ORIGINAL ARTICLE

The Risk Factors for Left Ventricular Hypertrophy in Patients of Stage IV Chronic Kidney Disease

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ABSTRACT

Background: Cardiovascular risk in renal insufficiency is perceived as an important public health problem and preventing and curing cardiovascular complications in patients with renal dysfunction is considered a true priority. Cardiovascularmortality rates in End stage renal disease (ESRD) patients are high and have been estimatedto be between 100 and 1000 times as compared to normal population. Cardiac failure and Left ventricular hypertrophy (LVH) are key prognostic variables. LVH has a prevalence of approximately40% in patients with chronic renal insufficiency, a figure thatrises to approximately 75% by the onset of ESRD. Therefore this study was designed to identify the risk factors for LVH in our pre-dialysis population of patients.

Aim: To determine the frequency of individual risk factors contributing to left ventricular hypertrophy in patients of stage IV chronic kidney disease.

Study Design: It was descriptive case series study.

Setting: Department of Nephrology, Sheikh Zayed Hospital Lahore, Six months from September 2012 to February 2013.

Methods: Ninety patients of Chronic kidney disease (CKD) stage IV having LVH were included in this study. Relevant data was entered in the specific predesigned proformas.

Results: Out of ninety (90) patients included in this study, 37 (41.1%) were males while 53 (58.9%) were females. Results showed that 83 patients(92.2%) were anemic, 17 (18.9%) had high calcium-phosphate product, 56 (62.2%) had deranged lipid profile, 26 (28.9%) had high CRP level, 68 (75.6%) were in volume overload state and 77 patients (85.5%) had systolic hypertension while diastolic hypertension was seen in 63 patients (70%).

Conclusion: Majority of patients of CKD stage IV having LVH were anemic emphasizing the great contribution of anemia in changing morphology of left ventricle.

Keywords:CKD, LVH, CVD, GFR

INTRODUCTION

Chronic kidney disease (CKD) is a common disease characterized by progressive deterioration of kidney function, which develops eventually into ESRD.[1] In order to identify individuals having CKD, it is important to estimate glomerular filtration rate (GFR) accurately using different methods like Modification of Diet in Renal Disease (MDRD) or Cockcroft-Gault formula[2].

Cockcroft- Gault equation:

$$\text{Estimated creatinine clearance (ml/min)} = \frac{(140 - \text{age in years}) \times \text{body weight (kg)}}{72 \times \text{plasma creatinine (mg/dl)}} \times 0.85 \text{ for women}$$

During last few years, various consensuses have classified CKD into five stages according to GFR[3] and presence of signs of kidney damage.

Table I:

Stages	GFR (ml/min)
I	>90
II	60-89
III	30-59
IV	15-29
V	<15

Cardiovascular disease (CVD) accounts for premature death in more than 50% of dialysis patients[4].The reason for this is the presence of various risk factors for CVD in renal patients. These risk factors are broadly divided into traditional as well as non-traditional risk factors[5]. Traditional risk factors are same as seen in general population and include diabetes, hypertension[6], high LDL cholesterol[7], low HDL cholesterol, smoking, elderly age, male gender, family history, white race, and menopause. Non-traditional risk factors are specific for renal patients. These include increase in extracellular fluid volume, anemia[8], abnormal calcium-phosphorous products[9], parathyroid hormone, raised inflammatory markers (CRP)[10,11] hyper-homocystienemia[12] and deranged lipid profile.

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Among various CVD complications, LVH is highly prevalent in CKD even in early stages, as compared to general non-selected population.This is mainly due to the multi-factorial pathogenesis of LVH in renal patients where both hemodynamic and non-hemodynamic stimuli synergically act inducing either an increase in left ventricular mass or LV dilation. It is a strong predictor of mortality in patients with end stage renaldisease.

Reported incidence of these CVD risk factors and LVH in pre dialysis patients is quiet high. According to one study in Delhi (India) it's about 40% in mild to moderate CKD and 97% in severe CKD. High prevalence of anemia and hypertension in CKD may also partly account for increased prevalence LVH[6 8].This prevalence is directly correlated with age of the patient, blood pressure, duration of arterial hypertension, severity of anemia, level of C-reactive protein (CRP), blood phosphorous concentration and inversely correlated with GFR, serum albumin and serum calcium levels[9].

Therefore the purpose of this study was to identify risk factors of LVH in patients with advanced stages of chronic kidney disease (CKD)[13].

