Insulin Resistance and Clustering of Cardiometabolic Risk Factors in Urban Teenagers in Southern India

AMBADY RAMACHANDRAN, DSC[1]
CHAMUKUTTAN SNEHALATHA, DSC[1]
ANNASAMI YAMUNA, PHD[1]
NARAYANASAMY MURUGESAN, PHD[1]
K.M. VENKAT NARAYAN, MD[2]

OBJECTIVE — We sought to study the occurrence of cardiometabolic risk variables, their clustering, and their association with insulin resistance among healthy adolescents in urban south India.

RESEARCH DESIGN AND METHODS — School children aged 12–19 years (n = 2,640; 1,323 boys and 1,317 girls) from diverse socioeconomic backgrounds were studied. Demographic, social, and medical details were obtained; anthropometry and blood pressure were measured. Fasting plasma glucose, insulin, and lipid profiles were measured. Clusters of risk variables were identified by factor analysis. Association of insulin resistance (homeostasis model assessment) with individual risk variables and their clusters were assessed.

RESULTS — One or more cardiometabolic abnormalities (i.e., low HDL cholesterol, elevated triglycerides, fasting plasma glucose, or blood pressure) was present in 67.7% of children (in 64.8% of normal weight and 85% of overweight children). Insulin resistance was associated with the above abnormalities except HDL cholesterol. It also showed significant positive association with BMI, waist circumference, body fat percentage, and total cholesterol ($P < 0.0001$). Factor analysis identified three distinct clusters, with minor differences in the sexes: *1*) waist circumference and blood pressure; *2*) dyslipidemia, waist circumference, and insulin; and *3*) waist circumference, glucose, and plasma insulin, with minor differences in the sexes. Insulin was a component of the lipid and glucometabolic cluster. In girls, it was a component of all three clusters.

CONCLUSIONS — Cardiometabolic abnormalities are present in nearly 68% of young, healthy, Asian-Indian adolescents and even among those with normal weight. Insulin resistance is associated with individual cardiometabolic factors, and plasma insulin showed association with clustering of some variables.

Diabetes Care 30:1828–1833, 2007

Insulin resistance is associated with obesity, type 2 diabetes, cardiovascular disease, and subclinical cardiometabolic risk markers, such as dyslipidemia, hypertension, and central adiposity (1,2). In fact, many have hypothesized that insulin resistance may be the common pathophysiological factor tying together a "syndrome" of cardiometabolic disturbance, affecting adiposity, glucose intolerance, dyslipidemia, and altered blood pressure control (2–4). On the other hand, the concept that such a syndrome exists has recently been challenged (5).

The association between insulin resistance and cardiometabolic risk factors is often confounded once the disease sets in. The ideal population for examining these associations in depth would be one that is: *1*) at high risk of insulin resistance, *2*) young and has not yet acquired clinical disease, and *3*) undergoing rapid environmental and lifestyle change.

Asian Indians are at high risk of type 2 diabetes and cardiovascular disease and have an insulin-resistant phenotype, characterized by low muscle mass, upper-body adiposity, and high percentage of body fat (6,7). While insulin resistance runs in families and may have a genetic basis (8), it is often lifestyle factors that trigger the cardiometabolic disease processes (9). With India undergoing rapid industrialization and urbanization, the consequent changes in the form of sedentary lifestyle are rampant (10,11).

In this study, among young and healthy adolescents (aged 12–19 years) from urban southern India, we examined the following: *1*) the occurrence of cardiometabolic risk variables; *2*) the distribution of insulin resistance and its association with the individual cardiometabolic risk variables, which included blood pressure, serum triglycerides, fasting plasma glucose, and HDL cholesterol; and *3*) how cardiometabolic risk factors cluster and how much of such clustering may be associated with insulin resistance. In the context of the rising prevalence of overweight and diabetes in India (11,12), especially at a younger age, these data will also serve toward policy formulation for preventive strategies.

RESEARCH DESIGN AND METHODS

— A school-based, cross-sectional survey was done among 2,640 children (1,323 boys and 1,317 girls) aged 12–19 years studying in 8th to 12th standards in 16 schools in Chennai, India. The schools were selected from different regions in the city and covered government and private schools attended by children across all socioeconomic groups. Adolescents aged 19 years (n = 16) were grouped with those aged 18 years. All subjects from each class were selected, and the response rate was 92%. Signed informed consent was given by parents. The ethics committee of the institution approved the protocol.

