Prevalence of Metabolic Syndrome and its Association with Coronary Artery Disease Among an Urban Elderly South Indian Population (CURES- 145)

Rajendra Pradeepa 1, Jayagopi Surendar 2, Karunakaran Indulekha 2, Sundarapandi Chella 3, Ranjit Mohan Anjana 4, Viswanathan Mohan 5

Abstract

Objective: The aim of this study was to assess the prevalence of metabolic syndrome (MS) and its association with coronary artery disease (CAD) among an elderly urban population in south India.

Methods: Individuals aged ≥60 years (n=222) were recruited from Phase 3 of the Chennai Urban Rural Epidemiology Study. Anthropometric and blood pressure measurements, oral glucose tolerance test, lipids and fasting insulin were carried out. Prevalence of MS was estimated using the World Health Organization (WHO), Modified National Cholesterol Education Program’s Adult Treatment Panel III (ATP-III) and International Diabetes Federation (IDF) criteria. Diagnosis of CAD was made by resting 12 lead ECG and/or past history of documented myocardial infarction.

Results: MS was identified in 45.9% (n=102) by modified ATP-III, 37.4% (n=83) by IDF and 45.5% (n=101) by WHO criteria respectively. Only 61 subjects (27.5%) were identified by all the three criteria. Female subjects had a significantly higher prevalence of MS compared to their male counterparts (45.8 vs. 31.0%, p=0.023 respectively) according to IDF criteria. It was observed that 59.8%, 53% and 45.6% of the subjects had all five abnormalities according to modified ATP-III, IDF and WHO, respectively. Subjects with MS had significantly higher prevalence of CAD compared to those without MS using all the 3 criteria (modified ATP-III -20.6 vs. 8.5%; IDF-20.5 vs.10.1%; WHO-19.8 vs.9.1% respectively). The odds ratio of developing CAD among MS subjects was 2.93, 2.39 and 2.48 compared to those without MS after adjusting for age, gender and family history of diabetes according to modified ATP-III, IDF and WHO, respectively.

Conclusion: Nearly 40% of the elderly urban south Indians have MS and it is strongly associated with CAD.

Introduction

The clustering of metabolic risk factors like central obesity, glucose intolerance, dyslipidemia, hypertension, hyperinsulinemia collectively defined as metabolic syndrome (MS)1 is observed in about one-third of urban South Asians.2 The prevalence of MS among urban Indians ranges between 25-45%.3,4 Globally, among the elderly population, MS prevalence is high and ranges from 45-65%,5,6 depending on the population studied and criteria used to define MS.

MS is considered as one of the major public health problems and is found to have high risk for CAD.7 Among men 45 years and

Editorial Viewpoint

• There is a rising incidence of metabolic syndrome (MS) among elderly, urban South Indian population.

• MS predisposes to coronary artery disease irrespective of age, gender or family history of diabetes.

• Impact of interventions like weight reduction and control of hypertension and diabetes on risk reduction needs to be studied further.
older and women 55 years and older, MS confers a moderately high risk of CAD (10-year risk of 10%–20%). Combined with the metabolic derangements of MS, insulin resistance (IR) is an important factor that may potentate the risk of premature CAD and type 2 diabetes. Several studies have published information on the prevalence of MS in the general population. However, only a few studies have reported MS and its association with CAD among the elderly, and none to our knowledge from India. Hence the present study was taken up to assess the prevalence of MS using three criteria (WHO, modified ATP-III and IDF) and evaluate its association with CAD among a representative elderly urban population in southern India.

