REVIEW PAPER www.lejacq.com id: 7392

The Metabolic Syndrome and Dyslipidemia Among Asian Indians: A Population With High Rates of Diabetes and Premature Coronary Artery Disease

South Asians have high rates of diabetes and the highest rates of premature coronary artery disease in the world, both occuring about 10 years earlier than in other populations. The metabolic syndrome (MS), which appears to be the antecedent or "common soil" for both of these conditions, is also common among South Asians. Because South Asians develop metabolic abnormalities at a lower body mass index and waist circumference than other groups, conventional criteria underestimate the prevalence of MS by 25% to 50%. The proposed South Asian Modified National Cholesterol Education Program criteria that use abdominal obesity as an optional component and the South Asian–specific waist circumference recommended by the International Diabetes Federation appear to be more appropriate in this population. Furthermore, Asian Indians have at least double the risk of coronary artery disease than that of whites, even when adjusted for the presence of diabetes and MS. This increased risk appears to be due to South Asian dyslipidemia, which is characterized by high serum levels of apolipoprotein B, lipoprotein (a), and triglycerides and low levels of apolipoprotein A I and high-density lipoprotein (HDL) cholesterol. In addition, the HDL particles are small, dense, and dysfunctional. MS needs to be recognized as a looming danger to South Asians and treated with aggressive lifestyle modifications beginning in childhood and at a lower threshold than in other populations. (JCMS. 2007;2:267–275) ©*2007 Le Jacq*

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The metabolic syndrome (MS) is a complex web of metabolic factors that are associated with a 2-fold risk of cardiovascular disease (CVD) and a 5-fold risk of diabetes (if not already present) within 5 years, with an even higher long-term risk.[1] Persons with MS have a 30% to 40% probability of developing diabetes and/or CVD within 20 years, depending on the number of components present.[2] Presence of MS also predicts unstable lipid-rich plaques and death from premature coronary artery disease (CAD).[3–6] Among men 45 years and older and women 55 years and older, the MS confers moderately high risk of CAD (10-year risk of 10%–20%).[6] This article reviews the prevalence, criteria, and consequences of MS and the role of dyslipidemia in magnifying the risk from MS among South Asians.

The term South Asian refers to all individuals who have ancestral origin in the Indian subcontinent (India, Pakistan, Bangladesh, Nepal, and Sri Lanka). The Indian subcontinent is home to 1.4 billion people, constituting 23% of the world's population. All South Asians share the dubious distinction of having the highest rates of premature CAD in the world; they also have high rates of diabetes. Both diabetes and CAD occur about 10 years earlier among South Asians than in any other population.[7–10] The terms South Asians and Asian Indians will be used interchangeably in this article.

National Cholesterol Education Program vs International Diabetes Federation Criteria

The human body is programmed to cope with fasting and feasting, so the steady excess consumption of food calories with reduced energy expenditure often leads to visceral fat deposition. Abdominal obesity measured as waist circumference (WC) is a simple and clinically useful measure of visceral fat accumulation, which is one of the driving forces in the development of MS. Although criteria of both the International Diabetes Federation (IDF) and the National Cholesterol Education Program (NCEP) incorporate abdominal obesity as a component of MS, they differ in their emphasis and in the WC cutoff points that define obesity. Abdominal obesity is an "essential" component according to IDF, but is an "optional" component according to the NCEP. Furthermore, among whites, the cutoff point for WC as designated by the IDF is 8 cm lower than that specified by the NCEP, in both men and women (Table I).[11,12]

Thus, the prevalence of abdominal obesity in the US population increases from 40% to 60% in men and from 63% to 82% in women when the IDF WC is substituted for the NCEP WC[12–14] (Table II). Because 70% of the overall