MATERIAL AND METHODS

Thisdescriptive case series studywas conducted in the Nephrology department Sheikh Zayed Hospital Lahore.Duration of data collection was six months starting from September 2012 to February 2013. Ninety patients of CKD IV having LVH were included in the study.Non- probability purposive technique was used.

Inclusion Criteria

- Stage IV CKD patients having LVH
- Age > 20 years.

Exclusion Criteria

- Co-morbid conditions like sepsis, congenital/ valvular heart diseases, cirrhosis and malignancy based on clinical examination and relevant laboratory investigation.
- CKD stage I, II, III and V patients

Data collection procedure: All patients fulfilling inclusion and exclusion criteria were enrolled in the study. Afterwards, required data regarding risk factors of left ventricular hypertrophy e.g. hypertension, anemia, dyslipedimias, high calcium and phosphorous product and high c-reactive proteins, was collected by taking detailed history, physical examination and relevant laboratory investigations. For measurement of blood pressure (BP) at least 3 readings on 3 different occasions were taken to confirm level of BP, mean was calculated and classified in appropriate class according to the British Hypertension Society. Systolic hypertension was labeled when systolic BP was ≥140 mm of Hg while diastolic hypertension was labeled with diastolic BP reading of ≥90 mm of Hg. Anemia was defined as hemoglobin of <13g/dl in men and <12g/dl in women. Dyslipedimias included triglyceride levels ≥500mg/dl, LDL ≥100mg/dl and non-HDL cholesterol ≥130mg/dl. Serum calcium and phosphorus levels (mg/dl) were done and their product was calculated, high product was defined as value > $55mg^2/dl^2$, C-reactive protein level of > 5mg/l was considered significant. Additional risk factor for LVH, the volume overload, was assessed by history and physical examination.

Data analysis: Data was analyzed by using SPSS18.0 version. Frequency of individual risk factors e.g. anemia, hypertension, dyslipedemias, abnormal calcium-phosphorus product and raised inflammatory markers contributing LVH werecalculated.

Operational Definitions

***Stage IV CKD*:** GFR 15-29ml/min

LVH: is defined as an increase in the mass of the left ventricle, which can be secondary to an increase in wall thickness, an increase in cavity size or both. The American Society of Echocardiography with the European Association of Echocardiography has issued the following criteria for LVH using modified Simpson's rule[14]:

Estimated LV mass of 201 to 227 g (102 to $116g/m^2$) for men and 151 to 171 g (89 to $100g/m^2$) for women

RESULTS

Total90 patients were included in the study out of which 37 patients (41.1%) were males while 53 patients (58.9%) were females. Their mean age was 55.7±11.0 years with age range of 30- 65years. Table II demonstrates results of thisstudy by showing distribution of cases by LVH, Anemia, high calcium-phophorous product (CaxP), dyslipidemias, high CRP levels, volume overload and hypertension

Table II: Distribution of cases by anemia, high calcium-phosphate product, dyslipidemias, high CRP levels, volume overload and hypertension(n=90)

Variables	n	%age
Anemia		
Present	83	92.2
Absent	07	7.8
Total	90	100
High Calcium-phosphate product		
Present	17	18.9
Absent	73	81.1
Total	90	100
Dyslipidemias		
Present	56	62.2
Absent	34	37.8
Total	90	100

High CRP levels		
Present	26	28.9
Absent	64	71.1
Total	90	100
Volume overload		
Present	68	75.6
Absent	22	24.4
Total	90	100
Blood pressure		
Systolic>140mmHg	77	85.5
< 140mmHg	13	14.5
Diastolic >90mmHg	63	70
< 90mmHg	27	30

Table III: Different variables included in the study as their mean values along with standard deviation
Mean values of different variables

Variables	**Mean**	**Standard Deviation**
Systolic BP	144.4	±13.2
Diastolic BP	87.2	±8.8
Hemoglobin (g/dl)	9.7	±2.2
Calcium-phosphorousproduct mg^2/dl^2	42.7	±11.6
Triglyceride (mg/dl)	191.6	±103.5
LDL (mg/dl)	133.8	±72.6
Non HDL cholesterol	211.3	± 93.6
CRP Levels	4.1	±2.0

DISCUSSION

Left ventricular hypertrophy (LVH) is highly prevalent in CKD even in early stages as compared to general non-selected population. This is mainly due to the multi-factorial pathogenesis of LVH in renal patients where both hemodynamic and non-hemodynamic stimuli synergically act inducing either an increase in left ventricular mass or LV dilation. Anemia and arterial hypertension seem to be the most important factors. Interventional studies have shown that partial correction of anemia through epopetin, together with an arterial hypertension successful therapy through renin-angiotensin system acting drugs, such as ACE-inhibitors, were able to induce a LVH regression in CKD. Indeed, the unfavorable outcome in patients with both CKD and LVH, whose survival is reduced and incidence of fatal and non-fatal CV events increased, can be reversed if LVH is regressed by therapy[15].

