The Egyptian Journal of Hospital Medicine (July 2017) Vol.68 (1), Page 1059-1068

The Relationship between Abdominal Aortic Calcification and Cardiac Abnormalities in Hemodialysis Patients

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ABSTRACT

Background: Abdominal aortic calcification (AAC) is a marker of subclinical atherosclerotic disease and an independent predictor of subsequent vascular morbidity and mortality.

Aim of the work: This study was conducted to investigate the association of abdominal aortic calcification with cardiac abnormalitiesin hemodialysispatient (HD).

Methods: This cross-sectionalobservational study wasperformed on 90 patients (50 males and 40 females)with chronic kidney disease, stage 5 (CKD)of varying etiologies from hemodialysis unit at Al-Hussein UniversityHospital. They wereundergoing regularhemodialysis for more than 6 monthes.Laboratory investigations were done including liver function tests, kidney function tests,complete blood count (CBC),C-reactive protein (CRP), fasting and random blood glucose,lipid profile, calcium, phosphorus,calcium phosphate productandparathormone(PTH).In addition, Echocardiography and X-ray plain radiography were determined.

Results: Out of 90 HD patients, 37 patients (41.1 %) had valvular calcification, all of them (41.1 %) had aortic valve calcifications and AAC score exceeded 6. Only 7 patients (7.8%)had mitral valve calcifications. Moreover, cases with mitral valve calcifications had aortic valve calcification and AAC score above 12. Seven patients (7.8 %) had mild**aortic regurgitation** (AR)and 4 patients (4.44%) had aortic stenosis.

Conclusion: AAC precedes the occurrence of cardiac abnormalities in HD patients and has been shown to have significant prognostic significance for cardiovascular events and mortality.

Keywords: Abdominal, Calcification, Cardiac, kidney disease, Chronic, Radiography.

INTRODUCTION

Vascular calcification (VC) is a common complication associatedwith chronic kidney disease (CKD) and the major cause of cardiovascular disease (CVD) in the patients with end stage renal disease (ESRD)[(1)].Furthermore, patients with chronic kidney disease exhibitaccelerated calcification of the intima, media, heart valves and likely the myocardium as well as the rare condition of calcificuraemic arteriolopathy (calciphylaxis)[(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 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 independant risk factor for mortality among those patients [(5)]. In addition, hyperphosphatemia is a key regulator involved in multiple mechanisms that induce and promote the progression of VC. Therefore, prevention of MBD and lowering the circulating levels of phosphate and calcium have become major targets in the treatment of VC [(6,7)]. 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 [(8)].

Calcification of the aortic and mitral valve on echocardiography has been linked to coronary atherosclerosis in the general population and carotid intima-media thickness (an indirect marker of atherosclerosis) among patients undergoing haemodialysis , suggesting that vascular andvalvular calcification might share common pathogenetic mechanisms[(9)].

Structural and functional cardiac abnormalities are common in patients with CKD. 70–80% of CKD‐5D patients have abnormal left ventricular (LV) structure and/or function and 74% of CKD stage 5 patients show evidence of LV hypertrophy (LVH) at the initiation of renal replacement therapy[(10)].

Therefore, this study wasperformed to assess the abdominal aortic calcification and to find out its relation to cardiac abnormalities in HD patients.

Received: 01 / 04 /2017
Accepted: 10 / 04 /2017
DOI : 10.12816/0038209

PATIENTS AND METHODS

This study included 90 subjects.They were divided into three groups as follow: **Group (I):** Included 30 patients (9) males and (21) females with mean age (39.1 ±4.72 years) and with mean hemodialysis duration (38.63 ±58.17 months). **Group (II):**Included 60 patients (41) males and (19) females with mean age (51.92 ±4.17 years) and with mean hemodialysis duration (86 ±56.55 months). **Group (II) were sub-classified into three subgroups based on AAC score as follow: Group IIa (score from 1 to 6)** Included 34 patients (28) males and (6) females with mean age (52.4 ± 3.75 years) and with mean hemodialysis duration (61.97±47.2 months). **Group IIb(score from 7 to 12)** Included 19 patients (9) males and (10) females with mean age (51.1 ± 5.2 years)and with mean hemodialysis duration (98.5 ±44 months).**Group IIc (score above 12)** Included 7 patients (4) males and (3) females with mean age (52 ± 2.9 years)and with mean hemodialysis duration (173± 28 months).

***** The protocol was explained to the patients and informed consent for all patients was obtained. This information on age, gender, duration of dialysis, diabetic status, and smoking (non-smoker, current or past smoker) of all patients on hemodialysis.

*The inclusion criteria were age ranged from 18 to 60yearswith CKD (stage 5) on maintenance heamodialysis for at least 12 month es.Exclusion criteria were patients with old myocardial infraction, rheumatic or congenital heart diseases and those with history of kidney transplantation.

