International Journal of Advances in Medicine
Meena OP et al. Int J Adv Med. 2022 Jul;9(7):796-800
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20221706

Original Research Article

A study on correlation of anemia with left ventricular hypertrophy in chronic kidney disease patients: a cross sectional study from Southern Rajasthan

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Received: 02 May 2022
Revised: 24 May 2022
Accepted: 02 June 2022

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ABSTRACT

Background: Chronic kidney disease is becoming epidemic of twenty-first century. With increasing burden of diabetes and hypertension, chronic kidney disease is becoming rampant in our country. Adverse outcome of CKD includes kidney failure, complications due to decreased kidney function and cardiovascular disease etc. Increasing morbidity and mortality of coronary artery disease in CKD patients make it necessary to develop further researches in these population. Aim and objectives of current study were to demonstrate the correlation of anemia with left ventricular hypertrophy in a cohort of CKD patients in a tertiary care centre.
Methods: This study was done over one year on 100 patients of CKD (stage III to V), aged 15-80 years, who had elevated serum creatinine and reduced glomerular filtration rate, haemoglobin <11 gm/dl with ultrasonographic evidence of renal parenchymal disease grade ≥2. The patients were assessed based on clinical history and a number of laboratory parameters including blood urea, serum creatinine, calcium, inorganic phosphorus, serum electrolytes, iPTH level, Hb, Hct, glomerular filtration rate and left ventricular mass index.
Results: There is a significant relationship between of anemia and left ventricular hypertrophy among chronic kidney disease patients. In our study, it was observed that left ventricle mass (left ventricular mass index) increases with increasing severity of anemia.
Conclusions: Anemia is widely prevalent in our CKD patients. Severity of anemia is correlated to left ventricular hypertrophy in these patients. Hence correction of anemia early in these group of patients can halt or prevent cardiovascular morbidity and mortality.

Keywords: CKD, RPD, Glomerular filtration rate, Left ventricular mass index, Intact parathormone

INTRODUCTION

The association of anemia with chronic kidney disease (CKD) has been recognized since the early 19th century. Moreover, various studies done over the years have shown not only a higher incidence of anemia, but also a significantly higher incidence of cardiac complications, particularly left ventricular hypertrophy in chronic kidney disease patients.[1,2] In chronic kidney disease patients, various uremia related risk factors for cardiovascular disease includes anemia, hyperparathyroidism, abnormalities of mineral metabolism, acidosis, of note, association of anemia have been consistently described in all population of kidney disease. Anemia is defined as decrease in either percentage of RBC (hematocrit) or decrease in haemoglobin concentration in sample of venous blood when compared to reference values. In our study reference value is taken as 11 g/dl for both male and female. Anemia of renal failure mainly caused by lack of sufficient quantity of endogenous erythropoietin production, partially due to iron deficiency which can be

attributed to increased demand due to increased erythropoesis in response to exogenous EPO, gastrointestinal bleed, ongoing blood loss with dialyzer and tubing and due to frequent sampling and venupuncture. Anemia has been cited as an independent risk factor for the development of left ventricular hypertrophy (left ventricular hypertrophy) in chronic kidney disease patients.[3] Anemia leads to hemodynamic as well as non hemodynamic adaptation. Non-hemodynamic adaptation includes increase in erythropoietin hormone and intraerythrocytic 2,3 DPG. Whereas hemodynamic adaptation takes place when Hb is <10 g/dl, includes increase cardiac preload and reduced SVR, both of which leads to high cardiac output, which if remains for long term leads to left ventricle remodelling (initial dilatation and subsequent hypertrophy). Left ventricular hypertrophy is premature CVD that develop rapidly during progression of chronic kidney disease and is strong indicator of mortality in patient with ESRD. It is known that anemia is a strong predictor of development of left ventricular hypertrophy and morbidity and mortality in ESRD.[4] The importance of anemia in ESRD dialysis patients was shown by the observation that decreases in Hb level of 1 g/dl incrementally increased mortality by 18-25% and left ventricular hypertrophy by ~50%. In fact the role of anemia as a cardiac risk factor was shown in an evaluation of 246 patients in which it was found that every 0.5 g/dl decrease in Hb increased the relative risk of left ventricular growth by 32% (p=0.04).[5] Also in a prospective study of recombinant erythropoietin use in pre-dialysis patients; increase in mean Hb of 2.7 g/dl was accompanied by a decrease in left ventricular mass index (left ventricular mass index) in almost all patients.[3] This even in the absence of improved blood pressure control, confirmed the role of anemia in the genesis of left ventricular hypertrophy.

