Section: Community Medicine

Original Research Article

ASSOCIATION OF PROTEINURIA AND GLOMERULAR FILTRATION RATE WITH LEFT VENTRICULAR MASS IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT

Background: Chronic kidney disease (CKD) is frequently accompanied by cardiovascular complications, including left ventricular hypertrophy (LVH), a significant risk factor for adverse cardiovascular outcomes. **Objective:** To evaluate the relationship between proteinuria, estimated glomerular filtration rate (eGFR), and left ventricular mass index (LVMI) in CKD patients.
Materials and Methods: A prospective cross-sectional study was conducted at Srinivas Institute of Medical Sciences and Research Centre, Mukka, Mangalore, from September 2022 to September 2023. The study included 100 CKD patients, aged 18 years or older, managed with medical therapy alone, excluding those on hemodialysis. Data collected included serum creatinine, urine protein-to-creatinine ratio (PCR) for proteinuria, and LVMI measured through 2D echocardiography. Demographic and clinical data were obtained via structured interviews and laboratory evaluations. Descriptive statistics summarized demographic data. Pearson's correlation coefficient and Chi-square tests were used to assess associations between LVMI and variables, including eGFR and PCR, with a significance level set at $p < 0.05$.
Results: The mean age of participants was 65.17 ± 11.56 years, with 66% males. Hypertension (83%) and diabetes (51%) were the most common comorbidities. Moderate to severe LVH was observed in 57% of patients. A significant association between proteinuria (PCR) and LVMI ($p = 0.014$) was found, with higher PCR levels corresponding to increased LVMI. However, no statistically significant association was observed between eGFR stages and LVMI ($p = 0.453$).
Conclusion: Proteinuria is significantly associated with LVH in CKD patients, emphasizing its importance as a marker for cardiovascular risk. Conversely, eGFR did not show a significant relationship with LVMI, suggesting that factors beyond renal function may influence LVH in CKD
Keywords: Chronic kidney disease, proteinuria, glomerular filtration rate, left ventricular hypertrophy, cardiovascular risk.

INTRODUCTION

CKD is defined by the criteria in which there is kidney damage for more than 3 months as defined by structural and functional abnormalities of kidney, with or without decreased GFR or GFR < 60 ml/min/1.73m2 for > 3 months with or without kidney damage.[1] Proteinuria is an independent risk factor for function of kidney and mortality.[2] Myocardial LVH are of concentric and eccentric. Concentric LVH is mainly due to the muscular mass resulting in low end - diastolic volume i.e. insufficient to maintain cardiac output leading to diastolic dysfunction which is seen in hypertension, inflammation whereas the eccentric mass is seen in case of volume overload, severe anaemia.[3] Several studies showed the risk of adverse cardiovascular involvement which was 43% higher in patients with

a GFR between 45 and 59 ml/min/1.73 m2 and 343% higher in those with a GFR <15 ml/min/1.73 m2. Stage V CKD patients, not on renal replacement therapy, showed mortality rates similar to those on dialysis therapy. Cardiovascular diseases account for 50% of deaths in CKD patients regardless of age.[4] In CKD multiple humoral factors and hypertension results in end organ damage in the form of cardiac remodelling resulting in increase in left ventricular mass and hypertrophy. Significant association between EGFR, proteinuria and left ventricular mass helps to initiate prompt therapy at the very beginning to help avoid or slow progression of cardiac remodelling in these patients. This study was done to assess whether there is a relationship between the amount of proteinuria and the glomerular filtration rate to the left ventricular mass in patients with CKD.

MATERIALS AND METHODS

This was a prospective cross-sectional study conducted over one year, from September 2022 to September 2023, at Srinivas Institute of Medical Sciences and Research Centre in Mukka, Mangalore. The study focused on patients diagnosed with chronic kidney disease (CKD) who met the inclusion criteria.