Details of demography, medical history, parental income, and family history

From the [1]Diabetes Research Centre, M.V. Hospital for Diabetes, World Health Organization Collaborating Centre for Research, Education, and Training in Diabetes, Royapuram, Chennai, India; and the [2]Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia.

Address correspondence and reprint requests to Dr. A. Ramachandran, MD, PhD, India Diabetes Research Foundation, 28 Marshalls Rd., Egmore, Chennai 600008, India. E-mail: ramachandran@vsnl.com.

Received for publication 13 October 2006 and accepted in revised form 19 March 2007.

Published ahead of print at http://care.diabetesjournals.org on 6 April 2007. DOI: 10.2337/dc06-2097.

Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Medians (interquartile range) of anthropometry and cardiometabolic variables among boys and girls and in categories of socioeconomic status*

Variables	Boys (n = 1,323)	Girls (n = 1,317)	Socioeconomic status		
			Category 1	Category 2	Category 3
Age (years)	15.0 (14.0–16.0)	16.0 (15.0–16.0)	16.0 (15.0–17.0)	15.0 (14.0–16.0)*	15.0 (14.0–16.0)†
BMI (kg/m^2)	18.1 (16.3–20.8)	19.3 (17.4–21.9)‡	18.4 (16.5–20.5)	18.8 (16.9–21.9)§	19.5 (17.3–22.6)†
Body fat (%)	8.8 (5.7–13.5)	17.3 (13.5–22.0)‡	12.7 (7.2–18.1)	13.5 (8.8–18.9)	14.2 (8.8–20.5)
Waist circumference (cm)	65.0 (60.0–72.0)	62.0 (57.0–68.0)‡	62.0 (57.0–67.0)	64.0 (59.0–71.0)*	67.0 (61.0–75.0)†¶
Systolic blood pressure (mmHg)	100.0 (90–110)	100.0 (90–100)	100.0 (90–110)	100.0 (90–110)	100.0 (95–100)
Diastolic blood pressure (mmHg)	70 (70–80)	70	70	70 (70–80)	70 (70–80)
Fasting plasma glucose (mmol/l)	4.9 (4.6–5.2)	4.8 (4.5–5.1)	4.81 (4.59–5.09)	4.92 (4.64–5.20)*	4.92 (4.70–5.20)†
Triglycerides (mmol/l)	0.81 (0.63–1.10)	0.84 (0.69–1.08)‖	0.81 (0.65–1.05)	0.84 (0.66–1.10)§	0.85 (0.67–1.15)**
Total cholesterol (mmol/l)	3.54 (3.14–4.00)	3.77 (3.35–4.21)	3.64 (3.25–4.10)	3.66 (3.27–4.13)	3.61 (3.19–4.18)
HDL cholesterol (mmol/l)	1.14 (1.01–1.30)	1.24 (1.09–1.40)‡	1.17 (1.01–1.35)	1.19 (1.04–1.37)	1.24 (1.06–1.40)¶**
Fasting insulin (pmol/l)††	72.6 (43.8–114.6)	94.2 (62.4–135.6)‡	72.6 (45.6–112.2	88.8 (58.2–130.2)*	98.4 (61.2–147.6)†
HOMA-IR	2.6 (1.6–4.2)	3.4 (2.2–4.9)‡	2.6 (1.6–3.9)	3.2 (2.1–4.8)*	3.6 (2.2–5.3)†

*$P < 0.0001$ for category 1 vs. 2; †$P < 0.0001$ for category 1 vs. 3; ‡$P < 0.0001$ for girls vs. boys; §$P < 0.05$ for category 1 vs. 2; ¶$P < 0.05$ for category 2 vs. 3; ‖$P < 0.05$ for girls vs. boys; and **$P < 0.001$ for category 1 vs. 3. ††Adjusted for age and BMI.

of diabetes and cardiovascular disease were obtained using a questionnaire, with parental help when necessary. Height and weight were measured without shoes. The subject was asked to stand erect with shoulders and heels flat against the wall, looking straight ahead. Height was measured to the nearest centimeter using a tape stuck to the wall. Weight was measured to the nearest 0.1 kg using a digital bathroom scale, which was checked each day using a standard weight. Waist was defined as the smallest girth between the coastal margin and the iliac crest. Blood pressure measurements were made with two cuffs of different sizes. The average of two readings taken in sitting position at an interval of 5 min was noted, and the values were rounded off to the nearest 5 mmHg. Body fat percentage was measured using Tanita body composition analyzer (Model TBF-300; Tanita, Tokyo, Japan). In girls, age at menarche was recorded at interview.