* Laboratory investigations were done including liver function tests, kidney function tests, Hemoglobin percent (HB%), lipid profile, calcium, phosphorus, calcium phosphate product and parathormone (PTH). In addition, Echocardiography and X-ray plain radiography were determined.

The study was done after approval of ethical board of Al-Azhar university and an informed written consent was taken from each participant in the study.

Statistical Analysis

Statistical analyses were performed using SPSS version20.0. Quantitative data were expressed as mean± sta ndard deviation (SD).
Qualitative data were expressed as frequency a nd percentage.Indepndant t-test of segnificance was used when comparing between two mean. ANOVA test for comparing more than two groups.

RESULTS

A total of 90 patients on regular HD(50 males and 40 females) fulfilling the inclusion and exclusion criteriawere included into the study.14 patients had diabetes mellitus(DM)and 36 patientshad hypertension (HTN), while18 patients were smokers as shown in **figures1,2 and** only 15.55%were diabetics **(fig.1)**. In addition, 40% of the study population were hypertensive **(fig. 2)**.Also, only20% of the study population were smokers**(fig. 3).**Moreover, 37 patients (41.1 %) had valvular calcification and hadaortic valve calcifications with AAC score exceeded 6.

On the other hand,7 patients(7.8%) had mitral valve calcifications. Population with mitral valve calcifications had aortic valve calcification and AAC score above 12. Seven patients (7.8 %) had mild aortic regurgitation and 4 patients (4.44%) had aortic stenosis as shown in **figure(4)**.Furthermore, patients without AAC had no valvular calcification either aortic or mitral. No patients had pulmonaryor tricuspid valve calcification. The duration of dialysis in group II patients was statistically significant higher than that of group I as shown in **figure(5)and table (1).** Moreover,the left ventricular end systolic diameter in group II patients (4.31 ± 1.01) was statistically significant higher than that of group I(3.48 ± 0.72). Also, the left ventricular end diastolic diameter in group II patients (5.84 ± 0.68) was statistically significant higher than that of group I (5.09 ± 0.43 **)(Fig. 6& table 2)**.

However, the mean of age, dialysis duration and Serum calcium of patients with valvular calcification (52.32 ± 4.44, 106.24 ± 57.18 and 8.71 ± 0.67 respectively) were statistically significant higher than those of patients who don't have valvular calcification (44.38 ± 7.43, 56.7 ± 38.45 and 8.62 ± 0.98, p 0.001, 0.001, 0.05 respectively) as shown in**figure (7) and table (3)**. The mean of ejection fraction and abdominal aorta calcification score in patients with valvular calcification (58.03 ± 6.43 and 8.22 ± 3.54 respectively) were statistically significant higher than those of patients who don't have valvular calcification (57.68 ± 5.19 and 1.28 ± 1.68 and 8.62 ± 0.98) as shown in **figure(8)and table (4)**. The data of **figure (9) and table (5)**showing a statistically significant higher mean duration of dialysis in patients with sever abdominal aortic calcification (173.14 ±

28.45) in comparison to other groups.**Figure (10) and table(6)** showing a statistically significant higher mean ejection fraction in patients with sever abdominal aortic calcification (62.43±4.12) in comparison to other groups, p = 0.01. It's also showing a statistically significant higher mean left ventricular mass index in patients with moderate abdominal aortic calcification (177.32±11.46) in comparison to other groups. It's finally showing It's also showing a statistically significant higher mean AAC score in patients with sever abdominal aortic calcification (13.86 + 0.9) in comparison to other groups.

