Original Article

Risk Factors for Premature Myocardial Infarction: A Matched Case-Control Study

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ABSTRACT

Background: Myocardial infarction in young age is increasing. Identifying risk factors could be important for health promotion. We studied classic atherosclerotic risk factors in premature myocardial infarction.

Methods: In this matched case-control study, atherosclerotic risk factors (hypertension, family history of coronary artery diseases, obesity, diabetes mellitus, dyslipidemia) of 98 patients affected by acute myocardial infarction aged under 50 years were compared with that of 98 healthy neighborhood controls.

Results: Mean levels of cholesterol, triglyceride, low-density lipoprotein, as well as systolic blood pressure and body mass index were significantly higher in cases than in controls. There was a positive association between coronary artery disease at younger age and dyslipidemia OR=2.8 [95% CI: 1.5, 5.2], smoking OR=6.4 [95% CI: 3.0, 13.5], systolic hypertension OR =3.1 [95% CI: 1.5, 6.3], family history of coronary artery diseases OR=10.9 [95% CI: 3.2, 37.9] and diabetes OR=2.5 [95% CI: 1.04, 6.2].

Conclusion: Smoking, systolic hypertension and dyslipidemia were the most common risk factors among patients with premature myocardial infarction.

Introduction

The World Health Organization (WHO) anticipated that non-communicable diseases (NCDs) would account for 7 of 10 deaths occurring in developing regions by 2020. In developing countries, NCDs not only tend to increase but also appear earlier in life\textsuperscript{1}.

Cardiovascular diseases (one of NCDs) are among the main causes of death worldwide. It is estimated that by 2030, almost 23.6 million people will die from cardiovascular diseases (CVDs), mainly from heart disease and stroke. In Iran, CVD is the most common cause of death\textsuperscript{2}. Most studies show that 4%-10% of patients with acute myocardial infarction (AMI) are below 45 years of age\textsuperscript{3}. Risk factors, clinical presentations, and prognosis of AMI are different between younger and older patients\textsuperscript{4}. Although the intra-hospital mortality of premature CAD is lower, its long term prognosis is
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poor (15-year mortality was 30%)\(^5\). Therefore, assessment of these young patients with AMI and looking for their potential risk factors are a priority that may help health authorities in designing primary and secondary preventive programs.

Several studies have been carried out on the occurrence of AMI regarding to the age in Iran\(^6,7\). However, the prevalence of potential CVD risk factors has not been extensively studied in premature MI patients and healthy people in Iran\(^8\). Accordingly, we designed the present case–control study in Birjand City, the east of Iran, in order to compare potential atherosclerotic risk factors in young adults aged under 50 years who experienced AMI for the first time.

Methods

This matched case-control study was carried out between 2005 and 2007 in Birjand City, the east of Iran. Cases were 94 young adult patients aged less than 50 years who experienced AMI for the first time and admitted to the coronary care units of Vali-Asr Hospital. Since this hospital is the only cardiac center in this city, the enrolled patients could be regarded as the representative of all the patients with AMI in the region. AMI was detected based on the presence of at least two of the following criteria\(^9\): (a) typical chest pain lasting for at least 30 minutes, (b) at least 1 mm ST elevation in two or more contiguous leads, with subsequent evolution of the changes on electrocardiography (ECG), (c) diagnostic cardiac enzyme changes: doubling of creatine kinase with at least 10% Creatine Kinase Myocardial Band (CKMB).

Neighborhood controls were selected. The cases and controls were frequently matched for age, sex, and residence. A standardized questionnaire was used for data collection. Demographic characteristics such as age, sex, tobacco use, family history of heart disease, diabetes mellitus, known history of hypertension and dyslipidemia were recorded.

Blood pressure was measured and recorded twice in the supine position using a mercury sphygmomanometer (ALPK2). Two trained nurses carried out all measurements adhering standardized protocols.

Body weight (in kilograms) was measured with an electronic scale (SECA; Germany). Body height was measured to as the subjects stood erected against a vertical wall mounted scale with heels, buttocks, and occiput in the Frankfort plane with anthropometric square. The subjects were dressed with light under cloth and wore no shoes throughout the measurements. BMI (kg/m\(^2\)) was calculated as the ratio of the body weight to the square of body height. Waist circumference was measured at the widest diameter between the xiphoid process of the sternum and the iliac crest. Hip circumference, was measured at the widest diameter over the greater trochanter.

