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Adiposity and Cardiovascular Risk Clustering in South Asians

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Abstract

Background: South Asians have increased risk for type-2 diabetes and cardiovascular disease, but the relationship between metabolic health and weight has not been described. This study establishes the prevalence of metabolic abnormalities in normal weight, overweight, and obese South Asians.
Methods: Participants were categorized by body mass index and waist circumference. Subjects with two or more cardiometabolic risk factors (blood pressure, glucose, insulin, triglycerides, high-density lipoprotein cholesterol, and C-reactive protein) were defined as metabolically abnormal.
Results: Forty-one percent of the sample ($n = 1015$) was metabolically abnormal, and 12% of those were normal weight. Of metabolically healthy individuals, 58% were overweight or obese. At a normal level of adiposity, women were more likely to be metabolically unhealthy, whereas men were more likely to be unhealthy with increasing adiposity.
Conclusions: Similar to other ethnic groups, a significant number of normal weight South Asians can be metabolically unhealthy.

Introduction

Wildman et al. used data from the National Health and Nutrition Examination Surveys 1999–2004 and six criteria to analyze the relationship between different degrees of adiposity and cardiometabolic risk factors associated with insulin resistance in three different racial groups.[1] Four of the criteria of cardiometabolic risk were those, excluding waist circumference (WC), used to diagnose the metabolic syndrome,[2] with the other two being high-sensitivity C-reactive protein (hsCRP) and homeostasis model assessment of insulin resistance (HOMA-IR). If two or more of the criteria were met, the subject was classified as being abnormal. Their results demonstrated that a substantial number of subjects whose body mass index (BMI) was ≤ 25 kg/m^2 were cardiometabolically abnormal, and a comparable number whose BMI was ≥ 30 kg/m^2 were cardiometabolically healthy. These findings were consistent with previous publications.[3,4] What makes the findings of Wildman et al. unique is that the heterogeneity they described in the relationship between adiposity and cardiometabolic risk was reasonably comparable in all three of the racial groups studied.[1]

The current analysis is an effort to extend the findings of Wildman et al.[1] and had three major goals that differentiate it from their study. First, we believed it important to evaluate the relationship between degree of adiposity and cardiometabolic risk in apparently healthy individuals, and for that reason excluded subjects with known cardiovascular disease (CVD), diabetes, hypertension, or dyslipidemia. Second, we wished to consider the possibility that the overall thrust of the findings described by Wildman and colleagues might have been somewhat confounded by their use of BMI as the primary index of adiposity, rather than WC. For example, it has been argued by Després et al.[5] that WC can differ significantly at a given BMI, and that the greater the WC, the more visceral adiposity, presumably the major factor leading to insulin resistance and associated cardiometabolic abnormalities. Thus, we thought it worthwhile to address the relationship between adiposity and cardiometabolic risk with both BMI and WC as our primary indices of adiposity, using ethnic specific criteria for abdominal obesity. Third, it seemed important to evaluate a different ethnic/racial group than the three studied by Wildman et al. and, in particular, a group in whom the findings might vary as a function of index of adiposity. We chose South Asians for this purpose

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because they have an increased prevalence of CVD, insulin resistance, hyperinsulinemia, and high triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C) concentrations.[6–8] It has been suggested that abdominal obesity accounts for these metabolic abnormalities and increased risk of CVD in these individuals.[9–11]

Methods

Study participants

The study sample consisted of 463 women and 552 men, part of a larger group of volunteers ($n=4797$) evaluated for cardiometabolic risk at the South Asian Heart Center, a not-for-profit organization providing CVD risk assessment and counseling to South Asians in the San Francisco Bay Area. The Institutional Review Board of El Camino Hospital, Mountain View, California, approved the study. All participants were in generally good health and older than 18 years. Individuals taking drugs to lower blood pressure, glucose, or lipid levels were excluded, as were those not fasting for at least 10 h. Glucose tolerance tests were not performed, but volunteers whose fasting plasma glucose concentration ≥ 7.0 mmol/L were considered to have diabetes and excluded from analysis, as were participants with a known history of hypertension, abnormal cholesterol, or CVD.