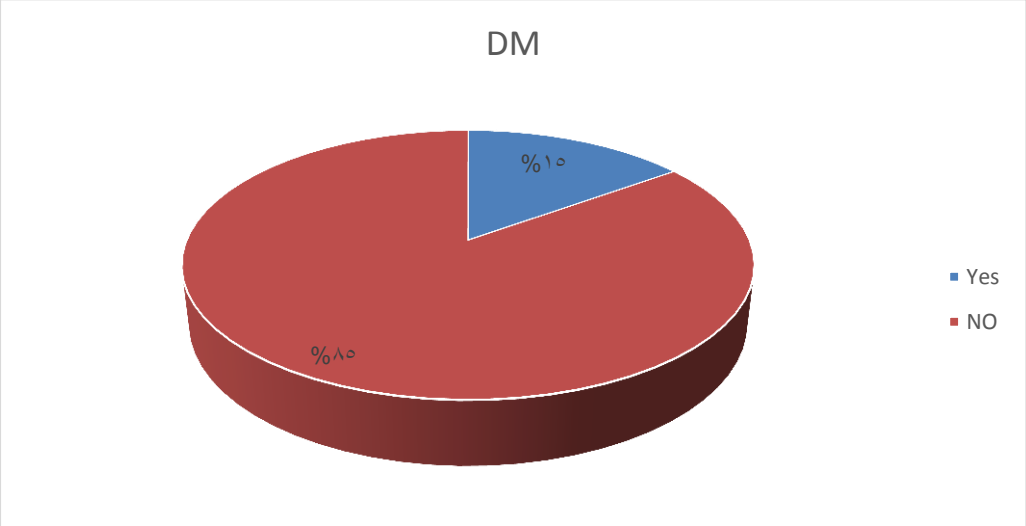

Figure (1): Distribution of the study population according to being DM patients

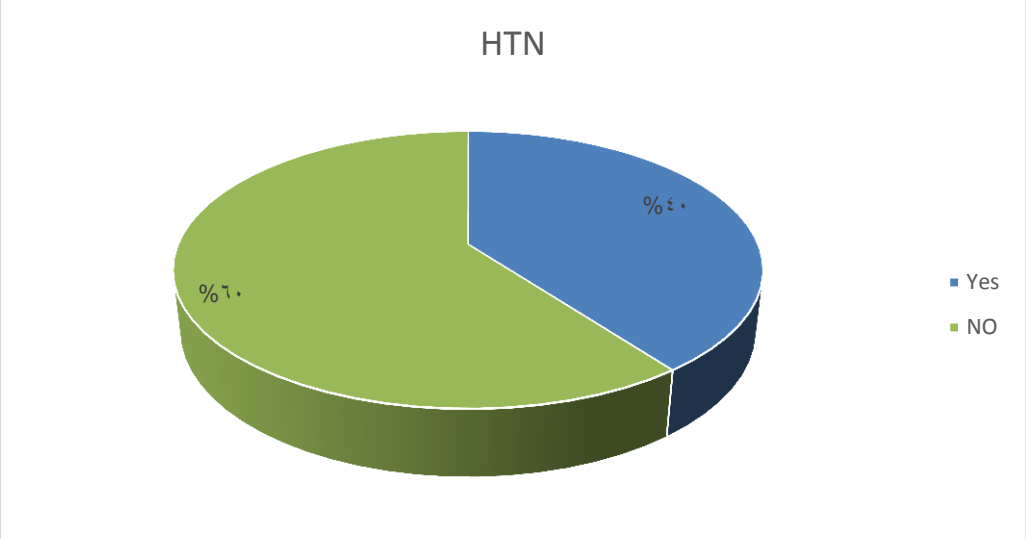

Figure (2): Distribution of the study population according to being HTN patients

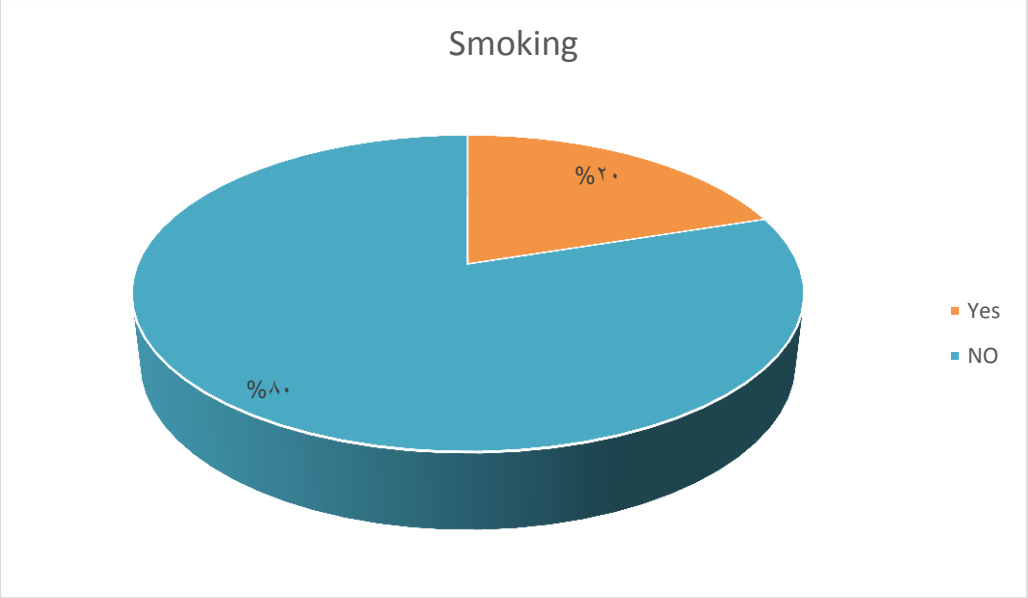

Figure (3): Distribution of the study population according to their smoking status

