Correlations between Echocardiography Findings for Detection of Some Cardiovascular Morbidities in Patients with Chronic Renal Failure on Regular Haemodialysis and Some Blood Biomarkers Including Fetuin A (Case Control Study)

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Abstract

Background: In dialysis patients, both atherosclerosis and arteriosclerosis are highly prominent. Fetuin A is a glycoprotein produced predominantly by the liver in adults. Fetuin A is known as the most powerful systemic inhibitor of vascular calcification.

Aim of Work: Is to study both carotid and valvular calcification in end-stage renal disease and some of biomarkers including fetuin-A, C-reactive protein (CRP), and Interlukin 6 (IL-6).

Patients and Methods: Fifty three patients with (ESRD) aged (31.2 ± 8.1 years); 32 patients were males and 21 were females, on regular haemodialysis (HD), divided into two groups; 27 of them of less than five years duration; and 26 of more than five years duration, compared with seventeen; apparently healthy persons. All studied persons were subjected to: CBC; lipid profile, serum albumin; calcium; phosphate; calculated calcium phosphate product (ca x p); serum for Fetuin-A, CRP, IL-6, performed by using ELISA kits. Doppler echocardiography.

Results: There were sixteen patients with calcified valves (30.2%); 23 calcified carotid arteries (43.4%). Fetuin-A was significantly reduced (p=0.002), and no significant difference in both CRP (p=0.400); and IL-6 (p=0.464) between ESRD patients and controls.

Conclusion: Patients with ESRD on chronic HD treatment are predisposed to morbidity from cardiovascular disease more than healthy persons. Controlling the process of vascular calcification (VC) can help patients with ESRD to limit these cardiovascular problems. Low fetuin-A was independent risk factor for VC which acts as inhibitory factor for this process.

Key Words: ESRD – Fetuin-A – Vascular calcification.

Introduction

RISK factors for atherosclerotic events and cardiovascular disease include male sex, increased age, elevated plasma total cholesterol and low density lipoprotein cholesterol, high blood pressure, smoking and diabetes mellitus. Approximately 50% of atherosclerotic coronary artery disease in the community occurs in the absence of these traditional risk factors [1].

One of the most common subjects of interest is the liability of renal failure patients to develop cardiovascular diseases [2]. It has been proven recently that even minor renal dysfunction constitutes a major risk to develop cardiovascular complications [3].

Cardiovascular diseases range from coronary heart diseases, valvular calcification, left ventricular hypertrophy, and myocardial fibrosis [4].

In renal failure many risk factors have been identified, some of them are related to the original illness which leads to the progression of renal failure such as hypertension. However few years ago new risk factors have been unveiled and those included vascular inflammation and vascular calcification [5]. It is now believed that renal failure patients are in a state of ongoing low grade inflammation with the resultant release of inflammatory markers which contribute to the vascular damage [6].

Hypoalbuminemia also acts in synergy with other factors to increase the cardiovascular burden.
in renal failure patients. However the most important of these factors drawing attention is vascular calcification [7]. There is vascular calcification in renal failure patients which involves both the media and intima [8]. Also renal failure patients are liable to develop valvular calcification; there is mitral annular calcification as well [9].

Some of the inhibitors of vascular calcification act locally at the site of the blood vessel and some of them are present circulating in the serum the so called systemic inhibitors of vascular calcification [10]. The main cells which seem to have the fundamental role in vascular calcification are the vascular smooth muscle (VSM) which acts to nucleate calcium in response to elevated serum calcium and phosphate levels [11].

Fetuin-A is a circulating plasma glycoprotein, produced abundantly during fetal development by multiple tissues, whereas in the adult, it is produced predominantly by the liver [12]. Fetuin-A is known as the most powerful systemic inhibitor of vascular calcification, its serum level is markedly decreased in renal failure patients on hemodialysis and this predisposes markedly to vascular calcification and accelerated cardiovascular morbidity [13]. Moreover other different actions of fetuin-A have been unveiled. Among those actions is its role in the mineral metabolism where fetuin-A has been proven to have regulatory role on the osteoblast and the signalling of the transforming growth factor B (TGF-B) [14].

