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ScienceDirect
Metabolism Clinical and Experimental 55 (2006) 1569–1573
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Simple anthropometric measures identify fasting hyperinsulinemia and clustering of cardiovascular risk factors in Asian Indian adolescents

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Received 3 January 2006; accepted 19 June 2006

Abstract

Correlations of easily measurable parameters of obesity (body mass index [BMI], waist circumference [WC], and subscapular skinfold thickness) with fasting hyperinsulinemia and cardiovascular risk factors (CRFs) have not been investigated in adolescents. We evaluated the screening performance of 3 anthropometric measurements, BMI, WC, and subscapular skinfold thickness, in identifying fasting hyperinsulinemia and clustering of CRFs in 680 male and 521 female adolescents and young adults aged 14 to 18 years in a cross-sectional population survey. CRFs considered were hypercholesterolemia, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, impaired fasting blood glucose, hypertension, and fasting hyperinsulinemia. The ability of the anthropometric measurements to identify the clustering of CRFs without (cluster 1) and with fasting hyperinsulinemia (cluster 2), and fasting hyperinsulinemia alone was evaluated. BMI, WC, and subscapular skinfold thickness identified the clustering of CRFs and fasting hyperinsulinemia better in males than in females. Among individual risk factors, WC was better in identifying the presence of 3 or more risk factors in cluster 1 for both males and females, and in cluster 2 in females. Subscapular skinfold thickness was better than BMI and WC in identifying hyperinsulinemia in males, and the presence of 3 or more risk factors in cluster 2 in females. All 3 measurements were more accurate in identifying fasting hyperinsulinemia than presence of 3 or more CRFs in either cluster 1 or cluster 2 with higher odds ratio for males. This study shows gender differences in identification of insulin resistance and clustering of CRFs by using simple anthropometric parameters in Asian Indian adolescents. These simple measurements are useful for preventing and predicting cardiovascular risk and for generating a correct definition of the metabolic syndrome.

1. Introduction

The presence of the metabolic syndrome increases risk for development of type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD). Insulin resistance is a central feature of the metabolic syndrome and is closely associated with obesity in children [1,2] and adults [3]. Obesity and the metabolic syndrome in children track into adulthood [4,5]; hence, detection of the metabolic syndrome at a young age is essential for the primary prevention of T2DM and CHD.

South Asians are more insulin resistant and have higher risk for T2DM and CHD than white Caucasians [6]. Furthermore, high prevalence of insulin resistance has been seen in South Asian children [7] and adolescents [8,9]. Insulin resistance in South Asians may be contributed by their body composition features: high body fat, truncal subcutaneous fat, and intra-abdominal fat [10]. It is particularly important to characterize and prevent the metabolic syndrome in Asian Indians at a young age for primary prevention.

Anthropometric measures (body mass index [BMI] and waist circumference [WC]) have been used to identify and follow up children and adolescents at risk for insulin resistance, T2DM, and CHD in ethnic groups other than Asian Indians [11-14]. Identification of anthropometric variables and their clustering as important markers of insulin resistance and cardiovascular risk has not been investigated in Asian Indian adolescents. Furthermore, although we showed that subscapular subcutaneous fat

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0026-0495/$ – see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2006.06.029

may be an important correlate of insulin resistance in adolescents in a small sample [8], this anthropometric variable has never been comprehensively analyzed and compared with BMI and WC in any ethnic group.

Therefore, the objective of this study was to identify the anthropometric measures of obesity that best identify insulin resistance and the clustering of cardiovascular risk factors (CRFs) in Asian Indian adolescents.

2. Methods

2.1. Subjects

The data for the present study were obtained from the Epidemiological Study of Adolescents and Young adults, which was conducted between 2000 and 2003. The sample included 1900 adolescents and young adults aged 14 to 25 years from schools and colleges located in southwest New Delhi. Multistage cluster sampling based on modified World Health Organization Expanded Program of Immunization Sampling Plan was used to collect a representative sample of adolescents and young adults [15]. Informed consent was obtained from individuals aged 18 years and older and from parents of subjects younger than 18 years. The institutional ethics committee approved the study. The data from 1201 subjects (680 males and 521 females) aged 14 to 18 years were analyzed in this study. The sample characteristics are represented in Table 1.

2.2. Clinical and anthropometric measurements

The assessment of anthropometric and body composition data (WC, hip circumference, BMI, waist-to-hip circumference ratio [WHR], skinfold thickness at 4 sites [biceps, triceps, subscapular, and suprailiac]) and blood pressure was performed according to the procedures described previously [8,16,17].

