Metabolic syndrome in Saudi Arabia

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ABSTRACT

Objectives: Metabolic syndrome (MS) is a well-established risk factor for the development of coronary artery disease (CAD). We designed this study to obtain the prevalence of MS and each of its components in Saudi Arabia. This study is part of Coronary Artery Disease in Saudi Study (CADISS).

Methods: We conducted this community-based national epidemiological health survey by examining Saudi subjects in the age group of 30-70 years of selected households over a 5-year period between 1995 and 2000 in Saudi Arabia. We interviewed all subjects, examined and took measurements of their blood pressure, weight, height, waist circumference, as well as fasting samples of plasma glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol. We obtained the prevalence of MS based on the presence of at least 3 of the following: abdominal obesity (waist circumference >102 cm (40 inch) in male and >88 cm (35 inch) in female), triglycerides ≥150 mg/dl (1.69 mmol/L), HDL cholesterol <40 mg/dl (1.03 mmol/L) in male and <50 mg/dl (1.29 mmol/L) in female, blood pressure ≥130/85 mm Hg, fasting glucose ≥110 mg/dl (6.1 mmol/L) as defined by the Adult Treatment Panel (ATP) III in 2001.

Results: We included 17,293 subjects in this survey during the study period. The overall age-adjusted prevalence of MS in Saudi Arabia obtained from this study is 39.3%. Age adjusted prevalence in males is 37.2% and crude prevalence is 40.9% (95% confidence interval [CI] 39.8-42), while females have a higher prevalence of 42% and crude prevalence of 41.9% (95% CI 40.9-42.9). Saudi subjects from urban areas have significantly higher prevalence of 44.1% (95% CI 43.2-45) compared to those living in rural areas of 35.6% (95% CI 34.3-36.7) ($p<0.0001$). Low HDL affects 81.8% of females and 74.8% of males with MS leading all other factors, and it continued to be consistent in all different age groups. Metabolic syndrome is a risk factor for CAD, as the prevalence of CAD was higher among patients with MS (6.7%) compared to subjects without MS (4.6%) ($p<0.0001$).

Conclusions: The prevalence of MS is high in Saudi Arabia. Low HDL cholesterol plays a major role in the contribution to the MS in Saudi Arabia. Therefore, we recommend routine assessment for the components of MS in patients with CAD, furthermore, we encourage aggressive management of the MS for primary prevention of CAD, particularly, measures to increase HDL cholesterol.

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Management of coronary artery disease (CAD) has evolved to include various strategies not limited to interventions after cardiac event secondary to CAD, but addressing the predisposing

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risk factors for primary interventions as well. The lifetime individual's risk for the development of CAD is determined by several well-known risk factors that have not accounted fully for all patients presenting with manifestations of CAD. Clearly, as living parameters are changing in societies towards western lifestyle with less physical activity and more prevalence of obesity, the risk for acquiring CAD is likely to increase. Metabolic syndrome (MS) is a cluster of disorders of metabolism including high insulin levels, excess body weight, high blood pressure and abnormal cholesterol levels that increase the risk for development of CAD. Gerald Reaven described Syndrome X (otherwise currently known as MS) in 1988.[1] Subsequently, other metabolic abnormalities have been associated with this syndrome, including microalbuminuria, and abnormalities in fibrinolysis and coagulation.[2-5] Among various names given to this syndrome (including the MS, the insulin resistance syndrome, the plurimetabolic syndrome, and the deadly quartet), "insulin resistance syndrome" has been commonly used and implies that insulin resistance is an important factor of the syndrome.[6-13] Due to its heterogeneity, an emerging need for a unifying definition of the MS lead the World Health Organization (WHO) to establish its criteria and proposed the components of the MS in 1998.[14] Obviously, despite the precise criteria set by the WHO, the difficulty in applying such criteria in clinical practice as well as epidemiological studies urged the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III in 2001 to provide a more practical criteria to clinically apply the definition for MS that does not include measuring urinary micro-albuminuria or performing an oral glucose tolerance test.[15] Guidelines from ATP III suggest that the clinical diagnosis of the MS is based upon the presence of any 3 of the following: abdominal obesity defined as waist circumference >102 cm (40 inch) in male and >88 cm (35 inch) in female, triglycerides ≥150 mg/dl (1.69 mmol/L), high-density lipoprotein (HDL) cholesterol <40 mg/dl (1.0[3] mmol/L) in male and <50 mg/dl (1.29 mmol/L) in female, blood pressure ≥130/85 mm Hg, fasting glucose ≥110 mg/dl (6.1 mmol/L). We designed this study with the objective of obtaining the prevalence of MS in Saudi Arabia.