Table I. Definitions of the Metabolic Syndrome

Risk Factors	SAM-NCEP (AHA/NHLBI, 2005)	IDF Consensus (2005)	NCEP (AHA/NHLBI, 2005)	WHO Criteria (1999)
Obesity/abdominal obesity	South Asians: WC ≥90 cm (M), ≥80 cm (F)	Caucasians: WC ≥94 cm (M), ≥80 cm (F) South Asians: WC ≥90 cm (M), ≥80 cm (F)	Caucasians: WC ≥102 cm (M), ≥88 cm (F)	Caucasians: BMI ≥30 kg/m^2 and/or waist-to-hip ratio >0.90 (M), >0.85 (F)
Blood pressure	≥130/≥85 mm Hg	≥130/≥85 mm Hg	≥130/≥85 mm Hg	≥140/≥90 mm Hg or taking medication
Fasting glucose	≥5.6 mmol/L or pre-existing diabetes	≥5.6 mmol/L or preexisting diabetes	≥5.6 mmol/L or preexisting diabetes	Diabetes, impaired glucose tolerance, or insulin resistance
Microalbuminuria	Not used for diagnosis	Not used for diagnosis	Not used for diagnosis	Urinary albumin excretion rate ≥20 μg/min
Triglycerides	≥1.7 mmol/L	≥1.7 mmol/L	≥1.7 mmol/L	Triglycerides ≥1.7 mmol/L and/
HDL-C	<1.04 mmol/L (M), <1.3 mmol/L (F)	<1.04 mmol/L (M), <1.3 mmol/L (F)	<1.04 mmol/L (M), <1.3 mmol/L (F)	or HDL-C <0.91 mmol/L (M), <1.01 mmol/L (F)
The metabolic syndrome–definition	At least 3 risk factors	Abdominal obesity plus 2 or more risk factors	At least 3 risk factors	Diabetes, impaired glucose tolerance, or insulin resistance plus any 2 or more risk factors

Abbreviations: AHA/NHLBI, American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement; BMI, body mass index; F, female; HDL-C, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; M, male; NCEP, National Cholesterol Education Program; SAM-NCEP, South Asian Modified National Cholesterol Education Program; WC, waist circumference; WHO, World Health Organization. Data from Grundy et al,[1] Alberti et al,[11] and Cheung et al.[12]

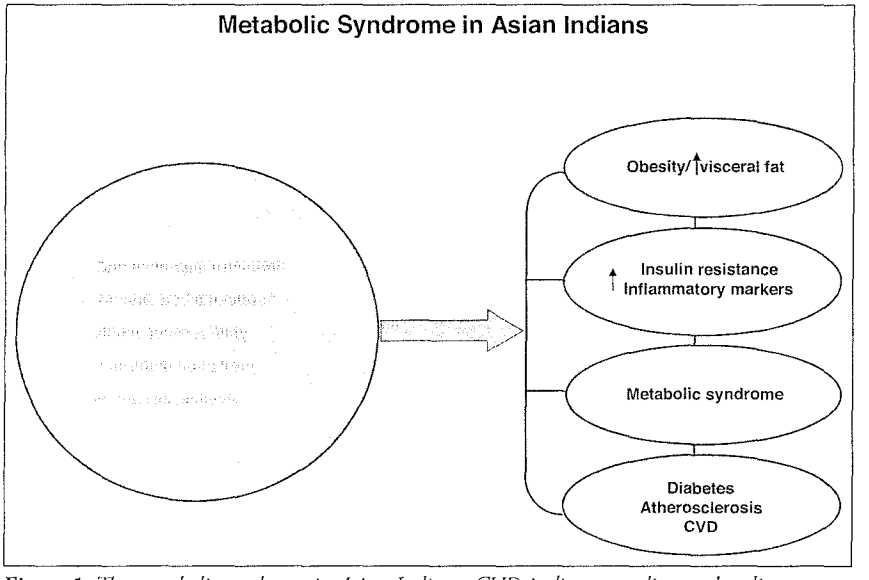

Figure 1. *The metabolic syndrome in Asian Indians. CVD indicates cardiovascular disease.*

US population has abdominal obesity by IDF criteria, whether abdominal obesity is essential or optional does not significantly affect the prevalence of MS in the US population—34% by NCEP and 40% by IDF criteria.[15]

Among Europeans, however, the NCEP criteria markedly underestimate the prevalence of MS. Among the German population, for example, the prevalence of abdominal obesity increases from 21% to 51% in men and from 23% to 45% in women if the IDF WC is substituted for the NCEP WC. The change also results in an increase in the prevalence of MS from 18% to 23% among German men and from 25% to 32% among German women.[13] In the Chinese population, the prevalence of MS is 31% by the NCEP criteria but increases to 46% using the IDF criteria.[16] These data demonstrate the futility of following guidelines made for the US population with other populations without making necessary adjustments for baseline characteristics among the populations. As explained below, both NCEP and IDF criteria appear to markedly underestimate the prevalence of MS among South Asians.