Fasting blood sugar (FBS), total serum cholesterol (TC), and triglycerides (TG) were measured by taking a sample of 5mL blood from the right brachial vein after 12 hours overnight fasting. The blood samples were sent to central lab of Vali-Asr Hospital. FBS, TC, and TG were measured by the standard enzymatic method (Pars Azmon kit, Iran). The plasma levels of low-density Lipoprotein (LDL) and high-density lipoprotein (HDL) were measured using commercially available enzyme assay kits (Pars Azmon kit, Iran).

The Ethics Review Committee of Birjand University of Medical Sciences approved this study. All cases and controls signed the informed consent. We used Chi-square test and \(t\)-test at 0.05 significant levels for data analysis using SPSS software version 11.5.

Results

Mean age was 45.25 [95% CI: 44.2, 46.3] and 44.8 [95% CI: 43.7, 45.8] years among cases and controls respectively (P= 0.520). Seventy-five subjects (80.9%) in each group were male.

The mean level of cholesterol, triglyceride, systolic blood pressure, BMI and LDL were significantly higher in the cases than in the controls (Table 1). The effect of dyslipidemia, smoking, hypertension, family history of coronary heart disease and diabetes mellitus were significantly higher in cases as well (Table 2).
Table 1: Comparison of various common risk factors among cases and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases Mean</th>
<th>95% CI</th>
<th>Controls Mean</th>
<th>95% CI</th>
<th>Difference Mean</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>211.0</td>
<td>204.0, 218.0</td>
<td>168.3</td>
<td>161.4, 175.2</td>
<td>42.7</td>
<td>29.2, 56.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum triglyceride (mg/dl)</td>
<td>134.6</td>
<td>121.3, 147.9</td>
<td>157.6</td>
<td>137.2, 178.0</td>
<td>-23.1</td>
<td>-49.6, 3.5</td>
<td>0.090</td>
</tr>
<tr>
<td>Serum LDL (mg/dl)</td>
<td>128.6</td>
<td>120.9, 136.3</td>
<td>102.0</td>
<td>97.0, 107.0</td>
<td>26.6</td>
<td>16.8, 6.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum HDL (mg/dl)</td>
<td>47.0</td>
<td>44.7, 49.3</td>
<td>63.2</td>
<td>60.0, 66.4</td>
<td>10.8</td>
<td>6.6, 15.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting Blood Sugar (mg/dl)</td>
<td>122.6</td>
<td>110.4, 134.8</td>
<td>86.3</td>
<td>80.6, 92.0</td>
<td>36.3</td>
<td>21.8, 50.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass Index (kg/m²)</td>
<td>27.1</td>
<td>26.2, 28.0</td>
<td>25.7</td>
<td>24.8, 26.6</td>
<td>1.4</td>
<td>0.1, 2.6</td>
<td>0.040</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td>123.1</td>
<td>120.2, 126.0</td>
<td>117.6</td>
<td>114.9, 120.3</td>
<td>5.5</td>
<td>1.4, 9.6</td>
<td>0.010</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>80.3</td>
<td>78.5, 82.1</td>
<td>79.1</td>
<td>77.1, 81.1</td>
<td>1.2</td>
<td>-1.5, 3.9</td>
<td>0.410</td>
</tr>
</tbody>
</table>

Table 2: The effect of various risk factors on premature myocardial infarction

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases N=94</th>
<th>Controls N=94</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>Chi²</th>
<th>Adjusted ORb</th>
<th>95% CI</th>
<th>Wald test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker</td>
<td>Yes 43</td>
<td>No 51</td>
<td>6.4</td>
<td>3.0, 13.5</td>
<td>0.001</td>
<td>5.8</td>
<td>2.8, 12.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Dyslipemic</td>
<td>Yes 43</td>
<td>No 51</td>
<td>2.8</td>
<td>5.0, 5.2</td>
<td>0.001</td>
<td>2.6</td>
<td>4.7, 5.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>Yes 31</td>
<td>No 63</td>
<td>3.1</td>
<td>1.5, 6.3</td>
<td>0.002</td>
<td>3.2</td>
<td>1.7, 6.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Positive family history of CVD</td>
<td>Yes 25</td>
<td>No 69</td>
<td>10.9</td>
<td>3.2, 37.9</td>
<td>0.001</td>
<td>10.2</td>
<td>3.1, 37.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetic</td>
<td>Yes 18</td>
<td>No 76</td>
<td>2.5</td>
<td>1.04, 6.2</td>
<td>0.035</td>
<td>2.4</td>
<td>1.03, 6.1</td>
<td>0.030</td>
</tr>
</tbody>
</table>

a Cases and controls are frequently matched on age, gender, and residence
b OR estimate adjusted for age and sex using logistic regression

Discussion

The present study assessed the relationship between classic atherosclerotic risk factors and premature AMI. We found strong positive association between dyslipidemia, smoking, systolic hypertension, positive family history of CVD, diabetes and premature CVD. In Chan's study, 19.8% of young adult patients aged less than 45 years with CVD had a positive familial history³. Having a positive familial history is an independent and non-modifiable factor for CVD. It is necessary to screen members of susceptible families earlier than usual. It is also necessary to pay more attention to their lifestyle, physical activities, and body mass index.