Fasting blood samples were drawn after a minimum fasting of 8 h and were transported to the laboratory on ice (4–8°C) for estimation of plasma glucose (fluoride-oxalate tube), plasma insulin (EDTA tube), and serum lipids. Plasma glucose was measured using the glucose oxidase-peroxidase method (13), serum total cholesterol (14) and triglycerides (15) by standard enzymatic procedures and HDL cholesterol by direct assay method (16). Biochemical assays were done on a Hitachi 912 autoanalyzer using regents from Roche Diagnostics, Mannheim, Germany with appropriate quality control methods. Plasma insulin was measured using a radioimmunoassay kit (Diasorin, Saluggia, Italy), which had a sensitivity of 4 μU/ml (<24 pmol/l) and intra and interassay coefficients of variation <10%. Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) (17).

In the absence of a national consensus on the normal cutoff values for anthropometric, lipid, and blood pressure parameters in Indian children, the criteria used in the Third National Nutritional Examination Survey for American adolescents were used in this study (18). Cutoff values were derived for BMI (≥85th percentile), waist circumference (>75th percentile for age and sex), and blood pressure (>90th percentile adjusted for age and sex). The cutoff values for triglycerides (≥1.1 mmol/l) and HDL cholesterol (<1.3 mmol/l for girls of all ages and boys aged <15 years; <1.17 mmol/l for boys aged 15–19 years) were also used as suggested by Ferranti et al. (18). Normal fasting glucose was taken as <5.6 mmol/l. The 75th percentile of HOMA-IR in normal weight children without any risk factors was considered the cutoff for normal. Cardiometabolic variables studied were blood pressure, triglycerides, HDL cholesterol, and insulin resistance (HOMA-IR) in groups dichotomized as overweight and normal weight (BMI). Waist circumference was also included as a risk variable in the factor analysis, as central adiposity may be a risk variable independent of overall adiposity (BMI).

Socioeconomic status was assessed based on the occupation and monthly income of parents, dwelling unit, and automobile ownership. Monthly income (Indian rupees [INR]) was divided into three categories: low (< 5,000 INR), middle (5,000–20,000 INR), and high (>20,000 INR). Those with professional jobs or employment in jobs likely to have a monthly income of >20,000 INR, who own or rent a house in costly areas, and who have cars were considered part of the high-income group, regardless of reported income.

Statistical analyses

Median values are reported for skewed variables, and group comparisons were made using median test or χ^2 test as relevant. Spearman rank correlations of insulin resistance (HOMA-IR) with other variables were evaluated. Factor analysis with principal component analysis was used to identify the domains that segregated among the risk variables (19). The risk variables included were log-transformed values of fasting insulin (as a surrogate for insulin resistance), systolic and diastolic blood pressure, fasting plasma glucose, HDL cholesterol, triglycerides, and Z values of waist circumference. Z values were calculated for age-standardized waist circumference. The principal component analysis method with orthogonal rotation identifies subsets of clusters of correlated variables (19). Interpretation is based on the correlations, called loadings (range −1.0 to 1.0), between the factors and the original independent variables greater than ±0.30—to interpret the resulting factor pattern as suggested by Cu-

Table 2—*Prevalence of cardiometabolic abnormalities and values of HOMA-IR in relation to presence of abnormalities*

Variables (abnormal cutoffs)	Prevalence of abnormalities	Median HOMA-IR values: Subjects with abnormalities	Median HOMA-IR values: Subjects with no abnormality	*P*
HDL cholesterol*	1,516 (57.4)	3.1	2.8	0.0019
Triglycerides (≥1.1 mmol/l)	637 (24.2)	3.8	2.8	<0.0001
Elevated blood pressure (> 90th percentile)†	158 (6.0)	5.4	2.9	<0.0001
Fasting plasma glucose (≥ 5.6 mmol/l)	154 (5.8)	4.6	2.9	<0.0001
Positive family history of diabetes	505 (19.1)	3.3	2.9	<0.0001

Data are *n* or *n* (%). *< 1.3 mmol/l for girls of all ages and boys aged <15 years and <1.17 mmol/l for boys aged 15–19 years. †Adjusted for age and sex.

reton and D'Agostino (19). SPSS package, version 10.1, was used for the analyses.

