Adult Metabolic Syndrome and Impaired Glucose Tolerance Are Associated With Different Patterns of BMI Gain During Infancy

Data from the New Delhi birth cohort

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OBJECTIVE — The purpose of this study was to describe patterns of infant, childhood, and adolescent BMI and weight associated with adult metabolic risk factors for cardiovascular disease.

RESEARCH DESIGN AND METHODS — We measured waist circumference, blood pressure, glucose, insulin and lipid concentrations, and the prevalence of metabolic syndrome (National Cholesterol Education Program Adult Treatment Panel III definition) in 1,492 men and women aged 26–32 years in Delhi, India, whose weight and height were recorded every 6 months throughout infancy (0–2 years), childhood (2–11 years), and adolescence (11 years–adult).

RESULTS — Men and women with metabolic syndrome (29% overall), any of its component features, or higher (greater than upper quartile) insulin resistance (homeostasis model assessment) had more rapid BMI or weight gain than the rest of the cohort throughout infancy, childhood, and adolescence. Glucose intolerance (impaired glucose tolerance or diabetes) was, like metabolic syndrome, associated with rapid BMI gain in childhood and adolescence but with lower BMI in infancy.

CONCLUSIONS — In this Indian population, patterns of infant BMI and weight gain differed for individuals who developed metabolic syndrome (rapid gain) compared with those who developed glucose intolerance (low infant BMI). Rapid BMI gain during childhood and adolescence was a risk factor for both disorders.

Diabetes Care 31:2349–2356, 2008

Approximately 10% of urban Indian men and women aged 40–49 years have type 2 diabetes, and a rising prevalence is predicted to produce 80 million diabetic patients in India by 2030 (1–3). Cardiovascular disease is also rising (4). Similar trends, thought to reflect increasing obesity, are occurring in other developing countries undergoing economic transition, and interventions to prevent disease are urgently needed.

Research in high-income countries has shown that factors linked to weight gain in early life contribute to the risk of developing diabetes and cardiovascular disease. Low birth weight (5,6) and accelerated gain in BMI during childhood and adolescence predict increased risk (7,8). The optimal pattern of infant weight gain (the first 1–2 postnatal years) is unclear; studies of adults suggest that low infant weight gain is a risk factor for later disease (7–9), whereas studies of children suggest the opposite (10,11). There are few data from developing countries.

In the New Delhi birth cohort (12,13), children were measured at birth and every 6 months throughout infancy, childhood, and adolescence. We reported earlier that low BMI in infancy and rapid childhood BMI gain were associated with an increased risk of adult diabetes or impaired glucose tolerance (IGT) (12). We have now examined other cardiovascular risk factors and the cluster of risk factors known as the metabolic syndrome.

RESEARCH DESIGN AND METHODS

— During 1969–1972, married women living in a 12-km^2 area of Delhi (n = 20,755) were followed up (12,13). There were 9,169 pregnancies and 8,181 live births. Trained personnel recorded the babies' weight and length within 72 h of birth and every 6 months until age 14–21 years. Gaps in funding interrupted measurements in 1972–1973 and 1980–1982. At recruitment, 60% of families had incomes of >50 rupees/month (national average 28 rupees/month) and 15% of parents were illiterate (national average 66%). Nevertheless, 43% of families lived in one room. Hindus were the majority religious group (84%), followed by Sikhs (12%), Christians (2%), Muslims (1%), and Jains (1%).

Current study

In 1998–2002 we retraced 2,584 (32%) of the cohort and 1,583 agreed to participate. Data on schooling, occupation,

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Received 16 May 2008 and accepted 27 August 2008.
Published ahead of print at http://care.diabetesjournals.org on 3 October 2008. DOI: 10.2337/dc08-0911.

household possessions, alcohol consumption, tobacco use, physical activity, and family history were obtained by questionnaire (12,13). Weight and height were measured using standardized techniques. Waist circumference was measured using fiberglass tape, in expiration, midway between the lower lateral costal margin and the iliac crest, with the subject standing. Blood pressure was recorded using an automated device (Omron 711) with the subject seated, after 5 minutes of rest (mean of two readings). Plasma glucose concentrations were measured fasting and 120-min after a 75-g glucose load. Glucose and fasting cholesterol and triglyceride concentrations were analyzed by enzymatic methods using Randox kits on a Beckman AutoAnalyzer, and HDL cholesterol was measured using the same method after phosphotungstate precipitation. IGT and diabetes were defined using World Health Organization criteria (14). Metabolic syndrome was defined using National Cholesterol Education Program Adult Treatment Panel III criteria (15,16). Insulin resistance (homeostasis model assessment [HOMA]) was estimated (17). The study was approved by the All India Institute of Medical Sciences research ethics committee, and informed verbal consent was obtained.