Anthropometric measurements

Height and weight were determined with subjects in light clothing and without shoes, and BMI was calculated by dividing weight (kilograms) by height (meter squared). WC was measured using the National Health and Nutrition Examination Survey III protocol during normal minimal respiration by placing a measuring tape around the waist just above the uppermost lateral border of the iliac crest.[12] Participants were classified using Asian-specific cut points as being normal weight (BMI < 23 kg/m^2), overweight (BMI 23–27.5 kg/m^2), or obese (BMI > 27.5 kg/m^2) and abdominally obese or abdominally normal on the basis of their WC (≥ 90 cm men, ≥ 80 cm women).[13] Blood pressure was measured with an automatic blood pressure recorder, using an appropriately sized cuff, with subjects sitting in a chair with feet on the floor and arm supported at heart level.

Laboratory measurements

After an overnight fast, blood samples were drawn for measurement of plasma glucose, insulin, TG, HDL-C, and hsCRP concentrations at the Berkeley Heart Lab.[14] Specifically, glucose concentrations were measured by enzymatic rate reaction, insulin by electrochemiluminescence immunoassay, triglycerides by blanked enzymatic method, HDL-C by a homogeneous direct assay, and hsCRP by particle-enhanced immunoturbidimetric assay. HOMA-IR was calculated from fasting glucose and insulin concentrations using the formula: ([fasting insulin (μU/ml)] · [fasting glucose (mmol/L)])/22.5.[15] The six criteria for identifying a cardiometabolic abnormality were those used by Wildman et al.[1] Criteria and cut points are given in Table 1, and it should be noted that sex-specific cut points for HOMA-IR and hsCRP were used in this and subsequent tables. Subjects were classified as metabolically healthy (< 2 abnormal findings) or metabolically abnormal (≥ 2 abnormities) on the basis of these definitions.

Table 1. Criteria for Defining a Cardio-Metabolic Abnormality

Measurement	*Cut point*
Elevated blood pressure	Systolic/diastolic blood pressure $\geq 130/85$ mmHg
Elevated glucose level	Fasting plasma glucose concentration ≥ 100 mg/dL
Elevated triglyceride level	Fasting plasma triglyceride concentration ≥ 150 mg/dL
Decreased HDL-C	Fasting plasma HDL-C < 40 (men) or < 50 mg/dL (women)
Insulin resistance	HOMA-IR $> 3.77 > 10^{th}$ percentile (> 4.07 (men) or > 3.1 (women))
Systemic inflammation	hsCRP $> 10^{th}$ percentile (> 4.2 mg/dL (men) or > 7.6 mg/dL (women))

HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; hsCRP, high-sensitivity C-reactive protein.

Statistical analysis

Descriptive statistics were used to provide means, ranges, standard deviations, and proportions for demographic and clinical variables. The Student *t*-test was used to assess for differences between continuous variables, and the Pearson chi-squared test was used to test for differences in proportions. All statistical tests were performed using STATA version 11 (College Station, TX).

Results

The sample was relatively young (age 39 ± 2 years), had nearly equal representation of men ($n=526$, 52% men) and women, and the majority of participants ($n=60$, 6%) were first-generation immigrants born outside the United States. Table 2 lists the demographic and metabolic characteristics of the metabolically healthy and metabolically abnormal groups based on their BMI category. Approximately one-quarter of the population was metabolically abnormal, and 13% ($n=34$) of these individuals were of normal weight. Of the 75% of individuals classified as metabolically healthy, 65% ($n=485$) were overweight/obese. It can be seen that the vast majority of subjects were nonsmokers, did not consume alcohol, and participated in some degree of physical activity on a weekly basis. Not surprisingly, the values of the six risk factors being evaluated were higher in the metabolically abnormal group. It should also be noted that when using race-specific criteria for indices of abdominal adiposity there was some discrepancy in categorizing the overweight/obese individuals as metabolically healthy or abnormal. In men, there were 184 (44%) categorized as overweight/obese by BMI with normal WC, and 12 (9%) abdominally obese by WC with a normal BMI. Among premenopausal women, 70 (27%) were overweight/obese with normal WC, and 26 (18%) were abdominally obese with normal BMI. There were 6 (15%) postmenopausal woman who were overweight/obese with normal WC, and 8 (50%) women who were abdominally obese with normal BMI.