Thus, the role of recombinant erythropoietin for correction of anemia which was shown to lead to the reversal of hypertrophy, came into significance. Thus, though heart disease is common in chronic kidney disease, not all cardiac disease in chronic kidney disease patients caused by conventional or atherosclerotic processes, nor due to ischemic changes. Instead, anemia is major independent risk factor for development of left ventricular hypertrophy in chronic kidney disease patients. Being a modifiable risk factor, if anemia is treated by intervening early in disease course, left ventricular hypertrophy can be arrested or to some extent reversed. In the same context, the present study was carried out.

Aim and objectives

The aim and objective of this study were to calculate left ventricular mass index in patients of chronic kidney disease stage III-V having hemoglobin level <11 g/dl with or without dialysis and to demonstrate development of left ventricular hypertrophy early in chronic kidney disease patients with mild to moderate anemia, so that early intervention with EPO with or without iron replacement can arrest or reverse the myocardial changes.

METHODS

This is an institution based comparative observational cross-sectional study conducted over 100 patients of either sex, age group of 15 to 80 years, from all socioeconomic status, admitted over a period of one year from 1 December 2017 to 30 November 2018. Diagnosed as CKD patients with varying degree of renal failure (grade III to V) with ultrasonographic evidence of renal parenchymal disease grade II or more and haemoglobin level <11 g% diabetic or non-diabetic, hypertensive or non-hypertensive and whether the patients were on dialysis or erythropoietin replacement or not. Out of 100 patients, 68 patients were hypertensive (controlled on medications). They were diagnosed as hypertensive between 2 to 4 years before commencing our study. Patients with post renal transplant status and those with uncontrolled hypertension who are known case of hypertrophic obstructive cardiomyopathy, rheumatic heart disease etc. were excluded from the study.

Investigations

Investigations included Hb, HCT, blood urea, serum creatinine, calcium, inorganic phosphorus, bicarbonate, serum electrolytes, iPTH level, urine chest X-ray, renal ultrasound for kidney size and echotexture, left ventricular mass index calculation by Modified Devereoux formula using electrocardiogram. Initial assessment included detailed clinical history with regard to duration of renal failure (in years), diabetes/hypertension if any, and whether the patients undergoing dialysis or erythropoietin replacement. Height, weight and blood pressure was noted in all patients. Laboratory tests including serum creatinine, Hb, Hct, calcium, creatinine clearance (calculated according to creatinine clearance by Cockroft-Gault equation. Calculation of left ventricular mass: As, both body size and body habitus are clearly associated with left ventricle dimension and mass, indexing for body size is required. Several index for body size correction have been proposed e.g. BMI, BSA, weight, free fat mass. Among all, BSA permits adequate classification of most patients in clinical practice incorporating in left ventricular hypertrophy determination. Left ventricular mass index was calculated by using the ratio of left ventricle mass to body surface area. left ventricle mass was derived by Modified Deveroux formula using 2D Echocardiography.

$$\text{left ventricle Mass} = 0.8 \times 1.04\,(\text{IVSd} + \text{LVIDd} + \text{LVPWd})3 - (\text{LVIDd})3 + 0.6\ \text{gms.}$$

Where IVSd=interventricular thickness in diastole in mm; LVID; d=left ventricular diameter in diastole in mm; LVPWd=left ventricular posterior wall thickness in diastole in mm, left ventricular hypertrophy is

categorically defined as left ventricular mass index >135 for males and >110 for females.

In our study, all patients had haemoglobin <11 g/dl. Looking into Indian perspective where poor diet, chronic infections and malnourishment is common, and for convenience of our study, we took Hb <8 g/dl as reference value and were taken as anemic in both male and female. 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

Majority of study population i.e. 63% is male, 37% is female (Figure 1). Most of the male patient i.e. 77.78% of the study population are having abnormal left ventricular mass index (135 g/m^2 is taken as normal value for male patients).

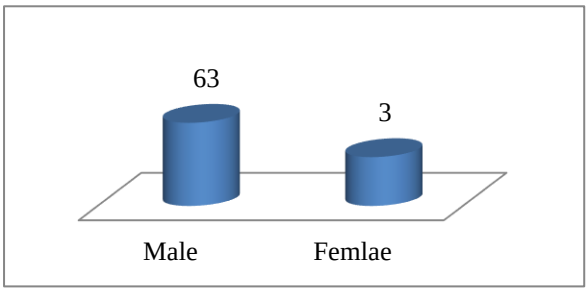

Figure 1: Sex wise distribution of study population.