Statistical analyses

Data from the whole original cohort was used to derive individual SD scores for BMI and weight at 6 months and birthdays from 1 to 21 years (12). Participants had a mean ± SD of 23 ± 5.5 observations. Interpolated values were used if measurements were made within 6 months (up to 1 year), 1 year (aged 2 years), 1.5 years (aged 3 years), and 2 years (all older ages). Back-transformation provided estimates of measurements at these ages. To measure changes in measurements in early life (e.g., from 2 to 11 years), we regressed SD scores at the end of the interval (11 years) on SD scores at the beginning (2 years) and at all preceding time points (birth, 6 months, and 1 year) and expressed the residuals as SD scores. This method produces uncorrelated variables describing change between specific ages (conditional SD scores). Quadratic terms were included when relationships between measurements at different ages were nonlinear. Associations between size in early life and adult outcomes were examined using regression. Outcomes with skewed distributions (HDL cholesterol and insulin resistance) were log-transformed.

Table 1—*Body measurements at birth, 2, 11, and 26–32 years and adult risk factors and components of the metabolic syndrome*

	Men	*n*	Women	*n*
n	886		640	
Birth				
Length (SD score)*	−0.44 ± 0.80	779	−0.45 ± 0.81	558
Weight (SD score)*	−1.06 ± 0.71	803	−1.17 ± 0.72	561
At 2 years				
Height (SD score)*	−1.54 ± 1.03	840	−1.55 ± 1.04	609
Weight (SD score)*	−2.01 ± 1.19	834	−2.27 ± 1.43	609
BMI (SD score)*	−0.78 ± 1.10	833	−0.85 ± 0.98	604
At 11 years				
Height (SD score)*	−1.11 ± 0.84	831	−1.37 ± 1.04	607
Weight (SD score)*	−1.56 ± 1.01	834	−1.87 ± 1.19	608
BMI (SD score)*	−1.23 ± 1.03	830	−1.31 ± 1.04	606
Adult				
Age (years)	29.2 ± 1.3	886	29.2 ± 1.4	640
Height (cm)	169.7 ± 6.4	886	154.9 ± 5.7	638
BMI (kg/m^2)	24.9 ± 4.3	886	24.6 ± 5.1	638
Waist circumference (cm)	90.2 ± 12.1	886	79.6 ± 12.4	640
Overweight (BMI ≥25) (%)	47.4	886	45.5	638
Obese (BMI ≥30) (%)	9.5	886	13.0	638
Any alcohol intake (%)	56.2	886	1.4	640
Ex-smokers (%)	5.1	886	0.2	640
Current smokers (%)	29.8	886	0.2	640
Systolic blood pressure (mmHg)	118.4 ± 11.4	880	106.6 ± 11.0	631
Diastolic blood pressure (mmHg)	77.9 ± 10.3	880	73.4 ± 9.2	631
Fasting				
Glucose (mmol/l)†	5.37 ± 1.21	869	5.28 ± 1.17	623
Insulin (pmol/l)†	34.4 ± 2.62	868	28.8 ± 2.64	623
Insulin resistance (HOMA)†	1.37 ± 2.73	868	1.13 ± 2.75	623
Total cholesterol (mmol/l)†	5.16 ± 1.14	869	4.75 ± 0.94	623
HDL cholesterol (mmol/l)†	1.12 ± 1.30	869	1.24 ± 1.29	621
Triglycerides (mmol/l)†	1.57 ± 1.69	868	1.05 ± 1.51	623
2-h glucose (mmol/l)†	5.93 ± 1.34	848	6.12 ± 1.28	591
Components of the metabolic syndrome				
High waist circumference (%): ≥90 cm (men) ≥80 cm (women)	51.5	886	45.5	640
Low HDL cholesterol (%) <1.0 mmol/l (men) <1.3 mmol/l (women)	34.2	869	55.6	621
High triglycerides (%) ≥1.7 mmol/l	41.2	868	10.6	623
High blood pressure (%): systolic ≥130 or diastolic ≥85 mmHg or receiving treatment for hypertension	27.6	880	12.3	632
High fasting glucose (%) ≥5.6 mmol/l	41.3	869	36.6	623
Metabolic syndrome (NCEP-ATPIII) (%)	35.6	869	20.2	623
Diabetes (%)	4.8	849	3.7	593
IGT (%)	11.2	849	10.3	593

Data are arithmetic means ± SD or % unless otherwise indicated. *SD scores are based on National Centre for Health Statistics data (18). †Geometric means ± SD. ATPIII, Adult Treatment Panel III; NCEP, National Cholesterol Education Program.