**Aim of work:** Is to study both carotid and valvular calcification in end-stage renal disease and some of biomarkers involved in the process of cardiovascular calcification of which fetuin-A, C-reactive protein (CRP), and interleukin 6 (IL-6).

**Patients and Methods**

Case control study has been performed on 70 persons at Assuit university hospital included in this study between February 2007 and December 2008, with informed consent and local ethical committee approval, divided into two groups:

**Disease group:** Which included 53 patients on chronic hemodialysis, 26 of them for more than five year duration and the other 27 for less than five year duration, their ages were less than forty five years; who has no history of smoking or cardiac disease, hyperlipidemia, diabetes mellitus, or history of systemic inflammatory disorders (systemic lupus, rheumatoid arthritis, or inflammatory bowel disease), or has underlying malignancy, chronic liver or lung diseases.

**Control group:** Which included 17 persons, who were apparently normal, matched with age and sex in the first group.

All the participants in the research had consented to the procedure after complete explanation of the steps, the objective and nature of the study.

**All patients and controls were subjected to the following:**

- Complete clinical history and physical examination.
- Peripheral haemogram.
- Kidney function tests (blood urea and creatinine).
- Lipid profile (total cholesterol, LDL, HDL, TG).
- Serum albumin, calcium, phosphate. Corrected calcium (calcium-c) = (40 - s. albumin) x0.8+s. calcium [18], and calcium phosphate product (ca x p product).
- Serum biomarkers:
  - CRP: By using high sensitivity CRP (hs-CRP), product code: 3/15-300, for quantitative determination of CRP concentration in human serum by a microplate immunoenzymometric assay.
  - Fetuin-A: Serum fetuin-A level was measured using an enzyme-linked immunosorbent assay kit (Biovendor Laboratory, cat. No: RD191037100R, for quantitative measurement of the human fetuin-A protein in serum.
  - Interleukin 6: Was measured by using (human IL-6 kit), which is an enzyme-linked immunosorbent assay for quantitative detection of IL-6.
- Body mass index (BMI) was calculated by the equation:
  \[ \text{BMI} = \frac{\text{weight in kilogram}}{\text{height in square meter}} \]
- ECG to detect the presence of ischemia and left ventricular hypertrophy (LVH).
- Echocardiography to assess calcification in the heart and Doppler for assessment carotid arteries and vascular access. Echocardiography using Agilent HP SONOS 4500 PHILIPS, U.S.A. with a 3.8MHz transducer. Echocardiography was done to evaluate valvular calcification, ejection fraction, LVH, (More than 1.2cm thickness was cosidered as LVH [16], systolic and diastolic dysfunction. Measurement of intima-media thickness (IMT) of the carotid artery was done using a computed color duplex sonography system (Voluson 730) which operates in several modes: real time B mode (that we used in our study),
color Doppler mode and spectral Doppler mode. Examination was performed with 3-5MHz convex transducer or 7-10MHz linear transducer. Measurements were made on the common carotid arteries (CCA), 2cm below its bifurcation. It was done for measurement of IMT, and to detect any atheroma in the wall of the artery. The arterial wall appears as two echogenic lines separated by a hypoechoic space. The interior, thin white line is formed by the intima; the outer echogenic thicker line is formed by the adventitia. The hypoechoic distance between these two lines corresponds to the media. IMT >1mm was considered thick [16].

Statistical methods:
Our data were analyzed using statistical program for social science (SPSS) computer software release for windows version 16. Those included: Unpaired t-test; Mann Whitney Willxon test; ANOVA (analysis of variance test); correlation co-efficient test (Pearson, or Kendall’s tau-b). p-value of <0.05 was considered to indicate statistical significance.