2.3. Metabolic parameters

Venous blood samples were obtained after an overnight fast of at least 12 hours. Estimation of levels of fasting blood glucose (FBG), total cholesterol, serum triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol were performed as described earlier [8]. Serum insulin levels were determined by using a radioimmunoassay kit (Medicorp, Montreal, Quebec, Canada) as described previously [8]. The assays for lipids and insulin were rigorously quality controlled by a consultant biochemist (KL) and frequently cross-checked with values obtained from another reference laboratory. Interassay and intra-assay variability of lipid parameters were less than 5%, and for serum insulin were 2.6% and 3%, respectively.

Table 1
Clinical, anthropometric, and biochemical profiles

Variable	Males n = 691	Females n = 523
Age (y)	16.2 (1.1)	16.1 (1.3)
Systolic blood pressure (mm Hg)	114.6 (9.3)	111.1 (9.0)*
Diastolic blood pressure (mm Hg)	74.4 (6.9)	72.6 (6.9)*
BMI (kg/m^2)	19.6 (3.4)	19.9 (3.2)
Waist circumference (cm)	70.4 (9.4)	66.3 (7.6)*
WHR	0.81 (0.05)	0.74 (0.06)*
Subscapular skinfold thickness (mm)	14.2 (9.2)	20.2 (8.2)*
Total cholesterol (mg/dL)	145.7 (25.3)	154.2 (22.9)*
Serum triglycerides (mg/dL)	88.2 (31.6)	94.0 (28.3)*
HDL-C (mg/dL)	47.7 (7.0)	49.9 (8.4)*
FBG (mg/dL)	90.2 (9.0)	88.0 (8.7)*
Fasting insulin (pmol/L)	114.5 (37.1)	153.5 (50.2)*

Values are means (SD).
* $P < .001$.

2.4. Statistical methods

Of the 1201 subjects included in the present analysis, data on fasting serum insulin levels were available in 653 subjects (341 male and 312 female). Gender and age showed a significant effect on the anthropometric and metabolic syndrome variables. Hence, the subjects of 2 genders were analyzed separately, and the variables were further adjusted for age by using regression analysis. The data for blood pressure were also adjusted for height.

The CRFs considered were: hypercholesterolemia, hypertriglyceridemia, low levels of HDL-C, impaired fasting blood glucose (IFG), fasting hyperinsulinemia, and hypertension. From these risk factors, the following 3 categories, including 2 clusters, were devised for statistical analysis:

1. Cluster 1: hypercholesterolemia, hypertriglyceridemia, low levels of HDL-C, IFG, and hypertension.
2. Cluster 2: hypercholesterolemia, hypertriglyceridemia, low levels of HDL-C, IFG, hypertension, and fasting hyperinsulinemia.
3. Fasting hyperinsulinemia alone.

For cluster 1, complete data were available for all the 1201 subjects, and for cluster 2, data from 653 subjects in whom fasting insulin values were available were considered. The rationale of including serum insulin levels in cluster 2 and as an independent risk factor was based on observations from our previous study that fasting hyperinsulinemia was the only biochemical abnormality in approximately 20% of the adolescents who did not have any anthropometric and biochemical abnormality or high blood pressure [17].

We studied the screening performance of 3 anthropometric measures, namely, BMI, WC, and subscapular skinfold thickness, in identifying the presence of each risk factor alone and in identifying clustering of 3 or more risk factors in the 2 clusters of risk factors, cluster 1 and cluster 2. These anthropometric measurements are easy to measure in a clinical setting, are well standardized, and were used by us in previous studies in adolescents [8,9].

The screening performances were analyzed by using receiver operating characteristic (ROC) curves. The ROC curve is a plot of true-positive rate and false-positive rate pairs resulting from continuously varying the decision

threshold over the entire range of results observed. Thus, ROC curves provide an index of accuracy of the test by demonstrating the limits of a test's ability to discriminate between alternative states of health over the complete spectrum of operating conditions. The area under the ROC curve (AUC) is the probability that a test will correctly identify a pair of patients with and without a disease who were randomly selected from the population, ie, a measure of the accuracy of the test. An AUC of 0.5 implies that the test is no better than chance, and an AUC of 1.0 indicates a perfect test. The optimal cutoff point or threshold of the test, which maximizes sensitivity and specificity, can be identified as the point closest to the top left corner of the ROC plot.

The diagnostic odds ratio (OR) (95% confidence interval [CI]) of the thresholds of the various anthropometric variables obtained from the ROC curves were used to identify hyperinsulinemia and the presence of at least 3 risk factors in clusters 1 and 2 in male and female subjects.