RESULTS — Of the 1,526 subjects attending the clinic, glucose tolerance category was definable for 1,442 and metabolic syndrome for 1,492. Compared with the remainder of the original cohort, more participants were male (58 vs. 52%, $P < 0.001$), mean birth weight was heavier (2,851 vs. 2,818 g, $P = 0.046$), and maternal literacy was 6% higher. BMI SD scores differed by −0.10 to 0.06 (mean −0.04) between

Table 2—*Mean waist circumference, HDL cholesterol and triglyceride concentrations, systolic blood pressure, fasting glucose concentration, prevalence of metabolic syndrome and IGT/DM, insulin resistance, and total cholesterol concentrations according to BMI at birth, age 2 years, age 11 years, and adulthood*

	n		Waist circumference (cm)	HDL cholesterol (mmol/l)*	Triglycerides (mmol/l)*	Systolic blood pressure (mmHg)	Fasting glucose (mmol/l)*	120-min glucose (mmol/l)*	Metabolic syndrome (NCEP-ATP III) (%)	IGT/diabetes (%)	Insulin resistance (HOMA)*	Cholesterol (mmol/l)
	Min	Max										
Fifths of BMI at birth (kg/m^2)												
Low	253	266	84.0	1.18	1.35	113.8	5.33	6.16	30.2	15.4	1.27	5.04
	255	268	85.8	1.17	1.33	113.7	5.47	6.06	29.7	16.9	1.35	4.99
	250	268	86.4	1.18	1.34	113.9	5.34	5.92	28.8	13.2	1.33	4.98
	255	268	86.5	1.16	1.33	113.8	5.29	5.97	31.6	12.9	1.22	5.05
High	251	267	86.5	1.16	1.31	112.6	5.26	5.89	24.7	15.5	1.19	4.93
P^1			0.02 (+)	0.9	0.4	0.5	0.06	0.03 (−)	0.1	0.4	0.3	0.7
P^2			0.1	0.8	0.09	0.05 (−)	0.04 (−)	0.009 (−)	0.002 (−)	0.2	0.004 (−)	0.3
Fifths of BMI at 2 years (kg/m^2)												
Low	267	286	82.5	1.18	1.31	112.5	5.36	6.31	29.3	19.9	1.22	4.99
	273	288	83.5	1.17	1.23	114.1	5.38	6.15	24.9	17.2	1.17	4.84
	273	288	85.8	1.19	1.42	112.8	5.33	5.93	29.2	12.5	1.25	5.09
	271	288	86.6	1.16	1.38	114.4	5.20	5.76	29.4	12.2	1.26	5.09
High	275	287	90.1	1.15	1.29	113.7	5.39	5.90	32.7	13.5	1.36	4.88
P^1			<0.001 (+)	0.3	0.6	0.1	0.6	<0.001 (−)	0.1	0.06	0.1	0.8
P^2			0.4	0.9	0.02 (−)	0.05 (−)	0.2	<0.001 (−)	0.01 (−)	0.002 (−)	0.002 (−)	0.02 (−)
Fifths of BMI at 11 years (kg/m^2)												
Low	267	287	78.2	1.20	1.25	111.8	5.33	6.09	18.2	15.7	1.06	4.91
	272	287	82.4	1.18	1.31	112.6	5.35	5.98	24.8	12.5	1.18	4.94
	271	288	84.7	1.19	1.31	113.5	5.29	5.98	29.1	16.2	1.18	5.03
	268	287	88.7	1.16	1.30	113.6	5.36	5.95	33.0	13.1	1.34	4.91
High	276	287	94.8	1.15	1.44	116.3	5.36	6.04	40.5	18.1	1.62	5.13
P^1			<0.001 (+)	0.8	0.002 (+)	<0.001 (+)	0.3	0.8	<0.001 (+)	0.09	<0.001 (+)	0.05 (+)
P^2			<0.001 (−)	0.02 (+)	<0.001 (−)	<0.001 (−)	0.3	<0.001 (−)	<0.001 (−)	0.2	<0.001 (−)	<0.001 (−)
Fifths of adult BMI (kg/m^2)												
Low	278	304	70.6	1.22	1.02	107.9	5.25	5.66	4.5	9.4	0.66	4.53
	288	305	80.3	1.18	1.28	112.1	5.28	5.89	12.7	11.8	0.94	4.93
	297	306	85.8	1.16	1.38	114.0	5.28	6.03	26.4	12.5	1.31	5.12
	292	305	91.3	1.17	1.43	115.5	5.38	6.08	43.7	18.8	1.63	5.12
High	286	304	100.9	1.11	1.57	118.1	5.47	6.38	57.9	23.1	2.36	5.23
P^1			<0.001 (+)	<0.001 (−)	<0.001 (+)	<0.001 (+)	0.001 (+)	<0.001 (+)	<0.001 (+)	<0.001 (+)	<0.001 (+)	<0.001 (+)