"Asian Indian" or "South Asian" Phenotype

Many Asian Indians fit into the model of metabolically obese, normal weight individuals.[17] This group comprises only 6% of all whites but a substantial segment of Asian Indians.[18] Many Asian Indians develop diabetes and MS with a body mass index (BMI) <25 kg/m^2, which is generally considered normal among whites. South Asians, in general, and Asian Indians, in particular, have certain unique clinical and biochemical characteristics that are collectively referred to as the "South Asian" or "Asian Indian" phenotype (Figure 1). Compared with whites at comparable BMI and age, Asian Indians have profoundly higher

Table II. Prevalence of Abdominal Obesity by Different Criteria Among Americans, Europeans, South Asians, and Asians

	Men		Women	
	NCEP WC ≥102 cm, %	IDF WC ≥94 cm, %	NCEP WC ≥88 cm, %	IDF WC ≥80 cm, %
US American	40	60	63	82
German	21	51	23	45
Urban Asian Indian[a]	6	39	29	58
Rural Asian Indian[a]	3	20	12	32
Chinese[b]	9	52	44	78

Abbreviations: IDF, International Diabetes Federation; NCEP, National Cholesterol Education Program; WC, waist circumference. Data adapted from Assmann et al,[13] Deepa et al,[14] Ford,[15] He et al,[16] and Chow et al.[49] [a]WC >90 cm in South Asian men and >80 cm in South Asian women. [b]Chinese same as South Asians.

Table III. Prevalence of the Metabolic Syndrome With and Without Abdominal Obesity and by SAM-NCEP Criteria Among Different Populations in Singapore and India

	No Metabolic Syndrome, No. (%)	Metabolic Syndrome With Abdominal Obesity, No. (%)	Metabolic Syndrome Without Abdominal Obesity, No. (%)	Metabolic Syndrome With SAM-NCEP Criteria, No. (%)
Total	3200 (73.8)	766 (17.7)	368 (8.5)	1134 (26.2)
Chinese in Singapore	2017 (79.2)	309 (12.1)	220 (8.6)	529 (23.7)
Malays in Singapore	637 (70.1)	206 (22.7)	66 (7.3)	272 (30)
Asian Indians in Singapore	546 (62.1)	251 (28.6)	82 (9.3)	333 (37.9)
Asians Indians in India (CURES)	1647 (70.1)	607 (25.8)	96 (4.1)	703 (29.9)

Abbreviations: CURES, Chennai Urban Rural Epidemiology Study; SAM-NCEP, South Asian Modified National Cholesterol Education Program. Data from Deepa et al[14] and Lee et al.[45]

rates of insulin resistance (measured by glucose clamp studies), diabetes, dyslipidemia, and hypoadiponectinemia; greater WC; thinner hips; short legs; and increased cardiovascular risk.[19,20] For any given WC, they also have increased visceral fat and insulin resistance[21,22] that are evident even among children aged 8 to 11 years.[23] For example, South Asian children with a WC of 80 cm have higher insulin levels than white children with a WC of 90 cm.[23] In sharp contrast, at a given level of BMI, blacks have less visceral fat compared with whites.[24] Despite a higher BMI among blacks overall, the WC among black men is 4 cm smaller than in white men but 5 cm larger in black women compared with white women.[25] In addition, South Asians also have significant procoagulant tendencies as shown by high plasminogen activator inhibitor-1 and fibrinogen concentrations.[26–28] These metabolic abnormalities also contribute to the increased predilection for diabetes and CAD.[7] Figure 2 shows an Asian Indian with MS and abdominal obesity.

Differing Criteria for Obesity and Abdominal Obesity Among Asians

Obesity guidelines based on Western populations markedly underestimate the risk among all Asians because Asians have greater body fat at a given BMI.[29] The World Health Organization (WHO) has, therefore, issued a lower cutoff point for overweight (BMI >23) and obesity (BMI >25) for all Asians.[11] By this criterion, 95% of South Asian diabetic patients were identified as overweight and 80% were obese in the United Kingdom Asian Diabetes Study (UKADS).[30] This study involved 401 South Asian diabetic patients with a mean age of 59 years and a mean duration of diabetes of 8 years.[30] Among Taiwanese, one-half of the population is overweight and one-quarter obese by this definition.[31]

