Cardiac valve sclerosis in patients with end stage renal failure

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تصلب الصمامات القلبية لدى المرضى الذين يعانون من فشـــل كلوي نهائي

الخلاصة

الخلفية والغرض المُجرّد

إنّ انتشار تصلب الصمامات القلبية لدى المرضى الذين يعانون من فشل كلوي مزمن ونهائي ، هو عالي ولكن المعلومات حول الأسباب التي تؤدي الى ذلك هي قليلة .

تصلب الصمامات القلبية له تأثيرات سلبية واضحة على حياة المرضى الذين يعانون من فشل كلوي مزمن .

الهدف من هذه الدراسة هو لمعرفة مدى انتشار تصلب الصمامات القلبية ومدى تاثير كل من العمر ، الجنس ، فترة ونوع الديلزة الكلويه ، نسبة كل من الكالسيوم ، الفوسفات ، الالبومين ، الكولسترول ، والترايكلسرايد ، حاصل ضرب الكالسيوم بالفوسفات ، بعض الادوية المتناولة من قبل المرضى والتي تشمل كل من حبوب الكالسيوم وفيتامين – D – وكذلك وجود كل من داء السكري وارتفاع ضغط الدم الشرياني على تصلب الصمامات القلبية عند هؤلاء المرضى .

الطرائق

تم اخذ عينة تتكون من ٦٠ مريض مصابون بالفشل الكلوي المزمن وتم فحصهم سريرياً بجهاز ايكو القلب للبحث عن وجود تصلب الصمامات القلبية . الفحوصات المختبرية التي تمت دراستها تشمل نسبة الكالسيوم ، الفوسفات ، الالبومين والدهون في الدم ، مع دراسة حاصل ضرب الكالسيوم بالفوسفات كذلك تم تقييم وجود او عدم وجود داء السكري وارتفاع ضغط الدم الشرياني لكل مريض . واخيراً تم تدوين عدد المرضى الذين يتناولون كل من دواء حبوب الكالسيوم وفيتامينD

تم اخذ عينه أخرى تتكون من ٦٠ شخص غير مصابين بمرض الفشل الكلوي وتم فحصهم بجهاز ايكو القلب للبحث عن تصلب الصمامات القلبية .

النتائج

نتيجة هذه الدراسة بينت ان تصلب الصمامات القلبية هي شائعة لدى المرضى المصابين بالفشل الكلوي المزمن والنهائي والمعتمدين على الديلزه الكلويه ، وان كل من عمر المرضى ، ارتفاع حاصل ضرب الكالسيوم بالفوسفات ، وهبوط نسبة الالبومين في الدم ، ارتفاع نسبة الترايكلسرايد في الدم وحبوب الكالسيوم المتناولة من قبل المرضى لها تأثير وعلاقة بحصول تصلب الصمامات القلبية عند هؤلاء المرضى .

الخاتمة

ان نتيجة هذه الدراسة اثبتت تأثير بعض العوامل في حدوث تصلب الصمامات القلبية لدى المرضى الذين يعانون من فشل كلوي مزمن وبالخصوص تقدم عمر المرضى ، ارتفاع حاصل ضرب الكالسيوم بالفوسفات ، وهبوط نسبة الالبومين في الدم ، ارتفاع نسبة الترايكلسرايد في الدم وادوية الكالسيوم المتناولة من قبل المرضى . ان الكشف المبكر عن العوامل التي يحتمل ان لها
تأثير في حدوث تصلب الصمامات القلبية عند هؤلاء المرضى ربما يمنع او يقلل حدة امراض القلب المصاحبة لتصلب الصمامات القلبية.

Abstract

Background:

The prevalence of cardiac valves sclerosis in end - stage renal disease patients is high and information regarding risk factors is scarce.Valvular heart sclerosis accounts for considerable morbidity and some mortality among patients with end stage renal disease

(ESRD).
the aims of this study were to determine the incidence of cardiac valve sclerosis and the impact of the age ,sex, duration and mode of dialysis , the presence or absence of hypertension and Diabetes mellitus, the product of serum calcium x phosphate, some medications taken by patients (including vitamin D analogue and oral calcium) and the levels of; serum cholesterol , serum triglyceride and serum albumin on the valvular sclerosis in these patients .