All available data was used; minimum (Min) and maximum (Max) numbers of subjects in each row are provided. Fifths of BMI were sex-specific. All values in the table are adjusted for age and sex, except for the binary outcome variables. *Denotes geometric mean. *P* values are derived from regression analysis, using all variables except binary outcomes as continuous. P^1 was adjusted for age and sex. P^2 was adjusted for age, sex, and adult BMI. Alongside statistically significant *P* values ($P \leq 0.05$) (+) denotes a positive association and (−) denotes an inverse association. ATPIII, Adult Treatment Panel III; NCEP, National Cholesterol Education Program.

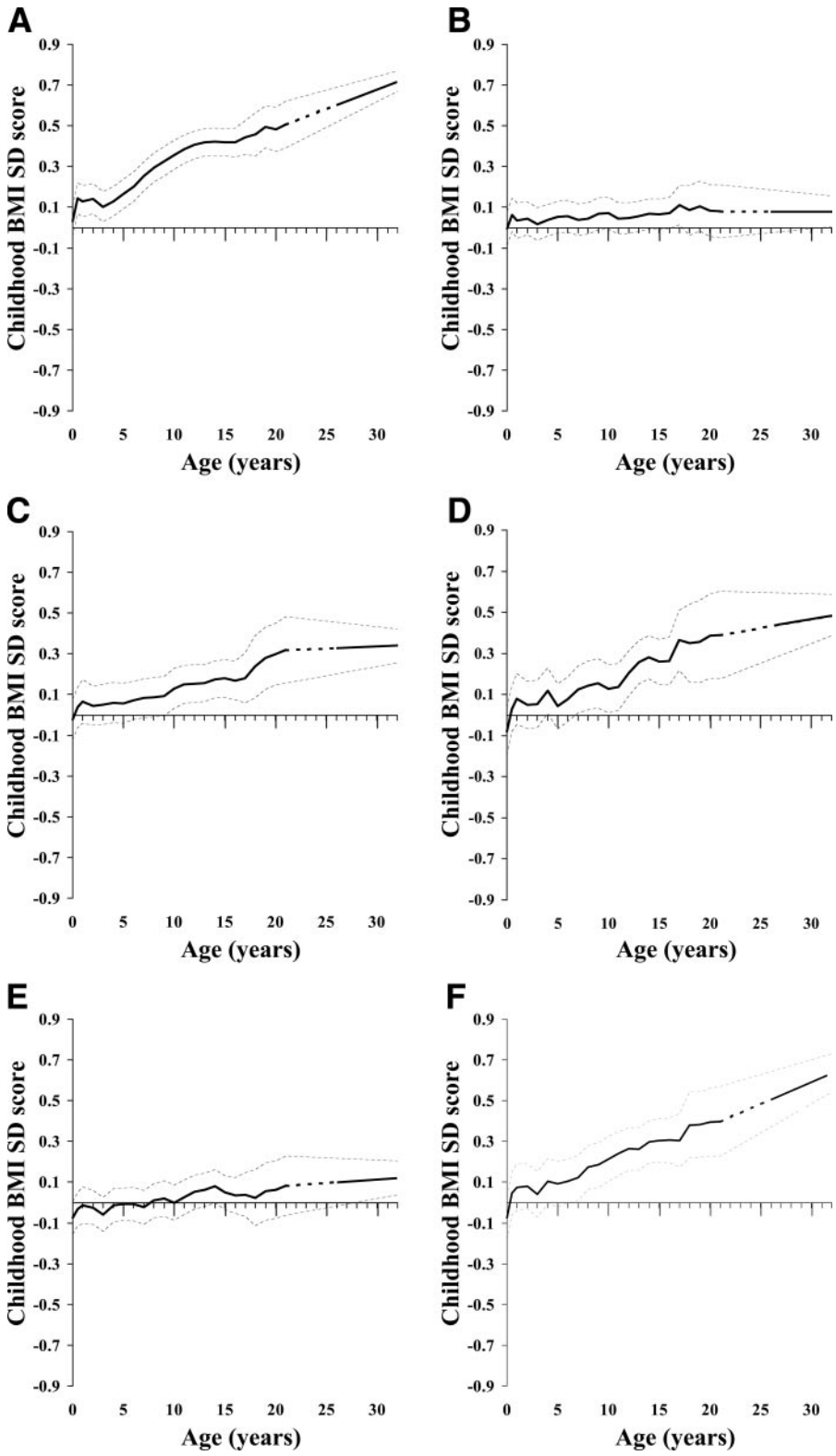

Figure 1—*Mean ± SD scores for BMI measured at earlier ages in subjects with components of the metabolic syndrome* (A–E) *and insulin resistance (HOMA)* (F) *above the upper quartile. High waist circumference* (A)*, low HDL cholesterol concentration* (B)*, high triglyceride concentration* (C)*, high blood pressure* (D)*, high fasting glucose concentration* (E)*, and insulin resistance (HOMA)* (F)*. The rest of the cohort is represented by the zero line in all graphs.*

birth and 21 years and were statistically significant at 11 and 12 years.

The children were short, light, and thin according to an international reference (18), but as adults almost half were overweight or obese (Table 1).

BMI (Table 2) and weight at birth and 2 years were positively related to adult waist circumference and inversely related to 120-min glucose concentrations. Eleven-year BMI was positively related to all outcomes except HDL cholesterol and glucose, and adult BMI was positively related to all outcomes except HDL cholesterol, to which it was inversely related. After adjustment for adult BMI, the associations with earlier BMI reversed, becoming significantly inverse for many outcomes. The associations were little changed after further adjustment for adult lifestyle factors (data not shown).