Results
A total of 53 patients (60%) males and (40%) females with mean age 31.2 ±8.1 years, ranging from 19-44 years were included in this study. Also 17 healthy control group 7 males and 10 females, with mean age 30.9 ±5.1 years, ranging from 22-42 years. No statistically significant difference in age and sex distribution (p=0.873), (p=0.165) respectively, and significant decrease in body mass index (BMI) (p=0.042), in diseased group than healthy controls. The correlation of chemical parameters between patients and controls was shown in (Table 1). There is statistically significant increase in corrected calcium (calcium-c) (p=0.008); phosphorus (p=0.000), and calcium phosphate product (Ca X P) (p=0.000), and significant decrease in serum albumin (p=0.018). As regard to the lipid profile, there was a statistically significant increase in serum TGS; and LDL-C; and significant decrease in cholesterol and HDL-C in diseased group than controls (Table 2).

Table (1): Chemical parameters for diseased and healthy control groups (data presented as mean ± SD).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Disease Group N=53</th>
<th>Healthy Control Group N=17</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (gm/l)</td>
<td>38.8±5.6</td>
<td>42.4±4.3</td>
<td>0.018 Sig</td>
</tr>
<tr>
<td>Calcium-c (mg/dl)</td>
<td>10.5±3.5</td>
<td>8.9±1.2</td>
<td>0.008 HS</td>
</tr>
<tr>
<td>Phosph. (mg/dl)</td>
<td>7.1±2.3</td>
<td>3.9±0.8</td>
<td>0.000 HS</td>
</tr>
<tr>
<td>Ca X P product</td>
<td>75.5±39.9</td>
<td>34.7±7.4</td>
<td>0.000 HS</td>
</tr>
</tbody>
</table>

Calcium-c: Calcium corrected. Phosph: Phosphorus. HS: Highly significant.

Table (2): Lipid profile for diseased and healthy control groups (data presented as mean ± SD).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Disease Group N=53</th>
<th>Healthy Control Group N=17</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>131.2±31.2</td>
<td>166.6±31.2</td>
<td>0.000 HS</td>
</tr>
<tr>
<td>TG.c (mg/dl)</td>
<td>143.8±63.7</td>
<td>107.1±59.1</td>
<td>0.037 Sig</td>
</tr>
<tr>
<td>HDL.c (mg/dl)</td>
<td>32.4±15.2</td>
<td>42.5±12.1</td>
<td>0.008 HS</td>
</tr>
<tr>
<td>LDL.c (mg/dl)</td>
<td>141.5±43.8</td>
<td>105.7±31.6</td>
<td>0.001 HS</td>
</tr>
</tbody>
</table>

TG : Triglycerides. HDL.c: High density lipoprotein cholesterol. LDL.L: Low Density lipoprotein cholesterol.

Table (3) presents the serological markers with statistically significant decrease in serum fetuin (p=0.002); and non significant difference in serum CRP (p=0.400), IL-6 (p=0.464) between diseased group and controls.

Fetuin-A did not correlate with sex, dialysis duration in months, calcium, phosphorus, albumin, IL6, and CRP in patients with CRF with dialysis.

Table (3): Serological markers for Disease and Healthy control groups (data presented as mean rank).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Disease Group N=53</th>
<th>Healthy Control Group N=17</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetuin (ng/ml)</td>
<td>31.3</td>
<td>48.8</td>
<td>0.002 HS</td>
</tr>
<tr>
<td>CRP (ug/ml)</td>
<td>36.7</td>
<td>31.8</td>
<td>0.400 NS</td>
</tr>
<tr>
<td>IL6 (pg/ml)</td>
<td>36.5</td>
<td>32.4</td>
<td>0.464 NS</td>
</tr>
</tbody>
</table>

CRP: C-reactive protein. IL6 : Interlukin 6.

As regard to the haematological results, a statistically significant decrease in RBCs (p=0.000), haemoglobin (Hb %) (p=0.000), and haematocrit value (HCT) (p=0.000) in diseased group than controls (Table 4).