Even among whites, substantial risk of premature CAD occurs at a WC of >90 cm and underscores the dangers of abdominal obesity.[32] Asians tend to have more metabolic abnormalities at lower WC than whites. The optimum WC among Chinese has been found to be 80 cm for both men and women[33] and in Asian Indians 85 cm for men and 80 cm for women.[34] A more recent study found WC of 87 cm for men and 82 cm for women as appropriate cutoff points to identify cardiometabolic risk factors including prediabetes in urban Asian Indians.[35] The WHO and IDF have also issued lower cutoff points for WC for the diagnosis of abdominal obesity for South Asian men (90 cm) and women (80 cm).[11] In a study of Asian Indians with a mean age of 22 years living in the United States, the mean WC was 87 cm for men and 79 cm for women.[36] Although these values are well within the NCEP WC value cutoff points, they are alarmingly high for this age group by IDF criteria. These values also portend an epidemic of MS and diabetes in the second and third generations of Asian Indians in the United States.

Prevalence of MS Among Asian Indians by NCEP and IDF Criteria

The prevalence of MS among South Asians varies widely depending on the

Table IV. Prevalence of Diabetes and the Metabolic Syndrome in Different Parts of India by Sex Compared With US Population

	Diabetes		The Metabolic Syndrome	
	Male, %	Female, %	Male, %	Female, %
Bangalore	12	9	25	46
Coimbatore	4	8	17	43
Chennai	15	12	37	35
Delhi	13	7	19	32
Dibrugarh	3	2	22	18
Hyderabad	15	12	27	47
Lucknow	13	8	25	33
Nagpur	4	4	15	23
Pune	10	7	13	40
Trivandrum	17	15	32	47
Indian population	8	9	29	46
US population	6	7	43	38

Data from Deepa et al,[14] Ford et al,[15] and Reddy et al.[50]

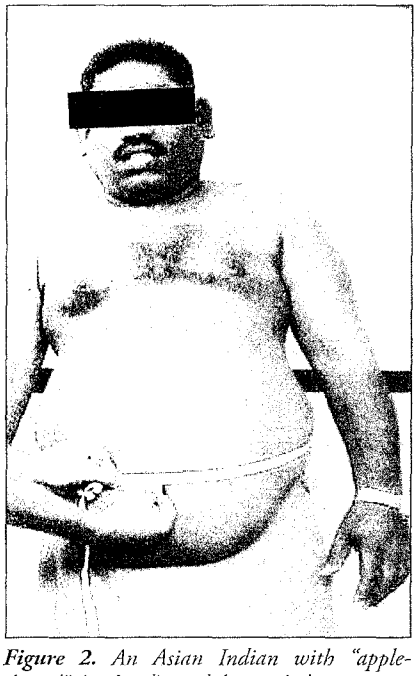

Figure 2. *An Asian Indian with "apple-shaped" (android) or abdominal obesity.*

criteria used and the countries studied. Among the overseas Indians, the prevalence of MS using NCEP criteria ranges from 12% in Mauritius, to 26% in Canada, to 34% in the United States.[37–39] In the United Kingdom, the prevalence of MS is 50% to 100% higher among South Asians than whites. In one study, 29% of South Asian men and 32% of women had MS compared with 18% of white men and 14% of women.[40] In another study, the prevalence of MS among South Asians was 28% in men and 38% in women, compared with 20% among both white men and women.[41]

Gupta and colleagues[42] have reported a prevalence of MS of 25% among urban Asian Indians (18% men and 31% women) using NCEP criteria. The Chennai Urban Rural Epidemiology Study (CURES), which evaluated 2350 individuals, reported a prevalence of MS of 25.8% with IDF criteria, 18.3% with NCEP criteria, and 23.2% with WHO criteria.[14] However, the concordance among the 3 sets of criteria was very poor; only 30% of the Indian population was identified to have MS by all 3 sets of criteria, unlike more than 93% of the US population.[14] Despite the fact that these 3 sets have most of the components in common, the criteria still appear to misclassify a large number of Asian Indians with respect to presence or absence of MS, underscoring the need for a South Asian–specific criteria for MS.[35]