Methods:

sixty uremic patients were assessed echocardiographically for the presence of valve sclerosis ,medical records were reviewed to assess presence or absence of diabetes mellitus and hypertension in each patient, consumption of oral calcium and vitamin D analogue was also noted. finally, the laboratory parameters studied were serum calcium, serum, phosphate ,CA x PO4 product, lipid profile and serum albumin.
Another sixty non uremic control group were also assessed echocardiographically for the presence of the valve sclerosis.

Results:

the results of this study showed that valvular sclerosis were common in uremic patients requiring dialysis , and the age of the patients ,duration of dialysis, calcium x phosphate product , oral vitamine D analogue and calcium medication , hypertriglyceremia and hypoalbuminemia were related to the occurrence of valvular sclerosis in uremic patients.

Conclusion:

the results of this study confirm numerous risk factors for cardiac valve sclerosis in patients with chronic renal failure, specifically older age ,duration of dialysis , high CA x PO4 product , oral vitamine D analogue and calcium medication , hypertriglyceremia and hypoalbuminemia.
Early identification of factors that might be related to valve sclerosis in uremic patients may prevent or hinder the extent of cardiovascular events associated with valvular sclerosis.

Key words: Uremia, Aortic sclerosis, Mitral sclerosis.

Introduction

Chronic renal failure refers to an irreversible deterioration in renal function which classically develops over a period of years ,hypertension develops in approximately 80% of patients with chronic renal failure[1], hypercholesterolaemia is almost universal in patients with significant chronic renal failure and increased triglyceride levels are also common in patients with chronic renal failure [1-2].
valvular calcification in end stage renal failure patients is almost constantly associated with widespread calcification of the myocardium, aorta and large or medium-sized arteries including coronary arteries [3]. The degenerative (wear and tear) etiology appears to underlie the dystrophic calcification of cardiac valves [4], aortic valves are submitted to cyclic mechanical stress, renal failure and dialysis superimpose further pathomechanisms,end stage renal failure promotes valvular disease by hemodynamic and biochemical mechanisms, the role of systemic hypertension in the pathogenesis of cardiac valve calcification is uncertain, although a significant correlation was found in some [5], but not all studies [6,7] .
In the general population, both diabetes mellitus and hypercholesterolemia are risk factors for development of the valvular lesion [4,8].

The pathogenesis of cardiac valve sclerosis in Patients with end stage renal failure is not fully understood. Hyperparathyroidism, uncontrolled hyperphosphatemia and high calcium-phosphorus (CaXpo4) product, older age, hypertension, hypoalbuminemia and dyslipidemia are all suggested risk factors for cardiac valve sclerosis, but these factors are not the sole causes of valve sclerosis in patients with end stage renal disease [9].

Aims of the study are to determine the incidence of cardiac valve sclerosis in our uremic patients in Hilla city and to examine some possible aetiological factors for its occurrence, including; age and sex of the patients, duration and mode of dialysis, hypertension, diabetes mellitus,the levels of serum calcium, serum phosphate, the product of serum calcium x serum phosphate, serum cholesterol, serum triglyceride , serum albumin and some medications taken by the patients (vitamin D analogue and oral calcium).

Patients and Methods

The participants were 120 persons that were divided into two groups, the first group included 60 uremic patients (age ranged 17-79 years old and the mean age 51.12 ±15.97) , thirty of them were undergoing regular hemodialysis (15 men and 15 women , age ranged 17-64 years) ,another 30 patients were on recurrent peritoneal dialysis (16 men and 14 women, age ranged 22-78 years) at Marjan Hospital in Hilla Iraq. Patients with history of rheumatic or congenital heart disease were excluded from this study.

The other group included 60 non uremic ,not hypertensive and not diabetic control persons who had negative past medical history of rheumatic or congenital heart disease (age ranged 16-80 years old and the mean age; 49.23±13.87) who were 32 men and 28 women and they were matched for both age and sex with the uremic patients group.