RESULTS — Table 1 shows the sex- and socioeconomic-specific characteristics of the study subjects (n = 2,640; 1,323 boys and 1,317 girls). Median of blood pressure was similar, waist circumference was significantly lower, and all other parameters were significantly higher in girls than in boys. Girls had significantly higher fasting insulin and insulin resistance than boys ($P < 0.0001$). Socioeconomic distribution of children was as follows: low income, 36.6%; middle income, 52.9%; and high income, 10.5%. Anthropometric variables, fasting plasma glucose, triglycerides, plasma insulin, and HOMA-IR values were all higher in the high socioeconomic group. The mean age of menarche in girls was 12.7 ± 1.0 years. We did not measure the stages of puberty in boys.

HOMA-IR showed significant ($P < 0.001$) inverse correlation with age ($r = -0.13$), whereas BMI ($r = 0.32$), waist circumference ($r = 0.24$), body fat percentage ($r = 0.34$), blood pressure (systolic $r = 0.13$; diastolic $r = 0.07$), fasting plasma glucose ($r = 0.28$), triglycerides ($r = 0.21$), and total cholesterol ($r = 0.12$) were positively correlated ($P < 0.0001$). HDL cholesterol and insulin resistance were not correlated ($r = 0.01$, $P = 0.51$).

HOMA-IR was significantly higher in children aged <14 years (median −3.3) than in those aged >14 years (HOMA-IR −3.0, $P = 0.002$). Multiple linear regression analysis showed that parameters independently associated with HOMA-IR were as follows: BMI ($\beta = 0.14$, SE $\beta = 0.02$, $P < 0.0001$, $r^2 = 8.5\%$), younger age ($\beta = -0.23$, SE $\beta = 0.03$, $P < 0.0001$, $r^2 = 1.5\%$), female sex ($\beta = 0.42$, SE $\beta = 0.10$, $P < 0.0001$, $r^2 = 0.3$), and waist circumference ($\beta = 0.02$, SE $\beta = 0.008$, $P < 0.004$, $r^2 = 0.3$). Fat percentage was not associated with HOMA-IR ($\beta = 0.03$, SE $\beta = 0.014$, $P = 0.446$).

A total of 1,790 children (67.8%) had abnormal values for one or more cardiometabolic risk factors (i.e., lipids, fasting plasma glucose, and blood pressure). The prevalence of each abnormality is shown in Table 2. Median values of HOMA-IR were higher in subjects with abnormal values for each parameter (Table 2). Family history of diabetes was reported in 19.1% of children, and HOMA-IR was significantly higher in those with a family history (Table 2).

Overweight children had higher prevalence and clustering of abnormalities (other than overweight and waist circumference) compared with those of normal weight ($P < 0.0001$) (Table 3). In overweight children, HOMA-IR values were significantly higher ($P < 0.001$) even in the absence of abnormalities. HOMA-IR values increased with increasing number of abnormalities in both subgroups. The cutoff for normal HOMA-IR was 3.62 in our study. The percentage with insulin resistance (HOMA-IR >3.6) showed an increasing trend with the increasing number of abnormalities ($P < 0.0001$). Overweight children showed higher rates of insulin resistance.

Elevated waist circumference (>75th percentile for age and sex) was present in a total of 625 (23.7%) children, in 285

Table 3—*Comparison of prevalence of abnormalities in relation to body weight and the influence of clustering on HOMA-IR values*

Abnormalities	Total	Nil	1	2	>2
n	2,640	850 (32.2)	1,181 (44.7)	545 (20.6)	64 (2.4)
Normal weight (n = 2,245)	2,245	790 (35.2)	1,006 (44.8)	420 (18.7)	29 (1.3)
Overweight n = 394	394	59 (15.0)	175 (44.4)	125 (31.7)	35 (8.9)
χ^2	—	61.84	NS	9.43	78.45
*P**	—	<0.0001	NS	0.002	$P < 0.0001$