This study showed the association between dyslipidemia and premature CAD. Mean levels of cholesterol and LDL in cases were significantly higher than that of controls. On the contrary, mean level of serum HDL among cases was significantly lower than that of controls. Positive correlation between serum cholesterol level and risk of cardiovascular diseases has been reported in some epidemiologic studies¹⁰.
The results of some clinical trials indicated that the treatment of hypercholesterolemia has been associated with reduction in cardiovascular events. Akosah et al. conducted a study on 449 patients younger than 50 years with acute coronary syndrome and showed that hypercholesterolemia (RR= 3.0), smoking (RR= 2.8) and diabetes (RR= 2.7) were associated with increased risk of early CVD. They estimated that total cholesterol must be even lower than National Cholesterol Education Program (NCEP’s) measures (lower than 200 mg/ml) to be effective in the prevention of coronary heart disease. Low HDL and hypertriglyceridemia are among other coronary risk factors. The serum HDL exerts its preventive effect on CVD through changing in the way of cholesterol transport. HDL removes extra cholesterol from the atherosclerotic plaque to liver. According to the results of Framingham study, 5 mg/dl reduction in HDL level is associated with 25% increased risk of AMI. However, the excess risk of coronary heart diseases due to increasing level of serum triglyceride is not clear. Recent investigations proposed that "high–rich-triglyceride atherosclerotic plaques" might tear and release free radicals.

This study, however, suggest a stronger positive association between smoking and CVD (OR=6.4). This finding is similar to that of other major epidemiologic studies. In a similar study in Athens, 100 patients younger than 36 years with AMI were compared with 100 healthy persons who were matched with respect to age and sex. Multivariate logistic regression analysis showed that current smoking increased 6-fold the odds of having AMI. Smoking is an independent risk factor for coronary artery disease. There is a clear association between smoking and coronary artery disease. The results of previous studies indicated that the relative risk of coronary artery disease reduces 36% subsequently to stop smoking cessation. Ramanthan et al. conducted a study on 254 patients with CVD and concluded that planning for quitting smoking should be started in cardiac rehabilitation centers. It seems regional attempts to quit smoking according to economic and cultural situation of the patients are more help full.

Hypertension is a very important risk factor of developing cardiac diseases. In one study, 12,000 male patients aged 40-60 years were followed for 25 years. It became evident that for each 10 mmHg increase in systolic blood pressure, the risk of coronary artery disease increases 1.25 times more. Akosah et al. found that hypertension and dyslipidemia, two major risk factors of CVD, are not well controlled in young adults. The reason is that researchers pay more attention to these two factors only in elderly. Another reason is that both physicians and patients control their blood glucose more strictly than their lipids and blood pressure. He suggested that young people should control their serum lipids and blood pressure more frequently.

In our study, diabetes mellitus was associated with increased risk of CVD. Similar results were reported in the previous studies. Both diabetic men and women are susceptible to coronary artery disease. The most common causes of death in these patients are cardiovascular diseases. Epidemiologic studies have shown that it is necessary to control blood pressure, lipid, and serum glucose levels in diabetic patients to reduce the risk of CVD.

Positive familial history of coronary artery disease was 26.3% among the cases. In Chan's study, 19.8% of young adult patients aged less than 45 years with CHD had a positive familial history. Having a positive familial history is an independent and non-modifiable factor for CVD. It is necessary to screen members of susceptible families earlier than usual. It is also necessary to pay more attention to their lifestyle, physical activities, and body mass index.

**Conclusion**

In conclusion, the present case-control study showed that CVD is associated with several common but mostly preventable risk factors. Hence, we recommend a national initiative to quit smoking, to have more physical activities, to improve life styles, and to promote healthy diets. We also propose screening programs for early detection of elevated blood pressure, high blood glucose, dyslipidemia, and control of these atherosclerotic risk factors to reduce CVD in young adults.
Acknowlegements

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Conflict of interest statement

There was no conflict of interest to be stated.

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References