Methods. Saudi Arabia encompasses approximately four-fifths of the Arabian Peninsula, and has inhabitants of 20.8 million people with 15.6 million being the local population (Saudis). A 5-year National Epidemiological Health Survey to study CAD and its risk factors was conducted between 1995 and 2000. Male and female Saudi subjects (aged 30 - 70 years), in rural and urban areas of the Kingdom formed the target population for this study. For the study, a Saudi is identified as a person holding (or a dependent of a holder) of a Saudi Nationality Identification Card (SNIC). Most previous studies on overweight and obesity from other parts of the world focused on a similar population that allows inter-countries comparison. A sample size of 20,000 participants was the target of the study to ensure a high reliability of our estimates of the prevalence of overweight and obesity. The subjects were selected using a 2 stage stratified cluster sampling procedure, urban and rural being the strata. The study population was drawn from the local primary health care centers' catchment areas, for practical and logistic reasons. The catchment population of each primary care center was taken as a cluster. The Kingdom of Saudi Arabia is subdivided into 14 administrative regions and samples were selected from each region. The first stage-sampling units were 1,623 primary health centers (PHCs) uniformly distributed in the Kingdom. Since the establishment of the PHCs was dictated by the population in each region, the allocation of the required number of PHCs were made proportional to be the number of PHCs in each region. Then, each region was stratified into urban and rural communities and a simple random sample of PHCs was selected. The number of PHCs selected from each community was based on the total number of PHCs in each rural and urban community. A total of 66 PHCs were selected from urban and 58 from rural areas. Then blocks were randomly selected from the catchment areas of each selected primary care center and used as cluster. One hundred households from urban PHCs and 50 households from rural PHCs were selected from these blocks. All subjects of age group of 30 - 70 years of selected households were interviewed at their house and examined at the PHCs. The questionnaire was developed, pre-tested, and validated in a pilot study. The questionnaire included basic demographic and socio-economic data as well as detailed medical history including intake of medications. A clinical examination was conducted, included height, weight, waist circumference, blood pressure, followed by obtaining 12 hours fasting blood samples (for measurement of fasting plasma glucose, fasting triglycerides, and fasting HDL) as well as performing an electrocardiogram (ECG). Well-trained primary care physicians conducted a clinical examination including measurement of blood pressure. Weight was measured with ordinary scales (non-electronic portable balance) with indoor clothing on without shoes, to the nearest 0.1 Kg. Height measurement was carried out in the standing position, without footwear, to the nearest mm by using measuring tape that is part of the weighing scale. Body mass index (BMI) was calculated by dividing the weight in kilograms by height in square meters. Weight and height were measured using standardized techniques and equipment (to be precise, healthcare workers were trained, for this study, to use the same technique of weight and height measurements for all subjects of the study population, using the same type of equipment such as blood pressure apparatus, weighing scale and ECG machine). Waist circumference was measured using ordinary non-stretchable measuring tape by centimeters (cm). We used the criteria defined by ATP III published in 2001 to establish the diagnosis of the MS in the subject population.[14] The data were analyzed using the Statistical Package for Social Sciences (Version 10) on PC. The estimate prevalence rate of MS and each of its components was calculated for the total sample, and sub-groups of gender, area of residence, income, marital status, educational level, occupation and age groups. Moreover, data were compared to seek differences at regional levels, and 95% confidence interval (CI) was calculated. A *p* value <0.05 was considered statistically significant. Logistic regression of determinants of MS was performed to develop a risk model.

