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Left Ventricular Hypertrophy (LVH) in Patients with Advanced Stages of Chronic Kidney Disease (CKD)

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FNK and IB conceived the idea, designed the project and did bench work. They also supervised the whole project. Authors SKS and HW wrote the manuscript and done the statistics. Authors SAR and SH helped in sampling, reviewing and extraction of data. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To determine the left ventricular hypertrophy (LVH) prevalence in patients admitted with advanced stage of Chronic kidney disease at Ziauddin hospital.
Methodology: This was a cross-sectional study conducted in department of Nephrology of Ziauddin University Hospital, Karachi from January to July 2016. The inclusion criteria involved patients with CKD stages 3-5 undergoing two-dimensional M mode Doppler echocardiography. The sample size of the study was 147. LVH was considered as positive when Inter-ventricular-septal-wall-thickness in diastole (IVSd) >11 mm, Left-Ventricular-Septal-Wall-Thickness in diastole (LVPWd) >11 mm and Left-Ventricular-Mass-Index (LVMi) >131 g/m2 for men and > 100 g/m2 for women. The exclusion criteria included patients with terminal illness, on mechanical ventilator support, valvular heart diseases and congenital heart diseases, liver diseases and patients with acute kidney injury on chronic kidney disease.

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Results: 88 male and 59 female patients were included. The mean duration of CKD was 7.02±1.60 years. 94(63.9%) study subjects were observed with left ventricular hypertrophy. A significant association of LVH was observed with gender and CKD Stages.
Conclusion: LVH can be easily diagnosed and assessed by M-mode or 2D echocardiography. The prevalence was high (60.5%) in stage 3–5 CKD patients.

Keywords: Left ventricular hypertrophy; chronic kidney diseases; end stage renal disease; obesity; CVD; CKD; LVH.

1. INTRODUCTION

Increased morbidity and mortality due to cardiovascular problems have been found more with comorbidity of chronic kidney disease (CKD) when compared with individuals without CKD of the same age. It is directly correlates with the severity of CKD [1,2]. After a certain period of time in CKD population, left ventricular hypertrophy is the robust and independent predictor of morbidity and mortality due to cardiovascular diseases. Diastolic dysfunction, congestive cardiac failure, arrhythmias and sudden dismissal are the potential outcomes of LVH [3]. LVH has a prevalence of 15–21% in in the general population. However, it gradually increases as renal function depreciates. During intermediate stages of CKD, LVH prevalence is found to be 50–70% that aggravates to 90% in patents with End-stage-kidney-disease (ESKD) [4,5,6]. The National kidney foundation task force reported that the risk of cardiovascular disease is higher in CKD patients, LVH and coronary artery disease being areas of accentuation [7,8].

The main culprits that holds the potential to cause LVH and congestive cardiac failure in CKD population came out to be hypertension, hypercholesterolemia, obesity and diabetes mellitus [9,10] [11]. Inflammation, oxidative stress, anemia, vascular abnormalities like endothelial dysfunction [12, 13] and activation of the sympathetic nervous system can also be the potential risk factors [14,15]. Various bone abnormalities and mineral metabolism dysfunction including serum phosphorus, magnesium and calcium can also aggravate this disease [16,17]. Certain hormones that control mineral metabolism, such as parathyroid hormone and vitamin D metabolites, have also been found to cumulate the risk of this disease. LVH has also been attributed to LV systolic dysfunction, represented as a reduced fractional shortening of mid-wall in systole. It has been highlighted that an impaired LV systolic function harbingers a reduction in renal perfusion. This pathological, highly pulsatile perfusion in the kidney microvasculature might accentuate a progressive reduction in kidney function in patients with pre-existing kidney damage [18].

This can be accredited to high prevalence of left ventricular (LV) abnormalities such as LVH, systolic dysfunction, and cardiac failure [19]. Moreover, since the prevalence of early stages of CKD is estimated to be 100-fold greater than the prevalence of ESRD [20], it is timely to remark that many CKD patients face mortality before ESRD appears with decreased GFR [21]. It has been observed that kidney function deteriorates as the prevalence of LVH rises. It was highest in patient on dialysis. In a study conducted at 5 Brazilian centers including 309 patients with CKD stages 3 and 4, the estimated risk of LVH was found to be 53% and of them, 60% were in Stage 4 CKD. This empirical evidence emphasizes the need for stringent diagnosis of CKD in order to prevent the occurrence of LVH before dialysis which will decrease the disease rate of CVD in such group [22] . In a study, LVH existed in 68-89% of patients before the advent of dialysis [23]. This elevated prevalence of LVH can increase the disease rate and hinders in the quality of life of the affected individuals. Reddy et al reported that LVH in dialysis patients is as high as 83% [24]. These reported studies suggest that LVH must be present in the earlier stages of CKD. Many patients with chronic kidney disease die prematurely before or after beginning dialysis. Cause behind these adverse outcomes is not understood.