Subjects with high adult waist circumference, triglycerides, blood pressure, and insulin resistance and those with metabolic syndrome had a higher mean BMI than the cohort mean at all ages from birth (Figs. 1 and 2*A*). The pattern for metabolic syndrome (Fig. 2*A*) matched that for overweight/obesity (Fig. 2*B*) but differed from that for IGT/diabetes (Fig. 2*C*), which was associated with high BMI during childhood and adolescence but a low BMI from 1 to 4 years.

Conditional regression analyses showed (Table 3) that greater BMI gain from birth to 2 years was associated with higher adult waist circumference and systolic blood pressure and lower 120-min glucose concentration. Weight gain in infancy was more strongly related to adult risk factors than BMI gain (Table 4, Fig. 2) and showed additional positive associations with triglycerides, insulin resistance, and metabolic syndrome. Greater BMI/weight gain from 2 to 11 years was associated with higher waist circumference, triglycerides, systolic blood pressure, and insulin resistance and a higher risk of IGT/diabetes and metabolic syndrome. Greater BMI/weight gain between 11 years and adulthood was associated with an increase in all risk factors (lower HDL cholesterol).

The inverse association between infant BMI gain and adult IGT/diabetes was stronger in subjects with lower birth weight (OR 0.74 [95% CI 0.58–0.95] for subjects weighing <2,850 g [median] compared with 1.05 [0.81–1.36] for subjects weighing ≥2,850 g, $P_{\text{interaction}} = 0.01$). There were no significant interactions at other ages or for other outcomes.

