MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.10.412.417

OPEN ACCESS

Key Words
CKD, RPD, glomerular filtration rate, left ventricular mass index, intact parathormone

Corresponding Author
V. Rajesh,
Department of General Medicine, KMC/MGM Hospital, Warangal, Telangana, India
rajeshvanam5@gmail.com

Author Designation
[1,3]Associate Professor
[2,4]Assistant Professor

Received: 15 August 2024
Accepted: 28 September 2024
Published: 1 October 2024

Citation: Chiluka Kiran, Durgam Venkatesh, Pulluri Sadanandam and V. Rajesh, 2024. Determining the Association of Anemia with Left Ventricular Hypertrophy in Chronic Kidney Disease Patients: A Cross -Sectional Study. Res. J. Med. Sci., 18: 412-417, doi: 10.36478/ makrjms.2024.10.412.417

Determining the Association of Anemia with Left Ventricular Hypertrophy in Chronic Kidney Disease Patients: A Cross-Sectional Study

[1]Chiluka Kiran, [2]Durgam Venkatesh, [3]Pulluri Sadanandam and [4]V. Rajesh

[1,2,4]Department of General Medicine, KMC/MGM Hospital, Warangal, Telangana, India

[3]Department of Community Medicine, GMC, Siddipet, Telangana, India

ABSTRACT

The aim to demonstrate development of left ventricular hypertrophy early in chronic kidney disease patients with mild to moderate anemia. This research examined 100 CKD patients (stage III to V) aged 15-80 with high serum creatinine, decreased glomerular filtration rate, hemoglobin <11gm/dl and renal parenchymal disease grade >2 over a year. Patients were evaluated based on clinical history and laboratory markers such blood urea, serum creatinine, calcium, inorganic phosphorus, serum electrolytes, iPTH, Hb, Hct, glomerular filtration rate and left ventricular mass index. The study population was 68% male and 32% female. Most male patients (75% of the study sample) had abnormal left ventricular mass index (135g/m2 is normal). Most women (87.5%) have abnormal left ventricular mass index. Association of anaemia (8g/dl reference value for this study group) with left ventricular mass index in male and female patients, p value is significant. Anaemia was strongly correlated with left ventricular mass index in both men and women. No relationship existed between DM and LVMI. In our CKD patients, anaemia was common. These individuals' left ventricular hypertrophy correlates with anaemia severity. In these individuals, early anaemia correction may avoid cardiovascular morbidity and death.

INTRODUCTION

Cardiovascular disease is the leading cause of illness and death in individuals with predialysis chronic kidney disease (CKD)[1,2]. Earlier, we stated that the occurrence of left ventricular hypertrophy (LVH) rose in a direct relationship with the advancement of CKD in individuals experiencing renal failure[3]. The incidence of left ventricular hypertrophy (LVH) rises in tandem with the advancement of renal failure. Prior to commencing dialysis, 85% of patients with stages 4 and 5 chronic kidney disease (CKD) have left ventricular (LV) remodeling. LVH is acknowledged as a significant risk factor for cardiovascular mortality in dialysis patients[4]. It is a robust indicator of cardiac failure, abrupt death, myocardial infarction and stroke[5]. A prior investigation identified systolic blood pressure, residual glomerular filtration rate and serum albumin (Alb) levels as prognostic indicators for LV mass index (LVMI), which were assessed using echocardiography at the commencement of haemodialysis[6]. Renal anaemia is a frequent consequence in people with chronic kidney disease (CKD)[7]. It often occurs due to a lack of erythropoietin. Previous research has shown that the average haemoglobin (Hb) level was greater in a group without complications related to left ventricular hypertrophy (LVH) compared to a group with combined LVH throughout the transition from pre-dialysis to dialysis beginning. This was seen when long-acting erythropoietin-stimulating agents (L-ESAs) were used[8].