2.5. Definitions

Hypercholesterolemia and hypertriglyceridemia were defined as values higher than the 75th percentile of the study sample. These values corresponded to the "borderline" total cholesterol and serum triglycerides values according to National Cholesterol Education Program, Expert Panel on Blood Cholesterol Levels in Children and Adolescents [18]. Low HDL-C levels were defined as values lesser than the 25th percentile of the sample [18]. Elevated blood pressure was defined as systolic blood pressure and/or diastolic blood pressure equal to or greater than 90th percentile after adjusting for age and height. This corresponded to the categories of prehypertension and hypertension in children as described by the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents [19]. Impaired FBG level was defined as 100 mg/dL or higher according to the American Diabetes Association guidelines [20]. Fasting hyperinsulinemia was defined as fasting serum insulin value greater than 20 μU/mL [17].

3. Results

3.1. Clinical, anthropometric, and biochemical profiles

Mean age and BMI were similar in both males and females (Table 1). Male subjects had higher values of blood pressure, WC, and WHR than females, whereas females had higher values of subscapular skinfold thickness than males. Mean value of FBG levels was higher in males, whereas the mean values of lipid parameters and fasting serum insulin levels were higher in females than in males. High blood pressure was observed in 20% of males and 13.2% of females. IFG was observed in 13.5% and 7.1% ($P < .001$), fasting hyperinsulinemia in 18.5% and 49.7% ($P < .001$), hypercholesterolemia in 21.4% and 28.9% ($P = .003$), hypertriglyceridemia in 22.9% and 28.7% ($P = .02$), and low HDL-C levels in 25.7% and 20.5% ($P = .03$) of males and females, respectively.

Table 2 presents the AUC and 95% CIs of the ROC curves with BMI, WC, and subscapular skinfold thickness as predictors and the presence of at least 3 risk factors in clusters 1 and 2 and hyperinsulinemia as the standards. Interesting gender differences in the ability of these anthropometric measures to predict clustering of CRFs and fasting hyperinsulinemia were noted. Overall, the accuracy of BMI, WC, and subscapular skinfold thickness to predict these abnormalities was significantly better in males than in females. Furthermore, the AUC was highest for subscapular skinfold thickness for cluster 1 in males and for cluster 2 in females (Table 2). In females, the AUC for BMI and subscapular skinfold thickness was similar but higher than WC with fasting hyperinsulinemia as standard. The AUC for BMI and WC were similar for all 3 variables in males and for clusters 1 and 2 in females.

Subsequently the optimum thresholds (with high sensitivity and specificity) of BMI, WC, and subscapular skinfold thickness were obtained from the ROC curves. The thresholds for BMI (in kilograms per meter squared, the same for males and females) were as follows: 14 years, 19; 15 years, 18.7; 16 years, 19.7; 17 years, 18.6; and 18 years, 19.5. Thresholds of WC (in centimeters) were as follows:

Table 2
AUC (95% CI) with anthropometric parameters as predictors

Standard (outcome variables)	AUC for anthropometric predictors					
	Males (n = 691)			Females (n = 523)		
	BMI	Waist circumference	Subscapular skinfold thickness	BMI	Waist circumference	Subscapular skinfold thickness
≥3 Risk factors in cluster 1	0.56 (0.48-0.65)	0.61 (0.53-0.70)	0.65 (0.57-0.73)*	0.57 (0.46-0.67)	0.57 (0.46-0.69)	0.57 (0.46-0.68)
≥3 Risk factors in cluster 2	0.69 (0.59-0.79)	0.72 (0.63-0.82)	0.72 (0.62-0.81)	0.56 (0.47-0.64)	0.51 (0.43-0.60)	0.60 (0.51-0.68)†
High fasting serum insulin	0.79 (0.72-0.85)	0.78 (0.72-0.85)	0.76 (0.68-0.83)	0.69 (0.63-0.75)	0.62 (0.56-0.68)‡	0.69 (0.63-0.74)§

* $P = .002$, BMI vs subscapular skinfold thickness.
† $P = .003$, WC vs subscapular skinfold thickness.
‡ $P = .01$, BMI vs WC.
§ $P = .01$, WC vs subscapular skinfold thickness.