**Methods**

The Chennai Urban Rural Epidemiology Study (CURES) is a large cross-sectional study done on a representative population of Chennai (formerly Madras) city in southern India with a population of about 5 million people. The detailed study design of CURES is described elsewhere and the sampling frame is shown on the web site (http://www.drmohansdiabetes.com/mdrf/CURES.pdf). Briefly, of the 155 Corporation wards in Chennai, 46 wards were randomly selected to provide a total sample size of 26001 individuals ≥20 years of age. Phase 1 of CURES was conducted in the field and involved a door-to-door survey of 26001 individuals. A detailed questionnaire was administered to all study subjects to collect information regarding demographic, socio-economic, behavioural and health status. A fasting capillary blood sugar, blood pressure and basic anthropometric measures were done in all eligible individuals. Phase 2 of CURES deals with studies on the prevalence of microvascular and macrovascular complications of diabetes among those identified with diabetes in Phase 1. Phases 1 and 2 are not discussed further in this article.

In Phase 3 of CURES, every tenth subject recruited in Phase 1 of CURES (n=2600) were invited to our centre for detailed anthropometric measurements and biochemical tests [response rate was 90.4% (n=2350)]. Out of these 2350 subjects, individuals aged ≥60 years (n=222) were included for the present study. The institutional ethical committee approval was obtained and written informed consent was obtained from all study subjects.

**Clinical and Biochemical Studies**

Anthropometric measurements including weight, height, hip and waist measurements were obtained using standardized techniques. The body mass index (BMI) was calculated using the following formula: weight (kg)/height (m)² and waist hip ratio (WHR) was calculated by dividing waist circumference (cms) by hip circumference (cms). Blood pressure was recorded in the sitting position in the right arm with a mercury sphygmomanometer (Diamond Deluxe Industrial Electronics and Products, Pune, India) and rounded off to the nearest 2 mmHg. Two readings were taken 5 minutes apart, and the mean of the two was taken as the blood pressure reading.

A fasting blood sample was taken for estimation of plasma glucose and serum lipids after an overnight fast of 8 hours. All study subjects underwent an oral glucose tolerance test (OGTT) using 75 gm glucose load, except self-reported diabetic subjects, for whom only fasting venous plasma glucose was measured. Fasting plasma glucose (glucose oxidase-peroxidase method), serum cholesterol (cholesterol oxidase-peroxidase-amidopyrine method), serum triglycerides (glycerol phosphate oxidase-peroxidase-amidopyrine method) and high-density lipoprotein (HDL) cholesterol (direct method – polyethylene glycol-pretreated enzymes) were measured using the Hitachi-912 Autoanalyzer (Roche Diagnostics/Hitachi, Mannheim, Germany). Urine samples were collected after an overnight fast. Microalbumin concentration was measured using an immunoturbidimetric assay (Hitachi 902 autoanalyzer, Roche Diagnostics, Mannheim, Germany). Serum insulin concentration was estimated using Dako kits (Dako, Glostrup, Denmark).

**Definitions**

**Diabetes:** Individuals diagnosed by a physician and on antidiabetic medications (self-reported) and/or those who had fasting plasma glucose (FPG) ≥126 mg/dl (³7 mmol/L) and/or 2 hour post load plasma glucose (2 h PG) ≥11.1 mmol/L (≥200 mg/dl).¹¹

**Impaired Glucose Tolerance (IGT):** Diagnosed if the 2 h PG was ≥7.8 mmol/L and <11.1 mmol/L (≥140 mg/dl and <200 mg/dl).¹¹

**Normal Glucose Tolerance (NGT):** If 2hPG was <7.8 mmol/L (<140 mg/dl).¹¹

**Coronary Artery Disease (CAD):** CAD was diagnosed based on a past history of documented myocardial infarction and/or electrocardiographic evidence of Q wave and/or ST segment changes.¹²

**Insulin Resistance (IR):** Calculated using the homeostasis assessment (HOMA) model using the following formula: fasting insulin (µLU/mL) × fasting glucose (mmol/L)/22.5. Subjects whose HOMA insulin resistance values were above the 4th quartile for the non-diabetic population (i.e.>2.58) were considered to have insulin resistance (homeostasis assessment insulin resistance (HOMA-IR)).³