South Asian Modified NCEP Criteria for MS

Although NCEP does not provide ethnic-specific cutoff points for WC, the 2005 American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement on MS endorses the lower WC for all Asian Americans (<90 cm for men and <80 cm for women).[1] We propose for the first time the South Asian Modified (SAM)-NCEP Criteria which follows the NCEP criteria for MS except for the inclusion of South Asian–specific WC cutoff points for abdominal obesity as recommended by the IDF[43,44] (Table I). Thus, unlike the IDF criteria, abdominal obesity is considered optional, not essential. Lee and associates[45] studied the prevalence of MS in the presence and absence of abdominal obesity in a multiethnic Asian population in Singapore. From the population-based cohort study (baseline 1992–1995), 4334 healthy individuals were grouped by the presence or absence of MS and abdominal obesity and followed up for an average of 9.6 years. The prevalence of MS was 17.7% by IDF criteria but increased to 26.2% by the SAM-NCEP criteria. This means 8.5% of the participants had 3 or more MS components in the absence of abdominal obesity when the SAM-NCEP criteria were applied. Thus, designating abdominal obesity as an essential rather than an optional component to diagnose MS would fail to identify a fairly large proportion of individuals with MS. Specifically, prevalence of MS among Asian Indians would increase by 50%. With application of the SAM-NCEP criteria, Asian Indians have higher rates of the MS (37.9%) than Chinese (23.7%) and Malays (30%)[44,45] (Table III).

The results of this pioneering study also showed that having MS either with or without abdominal obesity conferred similar CAD risk; there were 135 first-time CAD events. Cox's proportional hazards model was used to obtain adjusted hazard ratios for risk of a first-time CAD event. Compared with individuals without MS, those with MS and abdominal obesity were at significantly increased risk of CAD with an adjusted hazard ratio of 2.8 (95% confidence interval [CI], 1.8–4.2). Importantly, those with MS but no abdominal obesity also had an adjusted hazard ratio of 2.5 (95% CI, 1.5–4.0). This study has clearly demonstrated that designating abdominal obesity as an optional rather than essential criterion identifies more individuals at risk of

CAD. Conversely, this study suggests that including abdominal obesity as an essential component for the diagnosis of MS as proposed by IDF fails to identify approximately 50% of those who are at high risk of CAD. A similar 50% increase in MS is noted in other Asian populations when SAM-NCEP criteria are used (19.2% IDF vs 29.2% SAM-NCEP) without any decrease in the odds ratio for CAD.[46]

Prevalence of MS Among Asian Indians With SAM-NCEP Criteria

Among South Asians, the prevalence of MS is higher by 30% to 50% when SAM-NCEP criteria are applied compared with NCEP criteria and 20% higher compared with IDF criteria. The prevalence of MS for Asian Indians in Singapore increased from 27% with NCEP criteria to 35% with SAM-NCEP criteria.[47] In CURES, the prevalence of MS increased from 18% with NCEP criteria to 30% with SAM-NCEP criteria (V.M., unpublished data, 2007), whereas another study from the same city reported MS prevalence of 41% with criteria very similar to those of SAM-NCEP.[48] A recent study from rural Andhra Pradesh, India, involving 4535 adults aged 30 years and older showed a prevalence of MS by NCEP criteria of 26.9% in men and 18.4% in women, which increased to 32.5% and 23.9%, respectively, when SAM-NCEP criteria were applied.[49] In a large, contemporary, multicenter study involving 19,973 participants in India, the prevalence of MS was 26.6% with NCEP criteria but increased to 35.4% with SAM-NCEP criteria.[50] In addition, there was wide regional variation in the prevalence of MS from as low as 13% to as high as 47% (Table IV).

This increase in prevalence of MS in South Asians is in sharp contrast to that of the US population. If abdominal obesity were not a prerequisite, the prevalence of MS with IDF criteria would increase only slightly from 39% to 40%.[12] It appears that IDF criteria may be more appropriate for Europeans, NCEP for Americans, and SAM-NCEP for South Asians. MS is underestimated with IDF criteria because the overall prevalence of abdominal obesity is around 50% among Asian Indians when the IDF WC cutoff point is used and 10% to 20% when the NCEP WC cutoff point is applied[47] (Table III).[14,15,50] The overall prevalence of MS identified with SAM-NCEP criteria among Asian Indians is 30% to 40%, which is double that of Europeans (prevalence is 15%–20%) and similar to that of Americans (prevalence is 35%–40%).[40,41,48,51]