According to this study, the mean age of patients participating in the study was 55.7±11 years. Majority of the patients (67.7 %) are above the age of 50.The most common gender in our study is the female population 58.9% v 41.1%. But none of the single previous studies as well as our study has proved any correlation of sex with prevalence of LVH.

Among various risk factors of LVH, our study has proved anemia to be the most common and important risk factor present in 92.2% of cases. In one study done by Nasri H et al[16] in 2005, anemia was seen in 90% of patients. ARIC study by Sarnaket al[17] in 2002 has also proved the same that anemia has central role in cardiovascular mortality. In 2006,Mitsnefes MM et al[18] had also shown the importance of anemia. The same has been proved by our study. The statistical significance of anemia has also been proved by Tomilian et al[19] and also Levin A et al.[20] in which they said that for each 10 g/L decrease in hemoglobin, the risk of LVH increased by 6% (P = 0.0062).

Hypertension is the second most commonly associated risk factor especially systolic hypertension present in 85.5% cases as compared to diastolic hypertension present only in 70% patients. Again Nasri H et al[16] in 2005 and Tomilian et al[19] in 2007 have proved the statistical significance of hypertension. Their results are closely related to results of our study. In 2003,MacMahon et al[21] also determined the significant role of hypertension, by increasing the vascular volume which in turn leads to LVH, cardiac failure and ischemic heart disease in CKD patients. LVH in uncontrolled hypertensive patients is basically the end organ damage and brought about by certain hemodynamic changes.Levin et al[20]in 1996 and London et al[22] in 2001 had also proved the same. Levin et al[20] said that an increase in systolic blood pressure of 5 mm Hg leads to 3% increase in risk of LVH (p=0.0018).

Third most common risk factor according to this study is the volume overload which is seen in 75.6% cases.Levin et al[20] in 1996, London et al[22] in 2001 and Kimura et al[23] in 2007s also proved the statistical significance of volume overload.

The role of deranged lipid profile as one of the risk factor of cardiovascular mortality cannot be ignored and in our study it is seen in 62.2% of study population. In 2006, Amin K et al[24]study showed that hypertriglyceridemia was seen in 46% cases, low HDL cholesterol was present in 16% cases and high LDL cholesterol was found in 4% case. Another study done by Altaf A et al[25] in 2007 have also proved statistically significant less deranged lipid profile in patients on maintenance hemodialysis. The reason for this is the malnutrition. However, even less elevated lipid profile had been paradoxically associated with increase in CVD mortality in patients on maintenance hemodialysis. The reason for this high CVD mortality is due to malnutrition and inflammation, which are very common among CKD patients. This disturbed lipid pattern predisposes the patients to atherosclerotic complications and increased mortality due to cardiovascular and

cerebrovascular accidents. The CKD patients already having endothelial damage are more prone to it.

In this study, the contribution of abnormal calcium-phosphate product as a risk factor of LVH in CKD IV patients is minimal (only 18.9% cases). Similar results were shown in 2001 in a study conducted by Tomilina NA et al[19], where they showed that abnormal calcium-phopshate product as risk factor of LVH in CKD is not as statistically significant as in patients of end stage renal disease.

High CRP levels were seen in 28.9% of cases in our study however majority (71.1% cases) were those having normal CRP levels. According to the our study, high CRP level is not a significant contributing factor towards LVH but still it's statistical significance has been proved in one study by CottoneS et al[26] in 2007.So according to our study, anemia was the most commonly observed risk factor for LVH in CKD IV patients.

CONCLUSIONS

It is important to realize that incidence of LVH increases with the decline of GFR and LVH is an important risk factor for fatal cardiovascular events like myocardial infarction and heart failure. So it is crucial to identify various risk factors contributing to LVH in CKD patients. Among these factors, anemia proved to be most frequent and significant contributing factor in our study. This trend was demonstrated by various national and international studies as well. Therefore, early correction of anemia is of paramount importance in prevention of LVH.

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