Table (4): Hematological results for Disease and Healthy control groups (data presented as mean ± SD for continuous data).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Disease Group N=53</th>
<th>Healthy Control Group N=17</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC (million/mm³)</td>
<td>3.5±1.1</td>
<td>4.6±0.7</td>
<td>0.000 HS</td>
</tr>
<tr>
<td>HGB (gm%)</td>
<td>8.9±2.4</td>
<td>12±2</td>
<td>0.000 HS</td>
</tr>
<tr>
<td>HCT (%)</td>
<td>27.5±7.1</td>
<td>36.9±5.8</td>
<td>0.000 HS</td>
</tr>
</tbody>
</table>

Table (5) shows valve and carotid calcification correlations with some affecting variables in the study respectively, there was a statistically significant inverse correlation between the level of Fetuin A and both valvular and carotid calcifications. As regard to the albumin level there was inverse correlation with both valvular and carotid calcifications $r = -0.539, p = 0.000, r = -0.401, p = 0.000$ respectively (Tables 6,7). Table (7) shows a comparison of the radiological findings between the two studied groups. Fig. (1) shows normal carotid artery. Calcified lesions in the carotid artery were shown in Figs. (2-4), and Figs. (5-7) show valvular calcifications.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Valve Cal.</th>
<th></th>
<th>Carotid Cal.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$p$</td>
<td>$r$</td>
<td>$p$</td>
</tr>
<tr>
<td>D D M</td>
<td>0.164</td>
<td>0.154</td>
<td>0.377</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin</td>
<td>$-0.539$</td>
<td>0.000</td>
<td>$-0.401$</td>
<td>0.000</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0.256</td>
<td>0.027</td>
<td>0.293</td>
<td>0.011</td>
</tr>
<tr>
<td>Cor. calcium</td>
<td>0.545</td>
<td>0.000</td>
<td>0.408</td>
<td>0.000</td>
</tr>
<tr>
<td>Ca x P product</td>
<td>0.551</td>
<td>0.000</td>
<td>0.482</td>
<td>0.000</td>
</tr>
<tr>
<td>HDL</td>
<td>$-0.043$</td>
<td>0.712</td>
<td>$-0.186$</td>
<td>0.108</td>
</tr>
<tr>
<td>LDL</td>
<td>0.362</td>
<td>0.002</td>
<td>0.209</td>
<td>0.068</td>
</tr>
<tr>
<td>Fetuin</td>
<td>$-0.509$</td>
<td>0.000</td>
<td>$-0.405$</td>
<td>0.000</td>
</tr>
<tr>
<td>CRP</td>
<td>0.132</td>
<td>0.249</td>
<td>$-0.016$</td>
<td>0.886</td>
</tr>
<tr>
<td>IL 6</td>
<td>0.029</td>
<td>0.801</td>
<td>0.004</td>
<td>0.971</td>
</tr>
<tr>
<td>Carotid cal.</td>
<td>0.502</td>
<td>0.000</td>
<td>0.502</td>
<td>0.000</td>
</tr>
<tr>
<td>LV function</td>
<td>0.365</td>
<td>0.007</td>
<td>0.476</td>
<td>0.000</td>
</tr>
<tr>
<td>LVH</td>
<td>0.127</td>
<td>0.363</td>
<td>0.370</td>
<td>0.006</td>
</tr>
<tr>
<td>E.F</td>
<td>$-0.247$</td>
<td>0.074</td>
<td>$-0.383$</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table (6): Valve calcification and means of some correlated variables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>$-\text{Valve C}$</th>
<th>$+\text{Valve C}$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>D D M</td>
<td>55±36</td>
<td>73.5±39.9</td>
<td>0.122</td>
</tr>
<tr>
<td>Fetuin</td>
<td>33.2</td>
<td>12.7</td>
<td>0.000</td>
</tr>
<tr>
<td>CRP</td>
<td>28.6</td>
<td>23.8</td>
<td>0.249</td>
</tr>
<tr>
<td>IL 6</td>
<td>26.7</td>
<td>27.8</td>
<td>0.801</td>
</tr>
<tr>
<td>Albumin</td>
<td>41.2±3.7</td>
<td>33.2±5.2</td>
<td>0.000</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>6.6±1.9</td>
<td>8.2±3</td>
<td>0.052</td>
</tr>
<tr>
<td>Cor. calcium</td>
<td>9±1.8</td>
<td>13.9±4</td>
<td>0.000</td>
</tr>
<tr>
<td>Ca x P product</td>
<td>60.1±24.4</td>
<td>111±46.3</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL</td>
<td>33.3±16.3</td>
<td>30.3±12.5</td>
<td>0.461</td>
</tr>
<tr>
<td>LDL</td>
<td>128.9±39.3</td>
<td>170.6±40.5</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table (7): Comparison of the radiological findings between the two studied groups.

