Association between Vascular Calcification and Residual Renal Function in Chronic Kidney Disease Patients on Hemodialysis

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Abstract

Background: In CKD patients, the leading cause of mortality is cardiovascular disease. In most cases, it is related to vascular calcification. Among multiple risk factors for vascular calcification, decline of Residual Renal Function (RRF) is an important one. So far, data are scarce regarding this. To determine the association betweenvascular calcification and low RRF in HD patients.

Materials and methods: An observational study was performed on 60 CKD patients on MHD with low RRF attending in dialysis units of Chittagong Medical College Hospital in Bangladesh during the period from April 2018 to March 2019. Blood samples for biochemical analysis were collected in fasting condition and lateral lumbar radiography was done for vascular calcification score. Data were analysed using SPSS version 20. Continuous variables were expressed as mean and standard deviation, or as median and interquartile range according to distribution. Categorical variables were expressed as frequency distribution. Statistical analysis included unpaired t test for quantitative variables and χ^2 test for categorical variables. To assess the individual and combined influence of variables on Abdominal Aortic Calcification (AAC) score, univariate and multivariate linear regression were used respectively. Data were presented in tables and figures. Statistical significance was defined as $p<0.05$ and confidence interval set at 95% level.

Results: The prevalence of vascular calcification was present in 88.3% cases in patients with low RRF and the association was significant. There was also positive correlation of vascular calcification with FBS, CRP, iPTH, Cholesterol, BMI, serum calcium, serum phosphate, Ca x PO4 product and systolic BP but it was negative for serum Albumin, diastolic BP.

Conclusion: Vascular calcification is very common in patients with ESRD on MHD. Loss of RRF may be an important risk factor for vascular calcification.

Key words: Chronic kidney disease; End stage renal disease; Maintenance haemodialysis; Residual renal function; Vascular calcification.

Introduction

According to KDIGO reports, prevalence of CKD is approximately 10% of the global population.[1] In CKD stage 5 population, 80-85% of existing dialysis patients and 60% of new patients have some degree of Coronary Artery Calcification (CAC) or Aortic calcification.[2,3] Furthermore, it has been also reported that vascular calcification scores may be predictive of mortality, with lower survival in association with greater CAC.[4] Multiple risk factors are associated with VC in HD patients and RRF is one of the major risk factors. There is general belief that renal function rapidly declines after initiation of HD treatment. However, renal function can be preserved for several years after the start of HD in many patients, especially when ultrapure dialysis fluid and biocompatible dialyzers are used.[5,6] Previous observational studies have shown that, preservation of residual renal function in dialysis patients is a prognostic and independent factor in patient survival and quality of life.[7,8] So by preserving RRF, morbidity and mortality related to VC can be reduced. Several non-invasive methods e.g plain radiography, computed tomography, vascular ultrasound and so on are present to measure severity of VC. AAC is one of the measurements of VC that can easily be obtained by a semi-quantitative measurement in lateral lumbar radiography. AAC is an easy and fast measurement of VC used in HD patients.[9] Components of AAC are age, duration of dialysis

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and cardiovascular disease.[10] Traditional determinants for atherosclerosis, such as dyslipidemia, hypertension, smoking, gender and age only partly explain the calcification that seems to be more linked to the uremic milieu and abnormalities in mineral metabolism.[11] Relevant literature proved association between loss of RRF and VC in Peritoneal Dialysis (PD) patients but this association is still unclear in HD patients.[12] The aim of this study is to find out the association between loss of RRF and VC in HD patients.

Materials and methods

This observational study was conducted in Chittagong Medical College Hospital, Chattogram during April 2018 to March 2019. The study enrolled 60 CKD patients undergoing haemodialysis at dialysis units of the hospital consecutively.

The study included adult patients (Age ≥18 years) of either sex on haemodialysis through A-V fistula for >3 months and ambulatory patients with 24 hours urinary volume less than 200ml.

Patients on MHD for less than 3 months, on acute haemodialysis or on MHD through pump catheter and those who were not willing to participate were excluded.

Those patients who fulfilled the selection criteria were reviewed with their records. They were selected on the basis of measuring total amount of urine volume collected in the last 24 hours of a dialysis session. A 50-cc disposable syringe was used for urine volume measurement. Blood samples for biochemical analysis were collected in fasting condition. At the same day, lateral lumbar radiography was done for vascular calcification score. Lateral lumbar radiography and M-mode echocardiography was done in CMCH and biochemical tests were performed in a nearby reputed diagnostic laboratory. Demographic variables and haemodialysis duration were recorded after interviewing the patients. BMI was recorded after measuring weight by analog weight machine (Equinox BR 9201 weighing scale) and height by measuring tape (Foshan Guos Wintape measuring Tape Co. Ltd, China). Low RRF was considered in those patients with no urine output or 24 hours urine output less than 200 ml. Hypertension was defined as taking antihypertensive drugs without regard to the actual measurement of blood pressure or having a systolic blood pressure reading greater than 140 mm Hg or a diastolic blood pressure reading greater than 90 mm Hg.[13] BP was measured with a standard mercury sphygmomanometer and cuffs adapted to arm circumference. Before recording BP, the subject was kept in recumbent position for 10 minutes. Diabetes mellitus was defined as use of insulin or oral hypoglycemic agent or a fasting plasma glucose level of 126 mg/dL or more.[14] FBS was measured by auto analyzer Siemens Advia 1800. Venous blood was collected at morning after an overnight fast of at least 12 hours before starting a dialysis session. Whole blood was used for FBS and lipid profile. Serum was used for other biochemical analysis. Lipid profile, serum calcium and phosphate, serum albumin were assessed by automated clinical chemistry analyzer Siemens dimension EXL 200. Measurement of serum iPTH was done by chemiluminescence's method and CRP by nephelometry method.

