Prevalence of calcific aortic valve stenosis in haemodialysis patients at AL Hussein University Hospital.

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Abstract: Vascular calcification (VC) is common in chronic kidney disease (CKD) and associated with increased morbidity and mortality. This calcification starts to develop in the early stages of chronic kidney disease and is present in over 50% of patients at the time of dialysis commencement. The aim of this study is to assess the presence and extent of aortic valve calcification and stenosis in regular hemodialysis patients and chronic kidney disease patients and whether there is significant correlation between the age, Parathormonehormone (PTH), serum calcium, serum phosphorus, Ca x Ph product, cholesterol and triglycerides and these calcifications. The study was conducted on 100 individuals classified into three groups: 40 patients with stage 5 chronic kidney disease on regular hemodialysis for more than six months (group A), 40 CKD patients in predialysis period (group B) and 20 persons of normal individuals as control group (group C). All patients and control were subjected to full medical history, full clinical examination and laboratory investigations including serum calcium, Ph, (intact Parathormone hormone iPTH, Ca x Ph product, total cholesterol and triglycerides. Also transthoracic echocardiography was done to assess the severity of aortic valve calcification and degree of calcification. The results of aortic valve calcification showed a high significant difference between A and C& B and C ($P<0.01$). In dialysis patients aortic valve calcification showed a significant correlation with age, duration of haemodialysis ($p<0.01$). In pre-dialysis patients, aortic valve calcification showed significant correlation with age ($p<0.01$). This study suggested increased incidence of vascular calcification in chronic kidney disease patients on regular hemodialysis and pre-dialysis in comparison to the same age and gender of the healthy individuals. Vascular calcification in CKD patients is a very complicated multifactorial process which needs further studies.

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1. Introduction:

Vascular calcification is a common complication associated with CKD and the major cause of cardiovascular disease (CVD) in patients with end stage renal disease (ESRD) (1). The US Renal Data System reported that 38.3% of prevalent dialysis patients died from cardiovascular causes between 2008 and 2010. (2). The prevalence of VC increases as CKD progresses, from 40 % at stage 3 CKD to 80–99 % at stage 5 CKD on dialysis (3). Mineral and bone disorder (MBD) is also a frequent complication of CKD associated with increased risk of VC, arterial dysfunction, morbidity and mortality (4). A recent studies were revealed that every 1.0 mg/dL of serum phosphorus was associated with 18 % increase of the risk of death in patients with CKD, indicating that hyperphosphatemia is an independent risk factor for mortality among those patients (5). Hyperphosphatemia is increasingly considered the cause and a key factor inducing early and progressive VC in patients with CKD, implying that vigorous treatment of hyperphosphatemia with phosphate binders is essential to the prevention of VC (6). Dialysed patients showed increased calcium deposition within the cardiac valve apparatus, namely aortic and mitral valves. As a matter of fact, haemodynamically significant aortic valve stenosis is more prevalent and accelerated in ESRD patients when compared with subjects with normal kidney function (7). Structural and functional cardiac abnormalities are common in patients with CKD. 70–80% of CKD‐5D patients have abnormal left ventricular structure and/or function and 74% of CKD stage 5 patients show evidence of left ventricular hypertrophy (LVH) at the initiation of renal replacement therapy (8). The pathogenesis of CVD in CKD patients is in some ways similar to that in patients without kidney disease. However, uremic toxins resulting from renal dysfunction play a significant role in the development CVD. Recognizing that factor is very important, because prevention of CV death is achieved not only by delaying the progression of CKD, but also by modifying CV risk factors early in the course of the disease (9).

2. Materials and Methods

100 Subjects included in this study all were selected from Al- Hussein University Hospital, Al-Azhar University, They were classified into three groups.

Group (A):- Includes 40 patients 26 males and 14 females with mean age (47.37±10.8) on regular hemodialysis for more than six months with mean hemodialysis duration (62.7±38.2).

Group (B):- Includes 40 patients 26 males and 14 females with chronic kidney disease with mean age (48.27±13.17) matched for age and sex with group A.

Group (C):- Includes 20 apparently healthy controls subjects 12 males and 8 females with mean age (47.60±12.57) matched for age and sex with previous groups.

All subjects in this study will be subjected to the following:

1- Written informed concent for participation in the study.

2- Full history and clinical examination Demographic and hemodialysis data, drug history, history of peripheral or coronary heart disease.

3- Electrocardiogram (ECG).

4- Laboratory Investigation to evaluate Serum creatinine (S.Crt.), complete blood count (CBC), C-reactive protein (CRP), fasting (FBS) and random blood sugar levels (RBS)., lipid profile, Serum calcium (CA), phosphorus(PO4), calcium x phosphorus products, and iPTH.

