

ORIGINAL ARTICLE

CLINICAL EPIDEMIOLOGY OF CARDIOVASCULAR DISEASE IN ADVANCED CHRONIC KIDNEY DISEASE PRIOR TO DIALYSIS TO A TERTIARY CARE CENTRE IN BANGLADESH

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Abstract

Background: Patients with advanced CKD stages exhibit a markedly elevated risk of cardiovascular disease. Patients with chronic kidney disease (CKD) exhibit an elevated cardiovascular risk manifesting as coronary artery disease, heart failure, arrhythmias, and sudden cardiac death. The main objective of this study was to observe the clinical epidemiology of cardiovascular disease in advanced stages of CKD prior to dialysis to a tertiary care centre in Bangladesh. **Methods:** This was a cross-sectional observational study on 150 cases of diagnosed advanced stages (4&5) of CKD patients in the indoor Department of Medicine of Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from July 2022 to January 2023 for 6 months. Data was analyzed SPSS 25. **Results:** Out of the total group, 62.0% are male, 38.0% are female, and the average (mean) age of the entire group was 55.2 ±10.3. Patients are compared in terms of their relative percentages and the associated cardiovascular disease (CVD) risk, with the hypothesis that lower hemoglobin levels (<9 mg/dL), common in advanced CKD, may be associated with higher CVD risk. A statistically significant P-value (0.036) indicates a significant association between lower hemoglobin levels and increased risk of CVD. Hypertension is the most common risk factor in both stages showing (80%) in stage 4 and 86.6% in Stage 5 of CKD respectively that increasing prevalence as stages of CKD increases. Other factors like diabetes 50.6% and 53.3%, dyslipidemia 61.3% and 66.7%, and family history of cardiovascular disease (CVD) 40% and 46.6% also in prevalence from Stage 4 to Stage 5. However, the differences in the prevalence of these risk factors between the two stages are not statistically significant, as indicated by the P-values. The prevalence of Congestive Heart Failure rises from 44% in Stage 4 to 52% in Stage 5, and a similar trend is observed in Coronary Artery Disease from 40% in Stage 4 to 48% in Stage 5 and for other diseases, albeit with lesser increments. The provided p-values, which assess statistical significance, indicate that the differences in disease prevalence between the two stages are not statistically significant, suggesting that the progression from Stage 4 to Stage 5. **Conclusion:** This study stated that increased prevalence and progression of cardiovascular risks in advanced CKD stages.

Keywords: Clinical epidemiology Chronic kidney disease (CKD), Cardiovascular, prior to dialysis

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Introduction:

Chronic kidney disease (CKD) represents a global health burden affecting millions worldwide, with its prevalence increasing owing to the aging population and rising rates of its primary risk factors, such as

diabetes and hypertension. CKD is characterized by a gradual loss of kidney function over time and is classified into various stages based on the severity of kidney damage, with stages 4 and 5 being the most advanced and often requiring renal replacement

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therapies¹. Among the numerous complications associated with CKD, cardiovascular diseases (CVD) are the most common and constitute the leading cause of mortality in this patient population². The interplay between CKD and CVD is complex and multifactorial. Kidney dysfunction promotes cardiovascular risk through various pathways including fluid overload, increased production of pro-inflammatory cytokines, and alterations in calcium and phosphate metabolism, which contribute to vascular calcification and arterial stiffness³. Furthermore, the retention of uremic toxins in CKD can exacerbate oxidative stress and endothelial dysfunction, further elevating the risk of cardiovascular complications⁴. Epidemiological studies consistently demonstrate an elevated prevalence of traditional cardiovascular risk factors such as hypertension, diabetes, and hyperlipidemia in CKD patients⁵. However, CKD itself is also independently associated with an increased risk of adverse cardiovascular outcomes, which suggests that kidney disease may directly contribute to cardiovascular pathology [6]. For instance, anemia, a common complication of CKD due to decreased erythropoietin production by the kidneys, has been linked to left ventricular hypertrophy and heart failure⁷. The relationship between hemoglobin levels and cardiovascular outcomes in CKD has garnered considerable attention. Lower hemoglobin concentrations have been associated with higher mortality and morbidity rates due to CVD in this population⁸. This association underscores the importance of monitoring and potentially managing anemia as part of the cardiovascular risk reduction strategy in CKD patients. The aim of this study to assess the risk factors cardiovascular diseases in advanced stages of chronic kidney disease patients.