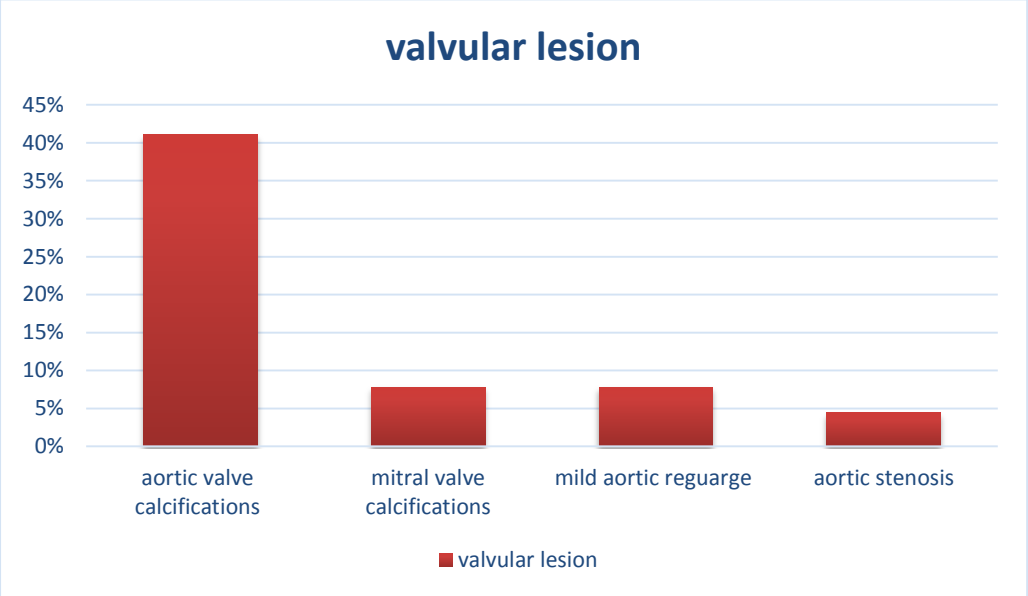

Figure (4): Distribution of our study population in terms of their valvular lesion.

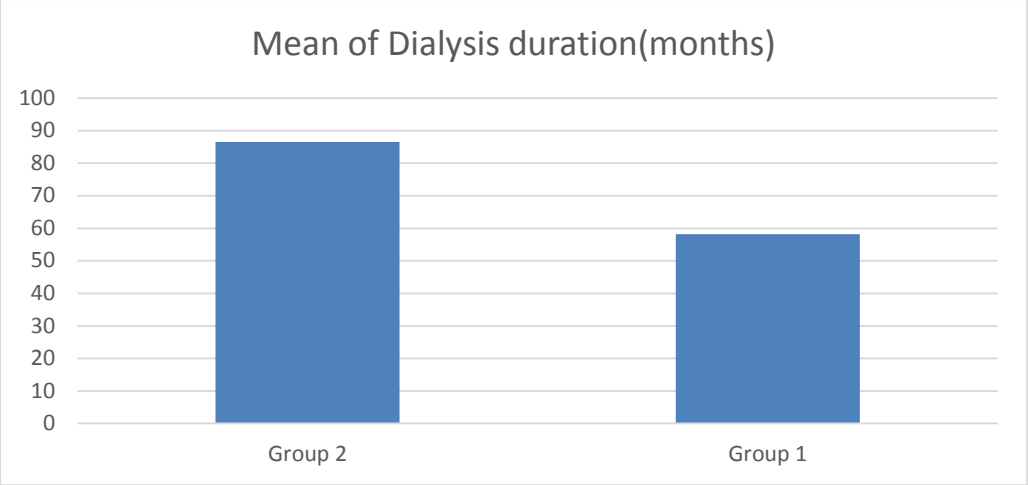

Figure (5): Comparison between the two study groups in terms of the mean duration of dialysis

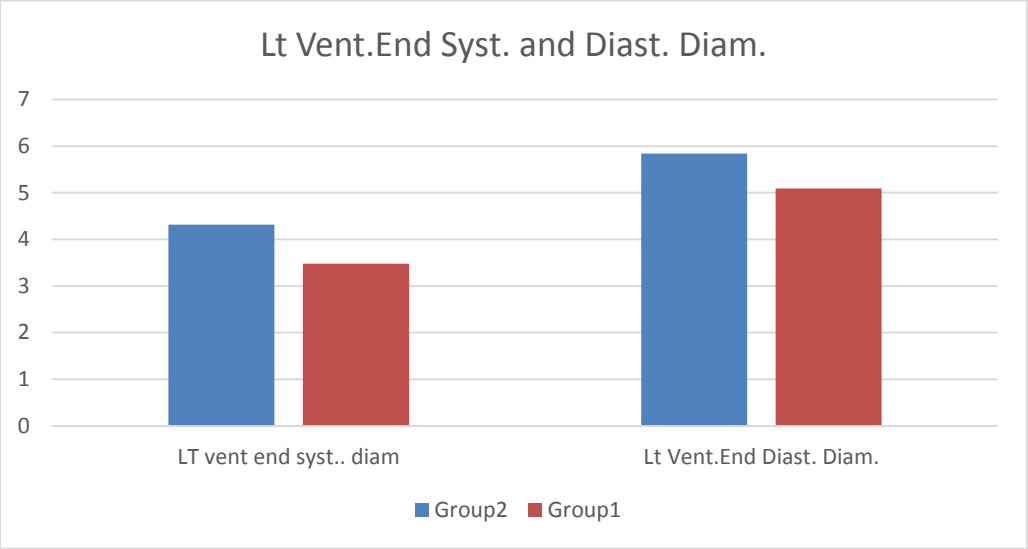

Figure (6): Comparison between the two study groups in terms of left ventricular end systolic and diastolic diameters