The study included both inpatients and outpatients with CKD, with a target sample size of at least 100 participants. Sample size calculation was based on a 95% confidence level and 90% power, using formula

$N=Z_{\alpha}^2\ s^2/\ d^2$

where $Z_{\alpha}=1.96$ at a 95% confidence level, s is the standard deviation (11.7), and d is the relative precision (10% of the mean), the minimum sample size was determined to be 100.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: patients aged 18 years and older diagnosed with CKD who were undergoing only medical management for their condition. Patients receiving hemodialysis were excluded to focus on those with stable CKD on conservative treatment. Additionally, patients with CKD who had pre-existing conditions that could impact cardiac function—such as aortic stenosis, hypertrophic obstructive cardiomyopathy (HOCM), or congenital heart disease—were excluded. This was to ensure that any observed cardiovascular changes were primarily related to CKD.

Data collection was carried out using a structured proforma designed for this study. Upon enrollment, a comprehensive medical history was taken for each patient, emphasizing the duration and severity of CKD symptoms, any related comorbidities, and the patient's management history. Laboratory assessments included the measurement of serum creatinine to evaluate kidney function, the urine spot protein-creatinine ratio (PCR) for proteinuria assessment, and a 2D echocardiogram to evaluate left ventricular (LV) mass. These data points provided insight into the cardiovascular risks associated with CKD.

Patients or their attendants were interviewed to obtain a detailed medical history, and routine laboratory tests were performed, including serum creatinine levels, urine spot PCR, and 2D echocardiography to assess LV mass. Blood samples were collected via venipuncture, and echocardiographic assessments were performed to identify left ventricular hypertrophy.

Data Analysis: Data analysis was conducted using SPSS software, version 23.0. Descriptive statistics summarized demographic and clinical characteristics. Pearson's correlation coefficient was used to examine correlations between LV mass and key variables, including serum creatinine and urine spot PCR. For categorical data, the Chi-square test was applied, with a p-value of <0.05 considered statistically significant.

Ethics Approval and Consent

Approval for the study was obtained from the institutional ethics committee of Srinivas Institute of Medical Sciences and Research Centre vide letter no. SIMSEC/SIMS&RC/2022/07/18. Informed consent was sought from all participants, or from their relatives when necessary, with a clear explanation of the study's objectives, procedures, and potential implications, presented in a language they understood.

RESULTS

A total of 100 patients with CKD were included in this study. The majority of patients (59%) were over 60 years old, followed by 28% in the 51-60 age group, and 13% in the 41-50 age group. The mean age of the participants was 65.17 years, with a standard deviation of 11.56 years. The youngest patient was 42 years old, while the oldest was 83 years old. Out of the total participants, 66 (66%) were male, and 34 (34%) were female. The study population shows a higher prevalence of chronic kidney disease among males compared to females, with almost twice as many male participants as female participants. Majority of patients in this study had moderate to severe kidney disease, with stages G3a, G3b, and G4 accounting for 75% of the participants. More than half of the patients (57%) had low albumin levels, which is a common finding in CKD patients.

Figure 1 presents the prevalence of various co-morbidities among the study participants. Hypertension was the most common co-morbidity, affecting 83% of patients, followed by diabetes (51%) and ischemic heart disease (37%).

Table 1 shows the distribution of patients based on their Left Ventricular Mass Index (LVMI). More than half of the patients (57%) had some degree of left ventricular hypertrophy, with 28% having

moderate to severe LVMI. This indicates a high prevalence of cardiac structural changes in CKD patients, which is a significant concern for cardiovascular health.

Table 2 shows the relationship between estimated Glomerular Filteration Rate (eGFR) stages and LVMI severity. The p-value of 0.453 indicates no statistically significant association between eGFR stages and LVMI. While there seems to be a trend of more severe LVMI in lower eGFR stages (e.g., 42.9% of G4 patients had severe LVMI compared to 0% in G1), the association is not statistically significant.