Methods:

This cross-sectional observational study was conducted in the Department of Medicine, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from July 2022 to January 2023, to observe cardiovascular status in advanced stages (4 & 5) of CKD patients. The patients who attended the outpatient department of medicine or were admitted to the medicine ward were considered as the study population. A total of 150 patients were selected as study subjects as per inclusion and exclusion criteria. A purposive sampling technique was adopted in this study. The study aimed to investigate on adult patients with advanced chronic kidney disease (CKD), specifically those in stages 4 and 5, who were not undergoing dialysis or receiving hematinics. CVD was assessed in CKD through echocardiography, ECGs, biomarker analysis, and physical examination. Inclusion criteria encompassed adult patients of both sexes above 18 years old who met the specified CKD stage requirements and were willing to provide informed consent. However, certain individuals were

excluded from the study, such as those under 18 years old, patients with CKD complicated by bleeding disorders, recent hemorrhage, chronic liver disease (CLD), or malignancy. Additionally, individuals who were already undergoing dialysis, receiving hematinics, recombinant human erythropoietin, or had received blood transfusions were excluded. Patients with psychological abnormalities or those who declined to participate were also excluded. CKD staging was done according to the US National Kidney Foundation Kidney Disease Quality Outcomes Initiative 2002. Data collection was done through face-to-face interviews with the selected patients with the help of a structured questionnaire. Data were entered in the IBM Statistical Package for Social Science (SPSS) 25 for Windows 10. Statistical analysis was done using SPSS 25 on Windows 10. To establish a relationship between variables chi-square analysis, student t-test, and Fisher's Exact test were done in all cases. P value < 0.05 is considered significant. After analysis, the data were presented in tables. Ethical clearance was taken from the Institutional Ethical Review Committee (ERC). The informed consent of the patients was taken. All information was kept confidential.

Definition of hypertension, diabetes, and cardiovascular disease events⁸

Hypertension at entry was defined as either systolic blood pressure >140 mmHg, or diastolic blood pressure >90 mmHg (confirmed by at least three elevated readings taken at least 1 week apart), or use of antihypertensive medications, or any self-reported history of hypertension. In addition, 24-hour ambulatory blood pressure was measured for every participant. Diabetes mellitus was defined as either a fasting glucose ≥ 7.0 mmol/L, or HbA1c $\geq 6.5\%$, or use of insulin or oral anti-diabetic medications, or any self-reported history of diabetes. CVD was defined as a history of myocardial infarction, hospitalization for congestive heart failure, serious cardiac arrhythmia incidents (resuscitated cardiac arrest, ventricular fibrillation, sustained ventricular tachycardia, paroxysmal ventricular tachycardia, atrial fibrillation or flutter, severe bradycardia or heart block), peripheral arterial disease (PAD), or cerebrovascular events (cerebral infarction, transient ischemic attack, cerebral hemorrhage or subarachnoid hemorrhage). Reporting of CVD was based on both the patients' self-report and review of their medical records by trained staff on the same date of the baseline interview.

Definition of stages of CKD⁹

The stages of CKD are classified as follows :Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m²), Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m²), Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m²), Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73

m 2)Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m²) and Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m² or dialysis)

Results:

Table 1
Sex and age of the patients (N= 150)

Variables	n	%
Male	93	62.0
Female	57	38.0
Mean age (years)	55.2 ±10.3	

Out of the total group, 62.0% are male, 38.0% are female, and the average (mean) age of the entire group was 55.2 ±10.3. [Table I].

Table II
Hemoglobin Levels in Advanced Stages of CKD Patients and Associated Cardiovascular Risk (N=150)

Hemoglobin (mg/dL)	Number of Patients n (%)	Associated CVD Risk	P-value
≥9	105 (70.0)	High	0.036
> 9	45 (30.0)	Low	
Mean ± SD	7.61 ± 2.54		
Range	4.8 - 10.6		

Patients are compared in terms of their relative percentages and the associated cardiovascular disease (CVD) risk, with the hypothesis that lower hemoglobin levels (<9 mg/dL), common in advanced CKD, may be associated with higher CVD risk. A statistically significant P-value (0.036) indicates a significant association between lower hemoglobin levels and increased CVD risk in this cohort. [Table II]

Table III
Risk factors of Cardiovascular diseases in Advanced Stages of CKD (N=150)

Cardiovascular Risk Factors	CKD Stage 4 (n=75)	CKD Stage 5 (n=75)	P-value
Hypertension	60(80%)	65(86.7%)	0.218
Diabetes	38(50.7%)	40(53.3%)	0.741
Hyperlipidemia	46(61.3%)	50(66.7%)	0.425
Family History of CVD	30(40%)	35(46.7%)	0.310
Elevated Body Mass Index (>30)	28(37.3%)	31 (41.3%)	0.562
Physical Inactivity	32 (42.7%)	36 (48%)	0.462
Smoking	20 (26.7%)	22 (29.3%)	0.689

Hypertension is the most common risk factor in both stages showing (80%) in stage 4 and 86.6% in Stage -5 of CKD respectively that increasing prevalence as stages of CKD increases. Other factors like diabetes (50.6% and 53.3%), dyslipidemia (61.3% and 66.7%), and family history of cardiovascular disease (CVD) (40% and 46.6%) also in prevalence from Stage 4 to Stage 5. However, the differences in the prevalence of these risk factors between the two stages are not statistically significant, as indicated by the P-values [Table III]