<table>
<thead>
<tr>
<th>Disease group</th>
<th>Healthy Control group</th>
<th>$p$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid state: Calcified</td>
<td>23 (43.4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Normal</td>
<td>30 (56.6%)</td>
<td>17 (100%)</td>
</tr>
<tr>
<td>Valve calcification: Calcified</td>
<td>16 (30.2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Normal</td>
<td>37 (69.8%)</td>
<td>17 (100%)</td>
</tr>
<tr>
<td>LV state: LVH</td>
<td>25 (47.2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Normal</td>
<td>28 (52.8%)</td>
<td>17 (100%)</td>
</tr>
<tr>
<td>LV diastolic dysfunction: Impaired</td>
<td>21 (39.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Normal</td>
<td>32 (60.4%)</td>
<td>17 (100%)</td>
</tr>
</tbody>
</table>

LV: Left ventricular.
LVH: Left ventricular hypertrophy.
EJ.FRA: Ejection fraction.
Fig. (1): Picture of normal carotid.

Fig. (2): Left carotid intima and media thickness, and calcified lesions.

Fig. (3): Intima and media thickness, and calcified lesion in the left bulb.

Fig. (4): Calcified carotid bulb.

Fig. (5): Echocardiogram reveals aortic sclerosis and calcification (arrow) of aortic valve leaflets.

Fig. (6): Image of the thickening and calcification of aortic valve.

Fig. (7): Echocardiography reveals mitral valve calcification.
Discussion

For the renal failure, traditional risk factors and new risk factors have a role in vascular inflammation and vascular calcification [5].

Our study shows there was a decrease in fetuin-A level in those patients who suffer from CRF, treated with dialysis in comparison with healthy controls and the presence of VC was negatively correlated with the level of fetuin-A. These results were consistent with other studies [4,17]. In dialysis patients, both atherosclerosis (mainly affecting the intima of the arteries) and arteriosclerosis (affecting predominantly the media of large- and middle-sized arteries diffusely) are highly prominent [18].

Also, these results go hand in hand with Wang and co workers [19] who noticed significant negative correlation between serum fetuin-A and valvular calcification as detected by echocardiography; patients with the lowest serum fetuin-A had the highest mortality.

A decrease in serum fetuin-A, the associations among valvular calcification, inflammation, carotid atherosclerosis, and arterial calcification suggest that valvular calcification is a marker of atherosclerosis and arterial calcification in patients with ESRD [20].

In our study, we had found that the diseased group had higher serum phosphorus level, however there is direct correlation with vascular calcification. This suggests that hyperphosphatemia could be regarded as a risk factor for vascular calcification and cardiovascular morbidity; however it has no direct mathematical correlation with the serum fetuin-A. This finding is supported by study done by Stevens and co workers [21] who found a direct association between hyperphosphatemia and cardiovascular morbidity especially left ventricular hypertrophy.

In this study there was no significant correlation could be detected between the triglycerides level, cholesterol level, duration of dialysis, age, and gender with the serum fetuin-A. These findings go hand in hand with a multinational cohort study [20]. Also our results agree with other study [22], which suggests that valvular calcification and the calcification milieu are part of the processes linking loss of residual renal function (RRF) and worsening cardiac hypertrophy.