	Median HOMA-IR values and percentage with value >3.6							
	Median	*n* (%)	Median	*n* (%)	Median	*n* (%)	Median	*n* (%)
Total	2.6	246 (30)	2.9†	404 (34)	3.9‡	301 (55)	7.1‡	52 (81)
Normal weight	2.5	198 (25)	2.6	272 (27)	3.3‡	189 (45)	5.4‡	18 (62)
Overweight	4.9§	48 (81)	5.0§	132 (75)	6.1‡§	112 (90)	8.0‡¶	34 (97)

Data are n (%) unless otherwise indicated. *Normal vs. overweight. †$P = 0.002$ vs. no abnormalities. ‡$P < 0.0001$ vs. no abnormalities. §$P < 0.0001$ vs. normal weight by median test; ¶$P < 0.05$ vs. two abnormalities.

Table 4—*Results of factor analysis showing the clusters of cardiometabolic risk variables*

	Total			Boys			Girls		
Variables	Factor 1	Factor 2	Factor 3	Factor 1	Factor 2	Factor 3	Factor 1	Factor 2	Factor 3
HDL cholesterol	−0.10	−0.74	0.21	−0.02	0.16	−0.78	−0.06	−0.77	0.09
Triglycerides	−0.02	0.74	0.23	0.02	0.38	0.66	−0.01	0.74	0.07
Z waist circumference	0.57	0.32	0.38	0.52	0.51	0.27	0.58	0.30	0.28
Systolic blood pressure	0.91	0.02	0.05	0.92	0.08	0.02	0.88	−0.19	0.06
Diastolic blood pressure	0.90	−0.16	−0.03	0.92	−0.02	−0.01	0.86	−0.04	−0.03
Fasting plasma glucose	−0.04	−0.22	0.75	−0.15	0.69	−0.33	−0.03	−0.14	0.88
Fasting insulin	0.19	0.31	0.68	0.20	0.71	0.23	0.37	0.38	0.57
Variance (%)	32.2	17.8	15.9	32.9	18.3	16.2	32.3	18.3	15.0
Total variance (%)		65.9			67.4			65.5	

Log-transformed variables were entered.

(12.7%) with normal weight and in 340 (86.3%) who were overweight.

Factor analyses identified three definite clusters of risk variables with some differences between boys and girls (Table 4). In the total group, the first cluster was the blood pressure factor, second was the lipid factor, and third was the glucose factor. Waist circumference was a component of all three factors. Insulin was associated with factors two and three. In boys, the second was the glucose and insulin factor. Waist circumference was a component of factors one and two in both sexes. In girls, insulin was associated with all of the three factors.

Type 2 diabetes was diagnosed in one boy aged 16 years, who had the following values: fasting plasma glucose 15.2 mmol/l, 2-h glucose 28.0 mmol/l, A1C 11.8%, total cholesterol 5.0 mmol/l, and triglycerides 6.7 mmol/l. These values improved in 2 months in response to metformin and medical nutrition therapy (fasting plasma glucose 5.6 mmol/l and 2-h glucose 5.7 mmol/l), and blood pressure was 130/90 mmHg.

CONCLUSIONS — In this population-based study, we found that 64.8% of normal weight children and adolescents had at least one cardiometabolic risk factor and that these factors clustered into three groups. Plasma insulin and waist circumference were strongly associated with these clusters. Waist circumference was a component of two clusters in both sexes.

Previous studies of cardiometabolic risk variables in children and adolescents have been mostly in obese subjects (20–23). In contrast, our study has shown the occurrence of these abnormalities even in children with ideal BMIs. However, abnormalities were more and tended to cluster more frequently in the presence of overweight. This was evident in the factor analysis, in which waist circumference was included as the index of overweight.

HOMA-IR values were significantly increased in subjects with cardiometabolic abnormalities. Blood pressure significantly correlated with insulin resistance in children. A positive association between insulin levels and blood pressure was reported in American children in some previous reports (24–28), while a few other studies did not find such a correlation (29,30). The factor analysis showed the association of plasma glucose with insulin in both sexes. Fasting hyperglycaemia was present only in a small percentage of children and adolescents.

The commonest cardiometabolic abnormality was low HDL cholesterol, followed by elevated triglycerides; the latter showed a strong association with insulin resistance. Low HDL cholesterol was seen in a large percentage of Asian-Indian adults in India (31) and in other countries (32). We had earlier suggested that elevated triglycerides could be used as a surrogate marker of insulin resistance in Asian-Indian, nondiabetic adults (33). We now confirm the findings in the children. The strong association of insulin resistance with dyslipidaemia had also been reported in childhood in other populations (20,28).