Unfortunately, we lack the data and estimates in our society its prevalence. Therefore, we aimed to determine the prevalence of LVH in present study which helped reviewing the prevalence of LVH in these patients. Because of geographical variation and lack of similar studies in this context within the Pakistani population, we planned to evaluate the LVH prevalence in CKD individuals. Familiarity with this factor helps in patient selection and the best treatment protocol

can be provided to decrease the burden of LVH in this patient population.

2. METHODOLOGY

This study was based on a Cross-Sectional study design. It took place in the Nephrology department of Ziauddin University Hospital, Karachi for six months from 9th January 2016 to 8th July 2016. This study is a dissertation-based article. The sampling technique used was non-probability consecutive sampling. 15-70 years range of patients were included of either gender, with CKD stages 3,4 and 5. While the patients who were not enrolled and were excluded patients with terminal illness, on mechanical ventilator support, with valvular heart diseases and congenital diseases of heart, acute or chronic kidney injury and those with liver diseases were excluded.

The Glomerular Filtration Rate (GFR) was used as a parameter to follow the renal function. GFR was calculated using the MDRD equation. Chronic Kidney Disease (CKD) was labeled as if diagnosed with renal failure for more than three months. The stages of CKD were classified as Stage 1; GFR normal for the age and weight but a persistent abnormal urinalysis or structural abnormality on ultrasound kidneys. Stage 2; decline in GFR between 60ml/min to 90ml/min. Stage 3; decline in GFR between 30 ml/min to 59ml/min. Stage 4; decline in GFR between 15ml/min to 29ml/min, and GFR less than 15ml/min is categorized as stage 5. The Left Ventricular Hypertrophy (LVH) was considered as positive when Inter-ventricular septal wall thickness in diastole (IVSd) >11 mm, Left-ventricular septal wall thickness in diastole (LVPWd) >11 mm and Left-ventricular mass index (LVMi) >131 g/m2 for men and > 100 g/m2 for women. American Society of Echocardiography's recommendations were taken into account. According to which Troy formula will be used to determine left ventricular mass: left ventricle mass (g)=1.05[(LVEDD+ IVS+PW)^3−LVEDD. Left ventricular mass was divided with body surface area to obtain the left ventricular mass index (LVMI).

The data collection involved 147 patients who were attended the department of Ziauddin University Hospital and fulfilled the study's inclusion criteria after informed consent. The principal investigator did the patients' demographics and clinical and physical history and duly filled in a predesigned Performa. All patients underwent 2D-M mode & Doppler echocardiography, which was executed by a consultant cardiologist with experience of more than 5 years. LVH was considered as positive when Inter-ventricular-septal-wall-thickness in diastole (IVSd) was >11 mm, Left-Ventricular-Septal-Wall-Thickness in diastole (LVPWd) was >11 mm and left-ventricular-mass-index (LVMi) was >131 g/m2 in men and > 100 g/m2 will be considered positive in women. Inclusion and exclusion criteria were sternly followed to control Bias and confounding variables.

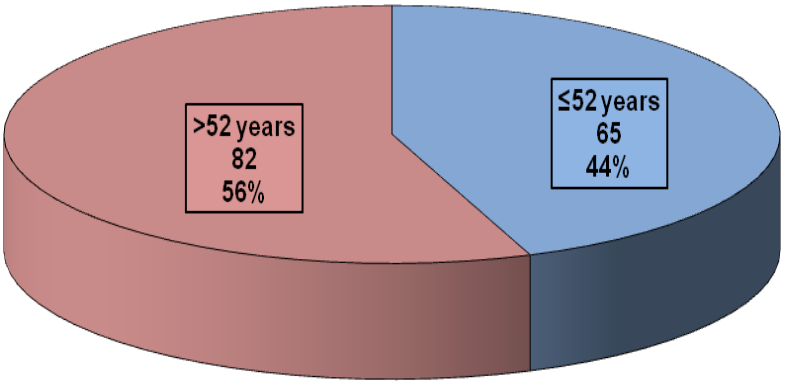
The sample size was based on the least prevalence of LVH (P)=75%,27 margins of error (d)=7% and 95% confidence level. The calculated sample size is 147 study participants, using WHO software for sample size calculation. Data were entered and analyzed in SPSS version 21. Statistical values will be taken as mean ± SD for continuous variables and % for categorical variables. Stratification was completed on age, gender, hypertension, and diabetes to check their effects on the outcome by Chi-square test, and a p-value of ≤0.05 was considered as statistically significant.