The correlation between anaemia and chronic kidney disease (CKD) has been recognised since the early 19th century. In addition, several studies conducted over the years have shown not only a greater prevalence of anaemia, but also a much higher occurrence of cardiac problems, including left ventricular hypertrophy, in patients with chronic renal disease[9,10]. Left ventricular hypertrophy is an early occurrence of cardiovascular illness that quickly develops throughout the evolution of chronic kidney disease. It is a significant predictor of death in patients with end-stage renal disease. Anaemia is a well-established predictor of the development of left ventricular hypertrophy and morbidity and death in end-stage renal disease (ESRD)[11]. The significance of anaemia in patients with end-stage renal disease (ESRD) undergoing dialysis was shown by the discovery that even a fall in haemoglobin level of 1g/dl resulted in a gradual rise in mortality by 18-25% and left ventricular hypertrophy by about 50%. The study of 246 individuals revealed that anaemia plays a significant role as a cardiac risk factor. Specifically, it was shown that for every 0.5 g/dl drop in haemoglobin (Hb) levels, the relative risk of left ventricular enlargement rose by 32% ($p = 0.04$)[12].

The purpose of this research was to determine the left ventricular mass index in patients with stage III-V chronic renal disease who had a haemoglobin level below 11g/dl. Additionally, the study aimed to illustrate the early development of left ventricular hypertrophy in chronic kidney disease patients with mild to moderate anaemia.

MATERIALS AND METHODS

Cross-sectional research was undertaken on a sample of 100 patients, including individuals of both sexes, aged between 15 and 80 years, from diverse socioeconomic backgrounds. The study spanned a period of one year. The patients were diagnosed with chronic kidney disease (CKD) and had different levels of renal failure (grade III to V). They also had evidence of renal parenchymal disease of grade II or higher based on ultrasound. Additionally, their haemoglobin levels were below 11g% and they could be either diabetic or non-diabetic, hypertensive or non-hypertensive. It was also noted whether the patients were undergoing dialysis or receiving erythropoietin replacement therapy.

Among a sample of 100 patients, 60 individuals were diagnosed with hypertension and were effectively managing their condition via medication. The participants were diagnosed with hypertension 2-4 years prior to the start of our research. The research excluded patients who had undergone kidney transplant and those with uncontrolled hypertension, who were also known to have hypertrophic obstructive cardiomyopathy, rheumatic heart disease and similar conditions.

Examinations: The investigations conducted consisted of measuring Hb (haemoglobin), HCT (haematocrit), blood urea, serum creatinine, calcium, inorganic phosphorus, bicarbonate, serum electrolytes, iPTH (intact parathyroid hormone) level, urine analysis, chest X-ray, renal ultrasound to assess kidney size and echotexture and calculation of left ventricular mass index using the Modified Devereoux formula with the assistance of an electrocardiogram. The first examination included obtaining a comprehensive clinical history, including the length of renal failure (in years), presence of diabetes or hypertension and information on whether the patients were having dialysis or receiving erythropoietin replacement therapy. Height, weight and blood pressure were recorded for all patients. The laboratory tests conducted include measurements of serum creatinine, haemoglobin (Hb), haematocrit (Hct), calcium levels, and creatinine clearance (estimated using the Cockroft-Gault equation). Computation of the mass of the left ventricle: Given the apparent correlation between body size, body habitus and left ventricle dimension and mass, it is necessary to adjust for body

size when analysing these factors. The left ventricular mass index was determined by dividing the left ventricle mass by the body surface area. The left ventricle mass was obtained using the Modified Deveroux formula with the assistance of 2D Echocardiography.

The mass of the left ventricle may be calculated using the formula 0.8 x 1.04 (IVSd+LVIDd+LVPWd)3-(LVIDd)3+0.6 grammes.

Left ventricular hypertrophy is characterized as having a left ventricular mass index more than 135 for males and greater than 110 for females. The left ventricular mass index is calculated using the measurements of IVSd (interventricular thickness in diastole in mm), LVID.,d (left ventricular diameter in diastole in mm) and LVPWd (left ventricular posterior wall thickness in diastole in mm).