The time of the study started from May 2009 to December 2009

Full history was taken regarding age, sex, presence of diabetes mellitus(the patient was considered diabetic if he had history of the disease or using anti hyperglycemic drugs or if the fasting blood sugar was >126 mg\dl(>7mml\dl) or random blood sugar >11 mml/dl(>200 mg/dl) [1], presence of hypertension (the patient was considered hypertensive if he had history of the disease ,using anti hypertensive medications or if the blood pressure was ≥140\90 mmHg) [1], duration of dialysis, mode of dialysis (haemo or peritoneal) and whether they were using vit D analogue and oral calcium drugs.

In each patient fasting venous blood sample was drown , the laboratory parameters studied were serum calcium ,serum phosphate ,CAXPO4 product , lipid profile (total cholesterol and triglyceride) and serum albumin. These biochemical parameters were measured by colorimetric methods

Two – dimensional echocardiography was performed in each case using an envisor HDI 5000 machine (Philips, Germany) with 2-4 MHz probe .each subject was examined in left decubitus position.

Cardiac valve sclerosis was defined as bright echoes of more than 1 mm diameter on one or more cusps of the mitral or aortic valve , or both. The participants were classified according to the echocardiographic findings into two subgroups one comprising individuals with valves sclerosis and other comprising individuals without valve sclerosis.

Statistical analysis

Correlation between variables assessed by chi square , P value < 0.05 is considered

significant. Spss version 15 is used to calculate statistical correlation.

Results

Echocardiography revealed valve sclerosis in 17 (28.33%) of the sixty uremic patients, in the hemodialysis group echocardiography revealed valve sclerosis in10(33.3%) of the thirty patients in whom one patient (3.3%) had mitral valve sclerosis , 7 patients (23.3%) had aortic valve sclerosis, and 2 patients (6.6%) had sclerosis of both valves .

In peritoneal dialysis patients, 7 cases (23.3%) of the thirty patients had valve sclerosis , one patient (3.3%) had mitral valve sclerosis , 5 patients (16.6%) had aortic valve sclerosis, and one patient (3.3%) had sclerosis of both valves.

In the control group the echocardiography revealed valve sclerosis in 3 (5%) persons (all of them were in the aortic valve) which was less than the valve sclerosis in the uremic patients (P value < 0.05)table(1).

Table 2 shows that there was no significant difference in the occurrence of the cardiac valve sclerosis in both sex (males and females) (P value > 0.05) but the patients with valve sclerosis were significantly older than those without valve sclerosis (P value < 0.05), There was no significant correlation between presence of diabetes mellitus and valve sclerosis (P value > 0.05) and there was also no significant correlation between the presence of hypertension and valve sclerosis (P value > 0.05) .

Table 3 shows that the duration of dialysis(ranged from 8 months up to 108 months in haemodialysis and from 1 month up 36 months in peritoneal dialysis) was not significantly correlated with the frequency of the valve sclerosis (P value < 0.05) and there was no significant difference in the frequency of valve sclerosis between the patients who were on hemodialysis mode or the recurrent peritoneal dialysis (P value > 0.05).

Table 4 shows that There was significant correlation between the vitamin D analogue which was taken by the uremic patients and the occurrence of valve sclerosis (P value < 0.05) ,there was significant correlation between the occurrence of cardiac valve sclerosis and the intake of the oral calcium medication (P value < 0.05) and the patients whom they had valve sclerosis had significantly higher level of CaXp04 product.

Table 5 shows that there was no significant correlation between the occurrence of cardiac valve sclerosis and the level of cholesterol (P value>0.05) but there was significant correlation between the the level of triglyceride and valve sclerosis (P value <0.05) and there was significant correlation between level of albumin and the occurrence of valve sclerosis (P value<0.05) .