Results. Seventeen thousand two hundred ninety-three subjects were included in this survey during the study period. **Table 1** shows the demographic variables of subjects studied and its relation with the prevalence of MS in Saudi Arabia. Widowed and divorced subjects have a high prevalence of MS. Lower income level in urban subjects shows a high prevalence of MS, while among rural subjects a high-income level shows a higher prevalence of MS. Illiterate subjects have been shown to have higher prevalence of MS compared to educated subjects, and this is statistically significant.

Table 2 shows the prevalence of MS categorized by gender, age groups, residence and region, and shows the prevalence is consistently increasing with age, which is statistically significant (p<0.0001). Saudi subjects from urban areas have a significantly higher prevalence of MS compared to Saudi subjects living in rural areas. The MS has variable prevalence when comparing the 5 different regions of Saudi Arabia with the highest prevalence affecting the eastern and northern regions. The prevalence of MS among overweight (BMI = 25–29.9 kg/m^2) and obese (BMI ≥30 kg/m^2) subjects is 38.8% and 59.5%, while the prevalence of MS among subjects with normal weight (BMI ≥18.5 - <25 kg/m^2) is 21.3%, and underweight (BMI <18.5) is 13%. The prevalence of overweight and obesity among subjects with the MS is 33.7% and 52.5%, while prevalence of normal weight and underweight among MS subjects is 13.5% and 0.4%. **Figure 1**

Table 1 - Prevalence of metabolic syndrome (MS) categorized by marital status, income and educational levels.

Factor/response	Prevalence of MS n	(%)	*p*-value	95% Confidence interval Lower	Upper
Marital status			<0.0001		
Single	119	(29.8)		25.3	34.3
Married	6431	(40.7)		39.9	41.5
Divorced	115	(51.3)		44.8	57.9
Widowed	497	(57.1)		53.8	60.4
Income level					
Urban			0.005		
SR 2,500	1168	(46.6)		44.7	48.6
SR 2,500 – 4,999	1752	(45.3)		43.7	46.9
SR 5,000 – 7,499	1140	(41.6)		39.8	43.4
SR 7,500 – 9999	517	(42.6)		39.8	45.4
SR 10,000 – 14,999	424	(43.8)		40.7	46.9
SR ≥15, 000	143	(44.4)		39.0	49.8
Rural			0.122		
SR <2,500	792	(35.0)		33.0	37.0
SR 2,500-4,999	649	(35.2)		33.0	37.4
SR 5,000 – 7,499	288	(36.2)		32.9	39.5
SR 7,500 – 9999	93	(34.6)		28.9	40.3
SR 10,000 – 14,999	87	(39.5)		33.0	46.0
SR ≥15,000	29	(51.8)		38.7	64.9
Educational level			<0.0001		
Illiterate	3941	(44.2)		43.2	45.2
Read and write only	813	(40.5)		38.4	42.7
School	1868	(37.7)		36.4	39.1
College and University	516	(37.9)		35.3	40.5
Total number of cases with MS	**7162**	**(41.4)**		**40.7**	**42.1**

Table 2 - Prevalence of metabolic syndrome (MS) categorized by gender, age groups, residence and regions.

Factor/response	Prevalence of MS n	(%)	*p*-value	95% confidence interval Lower	Upper
Gender			0.164		
Male	3373	(40.9)		39.8	42.0
Female	3789	(41.9)		40.9	42.9
Gender (adjusted*)					
Male	37.2				
Female	42				
Age group					
Male			<0.0001		
30 - 39	584	(27.2)		25.3	29.1
40 - 49	901	(41.3)		39.2	43.4
50 - 59	962	(48.8)		46.6	51.0
60 - 70	926	(47.4)		45.1	49.6
Female			<0.0001		
30 - 39	1029	(27.1)		25.7	28.5
40 – 49	1250	(45.9)		44.0	47.8
50 – 59	894	(58.5)		56.0	61.0
60 - 70	616	(61.8)		58.8	64.8
Residence			<0.0001		
Urban	5200	(44.1)		43.2	45.0
Rural	1962	(35.6)		34.3	36.7
Region			<0.0001		
Central	1549	(38.3)		36.8	39.8
Northern	698	(45.3)		42.8	47.8
Southern	1352	(37.6)		36.0	39.2
Western	2262	(41.4)		40.1	42.7
Eastern	1301	(49.2)		47.3	51.1
Total number of cases with MS	7162	(41.4)		40.7	42.1
Total (adjusted*)	39.3				