**Metabolic Syndrome Definitions**

WHO Criteria: MS was defined as the presence of diabetes, impaired glucose tolerance or insulin resistance plus any two or more of the following: body mass index ≥30 kg/m² and/or waist-to-hip ratio >0.90 for men and >0.85
for women; high blood pressure ≥140/90 mm Hg or antihypertensive medication; triglycerides ≥150 mg/dL; reduced HDL cholesterol <35 mg/dL for men or <39 mg/dL for women; and urinary albumin excretion rate ≥20 μg/min.11

IDF Criteria: MS was defined as the presence of central obesity defined using South Asian cut points for waist circumference (≥90 cm for men and ≥80 cm for women) plus any two of the following factors: high blood pressure ≥130/85 mm Hg or treatment of previously diagnosed hypertension; elevated fasting glucose ≥100 mg/dL or previously diagnosed type 2 diabetes; triglycerides ≥150 mg/dL or specific treatment for this lipid abnormality; reduced HDL cholesterol <40 mg/dL for men or <50 mg/dL for women or specific treatment for this lipid abnormality.13

Modified ATP-III Criteria: MS was defined according to the National Cholesterol Education Program–ATP III criteria for adults.14 MS was defined as the presence of any three of the following abnormalities: central obesity defined using South Asian cut points for waist circumference (≥90 cm for men and ≥80 cm for women); high blood pressure ≥130/85 mm Hg, elevated fasting glucose ≥100 mg/dL, triglycerides ≥150 mg/dL, reduced HDL cholesterol <40 mg/dL for men or <50 mg/dL for women.

Statistical Analysis

Statistical analysis was done using SPSS version 20.0 (SPSS, Inc., Chicago, IL) for Windows. Data are expressed as mean ± SD. Chi square test for trend was used to compare proportions among groups. Logistic regression analysis was performed to assess the association of MS with CAD, adjusted for multiple key variables.

Results

The mean age of the study population (n = 222) was 66 ± 6 years and 56.8% (n = 126) of the subjects were males. Figure 1 presents the prevalence of MS among the elderly subjects using the three criteria.

![Fig. 1: Prevalence of metabolic syndrome among the elderly subjects using various criteria](image1)

**Table 1: Clinical and biochemical characteristics of the elderly with metabolic syndrome**

<table>
<thead>
<tr>
<th>Variables</th>
<th>MS by modified ATP-III criteria</th>
<th>MS by IDF criteria</th>
<th>MS by WHO criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (n)</td>
<td>102</td>
<td>83</td>
<td>101</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.4 ± 5.0</td>
<td>63.8 ± 4.4</td>
<td>65.6 ± 5.9</td>
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<tr>
<td>Waist (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>92.1 ± 7.4</td>
<td>95.5 ± 4.9</td>
<td>90.6 ± 8.5</td>
</tr>
<tr>
<td>Female</td>
<td>88.2 ± 9.4</td>
<td>90.1 ± 8.3</td>
<td>88.4 ± 10.4</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.3 ± 2.5</td>
<td>23.7 ± 2.3</td>
<td>23.0 ± 2.6</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>141.0 ± 21.1</td>
<td>141.8 ± 21.9</td>
<td>141.6 ± 23.0</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80.6 ± 10.5</td>
<td>81.0 ± 10.6</td>
<td>80.6 ± 9.8</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>125.6 ± 56.0</td>
<td>127.2 ± 53.1</td>
<td>127.2 ± 55.7</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>199.3 ± 37.6</td>
<td>201.2 ± 37.4</td>
<td>194.6 ± 37.2</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
<td>171.6 ± 92.0</td>
<td>158.0 ± 78.8</td>
<td>164.2 ± 91.9</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38.6 ± 7.8</td>
<td>40.5 ± 6.9</td>
<td>40.3 ± 9.0</td>
</tr>
<tr>
<td>Female</td>
<td>43.2 ± 10.2</td>
<td>43.8 ± 10.4</td>
<td>44.3 ± 11.3</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>124 ± 34</td>
<td>127 ± 33</td>
<td>119 ± 33</td>
</tr>
<tr>
<td>Microalbuminuria (µg/mg)</td>
<td>36.0 ± 66.5</td>
<td>38.6 ± 72.3</td>
<td>35.4 ± 59.8</td>
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<td>HOMA-IR</td>
<td>3.01 ± 2.19</td>
<td>3.06 ± 2.13</td>
<td>3.21 ± 2.22</td>
</tr>
<tr>
<td>Insulin resistance (µU/mL)</td>
<td>44 (43.1)</td>
<td>38 (45.8)</td>
<td>55 (54.5)</td>
</tr>
<tr>
<td>Age group (years) n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>89 (87.3)</td>
<td>75 (90.4)</td>
<td>79 (78.2)</td>
</tr>
<tr>
<td>70-79</td>
<td>10 (9.8)</td>
<td>7 (8.4)</td>
<td>17 (16.8)</td>
</tr>
<tr>
<td>80+</td>
<td>3 (2.9)</td>
<td>1 (1.2)</td>
<td>5 (5.0)</td>
</tr>
</tbody>
</table>