Table 3 lists the demographic and metabolic characteristics of the metabolically healthy and abnormal groups based on their WC category. In general, the comparisons are similar to

Table 2. Demographic and Cardiometabolic Characteristics by Body Mass Index (Mean ± SD or *n* [%])

		Metabolically normal			*Metabolically abnormal*		
Characteristics	*Overall* n = *1015*	*Normal weight* n = *265*	*Overweight* n = *368*	*Obese* *n* = *117*	*Normal weight* n = *34*	*Overweight* n = *114*	*Obese* n = *117*
Age (years)	39 ± 9	38 ± 9	39 ± 8*	41 ± 9*	38 ± 10	38 ± 8	40 ± 9
Men (%)	526 (52)	100 (38)	184 (50)	49 (42)	23 (68)	92 (81)	78 (67)
Smoking status							
None	911 (90)	250 (94)	341 (93)	106 (91)	29 (85)	90 (79)	95 (81)
Former	65 (6)	11 (4)	16 (4)	7 (6)	3 (9)	17 (15)	11 (9)
Current	39 (4)	4 (2)	11 (3)	4 (3)	2 (6)	7 (6)	11 (9)
Alcohol intake							
<1 drink/day	977 (96)	255 (96)	353 (96)	115 (98)	34 (100)	109 (96)	111 (97)
1 drink per day	12 (1)	4 (2)	5 (1)	0	0	0	3 (3)
>1 drink per day	24 (2)	6 (2)	9 (2)	2 (2)	0	3 (3)	2 (2)
Physical activity							
None	198 (20)	44 (17)	59 (17)	31 (27)	10 (31)	28 (25)	26 (23)
1–2 days/week	213 (22)	62 (24)	76 (22)	18 (16)	10 (31)	29 (26)	18 (16)
3 days/week	222 (23)	63 (25)	80 (23)	24 (21)	4 (13)	21 (19)	30 (27)
>4 days/week	344 (35)	88 (34)	137 (39)	42 (37)	8 (25)	32 (29)	37 (33)
Systolic blood pressure (mmHg)	116 ± 14	111 ± 12	114 ± 12*	117 ± 11**	116 ± 15	124 ± 16*	128 ± 14**
Diastolic blood pressure (mmHg)	73 ± 9	69 ± 9	71 ± 8*	74 ± 8**	73 ± 9	77 ± 10*	79 ± 9*
Elevated blood pressure (≥130/85 mmHg)	194 (19)	22 (8)	38 (10)	14 (12)	7 (21)	48 (42)*	65 (56)*
HDL-C (mg/dL)	48 ± 13	55 ± 15	49 ± 10**	51 ± 10*	38 ± 8	38 ± 7	40 ± 9
Low HDL-C (<40 mg/dL men, <50 mg/dL women)	260 (26)	28 (11)	52 (14)	6 (5)	23 (68)	77 (68)	74 (63)
Triglycerides (mg/dL)	114 ± 63	84 ± 37	96 ± 37**	106 ± 41**	169 ± 64	184 ± 90	162 ± 69
Elevated triglycerides (≥150 mg/dL)	210 (21)	12 (5)	22 (6)	14 (12)*	23 (68)	77 (68)	62 (53)
Glucose (mg/dL)	86 ± 10	83 ± 9	85 ± 8*	85 ± 10*	88 ± 11	89 ± 11	92 ± 10*
Elevated glucose (≥100 mg/dL)	85 (8)	5 (2)	11 (3)	6 (5)	8 (24)	23 (20)	32 (27)
Insulin (μU/mL)	9.7 ± 5.7	6.6 ± 3.4	8.5 ± 3.6**	10.6 ± 4.2**	10.9 ± 5.3	12.4 ± 5.3	16.8 ± 8.6**
HOMA-IR	2.1 ± 1.3	1.4 ± 0.7	1.8 ± 0.8**	2.2 ± 0.9**	2.4 ± 1.3	2.7 ± 1.2	3.8 ± 2.0**
Elevated HOMA-IR (>10^{th} percentile)	101 (10)	3 (1)	8 (2)	10 (9)*	6 (18)	29 (25)	48 (41)*
Body mass index (kg/m^2)	25 ± 4	21 ± 1.6	25 ± 1**	30 ± 3**	21 ± 1	25 ± 1**	31 ± 3**
Waist circumference (cm)	86 ± 11	76 ± 7	84 ± 7**	94 ± 9**	82 ± 8	89 ± 6**	100 ± 9**
Elevated waist circumference (≥90 cm men, ≥80 cm women)	502 (49)	38 (14)	168 (46)**	107 (91)**	8 (24)	66 (58)*	115 (98)**
hsCRP (mg/L)	2.5 ± 3.7	1.6 ± 2.7	1.9 ± 2.9	3.7 ± 4.6**	3.3 ± 5.5	2.3 ± 2.6	5.3 ± 5.0*
Elevated hsCRP (>10^{th} percentile)	98 (10)	6 (2)	14 (4)	14 (12)**	7 (21)	14 (12)	43 (37)
Metabolic syndrome	172 (17)	0	8 (2)	5 (4)	7 (21)	64 (56)*	88 (75)**