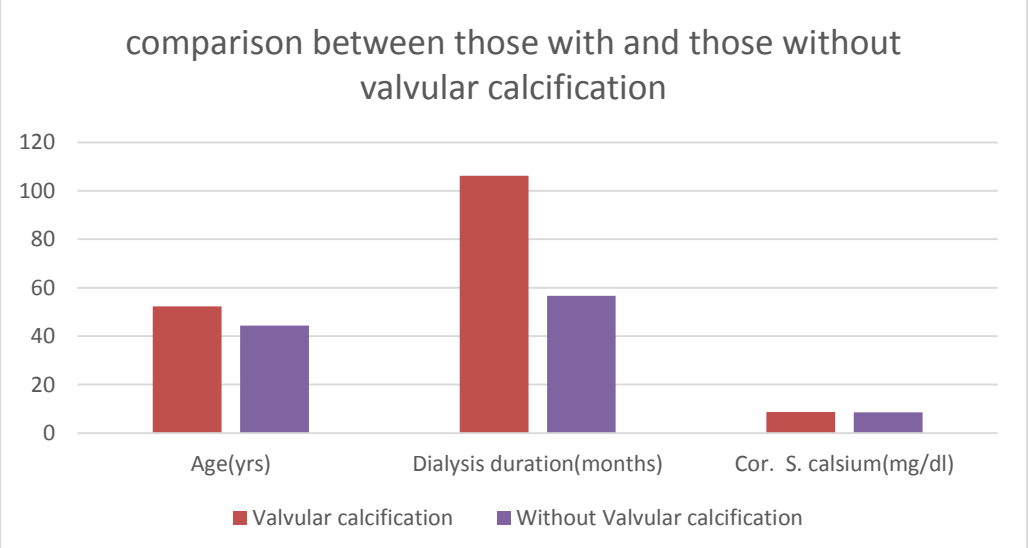

Figure (7): Comparison between the study population when classified according to presence of valvular calcification in terms of clinical and laboratory findings.

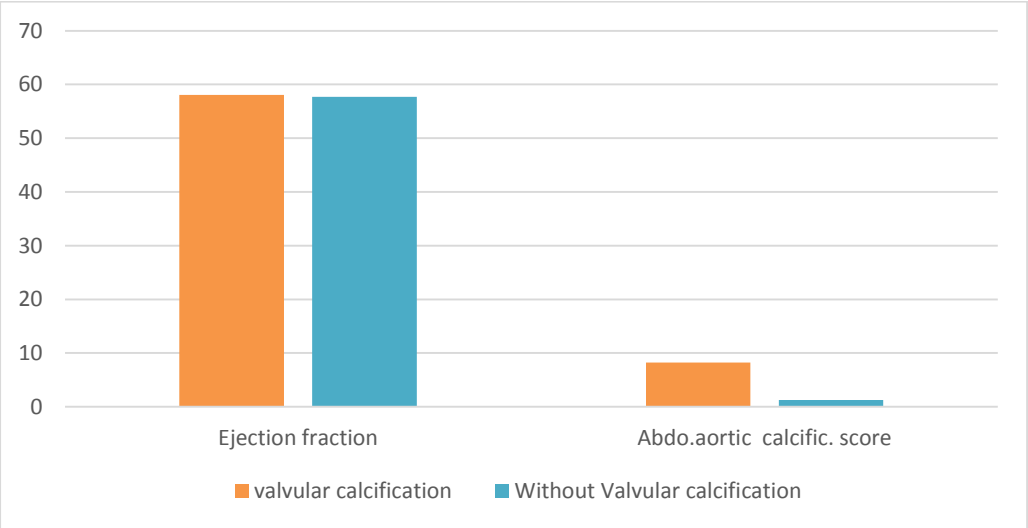

Figure (8): Comparison between the study population when classified according to presence of valvular calcification in terms of echocardiography findings.

