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Letters to the Editor

Modified criteria for determining cardiometabolic syndrome in Asian Indians living in the USA: Report from the diabetes among Indian Americans national study

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The disproportionate burden of cardiovascular disease (CVD) in the Asian Indian (AI) diaspora is well documented but not well understood [1–4]. Foucan et al. found AIs with type-2 diabetes mellitus (DM) had a 5-fold higher risk of cardiometabolic syndrome (CMetS) than the general US population [1]. Typical risk factors (RFs) like elevated low-density lipoprotein cholesterol (LDL-C) levels do not account for the high CMetS risk. Decreased levels of high-density lipoprotein subfraction 2b (HDL_{2b}) are associated with higher rates of coronary artery disease [5]. Higher levels of abdominal adiposity, visceral fat, dyslipidemia, insulin resistance, and high-sensitivity C-reactive protein (hsCRP) have also been reported as contributory factors [6–8]. In this study we aimed to propose an explanatory model of CMetS in AIs, controlling for confounders such as demographic variables, traditional risk factors, and novel biomarkers.

As the first randomized large-scale investigation of the prevalence and risk factors for DM and CVD in AIs in the US, the Diabetes among Indian Americans study included conventional and emerging CMetS RFs [2]. The primary outcome measure was prevalence of CMetS, which the International Diabetes Federation (IDF) defines as the presence of abdominal obesity (i.e., waist circumference [WC] ≥35.4 in for male and ≥31.5 in for female South Asians) and ≥2 other RFs [9]. Because AIs are at high risk for CMetS, progression in CMetS RFs was differentially examined based on a proposed set of AI-specific CMetS criteria (elevated WC and ≥1 other RFs).

Using computer randomization, 5000 participants were selected from a database of 43,000 AIs compiled from area telephone, ethnic association, faith-based organization, and professional association directories in seven US cities. Letters of invitation and follow-up phone calls resulted in 1038 telephone interviews completed by trained multilingual AI staff, fasting blood work, and anthropometric measurements. Sampling frame and data collection methodology were previously reported [2].

Analysis of variance examined 19 CMetS risk factors (total cholesterol [TC], HDL-C, HDL_{2b}, HDL_3, LDL-C, LDL-receptor, Lipoprotein(a), intermediate-density lipoprotein [IDL], total very low-density lipoprotein [VLDL], $VLDL_{1,2}$, $VLDL_3$, LDL density risk pattern [A—less-, A/B—intermediate-, B—most-atherogenic], triglyceride [TG], hsCRP, homocysteine, systolic blood pressure [BP], diastolic BP, WC, and fasting blood glucose [FBG]) by gender and body mass index (BMI) categories. Statistical significance was lowered to alpha = 0.002, a Bonferroni correction for multiple comparisons. Adjusted odds ratios (ORs) were calculated by estimating separate logistic regression analysis for CMetS using the IDF (elevated WC and ≥2 other RFs) and AI specific criteria (elevated WC and ≥1 other RFs), adjusting for demographic variables (age, education, gender, and years lived in the US), family history of CVD (DM, heart disease, and stroke), lifestyle behaviors (sedentary lifestyle, smoking, and fat intake), traditional risk factors, and novel biomarkers in the model.

Mean age and length of US residence were 45.7 ± 12.8 years and 18.5 ± 11.0 years, respectively. Most participants were male (61%), had access to health care (80%), and reported a family history of CVD (57%). Using AI criteria, 49.8% were obese (defined as ≥25 kg/m^2 [10]) and 61% had elevated WC.

The prevalence of CMetS using the IDF criteria was 41%. The following variables were significantly associated with the prevalence of CMetS after adjusting for the other variables: male gender (OR = 2.69; 95% confidence interval = [1.52, 4.75]), family history (2.07; [1.27, 3.35]), elevated hsCRP (1.17; [1.05, 1.30]), elevated homocysteine (1.08; [1.02, 1.14]), and LDL density risk pattern B (1.98; [1.08, 3.99]). Using the proposed AI-specific criteria, the prevalence of CMetS was 51%. All five aforementioned variables, and older age (1.02; [1.00, 1.05]), were significantly associated with CMetS prevalence (Table 1).