Table 3
OR (95% CI) of predictor variables for the clusters of risk factors and fasting hyperinsulinemia

Predictor variables	Diagnostic OR (95% CI)					
	Males (n = 691)			Females (n = 523)		
	≥3 Risk factors in cluster 1	≥3 Risk factors in cluster 2	High fasting insulin	≥3 Risk factors in cluster 1	≥3 Risk factors in cluster 2	High fasting insulin
Body mass index (>19.7 kg/m^2)	1.4 (0.8-2.4)	2.6 (1.2-5.3)	5.2 (2.8-9.9)	1.2 (0.6-2.4)	1.4 (0.7-2.5)	3.2 (1.9-4.8)
Waist circumference (males, >70 cm; females, >66.6 cm)	2.3 (1.3-4.2)	4.4 (2.1-9.2)	4.9 (2.7-8.9)	1.7 (0.8-3.4)	1.2 (0.7-2.2)	2.2 (1.4-3.5)
Subscapular skinfold thickness (males, >12.5 mm; females >19.4 mm)	2.2 (1.2-3.9)	3.9 (1.9-8.3)	5.8 (3.1-10.8)	1.6 (0.8-3.3)	1.6 (0.9-2.8)	3.1 (1.9-5.1)
Abnormal values of all the 3 variables	1.8 (1.0-3.2)	4.2 (2.1-8.6)	6.9 (3.8-12.5)	2.4 (1.2-4.9)	1.7 (0.9-3.1)	3.6 (2.1-6.2)

14 years, 69 and 62; 15 years, 68 and 67.6; 16 years, 70 and 68.6; 17 years, 69 and 68.3; and 18 years, 71.3 and 69 for males and females, respectively. Similarly, the thresholds of subscapular skinfold thickness (in millimeters) were as follows: 14 years, 13 and 20.3; 15 years, 11.8 and 18; 16 years, 13.7 and 23; 17 years, 12 and 25; and 18 years, 10.7 and 21 for males and females, respectively.

The diagnostic ORs (95% CI) of the thresholds obtained from the ROC curves for BMI, WC, and subscapular skinfold thickness are presented in Table 3. In both males and females, the accuracies of the 3 anthropometric variables to predict the presence of fasting hyperinsulinemia were better than their accuracy to predict the presence of 3 or more risk factors in either cluster 1 or cluster 2, and showed higher ORs for males. All the 3 anthropometric parameters had better accuracy in predicting the presence of 3 or more risk factors of cluster 2 than in cluster 1 in males.

4. Discussion

This is the first study in which the accuracy of common measures of obesity in identifying hyperinsulinemia, the surrogate marker of insulin resistance, and the clustering of the components of the metabolic syndrome have been analyzed in Asian Indian adolescents. Similar analysis of anthropometry and CRFs has not been done in adolescents of any other ethnic group.

In the current study, all 3 anthropometric parameters (BMI, WC, and subscapular skinfold thickness) identified fasting hyperinsulinemia better than they identified the other components of the metabolic syndrome (dyslipidemia and hypertension individually and their clustering). Among individual factors, WC had highest OR for presence of 3 or more risk factors in cluster 1 for both males and females and in cluster 2 for females. Furthermore, in the analysis of diagnostic ORs, interestingly, subscapular skinfold thickness emerged as more important than BMI and WC in identifying fasting hyperinsulinemia. Although debate continues on whether BMI or WC is important for cardiovascular risk in both adults and in children, it appears that BMI and subscapular skinfold thickness would be more important for development of clustering and hyperinsulinemia in Asian Indian adolescents. Furthermore, it is also possible that high fasting serum insulin levels might occur earlier than other risk factor clusters in Asian Indian males.

Interestingly, gender differences were seen in risk prediction. Overall, the 3 anthropometric measures of obesity performed better in males than in females in screening for the clustering of the components of the metabolic syndrome. Furthermore, higher ORs for high fasting insulin levels and clustering of risk factors (cluster 2) with high values of anthropometric variables in males indicate that when they become obese, they may be at a higher risk for developing other problems associated with insulin resistance than females. Similarly clustering of risk factors (cluster 2) may appear more in obese males than in females. However, the stage of puberty may also influence this to some extent.

Our study also provides cutoff values of BMI, WC, and subscapular skinfold thickness beyond which risk of hyperinsulinemia increases in Asian Indian adolescents. Furthermore, these observations are also important for development of appropriate definitions of the metabolic syndrome for adolescents, where insulin levels should be included as an important defining variable, and supports conclusions of our recent study [17].

More importantly, the risk prediction for clustering with the use of BMI, WC, and subscapular skinfolds in the present study was weaker than in white Caucasians [21,22]. The reason for this observation is not clear; however, it could be due to different sample size, cutoff points, different methodologies used in the studies, or due to the effect of ethnicity. Due to reasons of cultural and social sensitivity, it was not possible to examine the subjects, especially females, for Tanner staging. Sexual maturation has significant influence on insulin sensitivity, and the lack of control for Tanner staging is a major limitation of the study. The other limitation of this study is that accurate measures of body composition such as dual-energy x-ray absorptiometry (DEXA) scan (for total and regional body fat) and computerized tomography (for abdominal fat) were not used.

