

Cardiac Valve Calcification in End Stage Renal Disease Patients on Regular Hemodialysis

BHAGWAN DAS¹, BELLA DAYO², RAFIA MEMON³, FAZILA HASHMI⁴, AFREEN NAZ⁵, KISHOR KUMAR⁶

¹Assistant Professor, Department of Nephrology

^{2,3,5,6}Postgraduate Trainees, Department of Nephrology,

⁴Assistant Professor, Department of Surgery, Liaquat University of Medical & Health Sciences, Jamshoro

Correspondence to: Dr. Bhagwan Das E-mail: dr_jairamani@hotmail.com Cell 0333-2976340

ABSTRACT

Objective: The objective of the study was to determine the frequency of cardiac valve calcification in ESRD patients who are on maintenance hemodialysis.

Study design: Descriptive Cross-sectional study

Place and Duration of Study: Department of Nephrology (Dialysis Unit), Liaquat University of Medical & Health Sciences, Jamshoro from 1st August 2019 to 31st January 2020.

Methodology: One hundred and twenty patients with end stage renal disease on maintenance hemodialysis having age 18 to 70 years of either gender were included. Investigations were advised for Serum parathyroid hormone, C-reactive protein, calcium and phosphorus. Echocardiography was performed for the evaluation of cardiac valve calcification.

Results: The average age of the patients was 50.67±13.70 years. The cardiac valve calcification was found to be 62 (51.7%). Of 62 patients with cardiac valve calcification, mitral valve calcification was found to be 44 (71%), aortic valve 31 (50%), and mitral annulus 50 (80.6%) respectively. A significant association of cardiac valve calcification was observed with age (P<0.002), serum CRP level (P<0.001), serum phosphorus level (P<0.001) and hypertension (P<0.002).

Conclusion: The cardiac valve calcification in majority of the patients and mitral annulus was found to be higher 80% followed by mitral valve and aortic valve calcification.

Keywords: Cardiac valve calcification, End stage renal disease (ESRD), Mitral annulus, Mitral valve calcification, Aortic valve

INTRODUCTION

Chronic kidney disease is a prevailing, gradually increasing disease of all age groups and causes irreparable loss of function of kidneys.¹ It is a universal disease and occurs worldwide, and in our region like Pakistan diabetes, hypertension and renal stones are leading causes among others.² It is divided into five stages on the basis of glomerular filtration rate. Stage V disease has glomerular filtration rate less than 15 ml/min/1.73 m² also called end stage renal disease.³ Patient of chronic kidney disease stage V cannot sustain his or her life without renal replacement therapy either in the form of transplant or dialysis.⁴ The end stage renal disease populace requiring constant dialysis or renal transplantation is developing at a remarkable rate every year. Patients of end-stage renal disease on regular hemodialysis usually have structural abnormalities of the heart like calcified valvular sclerosis, left ventricular remodeling and left ventricular (LV) diastolic dysfunction, all these are related with high pace of cardiovascular mortality.⁵

Cardiovascular disease due to both traditional and non-traditional risk factors causes high morbidity and mortality in these patients.⁶ In patients with chronic renal impairment mortality due to cardiac related disease is 10-30 times higher than in patients without chronic kidney disease.⁷ In patients on regular hemodialysis cardiac valvular and vascular calcifications are progressively being perceived as the two risk factors of morbidity and mortality.⁸ The severity of valvular calcification can be estimated by certain labs.⁹ Past investigations dependent on echocardiography reporting have admitted that the prevalence of vascular calcification is 47% in patients on

maintenance hemodialysis.¹⁰ Dialysis cases with valve calcification (VC) had essentially elevated serum mineral levels and hormone levels as parathyroid. Additionally, cases with VC were notably over age, and have more number of diabetes. We also noticed relation between VC and time span of hemodialysis therapy.¹¹ The period of hemodialysis was escalated in cases with VC than cases without VC. Patients with vascular calcification remain at high risk of myocardial ischemia, valve dysfunction, conduction problems, endocarditis and cardiac failure.¹² It is also associated with atrial fibrillation and cerebrovascular events.¹³

The presence of VC confirmed on echocardiography is related with an elevated risk of mortality from cardiovascular causes in the dialysis populace. The rationale of our study was to analyze the frequency of VC in our local hemodialysis population as local on this topic is not available. If the magnitude is found to be high than policy could be made to screen ESRD patients on regular basis so that instant treatment may prevent from morbidity and mortality in such patients.