Detection of vascular calcification: Vascular calcification score of all patients were measured by a lateral lumbar radiography at the level of L_1 to L_4. Vascular calcification was graded as 0: no aortic calcific deposits: i) Small scattered calcific deposits less than one-third of the corresponding length of the vertebral level ii) Medium quantity of calcific deposits about one-third or more but less than two-thirds of the corresponding vertebral length iii) Severe quantity of calcifications of more than two-thirds or more of the corresponding vertebral lengths. The abdominal aorta score at each vertebra level was obtained by summing up the calcification of the anterior and posterior walls of aorta. Calcification score at each lumbar spine level was between 0 and 6. The scores of L_1 to L_4 were summed with a total AAC score ranging from 0 to 24. AAC was measured with the help of a radiologist who was blind about the study patients.

Data were collected by face-to-face interview, recording physical examination and reports of laboratory investigations using a structured questionnaire containing all the variables of interest. All the data were compiled in a preformed structured case record form.

After collection, all the data were compiled, edited and analysed using Statistical Package for Social

Sciences (SPSS) version 20. Continuous variables were expressed as mean and standard deviation, if normally distributed or as median and interquartile range where data were skewed. Categorical variables were expressed as frequency distribution. Statistical analysis included unpaired t test for quantitative variables and χ^2 test for categorical variables. To assess the individual and combined influence of variables on AAC score univariate and multivariate linear regression were used respectively. Data were presented in tables and figures. Statistical significance was defined as $p<0.05$ and confidence interval set at 95% level.

Before commence the study necessary permission was obtained from the proper authority.

Results

Table I Distribution of respondents according to socio-demographic characteristics, general risk factors and renal function-related variables (n=60)

Traits	Frequency (f)	Percentage (%)
Socio-demographic characteristics		
Mean age ± Standard deviation	50.33 ± 11.21	
Gender		
Male	43	71.7
Female	17	28.3
Residence		
Rural	39	65.0
Urban	21	35.0
Occupation		
Service holder	34	56.6
House wife	16	26.7
Businessman	10	16.7
Smoking status		
Smoker	23	38.3
Diabetes mellitus		
Diabetic	27	45.0
Hypertension		
Hypertensive	60	100.0
Renal-function related variables		
Duration of dialysis (Years)		
<2	26	43.3
2-4	24	40.0
>4	10	16.7

Table I demonstrates the socio-demographic variables .Mean age of the respondents was 50.33 ± 11.21 years. Majority of the participants were males hailing from rural areas.

Most of them were service holders by occupation (56.6%). Also demonstrates renal function-related risk factors of the respondents. Most cases were non-smoker (61.7%) and non-diabetic (55%). All 100% were found to be hypertensive. Etiology-wise, diabetes mellitus was predominant (45.0%). Duration of dialysis was found less than 2 years in majority of the cases (43.3%).

Table II Distribution of respondants according to RRF (n=60)

Residual renal function	Number (n)	Percent(%)
Moderately lost [urinary total volume in 24 hours: 100-200 ml]	32	53.3
Severely lost [urinary total volume in 24 hours: <100 ml]	28	46.7

Table II demonstrates with context to renal function-related risk factors, RRF was found moderately lost in majority (53.3%) of participants.

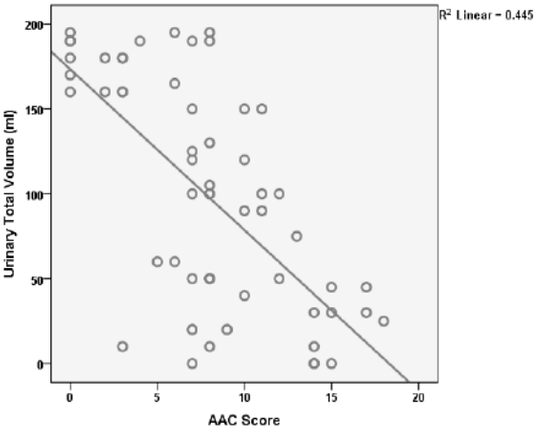

Figure 1 Negative linear correlation between AACS and urinary total volume (RRF)

Figure shows that abdominal aortic calcification score was negatively correlated with twenty four hours urinary total volume.