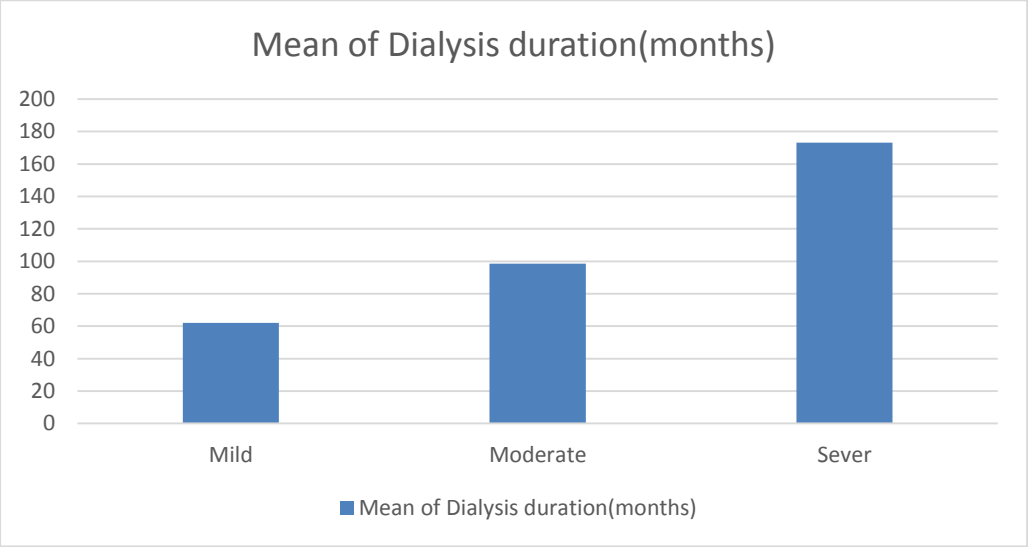

Figure (9): Comparison between grades of abdominal aorta calcification severity in terms of mean dialysis duration.

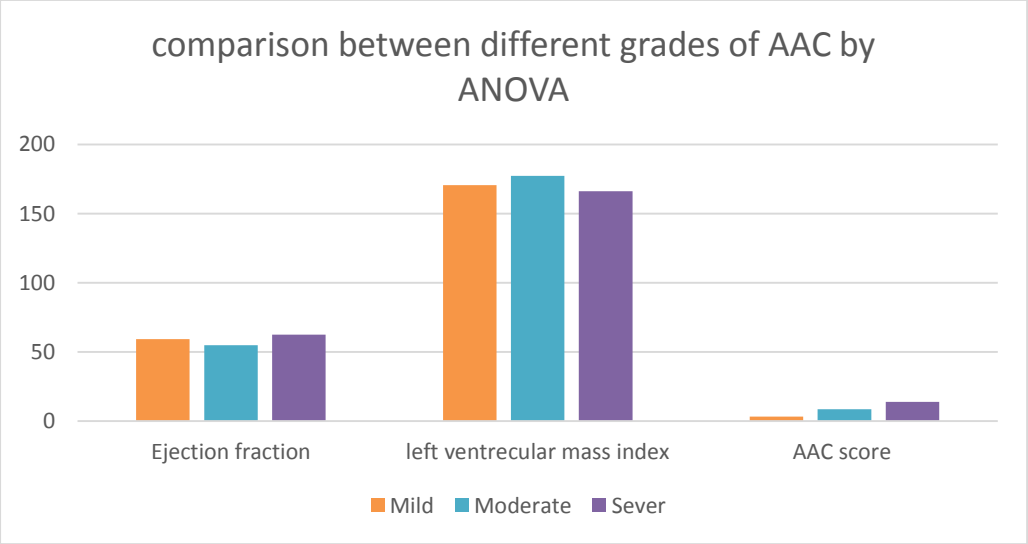

Figure (10): Comparison between different grades of Abdominal aortic calcification in terms of echocardiography findings

Table (1): Comparison between group I and group II as regard clinical and laboratory parameters.

	Group 2(N60)		Group 1(N30)		P value
	Mean	**SD**	**Mean**	**SD**	
Age(yrs)	51.9167	4.16723	39.1000	4.72229	NS
Dialysis duration(months)	86.52	56.551	58.17	38.632	.001
Kt/V	1.1250	.07120	1.1213	.07731	NS
Total cholesterol(mg/dl)	170.8583	38.87	169.5933	52.15969	NS
LDL(mg/dl)	127.8000	14.34	124.4667	17.13785	NS
HDL(mg/dl)	38.7933	5.40169	39.1667	6.33177	NS
Triglyserides(mg/dl)	146.4017	34.51	140.2333	31.91655	NS
Intact parathermone(pg/dl)	368.6217	348.03	489.6700	348.03929	NS
Corrected calcium(mg/dl)	8.7182	.81226	8.5400	.95072	NS
Phosphorus(mg/dl)	4.9942	1.27930	5.1100	1.21410	NS
Ca Phos Product	43.3250	10.95	43.1947	9.54224	NS
Potassium(mg/dl)	4.2050	.36750	4.1833	.39399	NS
Albumen(g/dl)	3.9433	.35719	3.9433	.45310	NS
Creatinin(mg/dl)	8.0217	1.75703	7.5233	1.35867	NS
Urea(mg/dl)	128.4833	36.76	126.5667	45.68081	NS
Hemoglobin(g/dl)	10.1100	1.07067	10.0400	1.09532	NS

Independent t-test. Data were represented as mean + SD
P≤0.05 significant.P≤0.001 considered highly significant. p >0.05 considered non-significant (NS).

Table (2): Comparison between group I and group II as regard Echocardiography findings.