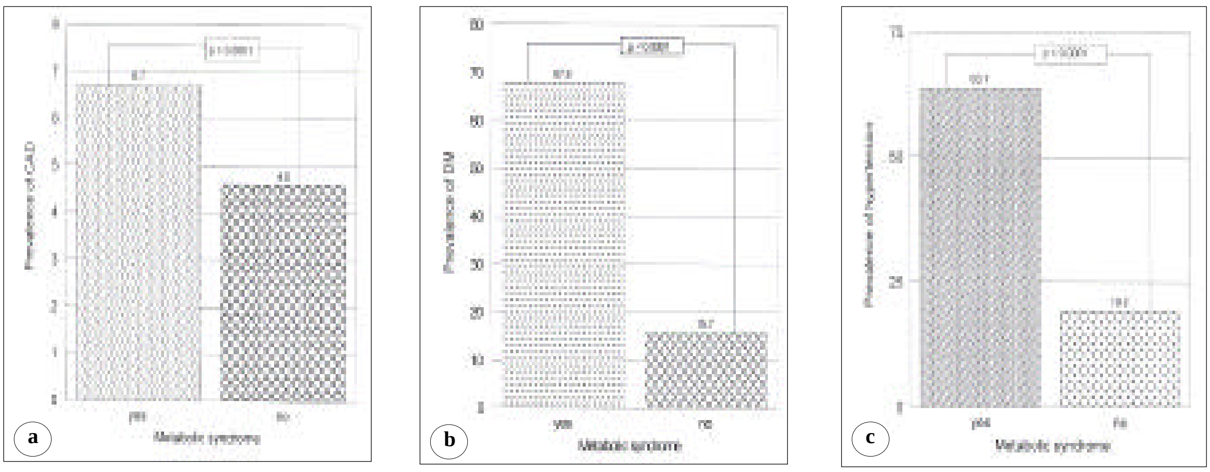

Figure 1 - Prevalence of **a)** coronary artery disease (CAD), **b)** diabetes mellitus (DM), and **c)** hypertension in subjects with metabolic syndrome.

Table 3 - Logistic regression of determinant of metabolic syndrome.

Variables	ß*	SE†	*p* value	Odds ratio
Age				
40-49 versus 30-39	0.779	0.042	<0.0001	2.180
50-59 versus 30-39	1.229	0.047	<0.0001	3.418
60-69 versus 30-39	1.219	0.052	<0.0001	3.383
Residence				
Rural/urban	-0.425	0.038	<0.0001	0.654
Region				
Central versus Eastern	-0.488	0.053	<0.0001	0.614
Northern versus Eastern	-0.123	0.067	0.067	0.885
Southern versus Eastern	-0.414	0.055	<0.0001	0.661
Western versus Eastern	-0.306	0.050	<0.0001	0.736
Gender				
Male	-0.236	0.035	<0.0001	0.790
Female	-	0.049	0.023	0.894
Marital status				
Married versus single	0.231	0.117	0.001	1.259
Divorced versus single	0.580	0.182	0.001	1.786
Widowed versus single	0.453	0.138	0.001	1.574
Income				
2500 - 4999 versus <2500	0.145	0.042	0.001	1.156
5000 - 7499 versus <2500	0.133	0.049	0.006	1.143
7500 - 9999 versus <2500	0.195	0.065	0.003	1.215
10000 - 14999 versus <2500	0.203	0.070	0.004	1.225
≥15000 versus <2500	0.266	0.112	0.018	1.304

*coefficient of regression, †standard error

Table 4 - Prevalence of each component of metabolic syndrome categorized by gender and age groups.