Table V. Indian Diabetes Risk Score

Items	Points
Age, y	
<35	0
35–49	20
≥50	30
Waist circumference, cm	
<80 (women), <90 (men)	0
80–89 (women), 90–99 (men)	10
≥90 (women), ≥100 (men)	20
Physical activity	
Regular vigorous exercise or strenuous (manual) activities at home/work	0
Regular moderate exercise or moderate physical activity at home/work	10
Regular mild exercise or mild physical activity at home/work	20
No exercise and/or sedentary activities at home/work	30
Family history of diabetes	
No diabetes in parents	0
Diabetes in 1 parent	10
Diabetes in 2 parents	20

Adapted from from Mohan et al.[61] Minimum score, 0; maximum score, 100; positive score, ≥60.

Impact of Sex, Age, and BMI on the Prevalence of MS

Many studies have shown a 50% to 75% higher prevalence of MS among South Asian women than men (Table IV). In India, the overall prevalence of MS was 29% in men and 46% in women.[50] In the United Kingdom, the age-adjusted prevalence was 41% higher among South Asian men and 140% higher among South Asian women compared with whites.[41] Furthermore, compared with whites, MS develops 10 years earlier among South Asian men and 20 years earlier among South Asian women. The prevalence of MS increases from 10% at age 20 to 29 years to 53% by age 60 years.[41] MS develops even among Indians with healthy weight and increases exponentially with the increase in BMI. In CURES, the prevalence of MS was 17.9% among those with a healthy BMI (18.5–22.9); 40.2% among overweight participants (BMI 23–24.9); and 53.2% among those who were obese (BMI 25–29.9).[14]

Risk of CAD With MS

Among the US population, the odds ratio (OR) for CAD is similar for MS diagnosed with NCEP (1.61) and IDF (1.65) criteria.[12] The OR for CAD among Asian Indians with MS appears to be similar or higher compared with whites. In the United Kingdom, the OR for CAD among people with MS was 2.1 for South Asians vs 1.6 for whites.[40] In Singapore, a study compared 4334 Asian Indians, Chinese, and Malays. Compared with individuals without MS, the OR for CAD was 2.8 (95% CI, 1.8–4.2) for MS diagnosed with IDF criteria and 2.5 (95% CI, 1.5–4.0) for MS diagnosed with SAM-NCEP criteria. The exclusion of diabetic patients did not greatly reduce the risk of CAD in MS with or without abdominal obesity.[45] In CURES, compared with those without MS, the OR

Table VI. Dyslipidemia Among South Asians Compared With Whites	
Lipid Variable	South Asians vs Whites
Total cholesterol	Similar or lower
LDL cholesterol	Similar or lower
HDL cholesterol	Lower
Triglycerides	Higher
Non-HDL cholesterol	Similar
Lipoprotein(a)	Higher
Small dense HDL	Higher
Small dense LDL	Similar
Apo B/Apo A ratio	Higher
Total cholesterol/HDL ratio	Higher
Triglyceride/HDL ratio	Higher
Abbreviations: Apo A, apolipoprotein A; Apo B, apolipoprotein B; HDL, high-density lipoprotein; LDL, low-density lipoprotein.	

for CAD among people with MS was 3.86 (95% CI, 2.37–6.29; $P<.001$) for WHO criteria; 2.19 (95% CI, 1.30–3.67; $P<.05$) for NCEP criteria; 1.90 (95% CI, 1.16–3.12; $P<.05$) for IDF criteria; and 2.11 (95% CI, 1.30–3.44; $P=.002$) for SAM-NCEP criteria (V.M., unpublished data, 2007). Thus, the association of CAD with MS in CURES with SAM-NCEP criteria was similar to that of NCEP and IDF.

These data indicate that among South Asians, MS is associated with CAD irrespective of the criteria used, and the risk is not substantially altered by the presence of abdominal obesity or diabetes. Furthermore, the risk of CAD among South Asians with MS identified with SAM-NCEP criteria is similar or higher than that reported in the US population.[52]

Risk Factors for MS Among South Asians

High carbohydrate intake (particularly high glycemic load) and low physical activity are 2 important contributors to the development of MS among Asian Indians.[53] In India, the prevalence of MS is higher in urban areas compared with rural ones and rises further with higher socioeconomic status.[54,55] In the Chennai Urban Population Study (CUPS), physical inactivity was associated with the components of MS and CAD; participants with the lowest level of physical activity had the highest prevalence of most of the components of MS.[56] South Asian children have higher BMI-adjusted blood pressure levels than white children in the United States. Ghee, a form of clarified butter, was positively and independently associated with high blood pressure in these children.[57] Ghee is very high in saturated fat and cholesterol oxide and is used liberally by affluent Indians worldwide.