	Group 2(N60)		Group 1(N30)		P value
	Mean	**SD**	**Mean**	**SD**	
Intervent. septal thickness	10.3517	.52448	10.4567	.54246	NS
Posteriow wall thickness	11.4600	.36786	11.5800	.42702	NS
left ventrecular mass index	172.1833	9.69622	172.4667	10.22078	NS
LT vent end syst..diam	4.3133	1.01187	3.4767	.72430	.04
Lt Vent.EndDiast. Diam.	5.8400	.67853	5.0900	.43419	.05
Fraction shortening	31.8000	7.23176	36.2000	5.65929	NS
Ejection fraction	58.1667	6.09019	57.1333	4.84756	NS

Independent t-test. Data were represented as mean + SD
P ≤0.05 significant.P≤0.001 considered highly significant. p >0.05 considered non-significant (NS).

Table (3) comparison between those with and those without valvular calcification as regard clinical and laboratory parameters.

	Valvular calcification(37)		Without valvular calcification(53)		P value
	Mean	**SD**	**Mean**	**SD**	
Age(yrs)	52.32	4.44	44.38	7.43	.001
Dialysis duration(months)	106.24	57.18	56.70	38.45	.001
Kt/V	1.14	.070	1.11	.074	NS
Total cholesterol(mg/dl)	162.75	31.50	175.8	49.74	NS
LDL(mg/dl)	129.78	15.51	124.53	14.95	NS
HDL(mg/dl)	38.26	4.59	39.38	6.36	NS
Triglyserides(mg/dl)	152.37	34.33	138.74	32.25	NS
Intact parathermone(pg/dl)	385.3	306.4	425.5	336.4	NS
Corrected calcium(mg/dl)	8.71	.67	8.62	.98	.05
Phosphorus(mg/dl)	4.93	1.38	5.10	1.17	NS
Ca Phos Product	42.65	11.18	43.72	9.99	NS
Potassium(mg/dl)	4.16	.35	4.22	.39	NS
Albumen(g/dl)	3.95	.34	3.94	.43	NS
Creatinin(mg/dl)	8.45	1.98	7.44	1.22	.01
Urea(mg/dl)	125.19	34.47	129.70	43.21	NS
Hemoglobin(g/dl)	10.24	1.014	9.98	1.11	NS

Independent t-test. Data were represented as mean + SD, P ≤0.05 significant.P≤0.001 considered highly significant.
p >0.05 considered non-significant (NS).

Table (4) comparison between those with and those without valvular calcification as regard Echocardiography findings.

	Valvular Calcification(37)		Without valvular calcification(53)		P value
	Mean	**SD**	**Mean**	**SD**	
Intervent.. septal thickness	10.31	.51	10.44	.54	NS
Posteriow wall thickness	11.47	.39	11.52	.39	NS
left vent.mass index	172.54	10.99	172.10	9.01	NS
LT vent end syst..diam	4.62	.89	3.62	.87	NS
Lt Vent.EndDiast. Diam.	5.91	.61	5.37	.69	NS
Fraction shortening	30.89	7.43	34.93	6.29	NS
Ejection fraction	58.03	6.43	57.68	5.19	.02
Abdo.aortic calcific. score	8.22	3.54	1.28	1.68	0.001

Independent t-test. Data were represented as mean + SD
P ≤0.05 significant.P≤0.001 considered highly significant. p >0.05 considered non-significant (NS).

Table(5) comparison between different grades of Abdominal aortic calcification as regard clinical and laboratoty parameters.

	Severe		**Moderate**		**Mild**		**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Age(yrs)	**52.38**	**3.75**	**51.11**	**5.22**	**51.86**	**2.91**	NS
Dialysis duration(months)	**61.97**	**47.23**	**98.53**	**43.76**	**173.14**	**28.45**	**0.01**
Kt/V	**1.12**	**.07**	**1.13**	**0.08**	**1.13**	**.08**	NS
Hemoglobin(g/dl)	**10.02**	**1.08**	**10.04**	**1.01**	**10.77**	**1.13**	NS
Urea(mg/dl)	**133.35**	**40.79**	**127.63**	**28.4**	**107.14**	**32.45**	NS
Creatinin(mg/dl)	**7.98**	**1.96**	**8.16**	**1.62**	**7.83**	**1.14**	NS
Potassium (mg/dl)	**4.25**	**0.38**	**4.16**	**0.308**	**4.13**	**.47**	NS
Albumen(g/dl)	**3.90**	**0.40**	**3.94**	**.308**	**4.14**	**.18**	NS
Total cholesterol(mg/dl)	**173.13**	**42.85**	**164.28**	**36.51**	**177.69**	**23.22**	NS
Triglyserides (mg/dl)	**145.35**	**38.26**	**140.25**	**27.89**	**168.21**	**25.37**	NS
LDL(mg/dl)	**125.32**	**13.56**	**129.89**	**14.59**	**134.14**	**16.70**	NS
HDL(mg/dl)	**39.68**	**5.93**	**37.71**	**4.80**	**37.43**	**3.78**	NS
Corrected Calcium(mg/dl)	**8.71**	**0.88**	**8.92**	**0.69**	**8.23**	**.62**	NS
Phosphorus(mg/dl)	**5.16**	**1.25**	**4.7421**	**1.38**	**4.86**	**1.17**	NS
Ca Phos Product	**44.83**	**11.21**	**41.86**	**10.80**	**39.97**	**10.25**	NS
Intact parathermone(pg/dl)	**307.74**	**291.24**	**420.25**	**398.76**	**524.20**	**404.6**	NS

Independent t-test. Data were represented as mean + SD
P ≤0.05 significant.P≤0.001 considered highly significant. p >0.05 considered non-significant (NS).

