MICROALBUMINURIA: ASSOCIATION WITH ISCHAEMIC HEART DISEASE IN NON-DIABETICS

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INTRODUCTION

Ischemic heart disease (IHD) is among the most frequent causes of morbidity and mortality worldwide. In the presence of this alarming epidemic, the case for identifying and targeting patients with IHD for aggressive treatment to reduce cardiovascular risk is well established. Risk factors for the development of IHD include age, gender, smoking, blood pressure, body mass index, and abnormalities of serum lipids. However, these conventional risk factors do not account for all cases of IHD. The interest in improving cardiovascular risk profile, focusing preventive measures and therapeutic measures. Microalbuminuria (MA) as a marker of cardiovascular risk is well established. Risk factors, such as age, hypercholesterolemia and hypertension, is an important prerequisite for identifying and targeting patients with IHD for aggressive treatment to reduce cardiovascular risk over and above the assessment of classic risk factors. The present descriptive study was undertaken at Combined Military Hospital, Lahore to determine the frequency of MA in nondiabetic IHD patients. Methods: One hundred consecutive non diabetic patients with IHD (73 males, 27 females). Patients showing clinical albuminuria and with other causes of proteinuria were excluded. Urinary albumin in first morning sample was estimated by immunoturbidimetry method. Albumin to creatinine ratio (ACR) was calculated as mg/g. Results: The frequency of MA (ACR > 30 mg/g) was 37% in patients. Frequency was highest in older age bracket for both genders. The mean ACR was 131.8±66.2 mg/g. Significant difference was observed in mean MA level among different age groups. Conclusion: MA is common in nondiabetics patients with IHD. The mean level of MA was higher in older patients.

Key Words: Ischemic heart disease, nondiabetics, microalbuminuria, cardiovascular risk.

MATERIAL AND METHODS

This descriptive study spanning over three months from Sep to Nov 2004 was conducted in the Departments of Medicine and Pathology of Combined Military hospital, Lahore. The study
population included one hundred non diabetic IHD patients (73 were men, 27 were women), consecutively reporting to the hospital. The majority of patients belonged to middle socioeconomic group. The diagnosis of IHD was based on finding of characteristic electrocardiographic changes, cardiac enzyme elevation, positive coronary arteriogram or hospital discharge diagnosis of IHD. Patients with diabetes, macroalbuminuria, renal disease, urinary tract infection and cardiac failure were excluded. After obtaining informed verbal consent, recording of demographic data, brief clinical history and physical examination of patients were carried out. A 12- lead electrocardiography was recorded. Fasting blood and first morning urine samples were collected. Two more urine samples were taken on the following days. Blood was tested for urea, creatinine and glucose. Routine urine examination was performed. Urinary albumin and creatinine were estimated and albumin to creatinine ratio (ACR) was calculated. Urinary albumin was measured by immunoturbimetric method using a commercial kit (Randox Laboratories, UK). All the chemical analyses were carried out on Auto Analyzer Selectra E (Vital Scientific, The Netherlands). Patients were considered microalbuminuric if ACR was between 30-300 mg/g in 2 out of 3 urine samples. Below this level they were regarded as normoalbuminuric. All the data was recorded on a Performa. Then data was entered and processed on SPSS software V. 11. It was presented as percentages, means and standard deviation. Analysis of variance F-test was applied to observe the mean difference.

RESULTS

Out of a total 100 selected non diabetic patients with IHD, 73 were men and 27 women. The mean ages were 59.1±13.7 (range 31-90), 60.3±9.9 (range 42-80) and 59.4±12.8 (range 31-90) years in men, women and all patients respectively. Frequency of MA in different age groups of study population is described in Table 1. The relative frequency was same in both sexes. However, it was higher in older patients. In patients over 70 years the frequency was highest (45.5%). Table 2. shows a comparison of level of albuminuria in microalbuminuric patients in relation to age. The level of albuminuria increased with increasing age (Fig. 1). The average level of MA was 131.8±66.2 mg/g in the study population. Significant difference was observed in mean MA levels among different age groups.

