

# Parathyroid Hormone Abnormalities Related with Mitral and Aortic Valve Calcification in Maintenance Hemodialysis Patients

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## ABSTRACT

Back ground: parathyroid hormone abnormalities and minerals disorder are common in hemodialysis patients which increase mitral and aortic valve calcification as well as mortality and morbidity.

The aim of the study: to verify the risk factors associated with valvular calcification and a benefit of Kidney Disease Improving Global Outcome guidelines for minerals level.

Patients and Methods: observation study of (52) hemodialysis patients divided into two groups (C) and (D) depend on the presence and absence of valve calcification by echocardiography then compared according to their association with risk factors and achievement of global guideline.

Results: group (C) 14 patients, group (D) 38, by comparison the age was a strong risk factor mean age for (C) =  $58.71 \pm (12.70)$  vs  $44.39 \pm (16.57)$  for (D) p- value = 0.005, for other risk factors, group (C) had longer duration of dialysis, higher use of drugs that increase calcium load, higher in hyperphosphatemia, hypercalcemia and a dynamic bone disease although the difference statistically not significant.

Discussion: all factors that mentioned were a risk factors for valvular calcification and global guidelines for minerals level were beneficial.

Conclusion: we should know these risk factors because many of them are treatable.

**Key words:** PTH (parathyroid hormone)–ca (calcium)–po4 (phosphate)–HTN (hypertension)–DM (diabetes) and ESRD (end stage renal disease).

## 1 INTRODUCTION

Parathyroid hormone (PTH) abnormalities and alterations of phosphate (po4) and calcium (ca) was common in maintenance hemodialysis patients (HD), they can associated with cardiac valve calcification (CVC) (1), and increase mortality and morbidity (2) (3) (4) (5) (6) only few studies failed to find an association with all these three factors or some of them. (7) (8) (9).

Guidelines applied for control of S. PTH, S. Po4 and S. ca like Kidney Disease Outcome Quality Initiative (K/DOQI) 2003 (10), and Kidney Disease Improving Global Outcome (KDIGO) 2009 which differ from the first one (11) (12), here S.PTH- 2 – 9 times the assay used, S. po4 and S. ca in their normal range and taken separately rather than product, these guideline was beneficial (13) and achieved by

minority of patients (10).

CVC was common in (HD) patients (14), prevalence of aortic valve calcification (52%), mitral valve (44.5%) both valves (58.7%) (9), it tend to occur earlier in age, rapid course, higher stenosis and/ or regurge, aortic valve affected more than mitral and higher association with coronary artery disease and early death than general population. (15) (16) (17) (18)

Risk factors for CVC include: advanced age, longer duration of HD (15), hypertension (HTN), diabetes (DM) (16), use of drugs that increase ca load (19) (20), hyperphosphatemia, hypercalcemia and hyperparathyroidism (9) (15) (16) a dynamic bone disease (ABD) (21), malnutrition, inflammation, atherosclerosis and decrease fetuin – A. (22)

CVC a kin atherosclerotic process with inflammation and tissue remodeling at areas of high shear stress. (23) (24) (25)

## 2 THE AIM OF THE STUDY

To verify the role of risk factors that contributed to aortic and mitral valve calcification and the importance and applicability of KDIGO guideline for S. PTH, S. ca, S.po4 in HD patients.

## 3 PATIENTS AND METHODS

Cross section study of (52) HD patients exclusion criteria history of congenital and Rheumatic valvular heart disease and HD less than three months.

All patients asked about their ages, duration of HD in months, use of drugs (ca. based po4 binders and vitamin D and it's analogue), subjective global assessment (SGA) using 7 point score with A= normal nutrition B= mild-moderate malnutrition and c= severe ,which was validated .

Blood sample for all patients for B. urea, S. creatinine S. po4 and corrected S. ca) in mg/dl, S. albumin in gm/l, C. reactive protein (CRP) , S.PTH in pg / ml , normal range for this assay ( 8 – 80 ) pg / ml and echocardiography for evidence of CVC (11).

