

## Metabolic syndrome in the Middle East

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### ABSTRACT

Metabolic syndrome (MS) is a combination of medical disorders that, in concert, increase the risk of developing cardiovascular disease and diabetes. It affects about one in four people in the Middle East, and prevalence increases with age. The aim of current review is to discuss the prevalence of MS and its component in different regions in the Middle East. The recorded high prevalence of the MS and its key cardiovascular risk factors (15-60%) among Middle East population mandates the need for a national and international prevention programs to combat obesity, diabetes, hypertension, dyslipidemia, smoking and related comorbidities. Consideration of early prevention and control is of utmost importance.

**Key words:** Metabolic syndrome, Middle East, obesity

### INTRODUCTION

Almost three decades ago, Dr Gerald Reaven identified a cluster of physiologic and metabolic characteristics that seek the company of one another. Originally known as “syndrome X”, the cluster has also been termed pluri-metabolic syndrome (MS), or Reaven’s syndrome. These characteristics, when found in the same person, are so ominous that they have also been called “the deadly quartet” or “the awesome foursome”.<sup>[1]</sup> Reaven and subsequently others postulated that insulin resistance underlies Syndrome X (hence the commonly used term insulin resistance syndrome).<sup>[2,3]</sup> Other researchers use the term MS for this clustering of metabolic risk factors. The National Cholesterol Education Program’s Adult Treatment Panel III (NCEP-ATP III) used this alternative. It consists of multiple, interrelated risk factors of metabolic origin that appear to directly promote the development of atherosclerotic cardiovascular disease. Five factors, identified NCEP-ATP III, are thought to comprise this syndrome—large waist circumference (WC; as indicator of central obesity),

elevated triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C) concentration, high blood pressure and elevated fasting plasma glucose. The concomitant presence of 3 or more of these confers an approximate 2-fold increased risk of atherosclerotic cardiovascular disease (CVD) and an approximate 5-fold increased risk of diabetes mellitus.<sup>[4]</sup> Other associated changes have also been described, including microalbuminuria, a prothrombotic and proinflammatory state.

### DEFINITION

Although the risk associated with the MS is well-documented, the definition of the syndrome is still in flux. To define any diagnostic criteria is not easy. It is even more complicated – what parameters, what thresholds, and what combinations should be used to define it?. In the absence of a diagnostic test, a number of definitions of the syndrome have been proposed.<sup>[5]</sup> They come from the World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), J-P Després’ group and NCEP-ATP III.<sup>[4,6,7]</sup> These various definitions include different factors and different thresholds for them.<sup>[5]</sup> For example the first definition, from the WHO, included microalbuminuria, which does not appear in the later definitions.<sup>[8]</sup> The EGIR definition did not include diabetic patients.<sup>[6]</sup> The most recent definitions are from the International Diabetes Federation (IDF) and from the American Heart Association/National Heart, Lung

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DOI:  
10.4103/2230-8210.91193

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and Blood Institute AHA/NHLBI.<sup>[9-11]</sup> The differences between these definitions are essentially the thresholds for the parameters to define a syndrome abnormality, the number of abnormalities before the syndrome is deemed to be present, and whether there is a compulsory abnormality which is required to be present. The IDF definition, with its differing thresholds for WC according to ethnic group, is likely to become the international norm, as it is supported by several international bodies.<sup>[5]</sup>