*p<0.05 compared to modified ATP-III criteria; ‘p<0.05, “p<0.01 compared to IDF criteria; #p for trend <0.001; MS: Metabolic syndrome"
Overall, MS was identified in 102 subjects (45.9%) by modified ATP-III criteria, in 83 subjects (37.4%) by IDF criteria and in 101 subjects (45.5%) by WHO criteria. The Venn diagram shows the overlap of subjects with MS based on the three definitions (Figure 2). Only 61 subjects (27.5%) were identified by all the three criteria. The κ statistics for agreement between IDF and modified ATP-III criteria was 0.77 (p <0.001), for IDF and WHO criteria it was 0.45 (p <0.001) and between the modified ATP-III and WHO criteria it was 0.56 (p <0.001).

Table 1 presents the clinical and biochemical characteristics of the elderly with MS using the three criteria. Subjects having MS according to WHO criteria were older (65.6 ± 6.0 years; p<0.05) compared to those with MS based on IDF criteria. For every 10 year increment in age, there was a decreasing trend in MS in the elderly population in both modified ATP-III (p<0.001) and IDF criteria (p<0.001) group. The prevalence of insulin resistance in the MS subjects was 43.1%, 45.8% and 54.5% using revised ATPIII, IDF and WHO criteria respectively.

The prevalence of metabolic risk factors as classified using the three different criteria in the elderly population was as follows; impaired fasting glucose (including self-reported diabetes) was observed in 42.8% and 39.6% of individuals on the basis of IDF and modified ATP-III criteria respectively. Abdominal obesity was present in 48.2%, raised blood pressure was seen in 63.1%, increased triglycerides in 29.3% and decreased HDL cholesterol levels in 54.1% of the elderly subjects, which is similar using both modified ATP-III and IDF criteria. According to the WHO criteria, abdominal obesity was present in 70.3%, increased triglycerides in 29.3% and decreased HDL cholesterol levels in 20.7%, raised blood pressure in 52.7% and microalbuminuria in 21.2% of the elderly population.

Figure 3 shows the prevalence of CAD in elderly subjects with and without MS according to different criteria. The overall prevalence of CAD in the study subjects was 14% (n=31). Subjects with MS had significantly higher prevalence of CAD compared to those without MS irrespective of the criteria used for defining MS (modified ATP-III: 20.6 vs. 8.5%, p= 0.009; IDF: 20.5 vs. 10.1%, p=0.030; WHO: 19.8 vs. 9.1%, p=0.022 respectively).