Metabolically healthy: 0–1 cardiometabolic abnormalities.
Metabolically abnormal: 2–6 cardiometabolic abnormalities.
Cardiometabolic abnormalities include blood pressure ≥ 130/85 mmHg, triglycerides ≥ 150 mg/dL, HDL-C < 40 mg/dL (men) or < 50 mg/dL (women), blood glucose ≥ 100 mg/dL, HOMA-IR > 4.07 (men) or > 3.1 (women), and C-reactive protein > 4.2 mg/dL (men) or > 7.6 mg/dL (women).
Normal weight, BMI < 23kg/m^2; overweight, BMI 23–27.5 kg/m^2; obese, BMI > 27.5 kg/m^2.
*$P < 0.05$ compared to normal weight group.
**$P < 0.001$ compared to normal weight group.
HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; hsCRP, high-sensitivity C-reactive protein.

Table 3. Demographic and Metabolic Characteristics by Waist Circumference (Mean ± SD or *n* [%])

	Metabolically healthy		*Metabolically abnormal*	
Characteristics	*Normal waist circumference* n = *440*	*Elevated waist circumference* n = *313*	*Normal waist circumference* n = *73*	*Elevated waist circumference* n = *189*
Age (years)	38 ± 8	41 ± 9**	37 ± 8	40 ± 8*
Men (%)	232 (53)	106 (34)	60 (82)	128 (68)
Smoking status				
None	407 (93)	289 (92)	65 (89)	150 (79)
Former	22 (5)	15 (5)	3 (4)	25 (13)
Current	11 (3)	9 (3)	5 (7)	14 (7)
Alcohol intake				
< 1 drink/day	422 (96)	304 (97)	70 (96)	181 (96)
1 drink per day	5 (1)	4 (1)	1 (1)	2 (1)
> 1 drink per day	12 (3)	5 (2)	2 (3)	5 (3)
Physical activity				
None	68 (16)	70 (23)*	15 (22)	45 (25)
1–2 days/week	104 (24)	54 (18)*	21 (30)	34 (19)
3 days/week	97 (23)	68 (23)	11 (16)	46 (25)
> 4 days/week	160 (37)	106 (36)*	22 (32)	56 (31)
Systolic blood pressure (mmHg)	113 ± 12	114 ± 12	122 ± 14	126 ± 15
Diastolic blood pressure (mmHg)	70 ± 8	72 ± 8*	76 ± 9	78 ± 10
Elevated blood pressure (≥ 130/85 mmHg)	40 (9)	34 (11)	27 (37)	93 (49)
HDL-C (mg/dL)	52 ± 13	51 ± 11	40 ± 9	39 ± 8
Low HDL-C (< 40 mg/dL men, < 50 mg/dL women)	55 (13)	34 (11)	43 (59)	128 (68)
Triglycerides (mg/dL)	91 ± 37	98 ± 40*	181 ± 90	169 ± 75
Elevated triglycerides (≥ 150 mg/dL)	21 (5)	28 (9)*	50 (68)	111 (59)
Glucose (mg/dL)	84 ± 9	85 ± 9	89 ± 11	91 ± 10
Elevated glucose (≥ 100 mg/dL)	12 (3)	8 (3)	17 (23)	48 (25)
Insulin (μU/mL)	7.2 ± 3.3	9.5 ± 4.2**	11.3 ± 5.1	15.3 ± 7.8**
HOMA-IR	1.5 ± 0.7	2.0 ± 0.9**	2.5 ± 1.2	3.4 ± 1.8**
Elevated HOMA-IR (> 10^{th} percentile)	5 (1)	15 (5)*	15 (20)	66 (35)*
Body mass index (kg/m^2)	23 ± 2	27 ± 3**	24 ± 2	29 ± 4**
Waist circumference (cm)	78 ± 7	90 ± 7**	83 ± 6	97 ± 9**
Elevated waist circumference (≥ 90 cm men, ≥ 80 cm women)	0	313 (100)	0	189 (100)
hsCRP (mg/L)	1.7 ± 2.9	2.7 ± 3.6**	2.3 ± 3.6	4.3 ± 4.6*
Elevated hsCRP (> 10^{th} percentile)	12 (3)	23 (7)*	13 (17)	50 (27)