5- TRANSthoracic Echocardiography (According to the standard protocol, a professional skilled cardiologist had performed echocardiographic examination to participants according to standard methods. Echocardiography for patients was done post hemodialysis session. M- mode, two dimensional echocardiography was performed using the commercially available device in our hospital (Philips IE 33). The following measures were reported:

a- Left ventricular end-systolic diameter (LVESD) (2-4 cm).

b- Left ventricular end-diastolic diameter (LVEDD) (3.7-5.7 cm).

c- Left ventricular posterior wall end-diastolic diameter (LVPWDd) (0.7-1.1cm).

d- Ejection fraction (EF) (53-75 %).

e- Fractional shortening (FS) (27-45 %).

f- Aortic valve area (AoVA) (3-4 cm2).

g- Maximal aortic velocity (AoVmax) > 2 m/s.

h- Aortic valve calcification (AVC).

The calcification of aortic cusps will be evaluated mainly from the long axis and short axis planes on 2D Echocardiography and degree of calcification will be scored according to the following criteria by rosenheketa 2000, as the follow:

1 – No calcification.

2 – Mildly calcified (small isolated spots).

3 _ moderately calcified (multiple large spots).

4 – Heavily calcified (extensive thickening and calcification of all cusps).

Statistical Analysis:

Data was analyzed by Microsoft Office 2010 (excel) and Statistical Package for Social Science (SPSS) version 16. Parametric data was expressed as mean ± SD and non parametric data was expressed as number and percentage of the total. Comparing the mean ± SD of 2 groups was done using the student's t test. Measuring the mutual correspondence between two values was done using the Spearman correlation coefficient. P value > 0.05 is considered non-significant, value < 0.05 is considered significant and value < 0.01 is considered highly significant.

3. Results

There was nostatistical significant difference (mean ± SD) of iPTH in group A patients (374.32±268.53) than group B (293.60±149.68 pg/ml) (P > 0.05) and there was highly statistical significant increase in (mean± SD) of iPTH in group A (374.32±268.53 pg/m) patients than group C (20.20±4.50 pg/ml) was found (P<0.01). Also there is highly statistical significant increase in mean ± SD of iPTH in group B than group C (293.60±149.68vs 20.20±4.50 pg/ml) (P< 0.01) (Table 1, 2, 3). There was no statistical significant difference in the level of corrected calcium between group A (8.9±1.3 mg/dl) and group B (8.5±.75 mg/dl) (P > 0.05), There was no significant difference in the level of corrected calcium between group A (8.9±1.3 mg/dl) compared to group C (8.89±.45 mg/dl) (P > 0.05). Also there is no significant difference was obtained on comparison between groups B (8.5±.75mg/dl) and group C (8.89±.45 mg/dl) (P> 0.05) (Table 1, 2, 3). Mean ±SD of serum Phosphorus level in dialysis group A show no significant difference with pre-dialysis group B (5.2±1.6 mg/dl & 4.95±1.51 mg/dl) (P> 0.05). Also there was highly statistical significant increase of serum Phosphorus in patients of group A (5.2±1.6mg/dl) and group B (4.95±1.51 mg/dl) than the control group (3.34±.78 mg/dl) (P<0.01) (Table 1, 2, 3). There was no statistical significant increase of Serum Ca x Ph product in patients of group A (47.05±17.9 mg/dl) than group B (42.9±14.5 mg^2/dl^2), but there was highly statistical significant increase of serum Ca x Ph of group A (47.05±17.9 mg/dl) than group C (29.72±6.85 mg/dl) (P< 0.01). and there is highly statistical significant difference of Ca x Ph product in group B (42.9±14.5 mg^2/dl^2) than group C (29.72±6.85 mg/dl) (P< 0.01) (Table 1, 2, 3). The (Mean ±SD) of EF in the patients of group A (56.15±12.69) show no significant increase than group B (50.90±14.42) and group C (61.9±7.96) (P< 0.05)

(P< 0.01), but there was highly statistical significant increase of EF between group B and C (50.90±14.42 VS 61.9±7.96) (P< 0.01) (Table 1, 2, 3).

Table 1: Comparative studies between group A and group B for all variables.

VARIABLE	Group A Mean ±SD	Group B Mean ±SD	P-value
iPTH	374.32±268.53	293.60±149.68	.067
Calcium	8.9±1.3	8.5±.75	.054
Phosphorus	5.2±1.6	4.95±1.51	.435
CaxPh	47.05±17.9	42.9±14.5	.222
Haemoglobin	10.35±1.6	10.3±1.6	.754
EF	56.15±12.69	50.90±14.42	.067
AoVA	3.04±.59	3.35±.29	.002
AoV max	1.72±.68	1.19±.42	.000

Table 2: Comparative statistics between group A and group C for all variables

VARIABLE	Group A Mean ±SD	Group C Mean ±SD	P-value
iPTH	374.32±268.53	20.20±4.50	.000
Calcium	8.9±1.3	8.89±.45	.743
Phosphorus	5.2±1.6	3.34±.78	.000
CaxPh	47.05±17.9	29.72±6.85	.000
Haemoglobin	10.35±1.6	12.5±1.49	.000
EF	56.15±12.69	61.9±7.96	.101
AoVA	3.04±.59	3.28±.27	.049
AoV max	1.72±.68	1.20±.32	.001

