The prevalence of silent myocardial ischemia and its association with cardiovascular diseases risk factors in dialysis patients in Imam Reza Hospital, Kermanshah, Iran in 2013-14

Mahnaz Hajemoradi¹, Hashem Kazerani²*, Hamidreza Omrani³

1. Kermanshah University of Medical Sciences, Kermanshah, Iran
2. Cardiology Department, Medical School, Kermanshah University of Medical Sciences, Kermanshah, Iran
3. Nephrology Department, Medical School, Kermanshah University of Medical Sciences, Kermanshah, Iran

*Corresponding Author email: Imamaliamozesh@yahoo.com

ABSTRACT: Cardiac diseases are the main cause of mortality among end stage renal disease (ESRD) patients. This study was done in order to determine the prevalence of silent myocardial ischemia in hemodialysis patients admitted to the Imam Reza Hospital, Kermanshah, Iran in 2013-14. This cross-sectional study was done on hemodialysis patients presented to the Imam Reza Hospital of Kermanshah, Iran in 2013-14. The sample size was calculated as 60 individuals. After interviewing with 248 hemodialysis patients and considering the inclusion and exclusion criteria, the required data were gathered from their medical records. All patients underwent dipyridamole scan with the SPECT (Single Photon Emission Computed Tomography) method. The data were analyzed by the SPSS (ver. 20.0) software using the independent t-test and Chi-squared test. Mean (±SD) age of the patients was 51.5 (±11.8) years and 38 subjects (63.3%) were male. None of the patients had previously diagnosed by a cardiac condition. Dipyridamole scan showed that 23.3% of the patients had silent myocardial ischemia. The analyses showed that none of the studied factors (including age, gender, diabetes mellitus, cigarette smoking, hypertension, serum total cholesterol, triglyceride, hematocrit, albumin, phosphate, calcium, parathyroid hormone, creatinine as well as hemodialysis duration) had significant association with silent myocardial ischemia (P> 0.05). The prevalence of silent myocardial ischemia was 23.3% which is lower compared to previous studies. However, we think that further studies are required in this field. In all patients, in particular those with cardiovascular diseases risk factors, screening is recommended.

Keywords: Silent myocardial ischemia; prevalence; hemodialysis; cardiac disease

INTRODUCTION

Cardiac diseases are the main cause of mortality among end stage renal disease (ESRD) patients. About 50% of causes of mortality in such patients are attributed to cardiac diseases (1, 2). The rate of coronary artery disease (CAD), which is the main cause in pathogenesis of cardiac disease, is 5-20% higher in ESRD patients than in normal population (3). In order to decrease the rate of mortality and complications of CAD in general population, effective programs and better interventions are implemented to control the risk factors of CAD. However, such programs are not usually introduced for ESRD patients (5). The risk factors of CAD are fully recognized in general population (6). The Framingham study and similar ones have described some atherogenic risk factors including aging, male gender, family history of CAD, hypertension, diabetes mellitus, cigarette smoking, and elevated serum cholesterol level. Recently, serum homocysteine and lipoprotein A have also been implicated as risk factors for developing CAD. Recognition of these risk factors necessitates development of strategies to control such factors (7, 8). Most of these conventional risk factors are seen in patients with renal failure (9-11). However, it is not clear that whether similar to general population, these factors are predictive of CAD in renal failure patients. This issue becomes prominent when knowing the fact that limited published studies have investigated the association between CAD risk factors and CAD among patients with ESRD.
High rate of CAD in new hemodialysis patients has postulated the assumption that uremic state per se is arterogenic. Anemia, hypoalbuminemia, hyperphosphatemia, and metabolic acidosis may be the responsible factors for high rate of CAD. Limited studies have been done regarding the effect of uremia on increasing the risk of cardiac diseases. Till now, hyperphosphatemia, hyperparathyroidism, and elevated serum levels of lipoprotein A and homocysteine have been associated to CAD in ESRD patients (10-14). In addition, a recent cross-sectional study on 400 subjects (257 with normal renal function and 160 with renal failure) reported that elevated serum level of lipoprotein A was significantly associated with atherosclerotic diseases among ESRD patients (14).