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Number</th>
<th>Positive</th>
<th>Relative Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>9</td>
<td>3</td>
<td>33.3%</td>
</tr>
<tr>
<td>41-50</td>
<td>18</td>
<td>6</td>
<td>33.3%</td>
</tr>
<tr>
<td>51-60</td>
<td>24</td>
<td>8</td>
<td>33.3%</td>
</tr>
<tr>
<td>61-70</td>
<td>27</td>
<td>10</td>
<td>37.0%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>22</td>
<td>10</td>
<td>45.5%</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>37</td>
<td>37.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Mean±SD (mg/g)</th>
<th>Minimum (mg/g)</th>
<th>Maximum (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>55.0±15.6</td>
<td>44.4</td>
<td>72.9</td>
</tr>
<tr>
<td>41-50</td>
<td>79.7±41.0</td>
<td>42.5</td>
<td>136.9</td>
</tr>
<tr>
<td>51-60</td>
<td>133.5±42.2</td>
<td>75.4</td>
<td>198.9</td>
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<tr>
<td>61-70</td>
<td>153.3±85.2</td>
<td>40.8</td>
<td>290.8</td>
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<tr>
<td>&gt;70</td>
<td>163.2±50.2</td>
<td>85.9</td>
<td>225.9</td>
</tr>
<tr>
<td>Total</td>
<td>131.8±66.2</td>
<td>40.8</td>
<td>290.8</td>
</tr>
</tbody>
</table>

DISCUSSION

Worldwide, ischemic heart disease is assuming an increasing role as a major cause of morbidity and mortality. From 1990 to 2020, the proportion of worldwide deaths due to cardiovascular disease including IHD is expected to increase from 28.4% to 33.7%. In terms of years of life lost, cardiovascular disease will jump from fourth to first place. For premature death and disability, cardiovascular disease will move from fifth to first place. However,
Despite the rising tide of this tragic disease, the physicians’ ability to predict the development of a cardiovascular event is limited by the low prognostic specificity of the traditional risk factors for atherosclerosis. This justifies the ongoing search for new biomarkers of atherosclerosis.

In the current study it was found that the frequency of microalbuminuria was elevated in the study population (37%). This is significantly higher as compared to the general population which ranges from 2.2% to 10.2% in various studies depending on variations in ethnic groups, specimen collection, the cut off value of albumin excretion and the analytical methods. This finding is similar to that found in studies in the west. The frequency and level of MA in our study was found to be highest in the older age brackets for both genders. This positive correlation with age may be related to a degree of nephrosclerosis as found in an earlier study.

Patients with renal or urinary tract disease or diabetes mellitus were excluded from this study, as urinary albumin excretion is elevated in these diseases for reasons other than atherosclerosis. The use of early morning urine sample was preferred to minimize the contribution of posture and exercise to urinary albumin excretion. By using the albumin creatinine ratio any variations in the urine volume were taken into account.

Despite the above-mentioned strengths of the study, it must be admitted that it has some limitations namely the small sample size and the fact that it is a hospital based study. However, these matters can be addressed by undertaking large population based and prospective studies.

The hypothesis of microalbuminuria as an atherosclerotic risk factor stems from diabetic research. Several studies have now demonstrated that MA is an independent predictor of cardiovascular morbidity and mortality in non diabetic populations as well. It has been postulated that MA is a marker of generalized endothelial dysfunction, which is thought to be the first stage of atherosclerosis. According to the above hypothesis urine albumin should be elevated and MA occur more frequently in these patients. Therefore, the results of this study support the hypothesis and underline the clinical relevance of MA as a cardiovascular risk indicator even in the absence of diabetes mellitus.

In addition to scientific and academic speculation there is a very important practical aspect to the intriguing association between microalbuminuria and ischemic heart disease, which is of special significance for the clinician. The detection of microalbuminuria is straightforward, easy and inexpensive to perform and may be used to identify subjects at increased cardiovascular disease risk and to prompt screening for other risk factors.

Also, as it has been shown that an early increase of urinary albumin is a strong independent predictor of adverse clinical outcome in both men and women with acute myocardial infarction, stratification of patients into low- and high-risk groups can be facilitated by ACR. So, it has been suggested that this measurement be included in the routine clinical work up of the patient with acute myocardial infarction. The aspect that makes it more attractive than some of the other emerging risk markers is that microalbuminuria is a modifiable risk factor whose correction, as in the case of hypercholesterolemia or arterial hypertension, would reduce, in its own right, the incidence of cardiovascular disease morbidity and mortality.

In short, our study highlights that MA is more frequent in non diabetic patients with IHD than the general population and thus may be an important emerging risk marker for it. Further large population based prospective studies are needed to assess the relationship between the occurrence of microalbuminuria and subsequent risk of IHD. Eventually the measurement of MA may prove to be useful in cardiovascular risk profiling and prevention of IHD and result in new therapeutic strategies in the prevention of this disease.

Though population wide screening is not recommended due to lack of definitive evidence, screening for microalbuminuria should be considered in high risk subjects e.g. those with a strong family history of IHD, smokers, those with hypertension and hypercholesterolemia to improve cardiovascular risk profiling.

REFERENCES

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