The patients then divided into two groups (C and D) according to the presence and absence of CVC then compared depend on their association with CVC risk factors.

The two groups also compared according to their percentage of hyperphosphatemia and hypercalcemia to determine the importance of KDIGO guideline.

The two groups compared at three levels, above the target of KDIGO for S. PTH ( > 9 times assay used), within the target 2 – 9 Of the assay used and below the target ( < 2 times) to determine the role of PTH abnormalities as risk factor for CVC and the benefit of KDIGO guideline.

## 4 STATISTICAL ANALYSIS

All results expressed as data of all patients in both groups with duplicates and percentages an t- test for two independent samples and chi- square test using SPSS V16, differences with P- value < 0.05 and P- value < 0.01 were considered as statistically significant.

## 5 RESULTS

Total of (52) patients, and (29) female, (23) male, mean age=  $48.25 \pm (16.76)$ , mean duration of HD=  $42.17 \pm (26.39)$  months, all their information was tabulated (table 1).

Aortic valve calcification = (50%), mitral valve calcification = (14%), both valve= (36%) table (3).

Group (C) patients with CVC No= 14 patients, (8) female and (6) male, Group (D) patients without CVC No= 38, (21) female, (17) male, all data tabulated (table 2 and 4).

Comparison of the two groups according to CVC risk factors and KDIGO guideline target show.

Group (C) patients were older than (D), mean age=  $58.71 \pm (12.70)$  vs  $44.39 \pm (16.57)$  year, p- value = 0.005 mean duration of HD for group (C) =  $44.21 \pm (26.57)$  month vs  $41.52 \pm (26.57)$  for D, p- value= 0.748.

Use of ca based po4 binders in (C) = 93% vs 82% in (D) , p- value= 0.317.

Use of vitamin D and it's analgue in (C)= 93% vs 87% in group (D), p- value = 0.317.

Hypertension in (C) = 50% vs 29% in (D), p- value = 0.157.

Diabetes in (C) = 29% vs 18% in D, p- value = 0.427.

SGA score (B) in group (C) = 29% vs 42%, p- value= 0.375.

(CRP) in group (C) = 14% vs 37% in group (D), p- value = 0.114.

Hypercalcemia in (C) = 14% vs 5% in D, p- value = 0.279.

Hyperphosphatemia in (C) = 86% vs 76% in (D), p- value = 0.462.

PTH above target in (C) = 7% vs 16% in (D), p- value = 0.719.

PTH within the target of KDIGO for (C) = 36% vs 31% for D, p- value= 0.719.

PTH below target in group (C) = 57 % in group (C) vs 53% in group (D), p- value = 0.719.

## 6 DISCUSSION

From these results CVC was common in maintenance HD patients and aortic valve affected more than mitral( aortic valve = 50% , mitral = 14% , both valve calcification = 36% ) , the age was the strongest risk factor as group (C), was older than (D) with statistically significant difference .

For other factors, duration of HD, use of drugs that increase ca load, hypertension, diabetes, hyperphosphatemia, hypercalcemia and ABD (less than lower limit of S. PTH guideline target), there is a difference although statistically not significant and also they are risk factors for CVC and global guideline for hyperphosphatemia, hypercalcemia and ABD was beneficial because they are a risk factors (15) (21).

Overlap results noticed for patients at level higher than guideline limits for S. PTH (2-9 times of the assay used for S. PTH) and within these limits because of a wide range for the guideline limits, there is no association between higher than recommended values for S. PTH and CVC noticed and no remarkable reduction in the risk of CVC for patients within these limits were hyperparathyroidism can be diagnosed at level of 400 pg/ml for S. PTH (27) and the upper limit of the target was = 720 pg/ml in this study according to that guideline which is much higher than S. PTH value that's diagnostic for hyperparathyroidism and many