Table 3: Comparative statistics between group B and group C for all variables

VARIABLE	Group B Mean ±SD	Group C Mean ±SD	P-value
iPTH	293.60±149.68	20.20±4.50	.000
Calcium	8.5±.75	8.89±.45	.210
Phosphorus	4.95±1.51	3.34±.78	.000
CaxPh	42.9±14.5	29.72±6.85	.002
Haemoglobin	10.3±1.6	12.5±1.49	.000
EF	50.90±14.42	61.9±7.96	.002
AoVA	3.35±.29	3.28±.27	.590
AoV max	1.19±.42	1.20±.32	.918

Table (4): Shows Correlation Study between AVC and the Other Studied Parameters in group A.

	AVC	
	R	p-value
AGE	.852	.000
EF	-.109	.502
FS	-.211	.192
AoVA	-.316	.047
AoVmax	.474	.002
CA	.082	.617
PO4	-.092	.574
CAxPO4	-.047	.774
iPTH	-.081	.620
CRP	.230	.154
Duration of HD	.669	.000

There was statistical significant difference of AoVA in patients of group A (3.04±.59) than group B (3.35±.29), but there was no statistical significant difference of AoVA in patients of group A (3.04±.59) with group C(3.28±.27) or in patients of group B (3.35±.29) with group C (3.28±.27) (P<0.05). (Tables 1, 2, 3). Mean ±SD of AoV max in dialysis group A (1.72±.68) show highly significant difference with pre-dialysis group B (1.19±.42) and group C (1.20±.32) (P<0.01) but there is no significant difference of AoV max between group B (1.19±.42) and group C (1.20±.32) (P > 0.05). Correlation study of aortic valve calcification in the dialysis group showed significant correlation regarding age, AoVmax and duration of haemodialysis but no significant correlation regarding CA, PO4, CA x PO4 product, and AoVA (Table 4). As regard CKD group there was significant correlation of aortic valve calcification

with age but no significant correlation with CA, PO4, CA x PO4 product, iPTH, AoVA and AoV max (Table 5).

Table (5): Shows Correlation Study between AVC and the Other Studied Parameters in group B.

	AVC	
	R	p-value
AGE	.593	.000
EF	.046	.695
FS	.036	.826
AoVA	.204	.826
AoVmax	-.016	.920
CA	-.002	.991
PO4	-.079	.626
CAxPO4	-.070	.669
iPTH	.013	.937
CRP	-.072	.657

4. Discussion

We found that the degree of AS progressed more rapidly in patients undergoing dialysis with aorticvalve calcification than without aortic valve calcification Using echocardiography as the screening method, Wang et al (10) demonstrated cardiac valve calcification to be a frequent complication with a prevalence of at least 30% in the patients with end-stage renal disease. In addition, Ventura et al (11) reported that AS is frequently found (6%) in patients undergoing dialysis. However, the rate of progression of AS in patients undergoing dialysis has not been fully elucidated. Roger et al (12)reported that the initial maximum aortic jet velocity was not related to progression of AS (2-2.4 m/s, 0.18 _ 0.22 m/s/y; 2.5-2.9 m/s, 0.32 _ 0.38 m/s/y; 3.0-3.4 m/s, 0.21 _0.33 m/s/y; and _3.5 m/s, 0.24 _ 0.52 m/s/y, respectively). In addition, it was reported that the presence of severe aortic valve calcification identifies patients with a rapid increase in maximumaortic jet velocity (increased by _0.3 m/s within 1 year).1 Thus, the assessment of aortic valve calcification by using echocardiographic examination is quite important to treat patients with AS.

It has been reported that standard risk factors for atherosclerosis, such as hypertension, diabetes mellitus, and hyperlipidemia, were similar to the factors associated with primary aortic valve calcification and AS (13-15).

On the other hand, in patients undergoing dialysis, aortic valve calcification was prevalent in accordance with earlier studies demonstrating the influence of reactive hyperparathyroidism (16-18). In this study, intact-PTH concentration was significantly higher in calcification group compared with noncalcification group. This finding suggested that aortic valve calcification might be influenced by not only atherosclerosis but also reactive hyperparathyroidism in patients undergoing dialysis. In addition, we revealed that the degree of AS was more severe and the progression of AS more rapid in patients undergoing dialysis with aortic valve calcification than without aortic valve calcification. Aortic valve calcification in patients undergoing dialysis was thought to be a condition favorable of AS, and in patients not undergoing dialysis. Our results suggest that assessment of the degree of aortic valve calcification by echocardiographic examination may yield important prognostic information in patients undergoing dialysis and serial evaluation of AS by transthoracic echocardiography might be requested in patients undergoing dialysis with aortic valve calcification.

Conclusion

The degree of AS progressed more rapidly in patients undergoing dialysis with aortic valve calcification than without aortic valve calcification. Serial evaluation of AS by transthoracic echocardiography might be requested in patients undergoing dialysis with aortic valve calcification.

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