ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

Original article

Correlation of Anemia with Left Ventricular Hypertrophy in Chronic Kidney Disease Patients

Dr. Harshal Vora[1], Dr. Jitendra Pareek[2]

[1]Assistant Professor, Department of General Medicine, Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat

[2]Associate Professor, Department of General Medicine, Pacific Medical College and Hospital, Udaipur, Rajasthan

***Corresponding Author: Dr. Jitendra Pareek**, Department of General Medicine, Pacific Medical College and Hospital, Udaipur, Rajasthan

Mob no: 81289 82840

Email address: dr.jitendrap84@gmail.com

Conflict of Interest: none

Source of Support: Nil

Abstract

Background and Aim: Cardiovascular disease (CVD) remains the major cause of death in patients with chronic kidney disease (CKD). Anemia is major independent risk factor for development of left ventricular hypertrophy in chronic kidney disease patients. 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.

Material and Methods: This is observational cross-sectional study conducted over 150 patients of either sex, admitted over a period of one year. 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. Left ventricular mass index was calculated by using the ratio of left ventricle mass to body surface area.

Results: There is strong correlation between Anemia and left ventricular mass index in both male and female patients. 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.

Conclusion: Severity of anemia significantly influences 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.

Key Words: Anemia, Cardiovascular disease, Chronic Kidney Disease, Left Ventricle

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

Introduction

Anaemia is the most common complication of chronic renal failure (CRF) and is characterized by a decrease in hemoglobin and red blood cells, which leads to reduced capacity of the blood to deliver oxygen to all tissues and organs. According to the WHO definition, anaemia is a decrease in hemoglobin below 130 g/l in men and below 120 g/l in women. 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 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 in chronic kidney disease patients.[3] Anemia leads to hemodynamic as well as non hemodynamic adaptation. Nonhemodynamic adaptation includes increase in erythropoietin hormone and intraerythrocytic 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]

The National Kidney Foundation Task Force about CVD in CKD has emphasized the high risk of CVD in patients with CKD, and has identified LVH and coronary artery disease as the major targets for intervention.[6] Left ventricular hypertrophy is an independent predictor of mortality in dialysis patients.[6,7] Its prevalence is very high among patients with ES-CKD starting hemodialysis, which suggests that it might be present in a large percentage of patients with CKD since early stages.[8]

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

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

or atherosclerotic processes, or due to ischemic changes. Instead, anemia is major independent risk factor for development of left ventricular hypertrophy in chronic kidney disease patients.

The objectives 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.

Material and Methods

This is observational cross-sectional study conducted over 150 patients of either sex, admitted over a period of one year. 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 150 patients, 100 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 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. 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 corrections 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 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.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

Results

Majority of study population i.e. 63.3% is male, 36.7% is female. Most of the male patient i.e. 78.94% of the study population are having abnormal left ventricular mass index (135 g/m2 is taken as normal value for male patients). It is evident that majority of female patients i.e., 91% have abnormal left ventricular mass index. Mean hemoglobin value in male was 8.12 g/dl and in females was 7.23 g/dl. There is strong correlation between Anemia and left ventricular mass index in both male and female patients. 23 out of 28 patients who were diabetic are having abnormal LVMI, whereas 91 out of 122 who were non diabetic were having abnormal LVMI, so there is no correlation between DM and LVMI.

Out of 68 male patients who were hypertensive, 58 patients had abnormal LVMI, and 11 patients out of 16 who are non-hypertensive had abnormal LVMI. Among female patients, 31 out of 32 (who were hypertensive) had abnormal LVMI and 20 out of 23 (who were non-hypertensive) had abnormal LVMI. Suggesting that HTN is also a contributory factor for LVH especially 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.

Table 1: Age wise distribution of study population

Age (Years)	Number	Percentage (%)
15-29	34	22.6
30-44	33	22
45-59	54	36
60-74	24	16
75 and more	5	31.25

Table 2: Distribution of normal and abnormal left ventricular mass index among both Genders

Gender	Left ventricular mass index (gm/m2)	Number	Percentage (%)
Male	<135 (Normal)	20	21.05
	>135 (Abnormal)	75	78.94
Female	<110 (Normal)	5	9.09
	>110 (Abnormal)	50	90.90

Table 3: Diabetes mellitus verses LVMI

Variable	Present	Absent
Male		
LVMI		
<135	5	16

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

>135	17	57
Female		
LVMI		
<110	0	5
>110	6	44

Table 4: Hypertension verses LVMI

Variable	Present	Absent
Male		
LVMI		
<135	10	11
>135	58	16
Female		
LVMI		
<110	1	3
>110	31	20

Discussion

The relationship between the kidneys and the heart in health and pathology has been long known. The decreased glomerular filtration rate is associated with hypervolemia and increased cardiac output. Haemodynamic loading leads to increased myocardial contractility by neurohumoral mechanisms and, over time, to LVH and heart failure.[8] The cardio-renal syndrome in patients with CKD was first described by R. Bright in 1836[9] but has been the subject of research and discussion since 1980, especially after the establishment of practical and widespread use of extrarenal methods for the treatment of CRF. The significant increase in the survival of patients with CRF undergoing organ replacement therapy, mainly related to the improvement of dialysis technology and the treatment of renal anaemia with epoetin after 1990, has also led to an increase in the incidence of chronic complications of CRF in which left ventricular hypertrophy and chronic heart failure play an essential role.[10]

In the present study the percentage of female in the study group was 55 and male was 95. Left ventricular hypertrophy was measured using echocardiography of heart by using Devereux formula.[6] The limit for left ventricular hypertrophy for females was >110 g/m2 . 50 female cases had increased left ventricular mass. The cut-off for left ventricular hypertrophy in males was

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

>135 g/m2 . 75 male cases had increased left ventricular mass according to Devereux formula. In our study, there is association between different age groups and increased left ventricular mass.

