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RISK FACTORS OF VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS

[1]*Dr. Sajeevkumar K. S., [2]Dr. Manoj T., [3]Dr. M. K. Mohana Das and [4]Dr. Induprabha Yadav

[1]Additional Professor in Nephrology, Govt Medical College, Thiruvananthapuram.
[2]Additional Professor in Radiodiagnosis, Govt Medical College, Thiruvananthapuram.
[3]Additional Professor in Nephrology, Govt Medical College, Aleppey.
[4]Additional Professor in General Surgery, Govt Medical College, Kollam.

***Corresponding Author: Dr. Sajeevkumar K. S.**

Additional Professor Gokulam, House Number 28 Peroorkada NCC Nagar Kerala India.

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ABSTRACT

Background: Vascular calcification is common in patients with chronic kidney disease doing dialysis and is associated with an increase in cardiovascular disease and death, an increase in the severity of vascular anastomoses (vascular grafts or AV fistulae). **Objectives:** Objective was to find a correlation of various risk factors with vascular calcification in CKD patients on hemodialysis. **Methods:** CKD patients aged 18-80 hemodialysis for at least three months from a teaching hospital in South India are selected. Patient enrolment period was for 6 months from March 2014. The clinical and biochemical parameters of these patients were recorded. Digtal X-ray of the adomen lateral view and non contrast MDCT abdomen [128 slice using Siemens machine] of these patients were taken. These patients were followed for 2 years. **Results:** Of the 80 patients, 62 (77.5%) were male. The average age of the study population was 49.9 +/-12.2 years. Age was found to be a major risk factor for Vascular calcification.odds ratio was 1.213 (95% CI 1.103-1.334), P value <0.001. Vascular calcification was present for CT in 63 patients and X-ray in 32. No statistical significance was found for male sex, number of years on dialysis and diabetic nephropathy. The level of C-reactive protein had a significant correlation with odds ratio of 1.138 (95% CI 1.016-1.274). Poor association of serum calcium, phosphorus, albumin, and calcium phosphorus product with vascular calcification. **Conclusion:** Age is the most important risk factor for vascular calcification in chronic kidney disease patients on hemodialysis.Inflamatory marker C reactive protein also has significant correlation with vascular calcification.

KEYWORDS:- Chronic Kidney Disease, Dialysis, Vascular calcification, Risk factors.

1. INTRODUCTION

Vascular calcification is common in chronic kidney disease patients especially patients on dialytic support. Calcification of tunica media of vessels are seen in elderly and is accelerated by chronic kidney disease. In fact CKD is a condition of accelerated vascular aging[1,2] Leading cause of morbidity and mortality in patients on dialysis is cardiovascular disease.[3] Susceptibility of these chronic kidney disease patients to cardiovascular disease are traditional and non traditional. Traditional risk factors are hypertension, obesity, hyperglycaemia, dyslipidaemia, smoking etc. Non traditional risk factors which are uraemia related include anaemia, hyper homocysteinemia, abnormal Calcium/ phosphorus metabolism, malnutrition, vascular calcification etc.[4] Vascular calcification is more prevalent in patients with chronic kidney disease compared to general population.[5] Recent evidence suggest that both non traditional and traditional risk factors play a role in vascular calcification in chronic kidney disease patients.[5]

The gold standard technique for detection of vascular calcification is the histological examination of post-mortem arterial specimens. plain X ray &CT scan can detect vascular calcification of different sites. Plain Xray has the advantage of being cost effective and non invasive & can differentiate between medial and intimal calcification to some extent. KDIGO guideline 2009 suggest the use of plain lateral abdominal Xray films to detect vascular calcification of abdominal aorta[6] CT scanning detects and quantify vascular calcification, but not able to differentiate between medial and intimal calcification.

Vascular calcification should be detected early in chronic kidney disease patients not only because it is associated with increased cardiovascular morbidity and mortality

but also associated with difficulty in vascular anastomosis[AV fistulae and vascular grafts].[7]

If vascular calcification is detected early, further progression can be prevented by modifying risk factors.

2. OBJECTIVE

To determine the association of various risk factors with vascular calcification.

3. MATERIALS AND METHODS

A case control study was done in CKD patients on hemodialysis to identify the factors associated with vascular calcification. This study was conducted in accordance with Declaration of Helsinki & was approved by the ethics committee of the Government Medical College,Trivandrum .Consecutive patients in the 18-80years age who were on hemodialysis at this institution were recruited after getting informed consent to detect those with vascular calcification. 80 patients were enrolled between March 2014 and August 2014. All these patients were undergoing twice weekly maintenance hemodialysis. X-ray of the Abdomen lateral view and non contrast MDCT abdomen [128 slice using Siemens machine] of these patients were performed to detect vascular calcification. X-ray and CT imaging were reported by various radiologists who were blinded by each other.

Factors associated with vascular calcification were assessed including patient and treatment characteristics like age, sex, diabetes and dialysis vintage time; as well as biochemical characteristics including serum albumin, serum calcium, serum phophorous, calcium phosphorous product, Alkaline phosphatase and C-reactive protein.