METHODOLOGY

This descriptive cross-sectional study was done in the Department of Nephrology (Dialysis Unit), Liaquat University of Medical & Health Sciences, Jamshoro from 1st August 2019 to 31st January 2020 and comprised 120 cases of ESRD patients on maintenance hemodialysis. The age from 18-70 years either gender with ESRD on hemodialysis for 3 months at least were included in the study. While patients with malignancy, chronic inflammatory disease, acute infections and congenital heart diseases

were excluded from the study. ESRD patients who was on hemodialysis and having GFR <15ml/min/1.73 m² visiting Nephrology department were included in the study. Informed consent was taken from all patients and benefits versus risks was thoroughly explained to the patients before considering them for study. History was taken by the principal investigator for diabetes mellitus (history diabetes for more than 2 years confirmed through physician prescription), hypertension (documented history of HTN for more than 2 years confirmed through physician prescription). Investigations was advised for Serum intact parathyroid hormone, C-reactive protein (CRP), calcium and phosphorus. Measurements was taken for height on stadiometer in meters without shoes. Weight was assessed on weighing machine nearest to 0.1 kg. Further BMI was noted by the formula weight in kg divided by height in meter square. Patient was referred for Echocardiography and using a 3.3 MHz probe two dimensional (2D) echocardiograms was obtained in cases in the left lateral position. 2D examination of valves was done with Doppler Ultrasound on the basis of the parasternal long-short-axis and apical 4-chambers views. Cardiac valve calcification described as bright echoes of more than 1 mm on one or more cusps of the cardiac valves. Information of all the above mentioned variables was obtained from patients and recorded. The statistics were analyzed by SPSS-21. Effect modifiers like age, gender, BMI, history of Diabetes Mellitus, Hypertension, Serum parathyroid hormone, CRP, calcium and phosphorus was addressed. Post stratification chi square test was applied considering p value less than or equal to 0.05 as significant.

RESULTS

The average age of the patients was 50.67±13.70 years. There were 76 (63.3%) patients with >50 years of age. Majority of the patients were males (n=68, 56.7%). Mean weight, height, and BMI of the patients was 60.11±5.12 kg, 1.54±0.06 m and 27.55±4.75 kg/m² respectively. There were 69 (57.5%) patients with ≤30 kg/m² BMI. Mean CRP, calcium, phosphorus, and parathyroid hormone level of the patients was 4.96±1.53 mg/L, 8.73±0.42 mg/dl, 4.29±0.70 mg/dl, and 97.81±12.14 pg/ml respectively.

Table 1: Descriptive statistics of the patients (n=120)

Variable	Mean±SD
Age (years) [range31-70]	50.16±13.76
Weight (kg) [range 53-66]	60.11±5.12
Height (meter) [1.51-1.63]	1.54±0.06
BMI (kg/m ²) [range 1.71-33.0]	27.55±4.75
CRP (mg/L) [range 2.72-7.40]	4.96±1.53
Calcium level (mg/dl) [range 8.1-9.5]	8.73±0.42
Phosphorus level (mg/dl [range 3.51-5.44]	4.29±0.70
Parathyroid hormone level (pg/ml) [range 82-122]	97.81±12.14
Duration of hemodialysis (years) [range 1-3]	1.89±0.73

The mean duration of ESRD and hemodialysis was 2.75±1.05 years and 1.89±0.73 years respectively (Table 1). Majority of the patients (n=89, 74.2%) had ≤3 years of duration of ESRD whereas 94 (78.3%) of the patients had ≤2 years of duration of hemodialysis. Frequency of diabetes and hypertension was found to be 76 (63.3%) and 71 (59.2%) respectively. Frequency of cardiac valve

calcification was found to be 62 (51.7%). Of 62 patients with cardiac valve calcification, mitral valve calcification was found to be 44 (71%), aortic valve 31 (50%), and mitral annulus 50 (80.6%) respectively (Table 2). A significant association of cardiac valve calcification was observed with age (P<0.002), serum CRP level (P<0.001), serum phosphorus level (P<0.001) and hypertension [P<0.002] (Table 3).

Table 2: Types of cardiac valve calcification (n=62)

Type	No.	%
Mitral Valve	44	71
Aortic Valve	31	50
Mitral Annulus	50	80.6

Table 3: Comparison of cardiac valve calcification with general characteristics of the patients (n=120)

Variable	Cardiac Valve Calcification		P value
	Yes (n=62)	No (n=58)	
Age (years)			
≤50	14 (22.5%)	30 (51.7%)	0.002
>50	48 (77.5%)	28 (48.3%)	
Gender			
Male	40 (64.5%)	28 (48.3%)	0.073
Female	22 (35.5%)	30 (51.7%)	
BMI (kg/m²)			
≤30	36 (58%)	33 (56.8%)	0.897
>30	26 (42%)	25 (43.4%)	
Duration of ESRD (years)			
≤3	43 (69.4%)	46 (79.3%)	0.213
>3	19 (30.6%)	12 (20.7%)	
Duration of hemodialysis (years)			
≤2	45 (72.5%)	49 (84.5%)	0.114
>2	17 (27.7%)	9 (15.5%)	
Serum parathyroid level (pg/ml)			
≤98	36 (58%)	34 (58.6%)	0.951
>98	26 (42%)	24 (41.4)	
Serum calcium (mg/dL)			
≤9	53 (85.5%)	47 (81%)	0.789
>9	9 (14.5%)	11 (19%)	
Serum CRP level (mg/L)			
≤4	20 (32.3%)	40 (64.6%)	<0.001
>4	42 (67.7%)	18 (35.4%)	
Serum phosphorus (mg/dL)			
≤4	32 (51.6%)	51 (87.9%)	<0.001
>4	30 (48.4%)	7 (12.1%)	
Diabetes mellitus			
Yes	41 (66.2%)	35 (60.3%)	0.511
No	21 (33.8)	23 (39.7%)	
Hypertension			
Yes	45 (72.5%)	26 (44.8%)	0.0
No	17 (27.5%)	32 (55.2%)	02