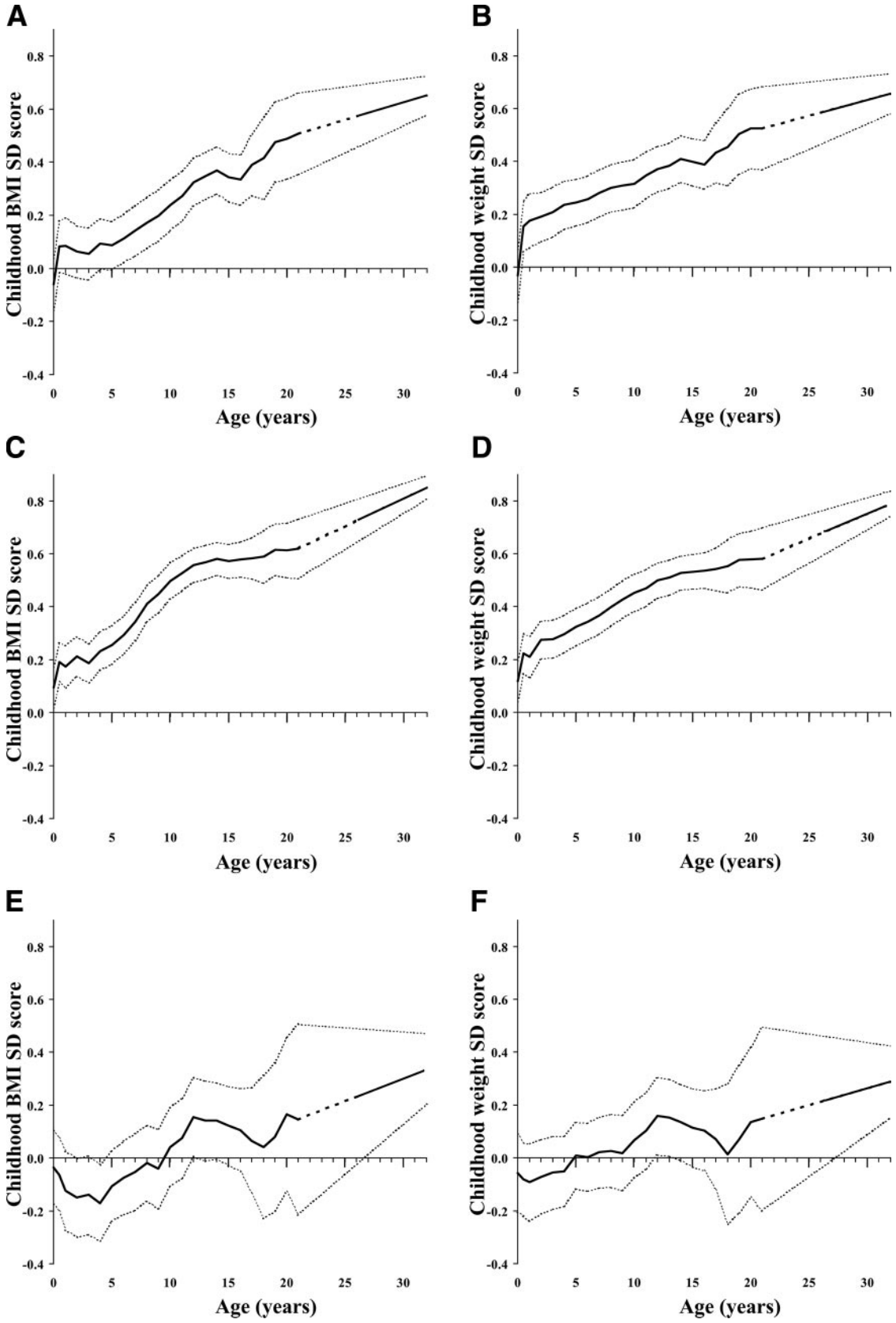

Figure 2—*Mean ± SD scores for BMI and weight measured at earlier ages for subjects who developed* (A *and* B) *metabolic syndrome,* (C *and* D) *overweight or obesity (BMI >25 kg/m*^{2}*), and* (E *and* F) *IGT or diabetes. The rest of the cohort is represented by the zero line in all graphs.*

Table 3—*Multiple linear and logistic regression analyses using conditional BMI SD scores in earlier life to predict adult outcomes*