4. STATISTICAL ANALYSIS

Data were entered into MsExcel and analysed using EpiInfo 7.2.4.0 (CDC). Quantitative variables were summarised as mean and standard deviation when normally distributed or into median and interquartile range. Categorical variables were summarised into percentages. A case control analysis was done in those with and those without vascular calcification. Odds ratio and 95% confidence intervals were calculated. P value of <0.05 was taken as significant.

5. RESULTS

Of the 80 patients enrolled in the study, 62 (77.5%) were male .49.9 + 12.2 was the mean age in this study .The baseline characteristics of the study population are listed in Table 1.

Table 1: Base line characteristics of the study population (N=80).

Age: Mean Range	 49.9 $\pm$ 12.2 years 18 - 78 years
Sex:	Males 62 (77.5%), Females 18 (22.5%)
Diabetic Nephropathy:	34 patients
Coronary artery disease:	25 patients
Dialysis vintage: Mean Range	 2.4 $\pm$ 1.2 years 0.5 - 7 years
Vascular accesses: Arterio-venous fistula Permanent tunnelled jugular catheter	 77 3
Corrected serum calcium: Mean Range	 8.4 $\pm$ 0.9 mg/dl 6.1 - 10.4 mg/dl
Serum Phosphorus Mean Range	 5.7 $\pm$ 1.17 mg/dl 2.9-9.1 mg/dl
Calcium Phosphorus Product Mean Range	 48.0 $\pm$ 12.2 mg^2/dl^2 20.9 – 91.9 mg^2/dl^2
Alkaline Phosphatase Mean Range	 139.8 $\pm$ 65.6 IU 41 – 446 IU
C - Reactive Protein Mean Range	 9.2 + 6.4 mg/dL 1.0 – 21.0 mg/dL
Serum albumin Mean Range	 3.2 + 1.4 g/dL 2.1 – 4.2 g/dL
Vascular calcification on CT abdomen	63 patients (78.8%)

Vascular calcification was detected by CT abdomen in 78.8 % patients.

Various risk factors for vascular calcification were analyzed **(Table 2&3)**

Table 2: Risk factors for vascular calcification in dialysis patients.

	P value	Odds ratio	95% C.I	
			Lower	Upper
Age	<.001	1.213	1.103	1.334
Male sex	.406	2.099	.365	12.071
Dialysis vintage time	.926	1.025	.611	1.718
Diabetic nephropathy	.548	1.621	.335	7.841

Age was found to be a significant risk for vascular calcification with odds ratio 1.213 (95% CI 1.103-1.334), P<0.001

Table 3: Association of biochemical parameters with vascular.

Calcification				
	P value	Odds ratio	95% C.I	
			Lower	Upper
Serum albumin	.784	.838	.236	2.976
Serum calcium	.859	.751	.032	17.781
Serum phosphorus	.610	.287	.002	34.616
Calcium phosphorus product	.611	1.157	.659	2.032
Alkaline phosphatase	.656	1.002	.992	1.013
C-Reactive Protein	.025	1.138	1.016	1.274

C-reactive protein level was found to have significant association with the vascular calcification with an odds ratio of 1.138 (95% CI 1.016-1.274), P value 0.02. No statistical significance was obtained for male sex, total dialysis duration and diabetic nephropathy. Serum calcium, serum phosphorus, calcium phosphorus product, and serum albumin measured at the time of enrollment to the study had no significant association with vascular calcification.

6. DISCUSSION

Risk factors for vascular calcification were analyzed in this study. Age was found have significant risk for vascular calcification. Age is an independent risk factor for vascular calcification in general population as well.[8] Inflammatory marker CRP has been shown to have positive correlation with vascular calcification in this study. One of the important factors involved in initiation and progression of vascular calcification is inflammatory processes. CRP levels have strong correlation with atherosclerosis,[11,12] cardiovascular disease[13-16] & mortality. Diabetes mellitus was found to have significant positive correlation with vascular calcification in many studies.[18] In our study diabetic nephropathy was not a significant risk factor for vascular calcification probably because advanced age and diabetic nephropathy became confounding factors when logistic regression analysis was performed. Dialysis vintage is generally associated with vascular calcification in previous studies[18] Most of our patients were having a short dialysis vintage [mean of 2.4 years]which may explain the reason for finding dialysis vintage poor correlation as a risk factor for vascular calcification in our study.

Abnormalities in the calcium and phosphorus metabolism is implicated in the pathogenesis of vascular calcification,[9] but in our study serum calcium, phosphorus, and calcium phosphorus product did not had any significant association with vascular calcification. Long term trends in these biochemical parameters are more likely to have association than point estimates.

Regular evaluation for vascular calcification in CKD patients on hemo dialysis is important as it is associated with increased morbidity and mortality, increased difficulty making vascular anastomoses (vascular grafts or AV fistulae) and effective coronary artery intervention (angioplasty, stenting, and coronary artery bypass). Assessment of risk factors of vascular calcification is of paramount importance as modification of these risk factors may slow further progression of vascular calcification & thereby reducing cardiovascular events, though age, the most important risk factor for vascular calcification in our study is not modifiable.

Drawback of our study is shorter dialysis vintage and majority of our patients were malnourished.

7. CONCLUSIONS

A good proportion of chronic kidney disease patients on maintenance hemo dialysis have vascular calcification**.** Age is the most important risk factor for vascular calcification in these patients. Inflamatory marker C reactive protein also has significant correlation with vascular calcification.

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