Although our patient ages were less than 45 years (mean age was 31.2±8.1 years) the presence of VC was similar to the result of previous study [23] who stated that young adults with childhood-onset CRF have a high prevalence of arteriopathy associated with indicators of microinflammation. Valve calcification in CRF, provides a new insight into the pathophysiology of cardiovascular calcification. Clinical studies have demonstrated that 50% of individuals with chronic renal disease (CRD) die of cardiovascular causes, including advanced calcified arterial and valvular disease. However, the mechanisms of accelerated calcification in chronic renal diseases remain obscure, and no therapies can prevent disease progression [24].

Our study shows no significance difference in CRP and IL-6 between diseased and healthy controls, and no correlation between these markers and VC. These results were supported by other studies which reported that a large intracardiac variation in inflammatory indexes is observed in HD patients. For the investigation of the factors influencing this variation, more longitudinal studies, including more patients and eventually more parameters (e.g. pro-inflammatory molecule gene polymorphisms) are needed [25,26]. At the same time our result was different from the results of other series [27-29] that recognized that about 30-50% of HD and peritoneal dialysis patients had elevated serum levels of CRP. In patients with CKD stage 5 patients, the serum fetuin-A concentration is significantly lower than in healthy individuals and is associated with increased levels of CRP and with enhanced cardiovascular mortality [30]. Previous study did not demonstrate such relations between serum fetuin-A concentrations and serum levels of CRP and albumin [25].

The role of inflammation in the medial aortic vascular calcification observed with CKD is uncertain. With this pathology, apoptotic bodies in the elastin-layer of the vessel media act as crystallization niduses in medial calcification [31]. This differs from atherosclerosis, which has inflammatory cells and lipid-deposition in the intima. It should be noted that there is controversy regarding this distinction between medial and intimal calcification [32,33].

In our study no correlation was found between CRP and VC. This is consistent with results of Sigrist and co workers [34] who found no association between CRP and VC; however, the importance of inflammation cannot be discounted, because no other circulating markers of inflammation were measured. There is no significant association between CRP and a decline in GFR in adults with renal disease [35].
Fetuin-A was a significant and independent predictor of vascular stiffness and calcification irrespective of dialysis vintage, implying that genetic polymorphisms may indeed play a role in an individual patient’s susceptibility to calcify, possibly by modulating the magnitude of change in fetuin-A production in response to a pro-inflammatory or pro-calcific environment. Also there is evidence to suggest that Asians may have a lower prevalence of inflammation compared to the Caucasians. The carotid intima-media thickness, CRP and serum albumin predict long-term mortality in ERSD patients. No correlation was evident between nutritional markers and inflammatory indexes. Data suggest that elevated CRP per se does not cause cardiovascular diseases (CVD); however, inflammation per se possibly contributes to CVD. Elevated CRP levels more likely is a marker for the extent of atherosclerosis or for the inflammatory activity and vulnerability of atherosclerotic plaques, and thus simply an innocent bystander in CVD.

There is a significant correlation between serum IL-6 and CRP levels and clinical outcome in young patients with IgA nephropathy.

The best-studied cardiovascular biomarker of inflammation is CRP, an acute-phase reactant produced predominantly by hepatocytes under the control of interleukin 6 (IL-6). Possible proatherogenic effects of CRP include activation of the complement system, binding to low-density lipoprotein (LDL) and very-LDL, and stimulation of tissue factor. On the other hand, because variations within the IL-6 gene were shown to affect the risk for CVD in a multiethnic dialysis cohort, this suggests that IL-6 should be the target for interventional studies.

IL-6 stimulates secretion of CRP from the liver, monocyte chemotactic protein (MCP-1) from macrophages, and adhesion molecules and cytokines from endothelial cells. Cellular sources of IL-6 include monocytes, fibroblasts, endothelial cells, and adipocytes. Adipocyte production explains the associations of abdominal obesity and CRP levels in CVD.