Indian Diabetes Risk Score: A Predictor of Diabetes and MS

Most persons with diabetes have MS, but the converse is not true. About 50% of whites with CAD have either diabetes (21%) or MS (29%). These rates are even higher among Asian Indians. In a study of nondiabetic Asian Indians with acute coronary syndrome, only 16% had normal glucose tolerance, 46% had prediabetes, and 37% had undiagnosed diabetes.[58] Diabetes is 3 to 6 times more common among South Asians than whites when adjusted for age and BMI. Furthermore, South Asian diabetics have a 2- to 4-fold higher mortality rate than whites and Chinese diabetics.[59,60] MS is strongly related to the development of diabetes among Asian Indians, as is true for all other populations.

Mohan and colleagues[61] developed an Indian Diabetes Risk Score (IDRS) for cost-effective screening to identify individuals with undiagnosed diabetes among Asian Indians. The IDRS uses 4 simple, safe, and inexpensive measures: age, WC, family history of diabetes, and physical activity. The IDRS results are graded as low (<30), medium (30–59), and high (>60) risk. A score of ≥60 was found to have optimum sensitivity and specificity for detecting undiagnosed diabetes (Table V). Moreover, the IDRS would help to do selective screening in the community instead of universal screening with a cost saving of 50% or more.

The ability of IDRS to detect MS and CAD was tested among the CURES population (No. = 2350). The mean IDRS increased significantly with worsening glucose tolerance (normal glucose tolerance [NGT]: 48±17; impaired glucose tolerance [IGT]: 57±16; newly diagnosed diabetes [NDD]: 61±15; and known diabetes [KD]: 68±12; P value for trend <.001). The proportion of participants with IDRS values ≥60 (the high-risk group) increased significantly with the increasing degrees of glucose intolerance, ie, 37% of NGT participants, 57% of IGT, 73% of NDD, and 88% of KD.

The IDRS is also a predictor of MS and CAD in subjects with NGT.[62] The prevalence of MS increased with the IDRS. The prevalence of MS was 1.8% in the low IDRS category, 14.6% in the medium, and 30.3% in the high (P value for trend <.001). The prevalence of CAD was 0.6%, 0.8%, and 2.2% in the low-, medium-, and high-risk IDRS groups, respectively. The prevalence of CAD in the high-risk group was significantly higher compared with the low-risk group ($P=.030$) and the medium-risk group ($P=.050$). Thus, NGT participants with medium-risk and high-risk IDRS results had significantly higher prevalence of cardiovascular risk factors compared with the low-risk IDRS group. It is remarkable that a simple measure such as the IDRS helps identify individuals with higher cardiovascular risk even at the NGT stage. Thus, it appears the use of such a risk score would be of great help in developing countries (eg, India) to cost-effectively identify individuals at high risk of developing MS, diabetes, and CAD.

Dyslipidemia Among Asian Indians

Prospective studies have shown that the incidence of and mortality from CAD among Asian Indians are at least 2-fold higher than among whites, even when fully adjusted for the high rates of insulin resistance, MS, and diabetes, as well as socioeconomic status.[59,63] This appears to result from the South Asian dyslipidemia that is characterized by high serum levels of apolipoprotein B (apo B), triglycerides (TG), and lipoprotein(a) (Lp[a]); borderline high levels of low-density lipoprotein (LDL) cholesterol; and low levels of apolipoprotein A1 (apo A1) and high-density lipoprotein (HDL) cholesterol (Table VI). Asian Indians have high ratios of total cholesterol (TC) to HDL, TG/HDL, and apo B/apo A1.[7,64,65] These ratios are highly correlated with premature incidence and severity of CAD, as well as acute myocardial infarction among Asian Indians.[66,67]

Asian Indians not only have low HDL, but also have a preponderance of small, dense, dysfunctional HDL particles that are associated with less efficient reverse cholesterol transport and less protection against CAD.[68] The level of HDL 2b, the most protective component of HDL, is low in >90% of Asian Indians.[69] However, physical activity is associated with significant increases in large HDL in this population.[70]