Variables	Total	Abdominal obesity (Men: >102cm; Female: > 88cm)	Triglycerides ≥ 1.69 mmol/L	HDL cholesterol (Men <1.03 mmol/L; Female <1.29 mmol/L)	Blood pressure ≥130/≥85 mmHg	Fasting glucose ≥6.1 mmol/L
Gender						
Male	**8253 (47.7)**	2023 (25.2)	3801 (47.6)	5911 (74.8)	3473 (42.2)	3248 (40.7)
Female	**9040 (52.3)**	4920 (55.2)	2968 (33.7)	7150 (81.8)	3015 (33.5)	3112 (35.4)
p-value		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Age group						
30-39	**5942 (34.4)**	2116 (36.4)	2015 (34.8)	4455 (77.7)	1123 (19.0)	1401 (24.2)
40-49	**4901 (28.3)**	2226 (46.5)	1983 (41.6)	3788 (79.9)	1763 (36.1)	1814 (38.1)
50-59	**3499 (20.2)**	1516 (44.0)	1568 (46.2)	2663 (79.4)	1812 (51.9)	1681 (49.6)
60-70	**2951 (17.1)**	1085 (37.6)	1212 (42.5)	2155 (76.4)	1790 (60.9)	1464 (51.5)
p-value		<0.0001	<0.0001	0.001	<0.0001	<0.0001
Total of each component (%) of study sample	**17293 (100)**	**6943 (41)**	**6778 (40.3)**	**13061 (78.4)**	**6488 (37.7)**	**6360 (37.9)**

Prevalence of metabolic syndrome among normal body mass index (18.5-25) subjects = 21.4%

demonstrates the prevalence of CAD (**Figure 1a**), diabetes mellitus (DM) (**Figure 1b**), and hypertension (**Figure 1c**) among subjects with MS, which is shown to be statistically significant. The association of metabolic syndrome with DM and hypertension is more pronounced among subjects with the metabolic syndrome compared to prevalence among subjects without the metabolic syndrome. Logistic regression of determinants of MS is shown in **Table 3**, with age, residence, gender and marital status, as well as income level being significant variables. **Table 4** shows the contribution of each factor of the MS among population in the survey. Low HDL leads all other factors contributing to the MS and is consistent in all different age groups. While elevated triglycerides rank second in contributing to MS among male subjects, abdominal obesity is found to be the second most prevalent contributing factor to MS among females.

Discussion. Among the studied population that represents the Saudi population, we found the MS to be highly prevalent in males and females. The age-adjusted prevalence also remains high for males and females. Thus, the overall prevalence of MS in Saudi Arabia is affecting slightly more than one third of the population as obtained from our data. This alarming figure places a large portion of the Saudi community at increased risk for the development of CAD, DM, and hypertension. The MS is considered a risk factor for incident CAD as has been shown by several studies.[16-22] Therefore, it is important to establish its prevalence in Saudi Arabia particularly, in light of recent data showing 5.5% overall prevalence of CAD in Saudi Arabia.[23] Our data are showing clear and unequivocal association of the MS with CAD as 6.7% of patients with CAD were found to have the MS, compared to 4.6% without the MS. Clearly, our population has a higher prevalence of MS (39.3%) compared to the age-adjusted United States of America (USA) prevalence of 23.7% (age 20-70 years), affecting nearly 47 million people in the US, placing them at increased risk for CAD.[24-28] Another survey from the USA reported an overall prevalence of 22% of the MS, as defined by the 2001 ATP III criteria, in 8814 adults (age ≥20 years) in the USA participating in the third National Health and Nutrition Examination Survey, with an age-dependent increase (6.7 for age 20-29, 43.5 for age 60-60, and 42% for age >70 years.[29] Additionally, reports from nearby Arab countries showed even lower prevalence of MS than our population (which may be attributed to younger age of studied populations compared to the 30-70 year age range studied in our population), as it is 21% in the Omani population (aged 20 years), and 17% among adult Palestinians.[30,31] A remarkable lower prevalence of the MS obtained from a cross-sectional study of individuals aged 30-60 years conducted in Japan found the prevalence of MS, using ATP III criteria, being 6% for the Japanese and 12% for the Mongolians.[32] Our population has more prevalence of MS than that affecting Arab Americans, as the reported age-adjusted prevalence of the MS was 23% (age 20-75 years).[33] Similarly, the prevalence of MS obtained from our survey showed higher rates compared to studies from Europe, as the age-adjusted prevalence of the MS was 23.6% among the adults Greek population.[34] Our population has similar prevalence rate of the MS compared to results obtained from a survey studying Indians (age 20-75 years) using ATP III criteria but with a modified waist circumference appropriate for Indians (male ≥90 cm, female ≥85 cm) and reported 41.1% prevalence of the MS.[35] Moreover, our data showed an increasing prevalence of the MS that is proportionate with increasing age, reaching 47.4% among males and 61.8% among females at age group 60–70 years that goes hand in hand with increasing prevalence of CAD among older populations. It is likely that the prevalence of MS will probably increase in the coming years due to the rapidly increasing prevalence of obesity among adults in Saudi Arabia, similar to data from the US that showed age-adjusted prevalence increased by 23.5% among females and 2.2% among males comparing data from 1994 and 2000.[36] The health hazards associated with the MS is not limited to CAD, DM, and hypertension; however, researchers established association with other disorders including fatty liver disease, polycystic ovary syndrome, sleep-disordered breathing and chronic kidney disease.[37-40]