	BMI change*											
	BMI at birth (SD score)			Birth–2 years (SD)			2–11 years (SD)			11–adult (SD)		
Risk factors	*B*	95% CI	*P*	*B*	95% CI	*P*	*B*	95% CI	*P*	*B*	95% CI	*P*
Waist circumference (SD)	0.07	0.05–0.09	<0.001	0.19	0.17–0.22	<0.001	0.43	0.41–0.46	<0.001	0.74	0.72–0.77	<0.001
HDL cholesterol (SD)	0.00	−0.05–0.05	1.0	−0.01	−0.07–0.05	0.7	−0.01	−0.07–0.05	0.7	−0.14	−0.20–−0.08	<0.001
Triglycerides (SD)	−0.01	−0.06–0.03	0.5	−0.00	−0.06–0.06	1.0	0.06	0.01–0.12	0.03	0.29	0.23–0.35	<0.001
Systolic blood pressure (SD)	−0.03	−0.07–0.02	0.3	0.06	0.01–0.12	0.02	0.11	0.06–0.17	<0.001	0.30	0.24–0.35	<0.001
Fasting glucose (SD)	−0.03	−0.08–0.02	0.2	−0.02	−0.08–0.03	0.4	0.03	−0.03–0.09	0.3	0.08	0.02–0.14	0.006
120-min glucose (SD)	−0.05	−0.09–0.00	0.05	−0.08	−0.14–−0.02	0.01	0.04	−0.02–0.09	0.2	0.19	0.13–0.25	<0.001
Insulin resistance (HOMA) (SD)	−0.01	−0.05–0.04	0.8	0.04	−0.02–0.09	0.2	0.15	0.09–0.20	<0.001	0.45	0.40–0.51	<0.001
Cholesterol (SD)	−0.01	−0.06–0.04	0.7	−0.03	−0.09–0.02	0.2	0.01	−0.04–0.07	0.6	0.19	0.13–0.25	<0.001
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Metabolic syndrome	0.91	0.81–1.02	0.1	1.09	0.94–1.26	0.3	1.48	1.28–1.71	<0.001	2.93	2.44–3.51	<0.001
IGT/diabetes	0.95	0.82–1.09	0.5	0.86	0.72–1.03	0.1	1.25	1.05–1.47	0.01	1.40	1.18–1.67	<0.001

*BMI changes are calculated as conditional measures; the standardized residuals of a BMI SD score value regressed on earlier SD score values. The continuous outcome variables were normalized so that *B* (regression coefficient) values for the associations with SD scores at birth and changes in early life indicate the SD change in the outcome per SD change in the predictor. All analyses are adjusted for age, sex, and lifestyle factors: alcohol consumption (four levels from none to heavy), physical activity (continuous measure estimated from reported activity levels, transformed, and expressed as a sex-specific SD score), tobacco use (categorized into never, ex-user, and current user), socioeconomic status in childhood based on father's occupation (ranging from 1 [low class] to 6 [high class]), socioeconomic status in adult life derived from education level, household possessions and occupation (ranging from 1 [low class] to 17 [high class]), and family history of any of high blood pressure, angina, myocardial infarction, stroke, or diabetes in a first-degree relative.

Mean ± SD age at adiposity rebound (lowest recorded childhood BMI) was 6.6 ± 1.7 years. Earlier rebound was associated with increased adult metabolic syndrome ($P = 0.07$) and IGT/diabetes ($P = 0.04$) and higher waist circumference ($P < 0.001$), systolic blood pressure ($P = 0.052$), triglyceride concentration ($P = 0.054$), and 120-min glucose concentration ($P = 0.01$). These associations became nonsignificant after adjustment for adult BMI.

CONCLUSIONS — The Delhi cohort represents an affluent, well-educated section of Indian society that has undergone considerable "transition." As children they were thin, but as young adults almost half were overweight and 29% had metabolic syndrome. Higher levels of all risk factors except IGT/diabetes were associated with BMI or weight above the average for the cohort as a whole (Figs. 1 and 2) and more rapid BMI or weight gain than the cohort average (Tables 3 and 4) from birth onward.

Strengths of the study were that it was population-based and children were measured by trained personnel, with exceptionally frequent follow-up throughout childhood. As with other birth cohorts, there was considerable loss to follow-up and participants are likely to be unrepresentative of the original sample. However, differences in their childhood sizes were small, and in a within-sample analysis, loss to follow-up would introduce bias only if associations between early BMI/weight and later disease differed between those studied and not studied, which seems unlikely given that inclusion was based only on subjects' availability.

Birth

Studies in high-income countries have shown increased metabolic syndrome in adults of lower birth weight (19). In Delhi, after adjustment for adult BMI, there were inverse associations with BMI at birth for metabolic syndrome and its components (Table 2), but these resulted from positive associations with childhood BMI gain, not from lower BMI at birth (Table 3). The absence of associations between metabolic syndrome and small size at birth in this population may be due to their young age, low mean birth weight, or different newborn body composition (20).