3. RESULTS

Total 147 individuals of both the gender ranging from 25 to 60 years, had advanced stages of Chronic kidney disease (Stage III, Stage IV, Stage V). They were evaluated to determine the prevalence of left ventricular hypertrophy. The mean age of subjects were included in this study was 52.29±7.00 years (Table 1). There were 59.9% (88) male and 40.1% (59) female patients (Table-2). The patients' age was further stratified into two groups. (Graph 1). The mean GFR of included participants was 16.69±14.33 ml/min while mean IVSD was 12.07±3.37 mm and mean LVPWD was 11.77±2.82 mm (Table 1). The overall mean ejection fraction of study subjects was 52.68±14.78% and mean LVDD was 50.088±8.73. The overall mean duration of CKD in study subjects was 7.02±1.60 years. (Table 1). Further stratification into two groups was done for the duration of CKD. Table 2 shows the percentage and the frequency of patients amongst these groups. As far as stages of CKD are concerned, it was observed that 12.9% were stage III, 17.7% were stage IV, and 69.4% were stage V of CKD as presented in Table-2.

Table 1. Demographic Variables

Demographic variables	Mean ±SD (n=147)
Age in years	**52.29±7.00**
Duration of CKD in years	7.02±1.60
GFR ml/min	16.69±14.33
IVSD (mm)	12.07±3.37
LVPWD (mm)	11.77±2.82
Ejection Fraction (%)	52.68±14.78
LVDD	50.088±8.73
Duration of HTN in months	12.69±6.07



Graph 1. Percentage of patients according to age groups (n=147)

Table 2. Frequency distribution & percentages (n=147)

Variables		Frequency (n)	Percentages%
Gender:			
Male		88	59.9%
Female		59	40.1%
	Stage III	19	12.9%
	A	5	19.2%
CKD STAGES	B	14	80.8%
	Stage IV	26	17.7%
	Stage V	102	69.4%
Diabetes Mellitus		91	61.9%
Hypertension		137	93.2%
LVH		94	63.9%

Out of total 147 study subjects 61.9% have diabetes mellitus (Table 2). The mean duration of diabetes mellitus was 15.12±9.52 months (Table 1). Among total study subjects 93.2% were hypertensive. (Table 2). The mean duration of hypertension was 12.69±6.07 months as presented in Table-1 respectively. There were n=89(60.5%) subjects found to have left ventricular hypertrophy. (Table- 2)

Stratification to gender, age, stage of CKD, duration of CKD, hypertension, duration of hypertension, diabetes mellitus, and duration of diabetes mellitus was taken into account to check the effect of these modifiers on the outcome (left ventricular hypertrophy). The results showed a significant association of LVH with gender (p=0.000) and CKD Stage (p=0.026). (Table 3). It was observed that among 94 LVH patients 16% were stage III, 22.3% were stage IV, and 61.7% were stage V. No significant finding was emerged with age (p=0.588), duration of CKD (p=0.944), diabetes mellitus (p=0.259), duration of diabetes mellitus (p=0.232), hypertension (p=0.747) and duration of hypertension (p=0.849). The details of frequency distributions and associations are presented in Table-3.

Table 3. Frequency and association of left ventricular hypertrophy

		Left ventricular hypertrophy		Total	P-Value
		Yes (n=94)	No (n=53)		
Gender	Male (n=88)	45	43	88	
	Female (n=59)	49	10	59	0.000*
Age in yrs					
	≤ 52 years (n=65)	40	25	65	
	> 52 years (n=82)	54	28	82	0.588
CKD stages	Stage III (n=19)	15	4	19	
	Stage IV (n=26)	21	5	26	
	Stage V (n=102)	58	44	102	0.026
CKD duration	≤ 7 years (n=81)	52	29	81	
	> 7 years (n=66)	42	24	66	0.944
DM	Yes (n= 91)	55	36	91	
	No (n=56)	39	17	56	0.259
DM Duration in months	≤ 12 months(n=59)	33	26	59	0.232
	> 12 months (n=32)	22	10	32	
	Yes (n=137)	88	49	137	
HTN	No (n=10)	6	4	10	0.747
HTN duration in months	≤ 12 months (n=74)	47	27	74	
	> 12 months (n=63)	41	22	63	0.849

Table 4. Frequency and association of left ventricular hypertrophy with hypertension according to stage iii patients