Table 3 shows the relationship between urine Protein-to-creatinine (PCR) levels and LVMI severity. The p-value of 0.014 indicates a statistically significant association between PCR and LVMI. There is a significant trend showing that as PCR increases (indicating more severe proteinuria), the likelihood of having more severe LVMI also increases. This suggests that proteinuria may be associated with left ventricular hypertrophy in CKD patients.

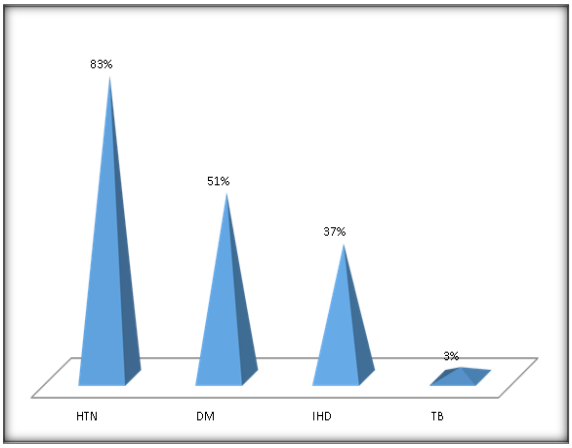

Figure 1: Distribution of patients according to co-morbidities

Table 1: Distribution of patients according to LVMI

LVMI	Frequency	Percentage
Normal	43	43%
Mild	29	29%
Moderate	14	14%
Severe	14	14%
Total	**100**	**100%**

Table 2: Association of eGFR with LVMASS among the study participants

	Normal	Mild	Moderate	Severe
G1 (>90)	4 (9.3%)	1 (3.4%)	0	0
G2 (60-89)	10 (23.3%)	4 (13.8%)	1 (7.1%)	0
G3a (45-59)	13 (30.2%)	8 (27.6%)	3 (21.4%)	1 (7.1%)
G3b (30-44)	10 (23.3%)	10 (34.5%)	6 (42.9%)	4 (28.6%)
G4 (15-29)	5 (11.6%)	5 (17.2%)	4 (28.6%)	6 (42.9%)
G5 (<15)	1 (2.3%)	1 (3.4%)	0	3 (21.4%)
Total	43 (100%)	29 (100%)	14 (100%)	14 (100%)
P value	0.453			

Table 3: Comparison of patients according to the PCR and LVMI

PCR	Normal	Mild	Moderate	Severe
Normal to mildly increased (<3mg/mmol)	35 (81.4%)	17 (58.6%)	5 (35.7%)	3 (21.4%)
Moderately increased (3-30 mg/mmol)	7 (16.3%)	11 (37.9%)	8 (57.1%)	9 (64.3%)
Severely increased (>30mg/mmol)	1 (2.3%)	1 (3.4%)	1 (7.2%)	2 (14.3%)
Total	43	29	14	14
P value	0.014*			

DISCUSSION

Chronic kidney disease (CKD) is a global health concern associated with significant cardiovascular morbidity and mortality. Left ventricular hypertrophy (LVH), as measured by left ventricular mass index (LVMI), is a common cardiovascular complication in CKD patients and serves as an independent risk factor for adverse outcomes. This study aimed to investigate the relationship between estimated glomerular filtration rate (eGFR), proteinuria and left ventricular mass in CKD patients. This study provides valuable insights into the complex interplay between renal function, proteinuria and cardiovascular health in this high-

Our study included 100 CKD patients with a mean age of 65.17 ± 11.56 years, with a predominance of males (66%). The majority of patients (75%) were in CKD stages G3a, G3b, and G4. These demographic findings are consistent with several other studies. For instance, Agarwal R et al. reported a slight younger age distribution of mean of 56 years with SD of 9 years and there was female predominance (56.15%) in their cohort of CKD patients.[5] In a study by Landler NE et al mean age for patients was 57.9 years (SD 12.7 yrs.) and 62% were males.[6]

Regarding CKD staging, our study found that the majority of patients (55%) were in stages G3a and G3b (eGFR 30-59 ml/min/1.73m²). This distribution differs somewhat from findings by Varughese and

Abraham, who reported a higher proportion of patients in more advanced stages (G4 and G5) in their review of CKD in India.[7] Our lower percentage of G5 patients (5%) compared to their findings might suggest earlier detection or referral in our study population.