Since there is no study in our country in order to determine the prevalence of silent myocardial ischemia in hemodialysis patients and in other foreign studies, the history of cardiac disease has not been controlled, we decided to study the prevalence of silent myocardial ischemia in hemodialysis patients admitted to the Imam Reza Hospital, Kermanshah, Iran in 2013-14.

**MATERIALS AND METHODS**

This cross-sectional study was done on hemodialysis patients admitted to the Imam Reza Hospital, Kermanshah, Iran in 2013-14. There were 248 patients who required hemodialysis. With considering the ischemia with a prevalence of 70% in these patients, alpha= 0.05, and power of 10%, the sample size was calculated as 60 persons.

To recruit the required sample size, firstly we conducted interviews with all 248 patients. During the interviews, the presence of any sign or symptom indicative of cardiac condition (i.e., chest pain, dyspnea, physical activity level, medications taken, previous history of cardiac disease) were asked. The patients who were asymptomatic and according to the definition of silent myocardial ischemia had never experienced any coronary artery event in the past, were not taking any medication, and were asymptomatic were selected. Those for whom the diagnosis of CAD had been made before or after hemodialysis, aged less than 25 years, or had received renal transplantation were excluded from the study.

After completing the interviews, 60 patients who were eligible for the study were selected and the required data were gathered by reviewing their medical records. These included medical history, laboratory findings, hypertension, diabetes mellitus, cigarette smoking, serum total cholesterol level, triglyceride level, hematocrit, albumin, phosphate, calcium, parathyroid hormone, and creatinine. The gathered data were controlled by repeated history taking from the patients.

At the next stage, the selected patients underwent dipyridamolescan with the SPECT (Single Photon Emission Computed Tomography) method. The SPECT method is one of the routine methods in nuclear medicine to study myocardial function. In this method, radioisotope is injected and uptake of the radioisotope from the bloodstream occurs by live myocardial tissue and the radioisotope remains for a short time in the myocardial tissue. In areas with ischemia, the uptake occurs slowly and in lesser amount. And in areas with myocardial cell death and scar, the radioisotope uptake does not occur at all. In this method, imaging is done at 3 levels (horizontal, vertical, and short oblique). Finally, those who had positive SPECT findings underwent medical treatment and a male patient underwent angiography which revealed two-vessel CAD. For this patient, drug-eluting stent was placed.

The gathered data were entered into the SPSS software (ver. 20.0) for analyses. To determine the association between qualitative variables and dependent variables, the Chi-squared test was used. To determine the association between quantitative variables and dependent variables, the independent t-test was used. The P value was set at 0.05.

**RESULTS**

Sixty hemodialysis patients with age range of 30-83 years and mean (±SD) age of 51.5 (±11.8) years were studied. There were 38 males (63.3%). None of the patients had previous history of cardiac disease. The results of dipyridamolescan showed that 14 patients (23.3%) had silent myocardial ischemia. During the study period which lasted for 1 year, two patients died. One of them was a 44-year-old male who had positive dipyridamolescan. The other was a 45-year-old female whose dipyridamolescan was negative.

According to the analyses, no significant association existed between the age of the patients and silent myocardial ischemia. Mean (±SD) age of those with and without silent myocardial ischemia were respectively 51.0 (±12.0) and 51.65 (±11.87); P= 0.85, 99% CI= 0.94-1.04. Although silent myocardial ischemia was more common in males (31.6%, 12 cases) than in females (9.1%, 2 cases), no significant association was observed between gender and ischemia (P= 0.06, odds ratio= 4.61; CI= 0.92-23.0).

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About 83.3% of the patients had hypertension and among these, 13 subjects had silent myocardial ischemia. Even though the rate of silent myocardial ischemia was higher in hypertensives, no significant association existed between hypertension and silent myocardial ischemia (P = 0.42).

There were 21 subjects who had diabetes mellitus (35%). Of this, 7 had positive dipyridamole scan results and in 14 no evidence of silent myocardial ischemia was found. Although silent myocardial ischemia was more common in diabetics (33.3%) than in non-diabetics, no significant association was found between diabetes mellitus and silent myocardial ischemia (P = 0.21). Of 20 smokers, 5 had silent myocardial ischemia. Likewise, there was no significant association between smoking and occurrence of silent ischemia (Table 1).