Table III Association between vascular calcification and residual renal function among respondents (n=60)

Vascular calcification	Severely lost RRF n %	Moderately lost RRF n%	Total N%	
No Vascular Calcification	0 (0.0)	7 (100.0)	7 (100.0)	
Mild Vascular Calcification*	11 (35.5)	20 (64.5)	31 (100.0)	
Moderate Vascular Calcification**	14 (73.7)	5 (26.3)	19 (100.0)	≤ 0.01 HS
Severe Vascular Calcification***	3 (100.0)	0 (0.0)	3 (100.0)	
Total	28 (46.7)	32 (53.3)	60 (100.0)	

* (AACS 1 – 8) ** (AACS 9 – 16) *** (AACS 17 – 24)
Figures within parentheses indicate percentages. p values were derived from χ^2 test (χ^2= 16.684). HS: Statistically highly significant.

*AACS=1-8, **AACS=9-16, ***AACS=17-24, hs=highly significant

Table III demonstrates the association between vascular calcification and residual renal function among the study respondents. In case of 31 out of 60 patients with mild VC, majority of the cases had moderately lost VC, which is 20 (64.5). It was also found that, out of those 19 patients who developed moderate VC, 14 (73.7) were detected to have severely lost RRF. The p-value was found by doing χ^2 test and the association between VC and RRF was seen to be statistically significant (p = <0.01).

Table IV Pearson's Correlation between vascular calcification scores (AACS) and other dependent variables (n=60)

Variables	Correlation Coefficient (r)	p-value
AACS and duration of dialysis	+0.345	0.007^{hs}
AACS and Serum Phosphate	+0.383	0.003^{hs}
AACS and Ca x PO_4	+0.339	0.008^{hs}
AACS and FBS	+0.271	0.036^{s}
AACS and Serum Albumin	-0.103	0.432^{ns}
AACS and Serum Calcium	+0.047	0.721^{ns}
AACS and BMI	+0.117	0.375^{ns}
AACS and Systolic BP	+0.037	0.778^{ns}
AACS and Diastolic BP	-0.092	0.486^{ns}
AACS and total Cholesterol	+0.016	0.902^{ns}
AACS and Triglyceride	-0.081	0.539^{ns}
AACS and HDL	+0.177	0.176^{ns}
AACS and LDL	+0.132	0.314^{ns}
AACS and Serum iPTH	+0.055	0.675^{ns}

vhs = Very Highly Significant (p< 0.001) hs = Highly Significant (p< 0.01) s = Significant (p<0.05) ns = Not Significant (p>0.05).

Table IV shows Pearson's correlation vascular calcification scores (Which is determined by Abdominal Aortic Calcification scores) and other dependent variables. It was clearly evident that, vascular calcification was significant positively correlated with duration of dialysis, serum Phosphate and Ca x PO_4 product (p>0.05).

Discussion

Previous studies on chronic kidney disease and diabetes patients demonstrated that age, diabetes mellitus, hypertension, male gender and duration of dialysis are closely associated with vascular calcification.[15-16] This study revealed similar results, except for the trait of duration of dialysis which could be for the fact of including most patients with shorter duration of dialysis.

Another study on general population suggested that, men are particularly more prone to vascular calcification than women.[17] Some studies on CKD patients also found close association of vascular calcification with male gender. In this study, male had more vascular calcification score than female. So, it supports the above studies. But these results may owe to the fact of recruiting higher number (71.7%) of male participants.[15-16]

Here, in case of respondents with loss of residual renal function, median abdominal aortic calcification score was significantly higher in severely lost group comparing with moderately lost group. This result is consistent with a study done at China Medical University Hospital on chronic haemodialysis patients.[18]

In this study, vascular calcification increased in proportional to reduced residual renal function and, patients with more severe vascular calcification status had more proportional loss of residual renal function. So, my result supports the above study.

CORD study found no significant relationship between AACS and SBP, DBP, serum PO4, Lipid.[10] However, in this study, I found positive correlation of AACS with SBP, serum PO4, serum Lipid though none of these were statistically significant. In addition, this study found negative correlation of AACS with DBP. This correlation was also found in similar studies.[19,17,20] It reflects the effect of vascular calcification that increases cardiac morbidity and mortality in maintenance haemodialysis patients.

Limitations

- The study was performed in only one center and only based on prevalence at a single point, no follow up records were included.
- There were relatively smaller sample size subgroups of vascular calcification which might have distorted the result of statistical analyses.
- Certain data may appear unusual as there were no restrictions on supplementary calcium, phosphate-binder medication or phosphate rich diet.

Conclusion

In this observational study conducted among the HD patients with loss of RRF revealed that, patients with severe loss of RRF (24 hours UTV <100 ml) had significantly (p value <0.01) raised vascular calcification. The more was the RRF loss, the more was the vascular calcification score.

Recommendation

Multicenter study with large sample size is recommended for proper scenario of whole community.

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Contribution of authors

HRC-Conception, acquisition of data, interpretation of data, drafting the article and final approval.
MA-Critical revision of content, drafting of article and final approval.
RBK-Data acquisition, critical revision of content and final approval
GMTA-Design, Drafting, revision of content and final approval
MNH-Interpretation of data, critical revision of content and final approval.
PKD-Data analysis, critical revision of content and final approval.

Disclosure

All the authors declared no conflict of interest.

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