Aortic Valve Calcification in Hemodialyzed Patients at the Iraqi Dialysis Center

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ABSTRACT:

BACKGROUND :

Aortic valve calcification in End Stage Renal Disease (ESRD) patients occurs ten to twenty years earlier than general population. It is associated with myocardial, coronary arteries and conduction system calcification and it is associated with rapid development of aortic valve stenosis.

OBJECTIVE:

To study the incidence of aortic valve calcification in hemodialysis patients and to look for risk factors associated with this calcification.

PATIENTS AND METHODS:

Forty six patients with End Stage Renal Disease (ESRD) on regular haemodialysis in Baghdad Teaching Hospital / Dialysis Unit and forty six patients with no renal disease as control group were studied between February 2005 - January 2006. Duration of dialysis, blood flow rate during dialysis, serum Calcium, serum Phosphorous and their products were included in this study. Echocardiography was done for all patients.

RESULT :

The incidence of Aortic Valve Calcification (AVC) in ESRD patients on haemodiaysis was 30 % and it was higher than that of general population (p value 0.0085) . It occurs 10-15 year earlier than in patients with no renal disease. End Stage Renal Disease patients with AVC were older than those with non calcified valves. Only 7.4 % of those ESRD patients with AVC have hemodynamic AV stenosis (p value 0.5). The mean duration of haemodialysis in ESRD patients with AVC was longer than that of ESRD patients without AVC which was statistically significant. Also there was statistically significant association between blood flow rate during haemodialysis and AVC. There was statistically significant association between Calcium phosphate products and AVC in ESRD patients.

CONCLUSION:

There is ahigher incidence of aortic valve calcification in ESRD patients on haemodialysis . This calcification occurs earlier than that in patients with no renal disease .The duration of haemodialysis is a risk factors for AVC .

KEYWORDS: aortic valve calcification, haemodialysis , echo study

INTRODUCTION:

Cardiovascular disorders are common in patients with end stage renal disease [1-4]. It accounts for half of all death among dialysis patients[5,6]. Moreover cardiovascular mortality among dialysis patients is higher than would be predicted simply by concurrent risk factors such as diabetes mellitus, hypertension and hyperlipidemia[7].Calcification of myocardium, coronary arteries and cardiac valves are frequently observed in patients with end stage renal disease on haemodialysis [8-11]. These calcifications are seen in dialysis patients at much younger age than general population [12], even adult less than 30 year of age on dialysis have high incidence of coronary arteries and valvular calcification , and these lesions progress at a relatively rapid rate [13].Retrospective autopsy study of pediatric end stage renal disease patients found high incidence of soft tissues, vascular and valvular calcification[12].

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Aortic valve calcification is a degenerative process of aortic valve involving accumulation of lipids; oxidized low density lipoprotein in particular association with chronic inflammatory process with accumulation of macrophage and T - lymphocyte and culminates in calcium deposits [14, 15].

Aortic valve calcification in haemodialysis patients occurs ten to twenty years earlier than general population [16, 17]. It is associated with myocardial, coronary arteries and conduction system calcification [22]. Also it is associated with rapid development of functionally aortic stenosis and subsequent increased morbidity and mortality [23].

End stage renal disease promotes valvular calcification by two mechanisms, haemodynamic and biochemical[23]. As a result of anemia , arteriovenous shunt, hypertension and over hydration, the cardiac output and heart rate increase which lead to increase transvalvular peak flow velocity and numbers of opening /closure cycle, and higher rate of repetitive stress which accelerate calcification of aortic valve [23]. So that numbers of years on haemodialysis correlate with presence of aortic valve calcification [20, 21].

Calcification of aortic valve is mostly associated with disorders of phosphorus and calcium metabolism, particularly an elevated Ca x PO4 products [22,23] .In end stage renal disease, secondary hyperparathyroidism can cause hypercalcaemia and high Ca x PO4 products, conditions favorable for development and progression of aortic valve calcification [24].The increased use of calcitriol and calcium containing phosphate binders, increases the entral calcium absorption and favors development of aortic valve calcification [22]. Few previous studies showed that, elevated serum phosphorus level in end stage renal disease was associated with increased risk of death in such patients, particularly from coronary arteries and valvular disease [25- 28].

Aim of the study is to look for the profile of aortic valve in hemodialysis patients and the objectives were:

1) Incidence of AVC with or without stenosis in ESRD patients on haemodialysis

2) Study the haemodialysis related risk factors and its effect on A.V calcification.