Table(6) comparison between different grades of Abdominal aortic calcification as regard Echocardiography findings.

	Sever		Moderate		Mild		P
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**value**
Ejection fraction	**59.18**	**5.79**	**54.79**	**5.79**	**62.43**	**4.12**	**.01**
Fraction shortening	**33.0**	**7.47**	**29.37**	**6.26**	**32.57**	**7.91**	NS
Intervent. septal thickness	**10.36**	**0.52**	**10.21**	**0.51**	**10.71**	**0.47**	NS
left ventrecular mass index	**170.56**	**8.13**	**177.32**	**11.46**	**166.14**	**5.18**	**.01**
LT vent end dias. diam	**4.08**	**1.01**	**4.64**	**0.95**	**4.56**	**1.00**	NS
Lt Vent.EndDiast. Diam.	**5.717**	**0.76**	**6.01**	**0.56**	**5.99**	**0.46**	NS
Posteriow wall thickness	**11.45**	**0.33**	**11.51**	**0.423**	**11.37**	**0.42**	NS
AAC score	**3.29**	**1.06**	**8.58**	**1.30**	**13.86**	**0.90**	**0.001**

Independent t-test. Data were represented as mean + SD
P ≤0.05 significant.P≤0.001 considered highly significant. p >0.05 considered non-significant (NS).

DISCUSSION

Vascular calcification plays a major role in ca rdiovascular disease which is one of the main causes of mortality in chron ic kidney disease patients[11]**.**Thus, we demonstrated in our study a high prevalence of vascular calcification among ESRD patients on HD and showed that was correlated to the presence of cardiovascular disease. HD patients were classified into two groups according to thepresence or absence of valvular calcification.In the present study, patients with valvular calcificationhave high AAC score**(p value=0.001)**. HD patients with valvular calcification were older in age, with a longer HD duration,showed normal phosphorus level and calcium x phosphorus products.These factors may be responsible for the development of cardiovascular diseas.

However, a number of non-invasive imaging techniques have been developed for detection and quantification of vascular calcification. The simplest technique is lateral lumbar X-ray plain radiography and is used to quantify Abdominal Aorta Calcification score (AACS). In our study, we found no significant correlations betweencalcification score and DM.This is not in agreement with **Raggi P** *et al.* who found that DM was associated with increasedvascular calcification indialysis patients[12].This may be because of a little number of diabetic patients in our study.Furthermore, the current study showed that there was significantassociation between AACS and age, wherecalcification scoreincreased rapidly with age.Thiscomes in agreement with**Honkanen H *et al*[13].**On the other hand, in this study there were other factors correlated withvascularcalcification (VC) such as phosphate level, triglycerides, parathyroid hormoneand dialysis adequacy. This factors notcorrelated uniformly withAACS. We particulary comment on the absence of strong correlations between phosphate level and AACS which is different from other previous studies[14] .This may be because of other confounding factors that may overshadow its statistical impact or relatively short period of phosphate monitoring inthisstudy. Ejection Fraction (EF) in our study not correlated positively with presence of valvular calcification.On the other hand, our study showed no significant association between serum calcium and PTH with both valvular calcification and AAC scoring.Our findings are in accordance with**Volkov*et al*.**who found that patients with valvular calcification receiving hemodialysis, had longer hemodialysis duration[15]**.**Also, our study was inconsistent withprevious study which was suggested that aortic and mitralvalvecalcification was associated with increased age.

The most commonly reported risk factors for valvular calcification were ageing, prolonged time on HD, hypercalcemia, hyperphosphatemia, hyperparathyroidism, increased Ca x P product and / or use of calcium containing phosphate binders, hypertension, diabetes, dyslipidemia and inflammatory markers[12].In consistent with our study**Volkov*et al*.**who found that HD patients presented with valvular calcifications showed higher levels of serum calcium, phosphorus & Ca x P product as compared with patients without valvular calcifications[15].In the current study, we found no significant correlations of aortic valve calcification with serum PTH levels.

CONCLUSION

lateral lumbar X- ray plain radiography and echocardiography are simple methods to detect AAC and cardiovascular morbidity & mortality in dialysis patients. Regular follow-up by X-ray and echocardiography could be useful method to reduce mortality risk in HD patients.

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