Metabolically healthy, 0–1 metabolic abnormalities; metabolically abnormal, 2–6 metabolic abnormalities.

Metabolic abnormalities include blood pressure ≥ 130/85 mmHg, triglycerides ≥ 150 mg/dL, HDL-C < 40 mg/dL (men) or < 50 mg/dL (women), blood glucose ≥ 100 mg/dL, HOMA-IR > 4.07 (men) or > 3.1 (women), and C-reactive protein > 4.2 mg/dL (men) or > 7.6 mg/dL (women).

Normal waist circumference, < cm (men), < 80 cm (women); elevated waist circumference, ≥ 90 cm (men), ≥ 80 cm (women).

*$P < 0.05$ compared to normal weight group.

**$P < 0.001$ compared to normal weight group.

HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; hsCRP, high-sensitivity C-reactive protein.

those presented in Table 2 when BMI was used to classify individuals. Thus, 28% of the metabolically abnormal individuals had a normal WC, and 42% of the metabolically healthy group were abdominally obese. As in Table 2, values of the six risk factors were higher in the metabolically abnormal group.

Figure 1 illustrates the prevalence of metabolically healthy and metabolically abnormal men and women when classified by the two indices of adiposity—BMI and WC. When stratified by BMI (Fig. A), we observe that 14% of normal weight men are metabolically abnormal, and 21% of obese men are metabolically healthy. It can also be seen that the prevalence of metabolically abnormal individuals essentially doubles as you go from normal weight to overweight, and again from overweight to obese. By contrast, there is quite a different pattern of prevalence of the metabolically healthy and abnormal groups in women. At the simplest, the prevalence of metabolically abnormal women is much less in any BMI category when compared to men; thus, only 14% of normal weight premenopausal and 18% of postmenopausal women are metabolically abnormal versus 25% of men, and 50% more obese women are metabolically healthy as compared to obese men (33% premenopausal, 30% postmenopausal vs. 21%). In addition, there is a higher prevalence of metabolic abnormality in all weight groups for premenopausal women compared to postmenopausal women.

Figure 1B compares the prevalence of metabolically healthy and metabolically abnormal men and women when classified on the basis of WC. In certain respects, these findings reflect the results in Fig. 1A. Thus, 21% of men with a normal WC were metabolically abnormal, as compared to 23% of men with a normal BMI. Furthermore, the prevalence of being metabolically abnormal was again much less in