## PREVALENCE OF METABOLIC SYNDROME IN THE MIDDLE EAST

Many reports have been published on the prevalence of the MS in the Middle East. A survey in Turkey reported a prevalence of 33.9% for MS, with a higher prevalence in women (39.6%) than in men (28%). The survey included random samples from both urban and rural populations in seven geographical regions of Turkey using ATP III guideline. The population for this analysis were 2108 men (1372 in urban and 736 in rural areas) and 2151 women (1423 in urban and 728 in rural areas) with a mean age of 40.9+/-14.9 years (range 20-90).<sup>[12]</sup> Another study was executed under the population study "The Healthy Nutrition for Healthy Heart Study" conducted between December 2000 and December 2002 by the Health Ministry of Turkey. Overall, 15,468 Caucasian inhabitants aged over 30 were recruited in 14 centers in different regions of Turkey. Overall, more than one-third (35.08%) of the participants were obese. The hypertensive people ratio in the population was 13.66%, while these ratios for diabetes mellitus and MS were 4.16% and 17.91%, respectively. The prevalence of hypertension, MS and obesity were higher in females than males, whereas diabetes mellitus was higher in males than females.<sup>[13]</sup>

In a study in Tunisia, MS prevalence was 45.5% based on the IDF criteria and 24.3% according to the ATP III definition, with significantly higher prevalence in women than in men. The two most common components were increased WC and low HDL-C. The study was a cross-sectional population-based survey, conducted in 1996 on a large nationally representative sample, which included 3435 adults (1244 men and 2191 women) of 20 years or older. Based on the ROC analysis, WC of 85 cm for both men and women was suggested as appropriate cut-off points to identify central obesity for the purposes of CVD and diabetes-risk detection among Tunisians.<sup>[14]</sup>

A study of adult female Saudi subjects found the prevalence of MS to be 16.1% and 13.6% according to IDF and ATP III definitions, respectively. Prevalence of the MS was

reported at 21.0% in one city in Oman, with low HDL (75.4%) and increased WC as the two most common components.

In a population in Northern Jordan, according to the ATP III definition, the prevalence of the MS was 36.3%, with a significantly higher prevalence in women than in men. The most common abnormality was low HDL-C in men (62.7%) and increased WC in women (69.1%). A cross-sectional survey conducted in 2005 to determine the prevalence of MS and other atherosclerotic cardiovascular disease risk factors among a sample of 342 Palestinians > or = 20 years in East Jerusalem. MS was found in 115 (33.6%) participants, with no significant difference between the sexes. The prevalence of obesity, diabetes and other cardiovascular risk factors was also high, with central obesity and obesity (BMI > or = 30 kg/m<sup>2</sup>) being significantly higher in women.

In a community-based, cross-sectional survey for establishing the normal value for WC among a rural district population in Basrah (Iraq), the optimal cutoff point for WC for the diagnosis of MS in the Iraqi adult rural population as 99 cm in women and 97 cm in men was proposed.<sup>[15-17]</sup>

Larger studies on the prevalence of MS in the Middle East have also been published. Nation-wide survey was conducted in 2007 on 3024 Iranians aged 25-64 years living in urban and rural areas of all 30 provinces in Iran. The age-standardized prevalence of the MS was about 34.7% based on the ATP III criteria, 37.4% based on the IDF definition, and 41.6% based on the ATP III//AHA/NHLBI criteria. By all definitions, the prevalence of the MS was higher in women, in urban areas, and in the 55-64-year age group compared to men, rural areas and other age groups, respectively. The burden of the MS was estimated to affect more than 11 million Iranians.<sup>[18]</sup>

A multinational study evaluated the prevalence and effect of MS on patients with acute coronary syndrome (ACS). The Gulf Registry of Acute Coronary Events prospectively enrolled 8716 patients with ACS from 65 centers in six Middle Eastern countries (Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, and Yemen). Patients were evaluated for the presence of MS based on IDF diagnostic criteria. MS was highly prevalent among Middle Eastern patients presenting with ACS. MS was associated with higher risk profile characteristics and increased risk for development of heart failure and recurrent myocardial ischemia without an increase in hospital mortality.<sup>[19]</sup>