Table 1: Age wise distribution of study population.

Age groups (years)	N	%
15-30	23	23
31-45	22	22
46-60	36	36
61-75	16	16
>75	3	3
Total	100	100

Table 2: Distribution of normal and abnormal left ventricular mass index among male patients.

Gender	Left ventricular mass index (gm/m^2)	N	%
Male	<135 (Normal)	14	22.22
	>135 (Abnormal)	49	77.78
Female	<110 (Normal)	3	7.89
	>110 (Abnormal)	34	92.10

It is evident that majority of female patients i.e., 92% have abnormal left ventricular mass index. Mean hemoglobin value in male was 8.09 g/dl and in females was 7.12 g/dl. Relation of anemia (reference value for this study population being taken as 8 g/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 is strong correlation between Anemia and left ventricular mass index in both male and female patients. 16 out of 19 patients who were diabetic are having abnormal LVMI, whereas 67 out of 81 who were non diabetic were having abnormal LVMI, so there is no correlation between DM and LVMI.

Table 3: Hb with left ventricular mass index in males and females.

Variables	Hb<8	Hb>8	Odds ratio	95% CI	P value	Remarks
Left ventricular mass index (male)						
<135	1	13	0.040	0.0049-0.3396	0.003	Significant
>135	32	17				
Left ventricular mass index (female)						
<110	1	2	0.067	0.0087-0.2912	0.04	Significant

Out of 46 male patients who were hypertensive, 39 patients (84%) had abnormal LVMI, and 7 patients out of 10 who are non-hypertensive (70%) had abnormal LVMI. Among female patients, 21 out of 22 (who were hypertensive) had abnormal LVMI and 13 out of 15 (who were non-hypertensive) had abnormal LVMI. Suggesting that HTN is also a contributory factor for LVH specially in advanced CKD.

There is linear inverse relationship between left ventricular mass index and Hb (g/dl) i.e., with decrease in Hb value, left ventricular mass index is increasing in male study population. There is linear inverse relationship between left ventricular mass index and Hb (g/dl) i.e.; with decrease in Hb value, left ventricular mass index is increasing in female study population as well.

DISCUSSION

In our study, we included 100 cases of known chronic kidney disease. The percentage of female in the study group was 37 and male was 63. Left ventricular hypertrophy was measured using echocardiography of heart by using Devereux formula.[6] Around 83% of the patients in this study had increased left ventricular mass on echocardiography. The limit for left ventricular hypertrophy for females was >110 g/m^2. 34% of the female cases had increased left ventricular mass (Table 1, Figure 1). The cut-off for left ventricular hypertrophy in males was >135 g/m^2. 49% of the male cases had increased left ventricular mass according to Devereux formula.[6] In our study, there is association between different age groups and increased left ventricular mass.

Table 4: Diabetes mellitus verses LVMI.

Variables	Present	Absent
Male		
LVMI		
<135	3	11
>135	12	37
Female		
LVMI		
<110	0	3
>110	4	30

Chronic kidney disease had an unequal distribution among age groups. The aetiology being inherited and congenital in the younger age group, with diabetes and hypertension dominating the picture in the older age groups.

Table 5: Hypertension verses LVMI.

Variables	Present	Absent
Male		
LVMI		
<135	7	7
>135	39	10
Female		
LVMI		
<110	1	2
>110	21	13

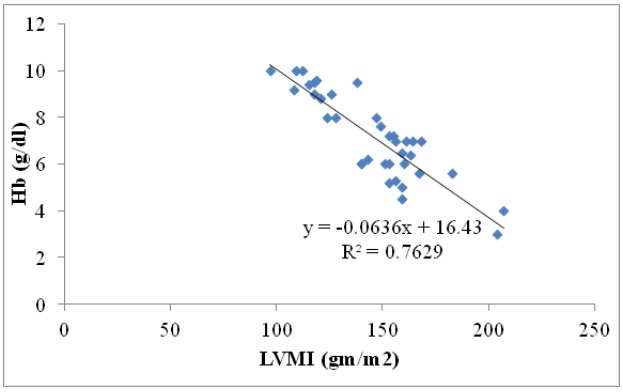

Figure 2: Correlation between Hb in g/dl with left ventricular mass index among male patients.