The relatively low proportion of patients in stages G1 and G2 (20% combined) is noteworthy. It may indicate delayed diagnosis of CKD in our setting, as early stages often remain asymptomatic. This underscores the need for improved screening and early detection strategies in the Indian healthcare system, as suggested by Jha et al.[8]

The majority of patients (60%) exhibited normal to mildly increased proteinuria, while 35% showed moderately increased proteinuria, and only 5% had severe proteinuria. These results highlight the variability of proteinuria in CKD patients and suggest that not all individuals with CKD necessarily present with severe proteinuria. The finding in the study generally consistent with those reported by Methven et al., who observed that approximately 70% of CKD patients had normal to mildly increased proteinuria. However, this study showed a slightly lower percentage in this category, which could be attributed to differences in study populations or disease stages.[9]

The prevalence of moderately increased proteinuria (35%) in this study is comparable to the findings of Toyama et al., who reported a prevalence of 30-40% in their cohort of CKD patients. This similarity reinforces the notion that a significant proportion of CKD patients experience moderate levels of proteinuria. Interestingly, this study found a lower prevalence of severe proteinuria (5%) compared to some previous reports.[10] The study done by Ruggenenti et al. observed severe proteinuria in approximately 10-15% of their CKD cohort.

One of the key findings of this study was the significant association between proteinuria, as measured by urine protein-to-creatinine ratio (PCR), and LVMI ($p = 0.014$). We observed that as PCR increased, indicating more severe proteinuria, the likelihood of having more severe LVMI also increased. The statistically significant difference ($p = 0.014$) in proteinuria distribution across CKD stages suggests a potential correlation between disease progression and the severity of proteinuria.[11] This finding aligns with the work of Hemmelgarn et al, who demonstrated that higher levels of proteinuria were associated with faster CKD progression.[12]

This study highlights the importance of regular monitoring of proteinuria in CKD patients, as it can vary significantly among individuals and may indicate disease progression or response to treatment. Furthermore, these findings support the use of proteinuria as a valuable prognostic marker in CKD management, as suggested by Levey et al.[13]

The association between proteinuria and LVH could be explained by several mechanisms. Proteinuria is not only a marker of kidney damage but also reflects widespread endothelial dysfunction and increased cardiovascular risk. It may contribute to LVH through activation of the renin-angiotensin-aldosterone system, increased sympathetic activity, and chronic inflammation.

Interestingly, this study did not find a statistically significant association between eGFR stages and LVMI severity ($p = 0.453$). While there was a trend towards more severe LVMI in lower eGFR stages, the relationship was not statistically significant. This finding contrasts with some previous studies. For instance, Park et al. reported a strong inverse relationship between eGFR and LV mass in CKD patients.[14] However, our results are in line with the study by Matteucci et al, which found that proteinuria, but not eGFR, was independently associated with LVH in CKD patients.[15]

The lack of a significant association between eGFR and LVMI in this study could be due to several factors. It's possible that other risk factors, such as hypertension and diabetes, which were highly prevalent in our cohort (83% and 51%, respectively), may have a more dominant influence on LVMI. Additionally, the cross-sectional nature of this study may not capture the long-term effects of declining renal function on cardiac structure.

CONCLUSION

The study highlights the complex relationship between renal function, proteinuria, and left ventricular mass in CKD patients. The significant association between proteinuria and LVMI underscores the importance of proteinuria as a marker of cardiovascular risk in CKD. The lack of a significant association between eGFR and LVMI suggests that factors other than renal function alone may influence left ventricular hypertrophy in these patients. These findings have important implications for risk stratification and management of cardiovascular complications in CKD patients.

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