In a nationwide exercise, six thousand seven hundred and

seventy three adult individuals (mean age 48 years  $\pm$  4, 42% were males and 58% were females) were screened for the key cardiovascular risk factors in Egypt.<sup>[20]</sup> Central obesity diagnosed by increased WC, > 102/88 cm (men/women), was markedly high in both men and women participating in the study. In addition, body mass index (BMI) which reflects total body obesity (> 30 kg/m<sup>2</sup>) was also high. Central obesity was estimated in the study to be 29% with a more prevalence in women. This is comparable to what was reported from several western countries, such as the United States (28.0% of men and 34.0% of women in a Survey of 4115 adult men and women conducted in 1999 and 2000 as part of the National Health and Nutrition Examination Survey, a nationally representative sample of the US population)<sup>[21]</sup> and the United Kingdom (23.0% in men and 25.0% in women).<sup>[22]</sup> This similarity could be due to common exogenous factors existing in the developing countries leading to the development of the MS such as sedentary life, psychosocial stressors and obesity.

## PREVALENCE OF OBESITY IN THE MIDDLE EAST

Obesity is a corner stone of the MS as an etiology or a sequel. It constitutes one of the elements of MS diagnosis.<sup>[23]</sup> Among different countries in the Middle East region there is significant heterogeneity in obesity (BMI > 30 kg/m<sup>2</sup>) prevalence.

Arab countries including Oman show prevalence of 30.8%, Qatar (40.8%), and Gaza and West Bank (41.5%) which is an extremely high prevalence of obesity. A community based cross-sectional survey representing all parts of Oman was designed in the year 2000. The crude prevalence of overweight and obesity (body mass index > 25 kg/m<sup>2</sup>) was 47.9% for the whole sample, and 46.2% for males, 49.5% for females. The crude prevalence of central obesity (abnormal weight hips ratio) was 49.3% for the whole sample, 31.5% for males, and 64.6% for females.<sup>[15,24]</sup> Overall, obesity was also found in several studies to be more prevalent in urban areas compared with rural regions. This is most likely because of rapid economic and nutritional transitions in this region as well as definite lifestyle changes. People became less sedentary and consuming more calories through non-healthy fast foods. Also, the overall prevalence of obesity in the Middle East region was considerably higher among women compared with men.

Although the exact explanation of such gender variations is not entirely clear, it has been reported that women are less active compared with men in certain areas. Physical and cultural barriers to physical activity have been reported

among women in Egypt and Saudi Arabia.<sup>[25,26]</sup> These include climatic conditions of extreme heat in the summer, limited exercise facilities devoted solely for women, lack of physical education or an emphasis on its importance in schools, and absence of women's participation in organized sports. Physical inactivity and sedentary lifestyle are major risk factors for the development of obesity and CVD.

New Egyptian WC cutoff points for abdominal obesity were developed based upon data from the Egyptian National Hypertension Project (ENHP).<sup>[27]</sup> These are 97.5 cm for men and 92.3 cm for women. Cutoff points recommended by IDF were 94 cm for men and 80 cm for women derived from the European cutoff points.<sup>[28]</sup> The prevalence of abdominal obesity in Egyptians based upon these European cutoff points was 30.2% for men and 70.9% for women while based on new Egyptian criteria, the prevalence of abdominal obesity in men was 37.1% and in women 50.8%.<sup>[20]</sup>

## METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS

Among Egyptian healthy adolescents 10 to 18 years of age, the overall prevalence of the MS was 7.4% with no sex or area of residence predilection. Results showed that adolescents with the full criteria of MS constituted nearly one-fourth of those exhibiting high values of different components, except for systolic blood pressure, where they were 42%, and TG, where they were 31%. Family history of obesity and diabetes mellitus increased the odds for MS significantly as well as inactivity. A high level of C-reactive protein was reported among affected adolescents. Homocysteine level did not have an influence on the prevalence of MS.<sup>[29]</sup>

In Lebanon, according to ATP III definition, the MS was identified in 26.4 and 4% of obese and overweight children, respectively, with a higher prevalence among girls than boys. The most common abnormalities among subjects with MS were elevated WC (100.0%), high triglyceride (91.7%) and low high-density lipoprotein cholesterol (66.7%) levels. Insulin resistance was identified in 70% of obese children and 75% of those having the MS.<sup>[30]</sup>