South-Asian adolescents have lower insulin sensitivity compared with European populations (34,35). This ethnic difference in insulin sensitivity was attributed to the higher body fat in South-Asian children (35) and may reflect differences in historical survival patterns.

In our study, girls had higher insulin resistance than boys, and this was not related to the higher percentage of body fat. The Early Bird Study in the U.K. among healthy children aged 5 years had reported that girls had an intrinsically higher insulin resistance than boys independent of the influence of body fat (36).

In our study, insulin resistance was higher in younger children who were in the peripubertal period. Interaction of various hormones during puberty may decrease insulin sensitivity (37–39). A longitudinal study of insulin resistance in American children showed that during puberty, insulin resistance decreased by ~50%, with a compensatory increase in plasma insulin (40). Decrease in insulin sensitivity was independent of the changes in body fat. The metabolic changes seen were increased lipolysis, decreased glucose oxidation, and a decrease in adiponectin levels. The changes were proposed to be partially mediated by increased growth hormone secretion (40). One of the limitations of our study was that we could not assess pubertal stages in boys. The age at menarche in girls was 12.7 ± 1 years. We noted that insulin resistance was higher in children aged ≤14 years and probably related to the stage of puberty.

Clustering of cardiometabolic abnormalities in our study subjects appeared to be associated with insulin resistance, more so in girls. Insulin resistance was found to be strongly associated with adiposity and glucose levels. Two previous studies in American children and adolescents had also demonstrated associations with insulin resistance using factor analysis (20,41). Independent associations of BMI and insulin resistance with cardiometabolic risk variables and of their clustering in children have also been shown (27). A recent prospective study in American children by Sinaiko et al. showed that insulin resistance begins at an early age, has an independent effect on cardiovascu-

lar risk, and may continue during adolescence (28).

Subjects with positive family history of diabetes were relatively more insulin resistant. Presence of a positive family history was known in 19.1%, and it is likely to be an underestimation, as it was elicited by history. The familial nature of insulin resistance, reported in adults in an earlier publication by us, was confirmed in the study (8).

Presence of overweight and cardiometabolic abnormalities were more common in the higher socioeconomic group, probably related to the differences in lifestyle. In an earlier study in school children, we noted that unhealthy lifestyle was common in the higher socioeconomic stratum (42).

In conclusion, there is a high prevalence of cardiometabolic risk factors even in healthy young children of normal weight in southern India, and we find evidence of clustering of several of these factors. Insulin resistance seems to be associated with elevated levels of fasting plasma glucose, blood pressure, and triglycerides and with their clustering. Given the fact that 64.8% of normal weight children had at least one cardiometabolic abnormality, our data also raise questions about what is normal weight in this population.

Lack of details on the pubertal stages, especially in boys, is a limitation of this study. However, we noted that insulin resistance was higher in younger children in the pubertal period than in adolescents. Blood pressure readings approximated to values of 5 may also have affected the sensitivity of the analysis to some extent. Identification of individual risk factors on a single cross-sectional analysis has limited predictive value. However, occurrence of multiple abnormalities confirms the existence of the risk in the study population.

Prospective studies are, therefore, needed to determine whether the clusters of risk variables predict future cardiovascular events more than individual risk factors or their sum. Furthermore, it is not known whether the three clusters found in our study each represent different aetiopathophysiological processes and risk factors and whether they may need different interventions.

Acknowledgments— We acknowledge the help of Tanita, Tokyo, Japan, for providing the body fat monitor. We thank the principals of schools, parents, and children for their cooperation. We acknowledge the help rendered by our epidemiology staff, Mary Simon, Sathish Cholayil Kizhakathil, Selvam Sundaram, Catherine Seeli, Muruganantham Manian, Lalitha Manjula, Jayanthi Jothikannan, and Latha Uthavkumar. We thank health inspectors Gangadharan Shanmugam, Sreedhar Gopal, Venu Purushothaman, Ramani Mani, Joseph Kulandairaj, and Mohan Anamala for their liaison work with the school authorities. We thank Bobby Alex and Vijaya Balaji for secretarial help.