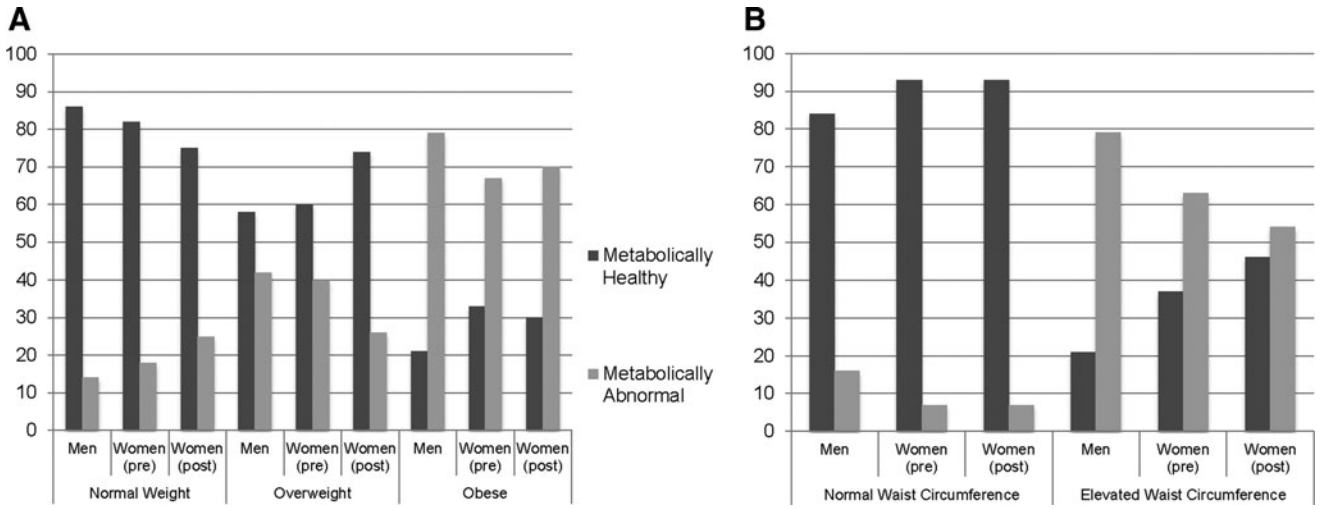

FIG. 1. Prevalence of cardiometabolically healthy and cariometabolically abnormal by adiposity index. **(A)** BMI. **(B)** Waist circumference and sex. Pre, premenopausal women; post, postmenopausal women.

women than in men—6% versus 21% in those with a normal WC and 23% versus 55% in individuals with an abnormal WC. A similar pattern was seen when women are compared by menopause status, with a higher proportion of premenopausal women ($n=410$) being metabolically abnormal compared to postmenopausal women ($n=55$).

Figure 2 displays the relationship between measure of adiposity and number of abnormalities. Not surprisingly, the more abnormalities present, the more obese the individual. Greater than half of those without any abnormality were obese/overweight by BMI classification and one-third were abdominally obese on the basis of their WC. At the other extreme, all participants with five abnormalities were obese/overweight or abdominally obese. Intermediate were those with two abnormalities, and it can be seen that at least two-thirds of the group with only two abnormalities had either an abnormal BMI or WC.

The results in Table 4 provide a more extensive analysis of the participants with two abnormalities by displaying the prevalence of the risk factor clustering that defined them as being metabolically abnormal. These data clearly identify dyslipidemia as the most common abnormality. Thus, the combination of a high TG and a low HDL-C concentration were present in approximately one-third of this population, and one or the other of these abnormalities was present in at least one-quarter of individuals with two other combined abnormalities.

Conclusions

At the simplest level, the current results generally support the findings of the relationship between adiposity and presence of cardiometabolic risk in non-Hispanic whites, non-Hispanic blacks, and Mexican Americans described by Wildman et al.[1] and extend them to a fourth racial group—South Asians. Specifically, their results and our findings demonstrate that substantial numbers of individuals who are overweight/obese by BMI criteria can be metabolically healthy, and individuals with a normal BMI can be metabolically abnormal.