		Left ventricular hypertrophy		Total	P value
		Yes	No		
HTN Stage III CKD	YES (n=22)	18	4	22	0.750
HTN Stage IV CKD	YES (n=16)	14	2	16	0.035
HTN Stage V CKD	YES (n=99)	56	43	99	0.728
DM Stage III CKD	YES (n=19)	15	4	19	0.698
DM stage IV CKD	YES (n=14)	10	4	14	0.179
DM stage V CKD	YES (n=58)	30	28	58	0.229

*Chi Square Test was applied, P-value ≤0.05 was considered as significant, * Significant at 0.05 levels*

The results showed that Stage-III, Stage-IV, and Stage V correlate the prevalence of left ventricular hypertrophy with hypertension and diabetes mellitus (Table 4). The results showed a significant association of LVH with hypertension at stage IV. No significant association of hypertension and diabetes mellitus was observed in remaining patients of Stage- III, Stage-IV, and Stage V. The results showed no significant association of left ventricular hypertrophy with hypertension and diabetes mellitus in patients of Stage-III, Stage-IV, and Stage The details of it are present in table 4.

4. DISCUSSION

Besides other factors, the main culprit behind increasing mortality and morbidity in end stage chronic kidney disease (ESCKD) is Cardiovascular disease. The associated cardiovascular disease accounts for ten to thirty times more death rate in these patients than the general population, affected mainly by Heart disease or heart failure [25]. It has been established that Left ventricular hypertrophy causes advanced cardiomyopathy.

The National kidney foundation task force has considered the LVH and coronary artery diseases as alarm features of cardiovascular disease risk in CKD patients. Hence, they marked LVH and coronary artery disease as the primary aims for intervention [26]. LVH was reported as an independent predictor of mortality in dialysis patients [13].

A study conducted in Japan revealed a high prevalence of pre-existing CVD. The stroke rate was highest with the prevalence of 12.4% followed by myocardial infarction 6.8% and then cardiac failure 5.7%, compared with the general Japanese population [27]. In a longitudinal analysis of CKD-JAC study, the results showed increased LVMI as CKD progressed. However, LVH was not identified in majority of the cases

(21.7%) [28]. Various studies identified increased prevalence of LVH around 34% to 74% in CKD patients and the LVF is inversely to renal function [29].

Nevertheless, differences in LVH have been seen to vary among some populations possibly due to differences in age, ethnicity, patients' proportion in different CKD stages, hypertension, methods for GFR evaluation. Cynthia et al evaluated the consequences of CKD that cause cardiovascular insult. The results were consistent with the previously literature reported in the western population. Early intervention in CKD was accentuated to avoid fatal consequences [30,31].

In CKD patients, LVH is a useful compensatory adaptation that helps to increase cardiac work and sustain constant wall tension.

In multivariate logistic regression analysis, systolic BP, even when it is well controlled (132.4±18.1 mmHg), can be an independent variable associated with LVH [32]. Foley et al has reported that in patients prior to dialysis, elevated pulse pressure and systolic arterial hypertension are being closely linked with LVH. This link can be because of fluid overload and elevated resistance due to stiffness in arteries leads to LVH before the advent of dialysis therapy [33].

To improve of LVH condition, excessive fluid monitoring and sustainability of a normal hydrodynamic state are crucial (34). Another multivariate logistic regression analysis study added to the literature, emphasizing that the occurrence of a prior CVD was significantly accompanying LVH [35].

A possible explanation for the acceleration of atherosclerosis in CKD patients is a source of clinical concern. The comorbidities that have an impact on CKD, particularly in older people, were suggested as one of four options. Second, CKD patients are given insufficient cardioprotective treatments. Third, the danger of a potentially detrimental outcome outweighs the treatment's benefit. Finally, vascular disorders in people with CKD can cause chaos. [36,37,38]. There was a certain limitation in our study. Firstly, it was a non-randomized design, with single center being involved and also low female presentation. The small sample size was small, and it was conducted in an urban setup; therefore, the results will not apply to the populations in general.

5. CONCLUSIONS

LVH is a consistent feature of CKD, and its diagnosis and assessment can be made by M-mode or 2D echocardiography. A strong association was found between CKD and LVH, and LVH was highly prevalent (60.5%) in stage 3–5 of CKD patients. Furthermore, gender and CKD stages are essential predictors of LVH Monitoring of LVH is a core in CKD management. Therefore, prevention and early diagnosis of LVH are highly recommended in CKD, preventing cardiovascular events.

CONSENT

Verbal and written informed consent were obtained from all patients.

ETHICS APPROVAL

Ethical approval was taken from the Chest Health and Education Society with the reference no. 1980320LAEM.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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