Factors leading to increased prevalence of the MS can be demonstrated from our data as we found the prevalence is higher among Saudis living in urban areas compared to those living in rural areas, which indicates that urbanization and adopting a western lifestyle (namely, eating fast food, driving rather than walking, spending more time on the couch watching television or glued to a computer either browsing the internet or playing video games) is an important factor in the development of the MS. Furthermore, the prevalence is significantly higher in the eastern and northern regions of Saudi Arabia that may be explained by either genetic predisposition or likely to be related to eating habits and physical inactivity. Interestingly, the higher income among studied population was associated with a higher prevalence of the MS. Conversely, a lower education level (illiterate) is associated with a higher prevalence rate. Other variables such as marital status, housing condition, occupation, and income level are not showing consistency to draw a conclusion probably because of confounders' effect, particularly, increasing age. Low HDL cholesterol was found to be the most contributing factor to the MS in our population with a prevalence of 81.8% in females and 74.8% in males. This may be explained by physical inactivity, genetic predisposition, as well as dietary habits of our population. Diet composition is a detrimental factor leading to the development of MS, as low-monounsaturated fat, high-carbohydrate diets have been criticized because they may raise triglycerides levels and lower HDL-cholesterol levels, thus aggravating the dyslipidemia of MS.[42] Moreover, the dyslipidemia seen in our population may be related to insulin resistance and higher prevalence of DM that have been recently reported to affect nearly one fourth of Saudis.[43] Despite the fact that obesity has been linked to higher prevalence of the MS, yet we found a 21.4% prevalence of the MS in normal weight subjects (BMI= 18.5-25). Therefore, having a normal weight is not exclusively protective from the MS, thus evaluating patients for the MS should not be limited to overweight or obese individuals, as normal weight may be deceiving. Other investigators had reported this observation as well, by finding individuals in the upper normal-weight and slightly overweight BMI range that have a relatively high prevalence and are at increased risk of having the MS.[44-48]

In conclusion, the current study demonstrates an alarming high prevalence of MS in Saudi Arabia that increases the burden of CAD and other disorders related to the MS specifically DM. The interpretations of the results of our study clearly dictate an action plan fighting the MS to be implemented sooner to prevent its consequences. Simple but active measures for health promotion such as encouraging healthier eating habits, increasing physical activity, maintaining a normal weight, along with controlling DM and hypertension are urgently needed; the outcome of which is a healthier society with containment of the costly management of complications secondary to the MS. Furthermore, we recommend active and aggressive measures to be taken against the MS in managing patients with CAD.

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