The difference between the age groups for normal and abnormal left ventricular mass index was statistically significant for male and female. In a study by Hamett et al the age was associated with the development of left ventricular hypertrophy after the initiation of dialysis.[2] 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.[11,12] Recent studies have shown that hemoglobin normalization does not benefit that population. On the other hand, anemia is known to be an important promoting factor of LVH.[13-15]

23 out of 28 patients who were diabetic are having abnormal LVMI, whereas 91 out of 122 who were non diabetic were having abnormal LVMI, so there is no correlation between DM and LVMI. Out of 68 male patients who were hypertensive, 58 patients had abnormal LVMI, and 11 patients out of 16 who are non-hypertensive had abnormal LVMI. Among female patients, 31 out of 32 (who were hypertensive) had abnormal LVMI and 20 out of 23 (who were non-hypertensive) had abnormal LVMI. Elevated systolic blood pressure is a well-known independent factor for left ventricular mass index. 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.[16,17] 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 remodeling. Strict control of blood pressure (BP) is known to be one of the best practices to prevent LVH.[18] In addition, diastolic BP was an independent determinant of LVH. This is a worrying result, because BP control should not be a difficult target to be reached, at least for most patients, considering the existing therapeutic armamentarium. We insist in the importance of strict BP control as an efficient measure for preventing both LVH and CKD progression.[19]

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.

Conclusion

Severity of anemia significantly influences 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. There was no significant difference in LVH incidence between patients with and without anaemia and those with and without hypertension. There was

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

a considerable dependence of left ventricular hypertrophy on the duration of chronic renal failure and dialysis treatment.

References

1. Kansz AT, Khan SS, Abichandani R. Management of patients with chronic renal insufficiency in the Northeastern United States. J Am Soc Nephrol. 2001; 7:1501-07.

2. Harnett JD, Kent GM, Foley RM, Parfrey PS. Cardiac function and hematocrit level. Am J Kidney Dis. 1995;25:S3-7.

3. Levin A, Thompson CR, Ethier J. Left ventricular mass index increase in early renal disease : impact of decline in hemoglobin. Am J Kidney Dis. 1999;34: 125-34.

4. Foley RN, Parfrey PS, Harnett JD. The impact of anemia on cardiomyopathy, morbidity and mortality in ESRD. Am J Kidney Dis. 1996;28:53-61.

5. Levin A, Thompson CR, Ethier J, Carlisie EJF, Tobe S, Mendelsson D, et al. Left ventricular mass index increase in early renal disease: Impact of decline in haemoglobin. Am J Kidney Dis. 1999;34:125-34.

6. Meyer KB, Levey AS. Controlling the epidemic of cardiovascular disease in chronic renal disease: Report from the National Kidney Foundation Task Force on Cardiovascular Disease. J Am Soc Nephrol. 1998; 9(Suppl12):S31-S42.

7. Parfrey PS, Harnett JD, Griffiths SM et al. The clinical course of left ventricular hypertrophy in dialysis patients. Nephron. 1990; 55:114-20.

8. Weiner DE, Tighiouart H, Vlagopoulos PT, Griffith JL, Salem DN, Levey AS, et al. Effects of anaemia and left ventricular hypertrophy on cardiovascular disease in patients with chronic kidney disease. JASN. 2005;16(6):1803-10.

9. Bright R. Cases and observations of renal disease accompanied with the secretion of albuminous urine. Guy's Hospital Reports. 1836;(1):338-79.

10. Kundurdjiev A. Cardiorenal syndrome. Sofia: Excelsior; 2019. Bulgarian.

11. Mcmahon LP. Development, prevention, and potential reversal of left ventricular hypertrophy in chronic kidney disease. J Am Soc Nephrol. 2004;15: 1640-7.

12. Yilmaz BA. Predictors of left ventricular hypertrophy in patients with chronic kidney disease. Ren Fail. 2007;29(3):303-7.

13. Drueke TB, Locatelli F, Clyne N et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006; 355:2071- 84.

14. Singh AK, Szczech L, Tang KL et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006; 355:2085-98.

15. Silverberg DS, Wexler D, Blum M et al. The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations. J Am Coll Cardiol. 2000; 35:1737-44.

16. .Cao XS. BMI, spKt/V, and SBP but Not DBP Are Related to LVH in Chinese maintenance hemodialysis patients. Renal Failure. 2011;33(3):269-75.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

17. Foley RN. Left ventricular hypertrophy in new hemodialysis patients without symptomatic cardiac disease. Clin J Am Soc Nephrol. 2010;5:805-13.
18. Berl T, Henrich W. Kidney-Heart Interactions: Epidemiology, Pathogenesis, and Treatment. Clin J Am Soc Nephrol. 2006;1:8-18.
19. Ruggenenti P, Perticucci E, Cravedi P et al. Role of remission clinics in the longitudinal treatment of CKD. J Am Soc Nephrol. 2008; 19:1213-24.