**Table 1. Demographic and Lab Variables for all Patients**

Variables		No.	percentage
Use of ca.bosed po4 binder	yes	44	85%
	no	8	15%
Use of vitamin D and its analogue	yes	46	88%
	no	6	12%
Causes of ESRD	HTN	19	36%
	D.M	10	19%
	ADPCKD	4	8%
	neurogenic bladder	2	4%
	Post acute Kidney injury	1	2%
	Rheumatiod arithritis	1	2%
	Lupus nephritis	1	2%
	Obstructive nephropathy	1	2%
Unknown causes	13	25%	
SGA	A ( normal nutrition )	32	62%
	B (mild- moderate )	20	38%
	mean		Std. deviation
Age / years	48.25		16.76
Duration of HD months	42.17		26.39
S.ca	7.78		1.717
S.po4	6.07		1.78
S.PTH	328.24		440.44
CRP	10.15		14.62
S.albumin	36.03		6.313
B.urea	152.93		97.67
S.creatinine	8.89		2.92

**Table 2. Group (C) Variables**

Variables		No.	percentage
HTN	yes	7	50%
	no	7	50%
D.M	yes	4	29%
	no	10	71%
SGA	A	10	71%
	B	4	29%
Use of Calcium based po4 binders	yes	13	93%
	negative	1	7%
Use of vitamin D or its metabolites	yes	13	93%
	negative	1	7%
	mean		Std. deviation
Age / years	58.71		12.70
Duration of HD months	44.21		26.57
S.ca	8.55		1.64
S.po4	5.76		1.22
S.PTH	242.76		270.08
CRP	6.35		10.80

**Table 3. Percentage of aorticand/ or mitral valve calcification for all patients**

	No.	percentage
Aortic value	7	50%
Mitral value	2	14%
Combined aortic and mitral value	5	36%

Table 4. Group (D)

Variables		No.	percentage
HTN	yes	11	29%
	no	27	71%
D.M	yes	7	18%
	no	31	82%
SGA	A	22	58%
		16	42%
Use of Calcium based po4 binders	yes	31	82%
	no	7	18%
Use of vitamin D or its metabolites	yes	33	87%
	no	5	13%
	mean	Std. deviation	
Age / years	44.39	16.57	
Duration of HD months	41.52	26.57	
S.ca	7.50	1.67	
S.po4	6.17	1.94	
S.PTH	359.53	487.85	
CRP	11.55	15.69	

patients with hyperparathyroidism would be missed within the recommended target, this study not found an association between malnutrition and inflammation with CVC , SGA score B in group C = 29% vs 42% for D and CRP higher than 6 ( positive ) in C = 14% vs 37% in D .

## 7 CONCLUSION AND RECOMMENDATION

Risk factors for CVC in HD patients should be known because many of them are treatable and global guideline for minerals was beneficial although the upper limit of S. PTH target need another review.

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**Table 5. Differences between(C) and (D)**

Variables		C = 14		D = 38		p-value
		No.	percentage	No.	percentage	
HTN	yes	7	50%	11	29%	0.157
	no	7	50%	27	71%	
D.M	yes	4	29%	7	18%	0.427
	no	10	71%	31	82%	
SGA	A	10	71%	22	58%	0.374
		4	29%	16	42%	
Use of Calcium based po4 binders	yes	13	93%	31	82%	0.317
	no	1	7%	7	18%	
Use of vitamin D or its analogue	yes	13	93%	33	87%	0.547
	no	1	7%	5	13%	
S.ca	Above 10.4	2	14%	2	5%	0.279
	Below 8.4-10.4	12	86%	36	95%	
S.po4	Above 4.5	12	86%	29	76%	0.462
	Below 2.8-4.5	2	14%	9	24%	
S.PTH	Above 720	1	7%	6	16%	0.719
	Between 160-720	5	36%	12	31%	
	Less than 160	8	57%	20	53%	
CRP	Result < 6	2	14%	14	37%	0.118
	normal	12	86%	24	63%	
		C = 14 mean	Std. deviation	D = 38 mean	Std. deviation	p- value
Age / years		58.71	12.70	44.39	16.57	0.005*
Duration of HD months		44.21	26.57	41.52	26.57	0.748

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