**Table 1. The association between background variables and occurrence of silent myocardial ischemia in hemodialysis patients admitted to Imam Reza Hospital**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Silent myocardial ischemia</th>
<th>All patients</th>
<th>Odds ratio (confidence interval)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>26 (31.7%)</td>
<td>12 (31.6%)</td>
<td>38 (63.3%)</td>
<td>4.61 (0.92-23.0)</td>
</tr>
<tr>
<td>Female</td>
<td>20 (22%)</td>
<td>2 (9.7%)</td>
<td>22 (36.7%)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>32 (82.1%)</td>
<td>7 (17.9%)</td>
<td>39 (65%)</td>
<td>2.28 (0.67-7.75)</td>
</tr>
<tr>
<td>Yes</td>
<td>14 (66.7%)</td>
<td>7 (33.3%)</td>
<td>21 (35%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>9 (90.9%)</td>
<td>1 (10%)</td>
<td>10 (16.7%)</td>
<td>3.16 (0.36-27.43)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes 7 (74%)</td>
<td>13 (26%)</td>
<td>50 (83.3%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>37 (77.5%)</td>
<td>9 (22.5%)</td>
<td>40 (66.7%)</td>
<td>1.14 (0.32-4.02)</td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes 15 (75%)</td>
<td>5 (25%)</td>
<td>20 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>DM = diabetes mellitus</td>
</tr>
</tbody>
</table>

Of background quantitative variables, mean (SD) serum total cholesterol, triglyceride, hematocrit, and calcium washigher in those who had silent myocardial ischemia compared to those whose dipyridamole scan was negative. On the other hand, mean (SD) serum albumin, phosphate, parathyroid hormone, and creatinine were lower in those with silent myocardial ischemia in comparison to others (Table 2).

**Table 2. The association between background quantitative variables and occurrence of silent myocardial ischemia in hemodialysis patients admitted to Imam Reza Hospital**

<table>
<thead>
<tr>
<th>Silent myocardial ischemia</th>
<th>All patients</th>
<th>Odds ratio (confidence interval)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 51.65 (11.87)</td>
<td>51.0 (12.9)</td>
<td>51.5 (11.8)</td>
<td>0.99 (0.94-1.04)</td>
</tr>
<tr>
<td>Cholesterol 123.36 (31.99)</td>
<td>139.71 (36.7)</td>
<td>127.18 (72.39)</td>
<td>1.01 (0.99-1.03)</td>
</tr>
<tr>
<td>Triglyceride 114.69 (75.55)</td>
<td>124.92 (62.77)</td>
<td>117.08 (72.39)</td>
<td>1.0 (0.99-1.01)</td>
</tr>
<tr>
<td>Hematocrit 31.47 (4.92)</td>
<td>34.77 (6.32)</td>
<td>32.24 (5.41)</td>
<td>1.13 (0.99-1.29)</td>
</tr>
<tr>
<td>Albumin 4.08 (0.53)</td>
<td>4.06 (0.57)</td>
<td>4.08 (0.54)</td>
<td>0.91 (0.93-2.79)</td>
</tr>
<tr>
<td>Phosphate 5.2 (1.17)</td>
<td>4.73 (0.91)</td>
<td>5.09 (1.13)</td>
<td>0.67 (0.38-1.19)</td>
</tr>
<tr>
<td>Calcium 9.3 (3.29)</td>
<td>11.74 (7.13)</td>
<td>9.87 (4.53)</td>
<td>1.1 (0.98-1.25)</td>
</tr>
<tr>
<td>PTH 347.96 (340.23)</td>
<td>188.14 (170.32)</td>
<td>310.1 (315.7)</td>
<td>0.99 (0.98-1.00)</td>
</tr>
<tr>
<td>Creatinine 8.76 (2.54)</td>
<td>8.49 (2.58)</td>
<td>8.7 (2.53)</td>
<td>0.95 (0.75-1.21)</td>
</tr>
<tr>
<td>Hemodialysis duration 39.56 (26.19)</td>
<td>30.28 (22.04)</td>
<td>37.4 (25.41)</td>
<td>0.98 (0.95-1.02)</td>
</tr>
</tbody>
</table>

PTH = parathyroid hormone; all data are presented as mean (standard deviation).