Our study shows significant increase in VC in relation to the duration of dialysis mainly in carotid calcification which agrees with a powerful study on 10.000 heart disease patients reported that coronary artery calcification (CAC) increased with the duration of dialysis. Other investigators such as Goodman et al also showed similar results regarding relation of duration of HD to CAC.

The impairments of the mineral metabolism, in particular phosphate and serum calcium, are very common in CKD patients and play an important role in the development of cardiovascular disease by promoting VC and being associated with higher mortality risk.

In this study, there was a good statistical relation between serum calcium (corrected); phosphorus and calcium phosphate product levels, and VC among HD patients. These results are similar to other studies who found that serum calcium was strongly associated with baseline coronary but not aortic calcium scores. They concluded that each 1 mg/dl increase in serum calcium was associated with a risk for VC, equivalent to five years of dialysis therapy. Furthermore, in patients with advanced CKD, other nonconventional CVD risk factors, such as calcium-phosphate product, inflammation, oxidative stress, and insulin resistance, are likely to have a significant contributory role.

In response to raised concentrations of extracellular Ca and/or P ions, VSMC calcification is accelerated under these conditions; VSMC shed numerous membrane-bound vesicles. These vesicles are a mixture of apoptotic bodies (AB) released from dying VSMC and matrix vesicles (MV) released from viable cells. Both have the capacity to nucleate basic calcium phosphate (BCP), and their accumulation in the VSMC matrix results in rapid and widespread calcification. The relation between serum calcium levels and VC among HD patients is still controversial. The results of several studies go against our result of the present study.

All of our patients at time of examination were taking calcium based oral phosphate binders (OPBs) in the form of calcium carbonate, and all patients received oral Vitamin D as well (one alfa). Other investigators such as Shahapuni, et al., were able to show that there was no significant relation between load of cumulative calcium intake given to HD patients and CAC. In 2002 came the first randomized prospective study that has shown that the progression of coronary and aortic calcification may be attenuated, and that the type of phosphate chelators used may have an influence on the extension of the calcification.

Our study showed hypoalbuminemia in diseased group which agree with several studies. It has been widely accepted by the nephrologists that malnutrition as defined by reduced levels of serum albumin predicts poor outcomes. Hypoalbuminemia...
in HD patients was considered multifactorial risk factor [58]. Increasing evidence supports the existence of a relationship between malnutrition, low serum albumin, and both overall and cardiovascular morbidity and mortality in dialysis patients [57, 59, 60].

There is also a role of hypoalbuminemia which acts in synergy with other factors to increase the cardiovascular burden in renal failure patients. However the most of these factors to draw attention is vascular calcification [7].

Malnutrition and chronic inflammation are frequently-occurring complications in dialysis patients. These conditions are associated with cardiovascular diseases and predict hospitalisation and mortality [61].

Our study has several limitations that need consideration. First, this is a prognostic rather than etiologic study. All parameters were measured on a single occasion at baseline and did not take changes over time into account. Multiple measurements would provide a more precise estimate of the true values. Second, echocardiography was used to detect VC and was unable to quantify the true values. Second, echocardiography was used to detect VC and was unable to quantify the true values.

We conclude from this study that patients with ESRD on chronic haemodialysis are predisposed to morbidity from cardiovascular diseases more frequently-occurring complications in dialysis patients. These conditions are associated with cardiovascular diseases and predict hospitalisation and mortality [61].

Low fetuin-A was independent risk factor for VC which acts as inhibitory factor for this process. So it may be used as a marker for calcification. There is debate about the role of IL6 and CRP in its significances.

We conclude from this study that patients with ESRD on chronic haemodialysis are predisposed to morbidity from cardiovascular diseases more than healthy persons; ranging from arterial and valvular calcification, hypertension, left ventricular hypertrophy, left ventricular diastolic dysfunction, impairment of ejection fraction.

References

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