3) Study the effect of the disturbance in Ca and PO4 metabolism on A.V calcification in ESRD patients.

PATIENTS AND METHODS:

A prospective study was performed between February 2005 and January 2006 to study the incidence of aortic valve calcification and stenosis in ESRD patients on haemodialysis and association of uremia and dialysis related risk factors with A.V calcification and stenosis.

Two groups of patients were included in this study: First group:-Forty six ESRD patients on regular haemodialysis with age range (20-60yrs) were studied at The Irqi Dialysis Center / Baghdad Teaching Hospital. Second group:-Forty six patients with no renal disease, with age range(20-60yrs) as control group were studied in Out Patients/Echocardiography Unit of Baghdad Teaching Hospital . Echocardiography was done for all patients on non dialysis day.

Echocardiography is a sensitive and specific method for detection of aortic valve calcification [29].It was done by a single doctor. For aortic valve calcification, two dimensional echocardiography with M mode was performed via the parasternal long axis and short axis views to assess the aortic valve.

Aortic valve calcification is defined as bright echoes more than 1 mm on one or more cusp [30]. For A.V stenosis, two dimensional echocardiography was performed using parasternal long axis, short axis and apical 5 chamber views to assess any limitations of movement, thickening and doming of A.V cusps at the same time, two-dimensional echocardiography with continuous wave Doppler echocardiography was performed via the apical 5 chambers view to assess the transvalvular peak gradient. A.V stenosis is defined as decrease in valve excursion to less than 1.5 cm and transvalvular peak gradient more than 10 mm/Hg. and its severity classified according to the peak gradient into [30].

1) Mild (peak gradient between 10-20 mm/Hg).
2) Moderate (peak gradient between 20-64mm/Hg).
3) Sever (peak gradient above 64mm/Hg).

For all patients the following uremic and dialysis related risk factors were studied:

1) Haemodynamic factors which include:-
   a) Duration of haemodialysis in months.
   b) Number of hours of dialysis per week.
   c) Blood flow rate during haemodialysis.
2) Biochemical factors which include:-

a) Serum Calcium. b) Serum Phosphorous . c) Ca x PO4 product.

Statistical analysis: Data was collected and analyzed by using statistical package of social science (SPSS) version 10. By using t.test to compare means of two different group . Chi – squire test used to compare between frequency variable

Statistical significant is considered when p-value <0.05

RESULTS:

Table 1 shows that the incidence of A.V calcification was higher in ESRD patients in comparison to control. It was 30. % Vs 8.90% , statistical significant with p-value of 0.0085 .One ESRD patient with A.V calcification has A.V stenosis , statistical not significant with p-value of 0.5 .

The mean age for 1st group patients with AVC was 47.79 (range 36-60y) and that of 2nd group patient with AVC was 57.5 (range 54-60y) as shown in table 2. The means age of 1st group patients with AVC was 47.79 and mean age of ESRD patients without AVC was 37.35 years and the difference was statistically significant (P value 0.004).

Table 3 shows that the mean duration of haemdialysis of 1st group patients with AVC was longer (mean l18.86 months , range 9-28 months) than that of patients without AVC 8.19 months (1-26) , also the mean of number of hours of haemodialysis per week was more (7.29 versus 6). The table also shows the mean of blood flow rate during dialysis of ESRD patients with AVC was 216.43 ml/min and that of ESRD patients without AVC was 197.5 ml/min. The last Table (4) revealed that the mean of Ca x Po4 products in ESRD patients with AV calcification was 56.84 (range 49.2-66) versus 38.09 (range 24.12-64.26) in ESRD patients without AV calcification.

Table 1: Aortic Valve Calcification in Haemodialysis and Control Groups.

Study group	AVC No. (%)	AVC with stenosis No. (%)
Haemodialysis (46)	14 (30 %) *	1 (7.4%)**
Control Group (46)	4 (8.9%)	0 (0%)

* p value 0.0085 (statistically significant)
** p value 0.5 (statistically not significant)

Table 2: Age and mean age of Hemodialysis and Control groups .

Group	With AVC	Without AVC	P value
Haemodialysis Age(mean year)	47.79 (36-60)	37.47 (20-60)	0.004
Control Age(mean year)	57.5 (54-60)	57.95 (54-60)	-
P value	0.038	-	

Table 3: Hemodynamic risk factor in Haemodialysis patients with and without Aortic Valve Calcification.