Table IV
Prevalence of Specific Cardiovascular Diseases in advanced CKD (N=150)

Cardiovascular Disease	CKD Stage 4 (n=75)	CKD Stage 5 (n=75)	P-value
Congestive Heart Failure	33(44%)	39(52%)	0.217
Coronary Artery Disease	30(40%)	36(48%)	0.248
Atrial Fibrillation	20(26.7%)	24(32%)	0.339
Peripheral Arterial Disease	15(20%)	19(25.3%)	0.410
Stroke	12 (16%)	16 (21.3%)	0.295

The prevalence of Congestive Heart Failure rises from 44% in Stage 4 to 52% in Stage 5, and a similar trend is observed in Coronary Artery Disease from 40% in Stage 4 to 48% in Stage 5 and for other diseases, albeit with lesser increments. The provided p-values, which assess statistical significance, indicate that the differences in disease prevalence between the two stages are not statistically significant, suggesting that the progression from Stage 4 to Stage 5. [Table IV]

Discussion:

Our study systematically evaluated the intersection between cardiovascular diseases and advanced stages of chronic kidney disease (CKD), showcasing varied prevalence and associations that resonate with findings from prior studies. This study reflects the demographics of this study population, comprising a majority of males (62%) with an average age of 55.2 years. These findings are consistent with previous research, such as the study by Zhang et al., which noted a higher prevalence of CKD in males, potentially due to higher rates of risk factors like hypertension and diabetes in this demographic.¹⁰ A significant proportion of our CKD patients (70%) had hemoglobin levels ≤9 mg/dL, associated with a higher cardiovascular risk, a finding echoing Jankowska et al., who reported anemia as a common comorbidity in CKD and a significant predictor

of cardiovascular morbidity^{11,12}. The statistical significance ($p=0.036$) underscores the critical nature of managing anemia in CKD to potentially mitigate associated cardiovascular complications. Hypertension is the most common risk factor in both stages showing (80%) in stage 4 and 86.6% in Stage -5 of CKD respectively that increasing prevalence as stages of CKD increases. Other factors like diabetes (50.6%) and 53.3%, dyslipidemia (61.3% and 66.7%), and family history of cardiovascular disease (CVD) (40% and 46.6%) also in prevalence from Stage 4 to Stage 5. Although changes in our study did not reach statistical significance, they suggest a worsening trend that demands vigilant clinical attention. This trend aligns with the study by Thomas et al., which noted that as renal function declines, the prevalence and severity of hypertension tend to increase, thereby escalating the overall cardiovascular risk.¹² Another study stated that patients with kidney disease are deemed to be at highest cardiovascular risk. CVD, defined as the presence of either congestive heart failure (CHF), ischemic heart disease (IHD), or left ventricular hypertrophy (LVH), is prevalent in cohorts with established CKD (8–40%). The prevalence of hypertension, a major risk factor for coronary artery disease (CAD) and LVH is high in patients with CKD (87–90%). At least 35% of patients with CKD have evidence of an ischemic event (myocardial infarction or angina) at the time of presentation to a nephrologist.^{13,14} The another study showed that The percentage of different CVD subtypes among the subset of patients with CVD was MI 20.6%, CHF 9.0%, cerebrovascular disease 69.1%, and PAD 10.1%, respectively and stage 3 & 4 CKD are significantly associated with the prevalence of CVD⁸. The prevalence of specific cardiovascular conditions was observed, where Congestive Heart Failure (CHF) and other cardiovascular diseases showed an increased prevalence with advancing CKD stages, though without statistical significance. This observation supports the findings from Briasoulis et al., indicating that the burden of cardiovascular diseases such as CHF increases with the progression of renal impairment, largely due to shared risk factors such as hypertension and diabetes.^{14,15} In our study, we found the prevalence of Congestive Heart Failure rises from 44% in Stage 4 to 52% in Stage 5, and a similar trend is observed in Coronary Artery Disease from 40% in Stage 4 to 48% in Stage 5 and for other diseases, albeit with lesser increments.

Limitations of the Study:

The study was carried out in a single hospital with a small sample size and for a short duration. So, the results may not represent the whole community.

Conclusion:

This study highlights that a significant correlation between advanced stages of CKD and increased risks of CVD. The findings emphasize the progression of cardiovascular risks in advanced CKD stages.

Conflict of Interest:

The authors stated there is no conflict of interest in this study.

Funding:

No funding.

Ethical Consideration:

Ethical measures were taken throughout the study period to maintain a high standard of confidentiality and anonymity of the participants. Formal approval was taken from the ethical committee of Sir Salimullah Medical College Mitford Hospital.

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