References

1. Ferrannini E, Muscelli E, Stern MP, Haffner SM: Differential impact of insulin and obesity on cardiovascular risk factors in non-diabetic subjects. *Inter J Obesity Relat Metab Disord* 20:7–14, 1996
2. Reaven GM: Banting lecture 1988: role of insulin resistance in human disease. *Diabetes* 37:1595–1607, 1998
3. Balkau B, Charles MA, Drivsholm T, Borch JK, Wareham N, Yudkin JS, Morris R, Zavaroni I, Van Dam R, Freskins E, Gabriel R, Diet M, Nilsson P, Hedblad B: Frequency of the WHO metabolic syndrome in European cohorts, and an alternative definition of an insulin resistance syndrome. *Diabetes Metab* 28:364–376, 2002
4. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group: The metabolic syndrome: a new world wide definition. *Lancet* 366:1059–1062, 2005
5. Kahn R, Buse J, Ferrannini E, Stern M: The metabolic syndrome: time for a critical appraisal. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia* 48:1684–1699, 2005
6. McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG: Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. *Circulation* 87:152–161, 1993
7. Ramachandran A, Snehalatha C, Vijay V: Low risk threshold for acquired diabetogenic factors in Asian Indians. *Diabetes Res Clin Pract* 65:189–195, 2004
8. Ramachandran A, Snehalatha C, Mohan V, Bhattacharyya PK, Viswanathan M: Decreased insulin sensitivity in offspring whose parents both have type 2 diabetes: *Diabet Med* 7:331–334, 1990
9. Steinberger J, Daniels SR: Obesity, insulin resistance, diabetes and cardiovascular risk in children: an American Heart Association scientific statement from the Atherosclerosis, Hypertension and Obesity in the Young Committee and the Diabetes Committee. *Circulation* 107:1448–1453, 2003
10. Wild S: Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 27:1047–1053, 2004
11. Ramachandran A, Snehalatha C, Baskar ADS, Mary S, Sathish Kumar CK, Selvam S, Catherine S, Vijay V: Temporal changes in prevalence of diabetes and impaired glucose tolerance associated with life style transition occurring in the rural population in India. *Diabetologia* 47:860–865, 2004
12. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, Rao PV, Yajnik CS, Prasanna KS, Nair JD; Diabetes Epidemiology Study Group in India (DESI): High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. *Diabetologia* 44: 1094–1101, 2001
13. Trinder P: Determination of blood glucose using an oxidase peroxidase system with a non-carcinogenic chromogen. *J Clin Path* 22:158–161, 1969
14. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC: Enzymatic determination of total serum cholesterol. *Clin Chem* 20: 470–475, 1974
15. Bergmeyer HU, Wahlefeld AW (Eds.): *Methods of Enzymatic Analysis*. 2nd ed. New York, Academic Press, 1974, p. 1831
16. Sugiuchi H, Uji Y, Okabe H, Jrie T, Vekama K, Kayahara N, Miyauchi K: Direct measurement of HDL cholesterol in serum with PEG modified enzymes and sulphated α-cyclodextrin. *Clin Chem* 41: 717–723, 1995
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RK: Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentration in man. *Diabetologia* 28:412–419, 1985
18. De Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N: Prevalence of the metabolic syndrome in American adolescents: Findings from the Third National Health and Nutrition Examination Survey. *Circulation* 110:2494–2497, 2004
19. Cureton EE, D'Agostino RB: *Factor Analysis: An Applied Approach*. Hillsdale, NJ, Lawrence Erlbaum Associates, 1983
20. Weiss R, Dziura J, Burget TS, Tamborlone WV, Taksali SE, Yeckel CW, Allen K, Lopes M, Savoye M, Morrison J, Sherwin RS, Caprio S: Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 350:2362–2374, 2004
21. Caprio S, Bronson M, Sherwin S, Rife F, Tamborlane WV: Co-existence of severe insulin resistance and hyperinsulinaemia in pre-adolescent obese children. *Diabetologia* 39:1489–1497, 1996
22. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH: Prevalence of a metabolic syndrome phenotype in adolescents:

findings from the third National Health and Nutrition Examination Survey: 1988–1994. *Arch Pediatr Adolesc Med* 157:821–827, 2003
23. Cruz ML, Goran MI: The metabolic syndrome in children and adolescents. *Curr Diab Reports* 4:53–62, 2004
24. Cruz ML, Weigensberg MJ, Huang TT, Ball G, Shaibi GQ, Goran MI: The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *J Clin Endocrinol Metab* 89:108–113, 2004
25. Raitakari OT, Porkka KVK, Ronnemaa T, Knip M, Uhari M, Akerblom HK, Vikari JS: The role of insulin in clustering of serum lipids and blood pressure in children and adolescents. *Diabetologia* 38:1042–1050, 1995
26. Cruz ML, Huang TT, Johnson MS, Gower BA, Goran MI: Insulin sensitivity and blood pressure in black and white children. *Hypertension* 40:18–22, 2002
27. Sinaiko AR, Steinberger J, Moran A, Prineas RJ, Vessby B, Basu S, Tracy R, Jacobs DR: Relation of body mass index and insulin resistance to cardiovascular risk factors, inflammatory factors and oxidative stress during adolescence. *Circulation* 111:1985–1991, 2005
28. Sinaiko AR, Steinberger J, Moran A, Hong CP, Prineas RJ, Jacobs DR Jr: Influence of insulin resistance and body mass index at age 13 on systolic blood pressure, triglycerides and high density lipoprotein cholesterol at age 19. *Hypertension* 48:730–736, 2006
29. Bergstrom E, Hernell O, Persson LA, Vessby B: Insulin resistance syndrome in adolescents. *Metabolism* 45:908–914, 1996
30. Berenson GS, Radhakrishnamurthy B, Srinivasan SR, Voors AW, Foster TA, Dalferes ER Jr, Webber LS: Plasma glucose and insulin levels in relation to cardiovascular risk factors in children from a biracial population: the Bogalusa Heart Study. *J Chron Dis* 34:379–391, 1981
31. Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V: Metabolic syndrome in urban Asian Indian adults: a population study using modified ATP III criteria. *Diabetes Res Clin Prac* 60:199–204, 2003
32. Dixon AN, Bellary S, Hanif MW, O'Hare JP, Raymond NT, Kumar S: Type 2 diabetes and cardiovascular risk in U.K. south Asian community. *Diabetologia* 49:2234–2246, 2006
33. Snehalatha C, Satyavani K, Sivasankari S, Vijay V, Ramachandran A: Serum triglycerides as a marker of insulin resistance in non-diabetic urban Indian. *Diabetes Res Clin Prac* 69:205–206, 2005
34. Whincup PH, Gilg JA, Owen CG, Odoki K, Alberti KG, Cook DG: British South Asians aged 13–16 years have higher fasting glucose and insulin levels than Europeans. *Diabet Med* 22:1275–1277, 2005
35. Ehtisham S, Crabtree N, Clark P, Shaw N, Barrett T: Ethnic differences in insulin resistance and body composition in United Kingdom adolescents. *J Clin Endocrinol Metab* 90:3963–3969, 2005
36. Murphy MJ, Metcalf BS, Voss LD, Jeffery AN, Kirkby J, Mallam KM, Wilkin TJ: Girls at five are intrinsically more insulin resistant than boys: the programming hypotheses revisited: the EarlyBird Study (EarlyBird 6). *Pediatrics* 113:82–86, 2004
37. Bloch CA, Clemons P, Sperling MA: Puberty decreases insulin sensitivity. *J Pediatr* 110:481–487, 1987
38. Cook JS, Hoffman RP, Stene MA, Hansen JR: Effects of maturational stage on insulin sensitivity during puberty. *J Clin Endocrinol Metab* 77:725–730, 1993
39. Goran MI, Gower BA: Longitudinal study on pubertal insulin resistance. *Diabetes* 50:2444–2450, 2001
40. Hannon TS, Janosky J, Arslanian SA: Longitudinal study of physiologic insulin resistance and metabolic changes of puberty. *Pediatr Res* 60:759–763, 2006
41. Goodman E, Dolan LM, Morrison JA, Daniels SR: Factor analysis of clustered cardiovascular risks in adolescence obesity is the predominant correlate of risk among youth. *Circulation* 111:1970–1977, 2005
42. Ramachandran A, Vinitha R, Megha Thayyil, Sathish kumar CK, Sheeba L, Joseph S, Vijay V: Prevalence of overweight in urban Indian adolescent school children. *Diabetes Res Clin Prac* 57:185–190, 2002