Statistical Analysis: Chi square test was applied to find relationship between the variables and odds ratio was calculated to determine the risk of abnormal values as compared to the normal values, p<0.05 was taken to be significant.

RESULTS AND DISCUSSIONS

Table 1: Age and Gender Wise Distribution of Study Population and Distribution of Normal and Abnormal Left Ventricular Mass Index among Male Patients

Age Groups (Years)	N	%	
15-30	25	25	
31-45	20	20	
46-60	36	36	
61-75	16	16	
>75	3	3	
Gender			
Male	68	68	
Female	32	32	
Gender	**Left Ventricular Mass Index (gm/m2)**	**N**	**%**
Male	**<135 (Normal)**	17	25
	>135 (Abnormal)	51	75
Female	**<110 (Normal)**	4	12.5
	>110 (Abnormal)	28	87.5

Majority of study population i.e. 68% was male, 32% was female. Most of the male patient i.e. 75% of the study population are having abnormal left ventricular mass index (135g/m2 is taken as normal value for male patients). Majority of female patients i.e., 87.5% have abnormal left ventricular mass index.

Table 2: Hb with Left Ventricular Mass Index in Males and Females

Variables	Hb<8	Hb>8	Odds ratio	95% CI	P-Value
Left ventricular mass index (male)					
<135	5	12			
>135	30	21	0.020	0.0047-0.3350	0.002
Left ventricular mass index (female)					
<110	1	3	0.067	0.0081-0.2940	0.03
>110	10	18			

Relation of anemia (reference value for this study population being taken as 8g/dl with left ventricular mass index in both male and female patients of study population, p value is significant for both male and female population. There was strong correlation between Anemia and left ventricular mass index in both male and female patients.

Table 3: Diabetes Mellitus Verses LVMI

Variables	Present	Absent
Male		
LVMI		
<135	5	12
>135	30	21
Female		
LVMI		
<110	0	4
>110	3	29

There was no correlation between DM and LVMI.

Left Ventricular Hypertrophy (LVH) often occurs in individuals with Chronic Kidney Disease (CKD) and is a significant poor prognostic factor[13,14]. Anaemia is a common occurrence in people with chronic kidney disease (CKD) and plays a significant role in the development of cardiac hypertrophy. This condition may lead to the increasing enlargement of the left ventricle (LV), the beginning of heart failure and even death[15]. Chronic kidney disease patients are at risk for cardiovascular disease due to many variables connected to uremia. These factors include anaemia, hyperparathyroidism, abnormalities in mineral metabolism and acidosis. It is important to highlight that the relationship between anaemia and kidney disease has been consistently seen in all populations. The reference standard for haemoglobin concentration in our research is 11g/dL, which applies to both males and females. Anaemia in renal failure mostly results from insufficient synthesis of erythropoietin, largely attributed to iron shortage. This shortfall may be caused by increasing demand, gastrointestinal bleeding, continuous blood loss and repeated blood collection and venipuncture. Anaemia has been identified as a distinct risk factor for the development of left ventricular hypertrophy (enlargement of the heart's main pumping chamber) in individuals with chronic renal disease[16].

Chronic Kidney Disease (CKD) is becoming more common worldwide, with a rising incidence and prevalence. This has led to its recognition as a significant public health issue[17]. The predominant result of CKD in most individuals is the development of End Stage Renal Disease (ESRD), which demands the use of renal replacement therapy (RRT). This involves an increasing reliance on dialysis and kidney transplants, which places a significant financial strain on healthcare systems[18]. The social and financial implications of CKD are significant, not only due to the morbidity and mortality associated with its progression to ESRD, but also because it increases the risk of developing cardiovascular disease (CVD) at a faster

rate[19,20]. Cardiovascular Disease is the primary cause of death in individuals with CKD, with mortality rates ranging from 10-100 times greater in Haemodialysis patients[21]. It is crucial to acknowledge that most patients with CKD succumb to CVD prior to attaining ESRD[22]. Left ventricular hypertrophy (LVH) is the primary structural change in the cardiovascular system of patients with chronic kidney disease (CKD). It is present in about 30-45 percent of CKD patients and the severity of LVH increases as the glomerular filtration rate (GFR) decreases[23,24].