Hemodynamic factors	Haemodialysis patients with AVC	Haemodialysis patients without AVC	P value
Hours of dialysis/ wk Mean (range)	7.79 (6 - 9)	6 (3 - 9)	0.02
Duration of haemodialysis in months Mean (range)	18.86 (9 -28)	8.19 (1-26)	< 0.001
Blood flow rate ml/min Mean (range)	216.43 (200- 250)	197.5 (150-250)	0.035

Table 4: Biochemical risk factor in Haemodialysis patients with and without AVC.

Biochemical risk factor	Haemodialysis patients with AVC	Haemodialysis patients without AVC	P Value
Serum Calcium mg/dl Mean(range)	9.18 (8.2 - 10.6)	8.44 (6.5-10.4)	0.015
Serum Phosphorous mg/dl Mean(range)	6.24 (5.6- 7.4)	4.53 (3.2- 6.3)	< 0.001
Product of Ca x po4 Mean(range)	56.84 (49.2-66)	38.09 (24.12-64.26)	< 0.001

DISCUSSION:

In this study we demonstrate the incidence of A.V calcification in ESRD patients on regular haemodialysis and non uremic control patients and the relation of the uremic and haemodialysis related factors with these calcification.

Regarding the prevalence, our study showed a higher prevalence of AVC in haemodialysis patients (30.4%) in comparison with control group (8.9%) which was statistically significant. This result is comparable with result of the Ribeiro S et al study[24] which showed that incidence of A.V calcification in haemodialysis patients was 25-55%. Our result was different from an Iraqi study done by Nabeel F Suliaman et al [30] which showed that the incidence of A.V calcification in haemodialysis patients was 5% and this difference could be explained by the limited number of patients in this study and difference in risk factors (as duration of haemodialysis) which was not mentioned in this study.

Regarding A.V stenosis , one patient (7.1 %) of ESRD patients with AVC have hemodynamically significant aortic valve stenosis .This result is comparable with the result of Urena P,et al study [22] which showed the prevalence of A.V stenosis in haemodialysis patients was 3-9%. However it was not statistically signification with comparism with non uremic patients in our study, this may be due to limited numbers of patients .

Regarding the age, our study showed that, the mean age of haemodialysis patient with AVC was less than that of non uremic patients with AVC (47.79 versus 57.5 years) which was statistically significant, so that A.V calcification in haemodialysis patients occurs earlier than patients with no renal disease due to presence of other factors related to haemodialysis This result is comparable with the results of Urena p et al study [22] which showed that A.V calcification in haemodialysis patient occurs 10-20 years earlier than in general population.

The mean age of haemodialysis patients with AVC was higher than that of haemodialysis patients without AVC which was statistically significant. This result is comparable with the result of Vincezo panuccio ,et al study [32] which showed that patients haemodialysis with AVC was older than those without AVC.

AVC in haemodialysis patient occurs earlier than in general population due to uremia and dialysis related risk factors which are either biochemical or hemodynamic ones. The disorders of Calcium (Ca+2) and Phosphate (PO4-3)metabolism and high Ca x PO4 product are the principle factors responsible for ectopic calcification in ESRD patients on haemodialysis. Cardiac valves are one of the common sites of metastatic calcification [11].

This study showed the mean of Ca x PO4 products in haemodialysis patient with AVC was higher than that in without AVC, which was statistically significant. This result is comparable with the result of London G M et al study [19]. Regarding the haemodynamic factors, there was a strong association between the duration of haemodialysis and AVC [20-21] because of more duration on haemodialysis, and more exposure to haemodynamic stress effect on A.V

Our study showed that the mean duration of haemodialysis (in months) and the mean numbers of hours of haemodialysis (per week) in haemodialysis patient with AVC was higher than that in those without calcification, which was statistically significant , this result is comparable with the result of Vincenzo panuccio, et al study [32].

Regarding blood flow rate during dialysis (ml/min), our study showed that the mean of blood flow rate during dialysis for haemodialysis patient with A.V C was higher than in those without , which was statistically significant. However the more blood flow rate during haemodialysis, the more

transvalvular velocity and the more stress on the valve which will accelerate the calcification

CONCLUSION :

We conclude that there was a high incidence of AVC and its complication in ESRD patients on haemodialysis. Aortic valve calcification in ESRD patients occurs earlier than in general population. ESRD patients with AVC were older than ESRD patients with non calcified aortic valve. Risk of AV and it's complication increase with increase duration of haemodialysis .

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