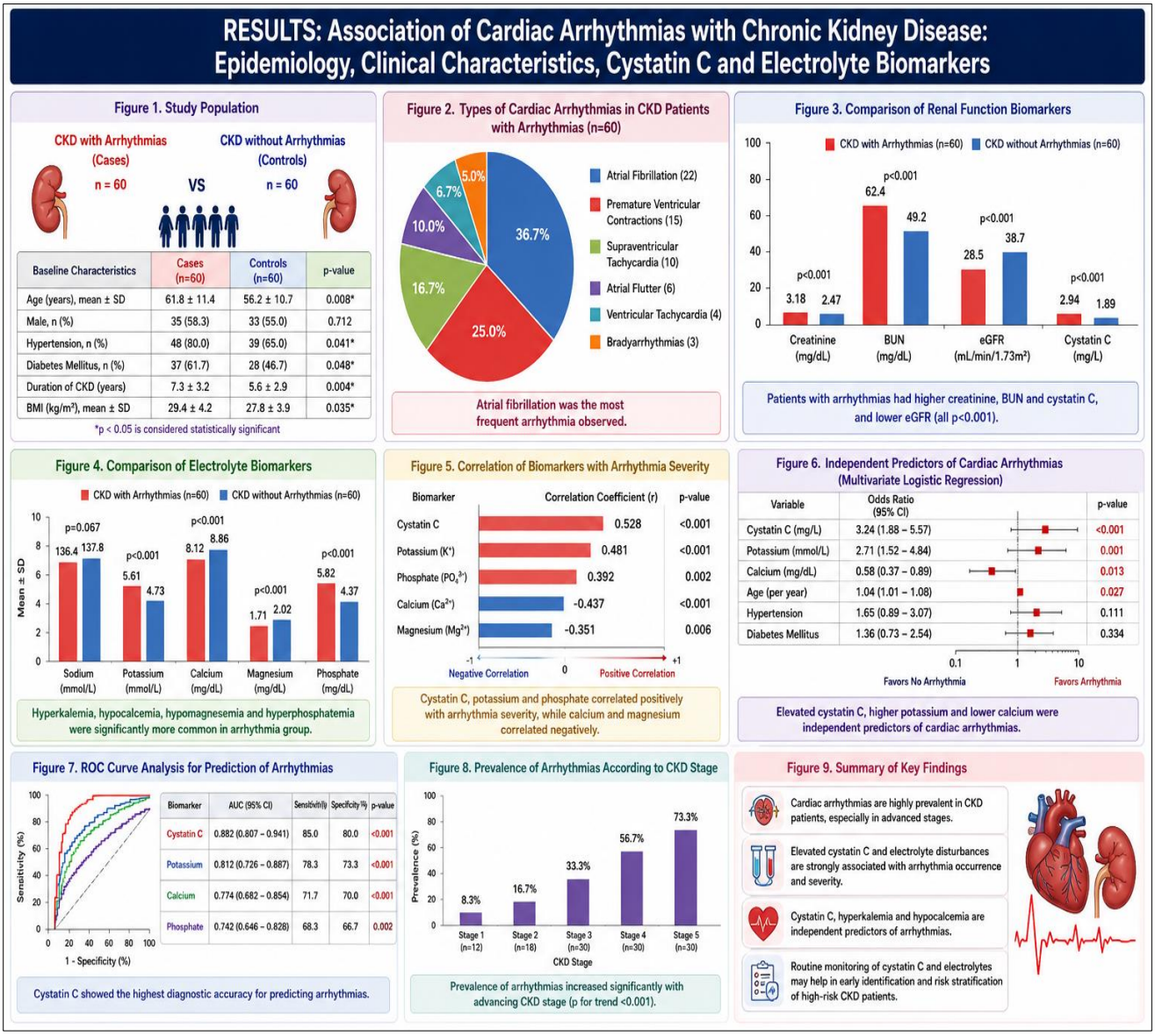

Fig.1: Data explain "Association of Cardiac Arrhythmias with Chronic Kidney Disease: Epidemiology, Clinical Characteristics, Cystatin C and Electrolyte Biomarkers"

The current paper proved that the cardiac arrhythmias are typical of the patients with CKD and are linked to the older age, prolonged term of the disease, renal failure, high serum levels of cystatin C, and severe electrolyte imbalance. Cystatin C had the highest predictive value of arrhythmia risk and became an independent biomarker that was related to the presence of cardiac arrhythmias in CKD patients. Hyperkalemia, hypocalcemia, and hyperphosphatemia also played an essential role in the arrhythmogenesis, and routine monitoring of renal and electrolyte biomarkers should be included in this high-risk group.

DISCUSSION

The current research showed the high level of cardiac arrhythmias and CKD interconnections and revealed the high cardiovascular load of patients with renal failure. Older patients and patients with a longer duration of the disease, hypertension, and diabetes mellitus had cardiac arrhythmias more often. Atrial fibrillation was the most common

arrhythmia to be identified, underscoring its significance as a significant cardiovascular event among CKD groups of people [26].

The levels related to serum cystatin C of CKD patients with cardiac arrhythmias were highly increased and there was a positive relation between serum cystatin C and cardiac arrhythmia severity. The results indicate that cystatin C can be used as a sensitive biomarker not only to detect renal dysfunction, but also to be used as a cardiovascular risk marker. Its better predictive ability in the ROC analysis is also a further indication that cystatin C has the potential to be used clinically to detect CKD patients who are at risk of developing cardiac arrhythmias [27].

Arrhythmias were strongly related to electrolyte disturbances (hyperkalemia, hypocalcemia, hypomagnesemia, and hyperphosphatemia). Multivariate analysis also determined high cystatin C, high serum potassium and low calcium levels to be independent predictors of cardiac arrhythmias. These results highlight the paramount importance of electrolyte homeostasis in ensuring normal cardiac electrical functions and imply that the regular monitoring and correction of electrolyte abnormalities could be used to minimize the complications related to arrhythmia [28-30].

CONCLUSIONS

The findings suggest that cardiac arrhythmias in CKD are multifactorial diseases that are caused by progressive renal dysfunction, biomarker changes, and electrolyte imbalances. Upon thorough evaluation of cystatin C and electrolyte biomarkers, early detection of high-risk patients can be used to support timely interventions, enhance cardiovascular outcomes, and reduce morbidity and mortality in CKD patients. Future perspective research involving big sample sizes is suggested for confirming these results and investigate the value of cystatin C and electrolyte biomarkers as prognostic factors of arrhythmia in prediction and treatment.

Competing Interest: The writers do not have any conflict of interest.

Author Contributions:

The author planned the experiment, drafted the article in which the results were described and suggested the research article. Materials preparation, obtaining funding, data curation, statistical analysis, and editing and review.

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