## INTERNATIONAL COMPARISONS

In other areas in the world, different studies report quite varied effects of gender on the MS in different populations using ATP III definition. In USA, MS is more prevalent in white males than in females.<sup>[31]</sup> In American blacks, Mexican Americans, Korea, Iran, India and Oman, women had higher prevalence of the MS than men.<sup>[32-35]</sup> The



combination of abdominal obesity and dyslipidemia was also reported as the most common combination among Chinese type-2 diabetics with MS.<sup>[36]</sup> Abdominal obesity is reported as one of the most prevalent risk factor among patients with MS in Greece. A cross-sectional analysis of a representative sample of Greek adults (4753 participants older than 18 years) were included in the final analysis. The age-standardized prevalence of the MS was 23.6%. The prevalence increased with age in both sexes. Depending on ATP III criteria, most of those with MS had three components of the syndrome (61%), 29% had four and 10% had all five components. Abdominal obesity (82%) and arterial hypertension (78%) were the most common abnormalities.<sup>[37]</sup>

It is well-documented that Asians have ethnic predisposition to adverse body fat distribution and MS, hence optimal cutoff points for WC have been established for South Asians. By using this cutoff, the prevalence of the MS in this populations is estimated to be 10-30%.<sup>[38]</sup> In India, a target sample of 1,800 adults (men 960, women 840) were randomly selected for epidemiological study among urban subjects in western India to determine prevalence of diabetes, MS and their risk factors. MS (using ATP III definitions) was present in 52 men (9.8%) and 114 women (20.4%) with age-adjusted prevalence of 7.9% in men and 17.5% in women with an overall prevalence of 12.8%. Other metabolic abnormalities of MS in men and women were high triglycerides in 32.1 and 28.6%, low HDL cholesterol in 54.9 and 90.2%; central obesity in 21.8 and 44.0%, and high normal blood pressure or hypertension in 35.5 and 32.4%.<sup>[34]</sup> In Pakistan, one study in Pakistan Institute of Medical Sciences showed a very high prevalence of the MS in type 2 diabetic population. Out of 106 patients, 91 (85.8%) had MS of whom 95% were females. Abdominal obesity was present in 91% females and 86% males. Low HDL levels were present in all females and 83% males. 78% females and 63% males had elevated levels of triglycerides. Hypertension was present in 68% and 73% females and males, respectively. Females were more affected than males in all respects. Thus, it appears that low HDL cholesterol and large WC are responsible for the high prevalence of MS in women in many populations.<sup>[39]</sup>

## CONCLUSIONS

As the syndrome does not have a known single cause, no single modality of treatment is able to manage MS. To delay the appearance of the syndrome or its manifestations, insulin sensitivity could be targeted, by lifestyle modification – loss of weight, increase in physical activity, a healthy diet or by pharmacological intervention. To treat the abnormalities of the MS, the first step is lifestyle modification, and even

modest weight loss may be effective.<sup>[40]</sup> Drug treatment should be used for the specific abnormalities according to current guidelines, and a more aggressive approach may be appropriate when more than one abnormality is present.<sup>[5]</sup>

The present review has highlighted the high prevalence of MS in adults and children across the Middle East. This epidemic has great negative public health potential, which is not limited to any single country, age group or gender. National health authorities in the Middle East, as well as across the globe, need to take immediate and urgent action to arrest the MS epidemic. Raising awareness about this lurking disease is but the first step in ensuring affirmative and aggressive action in tackling MS in the Middle East.

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**Cite this article as:** Sliem HA, Ahmed S, Nemr N, El-Sherif I. Metabolic syndrome in the Middle East. *Indian J Endocr Metab* 2012;16:67-71.

**Source of Support:** Nil, **Conflict of Interest:** None declared.