In summary, this study shows gender differences in metabolic correlates of regional adiposity and outlines the relative importance of anthropometric parameters in Asian Indian adolescents. These data would be important for risk prediction in adolescent males and females and for

generating correct definitions of the metabolic syndrome in Asian Indians. Furthermore, these data would be useful for planning prevention strategies for Asian Indians in the context of T2DM and CHD.

Acknowledgment

This study was fully supported by a financial grant from the Department of Science and Technology, Ministry of Science and Technology, Government of New Delhi, India. Mr Ramesh Giri assisted in anthropometry and body fat measurement. The cooperation of the children who took part in the study and the help extended by the principals, teachers, and staff of the various schools and colleges where the study was conducted are greatly appreciated.

References

[1] Caprio S. Insulin resistance in childhood obesity. J Pediatr Endocrinol Metab 2002;1:487-92.
[2] Goran MI, Ball GD, Cruz ML. Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents. J Clin Endocrinol Metab 2003;88:1417-27.
[3] Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988;37:1595-607.
[4] Bao W, Srinivasan SR, Wattigney WA, Berenson GS. Persistence of multiple cardiovascular risk clustering related to syndrome X from childhood to young adulthood. The Bogalusa Heart Study. Arch Intern Med 1994;154:1842-7.
[5] Katzmarzyk PT, Perusse L, Malina RM, Bergeron J, Despres JP, Bouchard C. Stability of indicators of the metabolic syndrome from childhood and adolescence to young adulthood: the Quebec Family Study. J Clin Epidemiol 2001;54:190-5.
[6] Mather HM, Chaturvedi N, Fuller JH. Mortality and morbidity from diabetes in South Asians and Europeans: 11-year follow-up of the Southall Diabetes Survey, London, UK. Diabet Med 1998;15: 53-9.
[7] Whincup PH, Gilg JA, Papacosta O, et al. Early evidence of ethnic differences in cardiovascular risk: cross sectional comparison of British South Asian and white children. BMJ 2002;324:635.
[8] Misra A, Vikram NK, Arya S, et al. High prevalence of insulin resistance in postpubertal Asian Indian children is associated with adverse truncal body fat patterning, abdominal adiposity and excess body fat. Int J Obes Relat Metab Disord 2004;28:1217-26.
[9] Vikram NK, Misra A, Pandey RM, Dwivedi M, Luthra K. Adiponectin levels in postpubertal Asian Indian adolescents: relationships with insulin resistance and C-reactive protein. Metabolism 2004;53:1336-41.
[10] Misra A, Vikram NK. Insulin resistance syndrome (metabolic syndrome) and obesity in Asian Indians: evidence and implications. Nutrition 2004;20:482-91.
[11] Pouliot MC, Despres JP, Lemieux S, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol 1994;73:460-8.
[12] Rankinen T, Kim SY, Perusse L, Despres JP, Bouchard C. The prediction of abdominal visceral fat level from body composition and anthropometry: ROC analysis. Int J Obes Relat Metab Disord 1999;23:801-9.
[13] Rexrode KM, Buring JE, Manson JE. Abdominal and total adiposity and risk of coronary heart disease in men. Int J Obes Relat Metab Disord 2001;25:1047-56.
[14] Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 1994;17:961-9.
[15] Lemeshow S, Stroh G. Sampling techniques for evaluating health parameters in developing countries. Washington, DC: National Academy Press; 1988.
[16] Dudeja V, Misra A, Pandey RM, Devina G, Kumar G, Vikram NK. BMI does not accurately predict overweight in Asian Indians in northern India. Br J Nutr 2001;86:105-12.
[17] Vikram NK, Misra A, Pandey RM, Luthra K, Wasir JS, Dhingra V. Heterogeneous phenotypes of insulin resistance and its implications for defining metabolic syndrome in Asian Indian adolescents. Atherosclerosis 2005;186:193-9.
[18] American Academy of Pediatrics. National Cholesterol Education Program: report of the expert panel on blood cholesterol levels in children and adolescents. Pediatrics 1992;89:525-84.
[19] National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555-76.
[20] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2005;28(Suppl 1):S37-S42.
[21] Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. Pediatrics 2004;114:e198-e205.
[22] Moreno LA, Pineda I, Rodriguez G, Fleta J, Sarria A, Bueno M. Waist circumference for the screening of the metabolic syndrome in children. Acta Paediatr 2002;91:1307-12.