Table (1) incidence of valve sclerosis in uremic patients and control group

	uremic patients No. 60	Control group No. 60
No valve sclerosis	43 (71.6%)	57 (95%)
Valve sclerosis	17 (28.3%)	3 (5%)

P 0.0006

Table (2) shows the relation of sex, age, presence of diabetes mellitus and hypertension with occurrence of valve sclerosis in uremic patients

Variable	NoValve sclerosis No. 43	Valve sclerosis No. 17	P value
Male / female	22 / 21	9 / 8	0.9011
Age (year)	44 ∓ 14	56 ∓ 13	0.0034
Diabetes mellitus	9	3	0.7745
Hypertension	23	12	0.2260

Table (3) shows the effect of duration and mode of dialysis on occurrence of valve sclerosis in uremic patients

Variable	No Valve sclerosis No. 43	Valve sclerosis No. 17	P value
Duration (month)	29 ∓ 3	33 ∓ 4	0.0001
Haemodialysis / peritoneal dialysis	20 / 23	10 / 7	0.3901

Table (4) shows the effect of using vit D analogue, calcium drug and level of $CAXPO_4$ on the occurrence of valve sclerosis in uremic patients

Variable	No Valve sclerosis No. 43	Valve sclerosis No. 17	P value
Vit D	39	12	0.0493
Calcium	37	10	0.0211
$CAXPO_4$ level	29 ∓ 1.1	4.8 ∓ 1.4	0.0001

Table (5) shows the relation between level of cholestrol, triglyceride and albumin with the occurrence of valve sclerosis in uremic patients

Variable	No Valve sclerosis No. 43	Valve sclerosis No. 17	P value
S. cholesterol	4.4 ∓ 0.8	4.1 ∓ 1.2	0.2637
S.Triglyceride	1.1 ∓ 0.3	2.3 ∓ 0.9	0.0001
S. albumin	38.01 ∓ 2.33	24.23 ∓ 5.81	0.0001

Discussion

The majority of cardiac valvular sclerosis observed in patients with renal failure are acquired, mostly secondary to dystrophic calcification of valvular annulus,cardiac valve sclerosis is a common complication of long term dialysis patients [10].

The echocardiography results from this study showed that the frequency of valve calcification in uremic patients was 28.33%, (33.3% in hemodialysis and 23.3% in peritoneal dialysis).

Previous studies based on imaging and echocardiography findings had revealed that the prevalence of calcification of aortic and mitral valves in uremic patients ranges from 30% to 50% [11,12].

Brown and co-workers reported that two-thirds of adult patients on hemodialysis had electron-beam computed tomography evidence of coronary artery calcification, and that more than one half of these individual also had cardiac valve sclerosis [13].

In accordance with previous findings [14] , our data revealed that calcification of heart valves was a frequent finding among hemodialysis and peritoneal dialysis patients and was more common than the valve sclerosis in the general population.

The reported prevalence of aortic valve sclerosis in hemodialysis patients ranged from 28% to 55% and from 10% to 40% of mitral valve [15,16].

The reported prevalence of valvular sclerosis in peritoneal dialysis patients ranged from 30% to 40% , 50%-70% affect the mitral valve and 30%-50% affect the aortic valve , this study revealed a higher frequency of aortic valve sclerosis alone (23.3% in hemodialysis , 16.6% peritoneal dialysis) than mitral valve sclerosis alone (3.3% in hemodialysis , 3.3% in peritoneal dialysis).

As with other study [14], there was no significant difference in the occurrence of valve sclerosis in both sexes.

Consistence with previous studies [11,13,16], our patients with valve sclerosis were older and there was significant correlation between older age group and frequency of valve sclerosis.

Age of patients who had valve sclerosis was lower than average age at which person in the general population develop these lesions compared with findings in the population with the normal renal function , cardiac valve calcification is more frequent and occur at younger age in uremic patients [15].

Increased atherosclerosis in patients undergoing dialysis and factors associated with dialysis treatment itself, may explain why cardiac valve sclerosis occurs at younger age in the uremic patients than in the general population [14].

In some studies, there is significant correlation between valve sclerosis and diabetes mellitus [17], but in other studies [14], as in our study there was no significant correlation between them probably because of the small number of the sample taken in this study.

Hypertensive nephrosclerosis is a presumed cause of end stage renal disease. The United State Renal Data system and European and Latin American registries have provided recent data on patients starting renal replacement therapy, and the statistics indicate that hypertensive nephrosclerosis is a frequent and increasingly important cause of this condition [18,19].