Genetically determined elevations in Lp(a) play an important role in accelerating atherosclerosis that results in premature myocardial infarction and stroke.[71] Among patients with Lp(a) excess, the CAD risk is increased to 3-fold in the absence of other risk factors and increases to 8-fold with low HDL, 12-fold with high LDL, 16-fold with diabetes, and 25-fold with high TC/HDL ratio.[71] Approximately 30% to 40% of Asian Indians have levels >20 to 30 mg/dL, generally considered as the threshold for high risk of CAD. Among 235 participants, a combination of high Lp(a) and low HDL, which confers a very high risk of CAD, was found in 42% of Asian Indians.[69] High levels of Lp(a) correlate with the prematurity, severity, extent, and progression of coronary atherosclerosis as well as the occurrence and recurrence of myocardial infarction among Asian Indians.[71,72] The adverse effects from elevated Lp(a) levels are magnified in this population because of concomitant abnormalities of lipoproteins, as noted above, as well as the high prevalence of MS and diabetes.[7]

Prevention and Control of MS

MS identifies patients at high risk of diabetes and CVD who are most responsive to lifestyle changes. There is growing evidence that efforts to prevent weight gain must begin in early life. Furthermore, low–birth weight followed by rapid excess weight gain in childhood and adolescence increases the risk of developing MS, diabetes, and CVD.

Lifestyle modifications to achieve a modest weight loss (5%–7%) in overweight individuals could reduce the prevalence of MS and its progression to diabetes. Weight loss requires attention to both energy intake and expenditure. Even small to moderate amounts of physical activity (<7 Kcal/min) are helpful in preventing MS. Food items with a high glycemic index (eg, refined grains and calorie-sweetened soft drinks) have an adverse effect on the development of MS, whereas modest intakes of animal and vegetable proteins, as well as healthy carbohydrates from fruits and vegetables, have a beneficial effect.[73]

Progression of prediabetes to diabetes is high among Asian Indians (18%/y) but can be significantly reduced by both lifestyle modification and metformin.[74] As the condition progresses, however, drug therapy directed toward the individual risk factors might be required.[44] Pioglitazone has significantly favorable effects on HDL particle size, markers of inflammation, and adipokines, and these actions contribute to its antiatherogenic effects.[75]

Patients with CAD and MS have higher risk of recurrent coronary events and derive incremental benefit from aggressive high-dose statin therapy.[76] It seems reasonable to achieve a TC/HDL goal of <4 in people with MS. The American Association of Physicians of Indian Origin recommends LDL cholesterol <100 mg/dL and non-HDL cholesterol <130 mg/dL for Asian Indians without CAD and diabetes. The recommended goal is LDL cholesterol <70 mg/dL and non-HDL cholesterol <100 mg/dL for Asian Indians with diabetes or CAD.[77] This is by far the simplest and most effective recommendation and is in agreement with the current literature.[7] Controlling abnormal lipid levels and hypertension to normal levels may prevent up to 50% of major acute coronary events; more importantly, controlling to optimal levels may decrease these events by 80% or more.[78]

Conclusions

Clinical diabetes and CAD are preceded by a constellation of risk factors that are also the components of MS, the prevalence of which among Asian Indians is approximately 25% with either NCEP or IDF criteria. The prevalence increases to 35% to 40% when the SAM–NCEP criteria are used. The prevalence of MS among South Asians is higher than in other Asians and Europeans. The prevalence among Asian Indian women is higher than in US women, but lower in Asian Indian men than in US men. The syndrome confers a 2-fold risk of CAD and a 5-fold risk of diabetes. Primary treatment of MS is lifestyle therapy and includes weight loss, increased physical activity, and an antiatherogenic diet. Adopting a healthy lifestyle beginning in childhood and adolescence is warranted in view of the malignant nature of CAD among Asian Indians. Because the adverse effects of these factors are greater in Indians, the benefits of modifying the factors are correspondingly greater and may prevent the onset of diabetes. Simple cost-effective tools like the IDRS can be used to screen for MS in developing countries, where measurement of the lipid profile is costly and often not feasible. Controlling dyslipidemia requires strategies appropriate to a patient's individual characteristics and the underlying lipid disorder.

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