On the other hand, there are substantial differences between the two studies. In the first place, we stratified participants into degrees of adiposity using conventional criteria

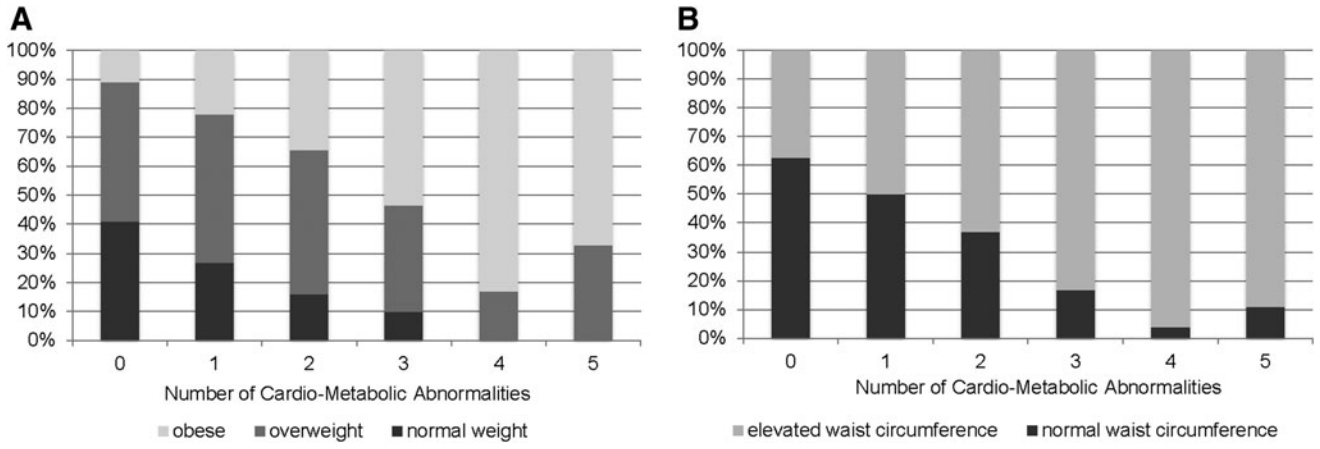

FIG. 2. Number of cardiometabolical abnormalities by adiposity. **(A)** Body mass index. **(B)** Waist circumference. Normal weight, BMI > 23 kg/m^2; overweight, BMI 23–27.5 kg/m^2; obese, BMI > 27.5 kg/m^2. Normal waist circumference, < 90 cm (men), < 80 cm (women); elevated waist circumference, ≥ 90 cm (men), ≥ 90 cm (women).

Table 4. Clustering of Two Cardiometabolic Risk Factors

Cardiometabolic risk factor cluster	*Frequency [*n *(%)]*
Low HDL-C and elevated triglycerides	59 (35)
Elevated triglycerides and elevated blood pressure	15 (9)
Low HDL-C and elevated blood pressure	14 (8)
Elevated blood pressure and elevated blood sugar	14 (8)
Low HDL-C and elevated hsCRP	13 (8)
All other combinations	55 (32)

Elevated blood pressure, >130/85 mmHg; low HDL-C, <40 mg/dL men, <50 mg/dL women; elevated triglycerides, ≥150 mg/dL; elevated glucose, ≥100 mg/dL; elevated hsCRP, >10th percentile (>4.2 mg/dL (men) or >7.6 mg/dL (women).

HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein.

based on both BMI and WC.[1,2] This decision was based on the view that abdominal obesity is more powerful than overall obesity as the link between excess adiposity and cardiometabolic risk in South Asians.[9–11] By so doing so, we found that the race-specific criteria for BMI was actually more conservative for estimating cardiometabolic risk in South Asians compared to WC, with the elevated WC group closely mirroring the obese but not the overweight BMI group. Specifically, 502 participants were abdominally obese (an elevated WC), and 189 of them were metabolically abnormal (38%). More (716) of the population were classified as being either overweight or obese by BMI criteria, but a similar proportion—265 (37%) of them—were metabolically abnormal. We cannot entirely place these data into the context of the findings of Wildman et al.[1] in the three racial/ethnic groups they studied, but they appear to be somewhat different. For example, Wildman et al.[1] state that "36.4 % of individuals with abdominal obesity expressed the metabolically healthy phenotype." By implication, it appears that ~64% of those with abdominal obesity were metabolically abnormal as compared to the ~40% abdominally obese South Asians who were metabolically abnormal in our study. In any event, it appears that measurements of BMI and WC in South Asians do not provide similar information as to the adverse impact of excess adiposity on cardiometabolic risk. Rather, the WC criteria more closely mirror the risk detected by the obese BMI criteria.