Hypertension is a major risk factor for atherosclerosis and an association between hypertension and valve calcification in uremic patients has been established. This suggests that good control of blood pressure in uremic patients may prevent progression of cardiac valve sclerosis [13,14].

In this study, there was no significant correlation between high blood pressure and the occurrence of valve sclerosis, probably because of the small number of the patients taken in this study.

In previous studies as in this study there was significant correlation between the

duration of dialysis and the prevalence of the cardiac valve sclerosis [20,21,22] for longer duration of the disease and dialysis makes the valves expose more to haemodynamic and biochemical mechansims that result in valve sclerosis.

The previous researches revealed no significant difference in the prevalence of the cardiac valve sclerosis between the two dialysis mode , the hemodialysis and peritoneal dialysis [15,17] and this was also observed in this study.

Disturbance of CAxPO4 metabolism is a well known contributor to the development of cardiac valve sclerosis in uremic patient.Uncontrolled hyperphosphatemia and high CAxPO4 product are established risk factors for cardiovascular calcifications, cardiac ischemia, and adverse cardiovascular outcomes in end stage renal disease patients [23,24,25]. In this study, high CAxPO4 product was associated with the presence of the valve sclerosis.

In this study, there was significant correlation with the intake of oral vitamin D analogue and valve sclerosis similar to other studies [14] and there was significant correlation between the intake of the oral calcium medication and the occurrence of valve sclerosis as with other study [25], increasing use of calcitriol and calcium-containing phosphate binders increases the enteral calcium absorption and may favor the development of hypercalcemia, increased CAXPO4 product, adynamic bone disease, and secondary hyperphosphatemia, all of these conditions favor the development of valvular calcifications[6].

In one study there was significant correlation between dyslipidemia and valve sclerosis [25] and in another study [23] there was no correlation between them, in this study there was significant correlation with hypertriglyceremia but not with hypercholesterolemia.According to recent studies, atherogenesis and presumably also degenerative disease of the aortic valves involve accumulation of lipids; oxidized LDL in particular is associated with a chronic inflammatory process with accumulation of macrophages and T lymphocytes and culminates in calcium deposits [26,27].

Some studies found no significant correlation between valve sclerosis and hypoalbuminemia [14,23]while other study[21] like our study found significant correlation between valve sclerosis and hypoalbuminemia, the pathogenesis by which hypoalbuminemia affect the valve sclerosis is vague.

Previous researchs had demonstrated a significant correlation between valve sclerosis and increased atherosclerosis in end stage renal disease [28,29,30,31]. In addition, an association between atherosclerosis and inflammation has been reported in dialyzed patients [32].Mohler and co-workers found that cardiac valve sclerosis lesions in this patients group have features that are also seen in arterial atherosclerosis plaque, specifically infiltration with inflammatory cells, lipoproteins, and calcium deposits in arterial walls [20].Previous researches suggest that valvular calcification may be a manifestation of atherosclerosis and may be considered as having similar pathogenic and prognostic significance as the other atherosclerotic complications [17].

Limitations of this study include the use of echocardiography instead of electron beam computed tomography to detect calcification, but despite this limitation, the echocardiography is more widely available, easier to perform and has no radiation .We defined the presence but not severity of valvular calcification, because assessing the severity of valvular calcification by echocardiography is very subjective and can be inaccurate.

Conclusion and Recommendations:

There is increased incidence of cardiac valve sclerosis in patients with end stage renal disease who are on renal replacement therapy (hemodialysis and peritoneal dialysis), and this is more common than the cardiac valve sclerosis in the general population,

older age group,duration of dialysis, elevated CAxPO4 product, oral vitamine D analogue and calcium medication, hypertriglyceremia and hypoalbuminemia are significantly associated with development of valve sclerosis while sex, mode of dialysis, hypertension, diabetes mellitus and hypercholesterolemia are not associated with development of valve sclerosis and so we recommend the use of echocardiography to assess possible valvular heart sclerosis in end stage renal disease for early identification and treatment of factors that might be related to valve sclerosis in dialyzed patients may prevent or retard the progression of the cardiovascular events associated with valve sclerosis. Additional prospective-controlled studies are warranted to confirm these results.

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