The study population consisted of a majority of males, accounting for 68% of the total, while females accounted for 32%. A majority of the male patients, namely 75% of the study group, exhibit an abnormal left ventricular mass index. It is worth noting that a normal value for male patients is considered to be 135 g/m2. 88.24% of female patients have an abnormal left ventricular mass index. Left ventricular hypertrophy was assessed using echocardiography of the heart, employing the Devereux formula[25]. Our investigation reveals a correlation between various age groups and an elevated left ventricular mass. There was a statistically significant difference in the age groups for male individuals when comparing normal and abnormal left ventricular mass index. Hamett *et al.* conducted research that found a correlation between age and the occurrence of left ventricular hypertrophy after the start of dialysis[26]. It was shown that individuals who acquired left ventricular hypertrophy were somewhat older than the control group at the beginning of the study. The explanation given was that as the ventricle ages, it becomes more responsive to the hypertrophic effect caused by an increased systolic blood pressure. A strong correlation was seen between anaemia and left ventricular mass index in both male and female individuals. The selected reference value for Hemoglobin (Hb) was 8g/dl[27,28].

The research found a strong correlation between anaemia (with a reference value of 8g/dl for this study group) and left ventricular mass index in both male and female patients. The p value was significant for both male and female populations. There was a significant link seen between Anaemia and left ventricular mass index in both male and female individuals. There was no association between DM (diabetes mellitus) and LVMI (left ventricular mass index). Concentric left ventricular hypertrophy (LVH) has been seen in patients with chronic kidney disease (CKD) and confirmed using echocardiography. It is present in 42% of patients at the initiation of dialysis and in up to 75% of patients who have been on dialysis for the last decade[29,30]. Arterial Hypertension is linked to Left Ventricular Hypertrophy (LVH) in patients with Chronic Kidney Disease (CKD) and research has shown that an increase in arterial stiffness causes LVH prior to the initiation of Haemodialysis. Additional risk factors contributing to the development of left ventricular hypertrophy (LVH) in individuals with chronic kidney disease (CKD) mostly include Body Mass Index (BMI), Anaemia, Hypertension and Ischaemic heart disease[31]. Left ventricular hypertrophy (LVH) is a robust indicator of mortality in patients with end-stage renal disease (ESRD) and is closely associated with a 60% increased risk of sudden death. Severe left ventricular hypertrophy (LVH) may ultimately result in left ventricular dilatation, which is itself a powerful indicator of a negative prognosis. The haemoglobin level has been shown to be sufficiently robust to predict the degree of left ventricular hypertrophy (LVH) in patients receiving extended haemodialysis. Each 1gm/dl decrease in haemoglobin is associated with a 6% increase in the risk of LVH. The number is[32]. For every 0.5 gm/dl decrease in haemoglobin level, the risk of LVH increased by 32%[33]. Therefore, anaemia has been shown to be a risk factor for the development of left ventricular hypertrophy (LVH) and negative outcomes in individuals with renal failure. Additionally, it may lead to an increase in cardiac output, which in turn may result in the enlargement and expansion of the left ventricle. This, along with other risk factors and metabolic abnormalities associated with chronic kidney disease (CKD), can contribute to the development of complications. Correction of anaemia might potentially lead to a partial regression of left ventricular hypertrophy (LVH) in dialysis-dependent patients[33].

CONCLUSION

The severity of anaemia has a considerable impact on the thickness of the left ventricular wall in individuals with chronic renal disease. These indicators of left ventricular mass may be readily assessed and have great sensitivity and specificity. When there is a suspicion of left ventricular hypertrophy, it is important to take strict efforts to address anaemia by using erythropoietin (EPO) with or without iron supplementation and blood transfusion. This will help enhance the patient's chances of survival from cardiovascular disorders.

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