The analyses showed that no significant association was observed between serum cholesterol, triglyceride, hematocrit, albumin, phosphate, calcium, parathyroid hormone, creatinine, and hemodialysis duration with occurrence of silent myocardial ischemia (P > 0.05); Table 2.

**DISCUSSION**

In this study we decided to determine the frequency of silent myocardial ischemia among hemodialysis patients who presented to the Imam Reza Hospital. Hence, 60 cases were selected and underwent SPECT method. It was revealed that the prevalence of silent myocardial ischemia was 23.3%. This figure is lower than the previously reported data (15-17). However, since in previous studies some included patients had previous history of cardiac condition, this discrepancy may be justified. Since, in our study none of the patients had previous history or cardiac disease and even they did not have any symptom indicative of cardiac disease, the obtained prevalence is considerable.

In the current study, no significant association was observed between age of the hemodialysis patients and occurrence of silent myocardial ischemia. The youngest patient aged 41 years and the oldest one aged 67 years. This indicates the importance of early screening for silent ischemia in hemodialysis patients. In Pochmalicki study et al. (1990) in Mondor hospital in France, age was one of the factors which has significant association with silent ischemia (16) which is not in agreement with our results. But in Narula et al. study (2000) in India, even though the prevalence of silent ischemia was different in the two studied groups, no significant difference was observed regarding the age of the two groups (17).
In the present study, of 14 patients who had silent myocardial ischemia, 12 were male (31.6%) and 2 were female (9.1%). Although no significant association was detected between gender and silent myocardial ischemia, this event was more common in males. In Stack (2001) and Soubassi (2007) studies, the prevalence of CAD was more common in males (18, 19). In the report by Hadj-Abdelkder 92003), silent ischemia was more common in males (15).

In this study, hypertension with a prevalence of 83.3% was the most common disease observed in hemodialysis patients. But no significant association was seen between hypertension and silent ischemia. This is in agreement with the report made by Hadj-Abdelkder (2003) who reported that hypertension, with a prevalence of 75%, was the most common comorbidity (15). The high rate of hypertension in the studied sample necessitates screening for hypertension in hemodialysis patients and paying more attention to this condition and its treatment.

Diabetes mellitus with a prevalence of 35% was the second most common disease in hemodialysis patients. The rate of silent ischemia in this group of patients was 33.3%. However, no significant association was observed between diabetes mellitus and occurrence of silent ischemia. In contrast, Pochmalicki et al. (1990) reported that diabetes had significant association with silent ischemia (16). Also, the prevalence of diabetes mellitus in Hadj-Abdelkder (2003) was 30% which is close to the current results (15).

Cigarette smoking was reported in 33.3% of the patients and the rate of silent ischemia in smokers was 25%. The analyses showed no significant association between smoking and occurrence of silent ischemia. In Hadj-Abdelkder (2003) study, the rate of smoking was 65% (15) which is higher than the current findings. Also, according to Pochmalicki et al. (1990), significant association existed between smoking and silent ischemia (16) which is in contrast to what we observed here.

In the current study, no significant association was detected between serum cholesterol, triglyceride, hematocrit, albumin, phosphate, calcium, parathyroid hormone, creatinine, and hemodialysis duration with silent ischemia. Mean (SD) cholesterol, triglyceride, and calcium was higher in those who had silent ischemia. Mean (SD) phosphate, albumin, parathyroid hormone, creatinine, and hemodialysis duration was lower in those with silent ischemia. This is in compatible with the results of Stack et al. study (2001) regarding lower albumin level, higher remaining renal function, and higher level of hematocrit (18).

Also, in the current study, two patients died during the one-year follow-up period. These included a 44-year-old male with positive dipyridamolescan and a 45-year-old female with negative dipyridamolescan. Also, mean age of patients with positive dipyridamolescan was 51.56 years. This indicates necessity for implementing early screening for cardiac diseases in hemodialysis patients.

CONCLUSION

The obtained results show that the prevalence of silent myocardial ischemia in hemodialysis patients was 23.3% which is lower compared to previous studies. However, further studies are required in this field. Screening for cardiac diseases for all hemodialysis patients, in particular those with cardiovascular diseases risk factors is recommended.

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