A more dramatic difference between our results and those of Wildman et al.[1] is the apparent impact of sex on the relationship between adiposity and cardiometabolic risk. Thus, Wildman et al.[1] found that "normal-weight men were 34% more likely than normal-weight women to have 2 or more metabolic abnormalities." In contrast, the comparisons in Fig. 1 indicate that normal weight South Asian men are less likely to be metabolically abnormal [14% vs. 18%% (premenopausal) or 25% (postmenopausal)] than normal weight South Asian women. However, South Asian men with a normal WC were twice as likely to be metabolically abnormal than were South Asian women with a normal WC (17% vs. 6%). Thus, in this relatively young group of South Asians (mean age of ~40 years), the adverse impact of excess adiposity on cardiometabolic risk depends on the selected measure of adiposity (BMI or WC).

We also found that, for overweight BMI and elevated WC groups, premenopausal women have a higher prevalence of metabolic abnormality than postmenopausal women. This is certainly an unexpected finding. Possible explanations include sample bias, in the case that women who are metabolically abnormal prior to menopause subsequently develop frank diabetes, hypertension, or dyslipidemia, and thus were excluded from our analyses. A second possible source of sample bias is the result of the convenience sampling method; a disproportionate number of young women with a family history or known presence of cardiovascular risk factors may have volunteered to participate in this risk reduction program.

Another, and not unexpected, difference between our findings in South Asians and those of Wildman et al.[1] in the three racial/ethnic groups they analyzed was the specific abnormalities that clustered together. Thus, they state that the two most common combinations were "a high triglyceride level/low HDL-C level and high blood pressure/high glucose level." It is obvious from Table 4 that our findings were similar with regard to the high TG and low HDL-C cluster, but without any predilection for the glucose and blood pressure combination. Given the increased prevalence of these lipid changes in South Asians,[6–11] it is not surprising that they were commonly present in the metabolically abnormal individuals in the current study. It should also be noted that we excluded patients with known hypertension and diabetes from our study group, and this may well explain why did not observe an increased clustering of high glucose with high blood pressure.

Although our findings seem relatively straightforward, they need to be in viewed within the limitations of our study protocol. Thus, the population was not selected at random, but had responded based on their awareness of a screening program being conducted to identify cardiometabolic risk factors in South Asians. The decision to use the six criteria employed to define cardiometabolic risk was based on the prior publication of Wildman et al.[1] and there is no *a priori* evidence that this is the "best" approach to evaluate the relationship between excess adiposity and cardiometabolic risk. Limiting our analysis to apparently healthy individuals had the advantage of identifying disease risk, rather than disease, but likely contributed to the relatively young age of our study group. Thus, they had a mean age of ~40 years, and at least 80% of the women were premenopausal. Additionally, the large majority of the participants were born outside the United States, which is an important consideration for generalizability of these findings.

On the other hand, to the best of our knowledge, our report represents the largest study in which standard values for cardiometabolic risk have been reported in South Asians, and the relationship of these abnormities to both BMI and WC quantified. Furthermore, given the relatively young age and exclusion of subjects with known disease, we have been able to provide an estimate of cardiometabolic risk in an apparently healthy population of South Asians, a group recognized to be at high risk to develop type 2 diabetes and/or CVD.[6–11] Finally, from a public health perspective, our data support two clinically useful conclusions that seem to apply to a relatively young and apparently healthy population of South Asians: (1) Measurements of BMI or WC differ in their ability to identify those with a metabolically abnormal phenotype; and (2) the relationship between adiposity

and cardiometabolic risk in men and women differs according to the index and category of adiposity, with women being higher risk at a normal BMI, but men being higher risk at a normal WC. For both indices, increasing adiposity is associated with higher risk in men compared to women.

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Author Disclosure Statement

Elena Flowers has no conflicts of interest to disclose. Cesar Molina and Ashish Mathur are principally employed by the South Asian Heart Center, where all data collection took place. Gerald Reaven has no conflicts of interest to disclose.

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