Chi-square test applied (P<0.05 taken as significant)

DISCUSSION

Patients of ESRD on regular hemodialysis usually have structural abnormalities of the heart like calcified valvular sclerosis, left ventricular remodeling and LV diastolic dysfunction, all these are associated with high rate of CV mortality.⁵ Cardiovascular disease due to both traditional and non-traditional risk factors causes high morbidity and mortality in these cases.⁶ In cases with chronic kidney impairment, mortality due to cardiac disease is 10-30 times more than in cases without.⁷ In patients on regular hemodialysis cardiac valvular and vascular calcifications

are progressively being perceived as the two causes and markers of morbidity and mortality.⁸ The severity of valvular calcification can be estimated by x-rays, ultrasound, echocardiography and CT.⁹ Former literature on echocardiography noting have described that the prevalence of vascular calcification is 47% in patients on maintenance hemodialysis.¹⁰ Dialysis patients with VC had elevated serum calcium, phosphate, parathyroid hormone and CRP than those with no valvular calcification. Additionally, cases with VC were of higher age, and have more incidence of diabetes. We also noticed relation between VC and time period of hemodialysis.¹¹ The duration of hemodialysis was more in cases with VC than without. Patients with vascular calcification remain at high risk of myocardial ischemia, valve dysfunction, conduction problems, endocarditis and cardiac failure.¹² It is also associated with atrial fibrillation and cerebrovascular events.¹³ The presence of VC confirmed on echocardiography is related with high risk of mortality from cardiovascular related issues in the haemodialysis populace.

The findings of our study showed frequency of cardiac valve calcification was found to be 62 (51.7%). Of 62 patients with cardiac valve calcification, mitral valve calcification was found to be 44 (71%), aortic valve 31 (50%), and mitral annulus 50 (80.6%) respectively. Furthermore, a significant association of cardiac valve calcification was observed with age ($P < 0.002$), serum CRP level ($P < 0.001$), serum phosphorus level ($P < 0.001$) and hypertension ($P < 0.002$).

The witnessed prevalence by literature of coronary artery calcification in the ESRD patients ranged from 40% to 100%.^{14,15} Very scant data in PD cases but the assessable evidence presents that vascular and valvular calcification is an eventually by most prevalent complication in the PD populace. Among two small surveys, about 60% to 80% of the PD cases, were affected with coronary artery calcification.¹⁶ The prevalence of cardiac valvular calcification reports about 32%-47% in PD cases.¹⁷ In contrary to 19%-84% in hemodialysis patients, a quite significant ratio.^{18,19}

Another research in hemodialysis cases reported a near association in between the coronary artery calcification and prevalence of atherosclerotic vascular disease.¹⁵ This is with regards to ongoing comparative analysis in PD cases describing that the severity of coronary artery calcium range was related with the prevalence of atherosclerotic vascular disease. The severity of coronary artery calcium score is probabilistic of arterial narrowing in cases with CKD.²⁰ and is related with elevated risk of left ventricular hypertrophy.²¹

The elevated incidence of vascular/valvular calcification in PD cases is caused by both common and so-called nontraditional uncommon risk elements. Aging is one of the most clinical element related with vascular/valvular calcification in hemodialysis affecties.^{14,17,20,22} Few studies noticed that the degree of coronary or valvular calcification escalates with time of dialysis.¹⁷ Deranged minerals with resulting hyperphosphatemia has been caused to play a most important aspect for vascular/valvular calcification in ESRD cases.^{14,17}

Two other studies have investigated the impact of different agents of valvular calcification progression. In a post hoc analysis by, Raggi and coworkers²³ observed in a cohort of 132 prevalent hemodialysis patients that 52 weeks of sevelamer HCl use was associated with a significant attenuation of cardiac calcification when compared with calcium salts.²³ In particular, the authors reported a significantly greater number of sevelamer-treated subjects experiencing an arrest (45% vs. 28%, $p = 0.04$) or regression (26% vs. 10%, $p = 0.02$) in total valvular and vascular calcification.²³ In a more recent study, the impact of cinacalcet plus low-dose vitamin D with pliable doses of vitamin D, on cardiac calcification was tested.²⁴ As highlighted in a subsequent post hoc analysis, prevalent hemodialysis subjects with evidence of aortic valve calcification were likely to benefit from the combined treatment with cinacalcet and low doses of vitamin D and experience significant cardiac valve calcification progression attenuation.²⁵

CONCLUSION

The cardiac valve calcification in most of the ESRD patients who are on maintenance hemodialysis was found to be higher 80.6% in mitral annulus followed by 71% in mitral valve and 50% in aortic valve calcification.

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