To assess the association of CAD with MS, multiple logistic regression analysis was done using CAD as the dependent variable (Table 2). The risk for developing CAD in subjects with MS was 2.9 times higher (p=0.012) than those without MS based on modified ATP-III criteria, 2.4 times higher (p=0.037) than those without MS based on IDF criteria and 2.5 times higher (p=0.028) than those without MS based on WHO criteria after adjusting for age, gender and family history of diabetes.

**Discussion**

The study highlights the following findings 1) A high prevalence of MS was observed in this elderly South Indian urban population based on the modified ATP-III, IDF and WHO criteria for MS. 2) Subjects with MS by all the three criteria were significantly associated with CAD after adjusting for potential confounders like age, gender and family history of diabetes.

In the past few decades, increased attention given to MS has led to several attempts to develop a definition that is accepted worldwide. However, there is as yet no internationally agreed definition for MS and, hence, prevalence of MS varies substantially depending on the criteria used. The World Health Organization (WHO) proposed a
set of diagnostic criteria, in 1998 followed by definitions from the National Cholesterol Education Program’s Adult Treatment Panel III (ATP-III) and the International Diabetes Federation (IDF). These definitions agreed that hyperglycemia, obesity, dyslipidaemia, and hypertension are core components of MS, but they differed in the details and criteria. In 2005, a modification (ATP-III) by the American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) was proposed with a reduced threshold for hyperglycemia and some minor modifications.

A wide variation is demonstrated in the MS prevalence among the elderly with a study from France showing 11.3% and 12.5% in women and men respectively as having MS according to modified ATP-III criteria. Use of the IDF criteria in a Greek population resulted in 69% of the elderly subjects having MS. Our study showed 45.9% and 37.4% of the elderly subjects, as having MS according to the modified ATP-III and IDF criteria respectively. These differences could be attributed to population specific factors and different diagnostic criteria applied. Moreover, our study showed an increased prevalence according to the modified- ATP-III criteria, whereas in other populations, a higher number of MS individuals was captured by the IDF criteria. Since the ATP-III criteria adopt ethnicity specific cut points, the prevalence rates might have been higher. Due to the variations in the prevalence of MS and the differential diagnostic ability of the criteria observed amongst different populations, it is necessary to obtain data for each country.

MS has been established as a strong predictor of cardiovascular disease and mortality in the general population and these findings have been extended to the elderly population as well in recent reports. In our study participants, the prevalence of CAD was nearly 20% in MS subjects categorized by ATP-III, IDF and WHO criteria showing a high degree of concordance between the three criteria. This agreement between ATP-III and IDF criteria has been recorded in other reports as well. The higher rates of insulin resistance observed in our elderly subjects (>40%) might be because of the tendency of Asian Indians towards higher visceral (abdominal) fat deposition and the direct causal link between abdominal fat and insulin resistance, might augment the prevalence of insulin resistance in our subjects.

In subjects with MS, intervention strategies for the control of hypertension, hyperglycemia and dyslipidemia would lead to reductions in the subsequent cardiovascular mortality. Moreover, approaches like weight reduction in the elderly might increase their insulin sensitivity. Implementation of these strategies is important in the elderly population as they are at increased MS risk due to age associated physiology.

There are some limitations for our study. Due to the cross-sectional design of the study, no cause/effect relationships can be made. Lifestyle factors like physical inactivity and their effect on occurrence of MS in the elderly were not assessed. However, ours is the first estimate of the burden of the metabolic syndrome in elderly subjects in India to report on population based study and hence the findings are of significance.

In conclusion, we report that nearly 40% of the elderly urban south Indians have MS using all three criteria, although they seem to identify different individuals. In addition, MS is strongly associated with CAD in the elderly subjects.

Competing Interests
None to declare.

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Author Contribution
VM conceived and designed the study. RP, JS, KI and SC analysed the data and wrote the manuscript. RMA and VM helped revising the manuscript critically for important intellectual content, read and approved the final manuscript.

References