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Table 1
Adjusted odds ratios expressing the relationship among demographic factors and traditional and novel biomarkers with cardiometabolic syndrome (CMetS).

Independent variable	Proposed criteria for Asian Indians (elevated WC + ≥1 other risk factors)			International Diabetes Federation definition (elevated WC + ≥2 other risk factors)		
	No CMetS vs. CMetS			No CMetS vs. CMetS		
	Adjusted odds ratio	95% Confidence interval	*p*-Value	Adjusted odds ratio	95% Confidence interval	*p*-Value
Age (years)	1.02	[1.00, 1.05]	0.048[a]	1.02	[0.95, 1.04]	0.1
Gender (male)	2.08	[1.21, 3.58]	0.008[a]	2.69	[1.52, 4.75]	0.001[a]
Family history of chronic disease (heart disease, diabetes, or stroke)	2.12	[1.35, 3.34]	0.001[a]	2.07	[1.27, 3.35]	0.003[a]
hsCRP (mg/dL)	1.26	[1.11, 1.42]	<0.001[a]	1.17	[1.05, 1.30]	0.003[a]
Homocysteine (mg/dL)	1.09	[1.02, 1.17]	0.005[a]	1.08	[1.02, 1.14]	0.011[a]
LDL density pattern B (most atherogenic)	1.10	[1.01, 2.35]	0.050[a]	1.98	[1.08, 3.99]	0.012[a]

Odds ratio (OR) calculated from logistic regression analysis. Variables not significant (NS) in the model were education, number of years lived in the USA, lifestyle behavior (dietary behavior, physical activity, and stress management), Lipoprotein(a), high-density lipoprotein (HDL) and subfractions, very low-density lipoprotein (VLDL) subfractions 1 and 2, intermediate-density lipoprotein, low-density lipoprotein (LDL) receptor, and total LDL. hsCRP—high-sensitivity C-reactive protein, N/A—not applicable, WC—waist circumference.
[a] Statistically significant.

The odds of increased risk were similar for all five variables at approximately similar rates in both models, suggesting that a redefinition of CMetS for Asian Indians may offer a simplified approach for predicting CMetS in this population. The analysis revealed that elevated WC and one additional RF may be sufficient to define CMetS in this high-risk group. Results also highlight the need to focus investigations on novel emerging CMetS RFs. For example, males with a family history of CVD and an abnormal LDL density risk pattern were at higher risk of CMetS (and in turn CVD), even in the presence of normal LDL levels.

The proposed AI-specific criteria for CMetS delineated significant differences ($p<0.002$) in all the 19 RFs except TC, LDL, Lipoprotein (a), and hsCRP. Mean LDL-C levels, although not alarmingly elevated in AIs, may give a false sense of security if the lipoprotein subfractions are not measured. The predictive capability of WC makes it an important biometric for identifying CMetS in the AI population. WC has been shown to be a predictor of heart failure rate (even for individuals with normal BMI) [11], CVD [7], and related mortality [12]. LDL density risk pattern B (the most atherogenic) was significantly associated with increased WC and predictive of CMetS.

Researchers have advocated updating guidelines for managing CMetS in the South Asian patient population, lowering thresholds for biomarker monitoring, and involving the mass media and physicians in behavioral change [13]. The need for aggressive monitoring of biomarkers and biometrics in AIs was reiterated in a joint scientific statement by the American Heart Association and National Heart, Lung, and Blood Institute because South Asians are "susceptible to developing the metabolic syndrome at waist circumferences below NCEP/ATP III cut-points" [14].

These results must be considered in the context of the study's limitations, which include self-reported behavioral data, moderate response rate, and a cross-sectional design that does not provide insight into firm event endpoints and correlations with their risk. However, these AI-specific data can be used in clinical algorithms with greater attention to CMetS for patients with the following profile: male, family history of CVD, LDL density risk pattern B, elevated WC, elevated hsCRP, and elevated homocysteine. Early assessment for CMetS risk is important to establish optimal treatment strategies in this high-risk group.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology (Shewan and Coats 2010;144:1–2). The study was funded by the American Association of Physicians of Indian Origin.

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