The difference between the age groups for normal and abnormal left ventricular mass index was statistically significant for male (p=0.0049) and female (p=0.021). In a study by Hamett et al the age was associated with the development of left ventricular hypertrophy after the initiation of dialysis.[7]

They found that cases that developed left ventricular hypertrophy were significantly older than controls at baseline; the reason cited was that the aging ventricle is more sensitive to the hypertrophic stimulus of an elevated systolic blood pressure. There was significant relation between anemia with left ventricular mass index in both male and female patients. Anemia being expressed in haemoglobin (g/dl). The reference value taken was 8 g/dl for Hb.[8,9]

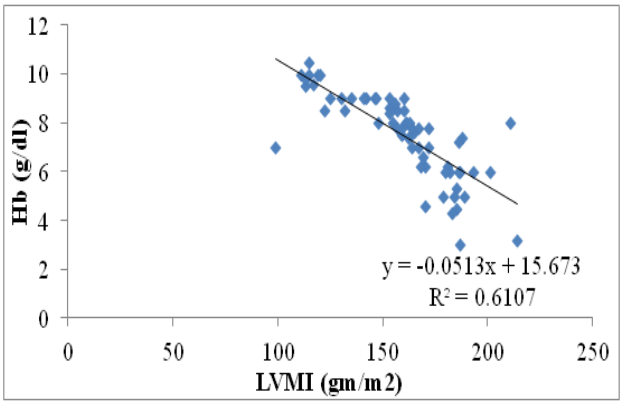

Figure 3: Correlation between Hb in g/dl with left ventricular mass index among female patients.

Among male patients 32 out of 33 with Hb<8 g/dl had abnormal left ventricular mass index and 17 out of 30 with Hb>8 g/dl had abnormal left ventricular mass index, odd's ratio being 0.0409 (p value=0.0031). Among female patients 24 out of 25 with Hb<8 g/dl had abnormal left ventricular mass index and 11 out of 13 with Hb>8 g/dl had abnormal left ventricular mass index, Odd's ratio being 0.067 (p value=0.04). In our study, hypertensive patients who were under control with medications were taken as the study population; to eliminate the bias of uncontrolled hypertension inducing left ventricular hypertrophy. Elevated systolic blood pressure is a well-known independent factor for left ventricular mass index. Out of 46 male patients who were hypertensive, 39 patients (84%) had abnormal LVMI, and 7 patients out of 10 who are non-hypertensive (70%) had abnormal LVMI.

Among female patients, 21 out of 22 who were hypertensive (95%) had abnormal LVMI and 13 out of 15 who were non-hypertensive (87%) had abnormal LVMI. suggesting that HTN is also a contributory factor for LVH especially in advanced CKD. These patients were diagnosed as hypertensive between two to four year before commencing this study and their blood pressure was controlled on medication. Thus in this study, it was observed that decrease in haemoglobin concentration is associated with increase in left ventricular mass index (left ventricular mass index) and therefore increase in cardiovascular morbidity and mortality.

Severity of anaemia could very well predict the left ventricular dimension and thickness in both male as well as female patients, and therefore risk of CVDs.[10,11] This study points towards importance of timely administration of anaemia correcting measures in form of EPO or blood transfusion which could herald or reverse left ventricle remodelling. In the study by Jesuorobo et al the hemoglobin levels of the study population had a negative

correlation with left ventricular mass index and it was statistically significant.[12]

Limitations

Limitations of current study were; early diagnosis of diseases like diabetes, hypertension and CKD is not possible in all the patients. Hence the duration of the underlying risk factors, control of blood pressure and glycemic control prior to the treatment could not be commented. CKD patients who were managed conservatively as well as who were subjected to hemodialysis were the subjects. Thus, the effect of hemodialysis and its effect on LVMI could not be omitted from this study. As many patients were treated for anemia by means of blood transfusion or EPO, correction of anemia and its effect on LV mass could not be studied, as follow up study measuring and monitoring LV mass could not be done.

CONCLUSION

Severity of anemia significantly influence the left ventricular wall thickness in chronic kidney disease patients. These predictors of left ventricle mass could be easily measured and are highly sensitive and specific for the same. On arriving at a suspicion of possible left ventricle hypertrophy, rigorous measures should be taken to correct anemia by EPO with or without iron administration and blood transfusion, to improve the patient's survival from the deadly cardiovascular diseases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Meena OP, Meghwal H, Meena R, Gurjar S. A study on correlation of anemia with left ventricular hypertrophy in chronic kidney disease patients: a cross sectional study from Southern Rajasthan. Int J Adv Med 2022;9:796-800.