Infancy

Consistent with studies of adults in high-income countries (8,9), greater infant BMI/weight gain was associated with a lower risk of diabetes, especially in lower-birth-weight infants. However, it was associated with an increased risk of metabolic syndrome and its components, which is consistent with recent studies showing higher BMI, blood pressure, and insulin concentrations in children who had greater infant weight gain (10,11,21). Understanding these apparently paradoxical findings is important. Effects may differ among populations according to body composition at birth and fat and lean mass accrual during infancy and may vary for different outcomes according to critical periods of development for different tissues. In developing countries, greater infant weight gain is beneficial for survival, growth, and neurocognitive development (22). However, it may become disadvantageous as obesity-related adult chronic diseases emerge (23). The balance of benefits and risks will become clearer as the cohort ages enough to assess cardiovascular disease and mortality. In an intervention study with relevant adult outcomes, protein-energy supplementation in infancy produced no increase in adult cardiovascular risk factors (24).

Childhood and adolescence

A clear message from our study, consistent with studies in high-income countries, is that rapid BMI gain in childhood and adolescence and earlier adiposity rebound are associated with adult metabolic syndrome and IGT/diabetes. This result probably reflects the known correlation between childhood and adult BMI. Thus, even in underweight children in developing countries, increasing BMI SD scores ("becoming obese relative to oneself") is a risk factor for later disease. Reinforced by evidence that risk factors in Indian children are already high (25), our study supports efforts to prevent childhood obesity. It also suggests that interventions to control adiposity should be targeted not only to obese children, but also to "normal" weight children with rising BMI SD scores.

Acknowledgments— The original study was funded by the Indian Council of Medical Research and National Institutes of Health (U.S.); the current study was funded by the British Heart Foundation and the Medical Research Council (U.K.).

Table 4—*Multiple linear and logistic regression analyses using conditional weight SD scores in earlier life to predict adult outcomes*

	Weight at birth (SD score)			Weight change*							
				Birth–2 years (SD)			2–11 years (SD)			11–adult (SD)	
Risk factors	*B*	95% CI	*P*	*B*	95% CI	*P*	*B*	95% CI	*P*	*B*	95% CI	*P*
Waist circumference (SD)	0.15	0.13–0.17	<0.001	0.30	0.27–0.32	<0.001	0.41	0.38–0.43	<0.001	0.74	0.72–0.76	<0.001
HDL cholesterol (SD)	−0.03	−0.09–0.02	0.3	−0.03	−0.09–0.03	0.3	−0.03	−0.09–0.03	0.3	−0.14	−0.20–−0.08	<0.001
Triglycerides (SD)	−0.03	−0.09–0.02	0.3	0.09	0.03–0.15	0.004	0.07	0.01–0.12	0.02	0.28	0.22–0.34	<0.001
Systolic blood pressure (SD)	−0.02	−0.07–0.04	0.5	0.11	0.05–0.17	<0.001	0.11	0.06–0.17	<0.001	0.30	0.24–0.35	<0.001
Fasting glucose (SD)	−0.02	−0.08–0.04	0.5	0.04	−0.02–0.10	0.2	0.04	−0.01–0.10	0.1	0.07	0.01–0.13	0.01
120-min glucose (SD)	−0.04	−0.10–0.02	0.2	−0.04	−0.10–0.02	0.2	0.06	−0.00–0.12	0.06	0.17	0.11–0.23	<0.001
Insulin resistance (HOMA) (SD)	0.00	−0.05–0.06	0.9	0.08	0.02–0.13	0.005	0.15	0.10–0.20	<0.001	0.44	0.39–0.49	<0.001
Cholesterol (SD)	−0.04	−0.10–0.02	0.2	0.00	−0.06–0.06	1.0	0.01	−0.05–0.07	0.7	0.16	0.10–0.22	<0.001
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Metabolic syndrome	0.93	0.80–1.08	0.3	1.45	1.23–1.70	<0.001	1.53	1.32–1.77	<0.001	2.83	2.36–3.38	<0.001
IGT/diabetes	0.93	0.78–1.10	0.4	0.94	0.79–1.13	0.5	1.26	1.06–1.49	0.008	1.31	1.11–1.56	0.002

*Weight changes are calculated as conditional measures; the standardized residuals of a weight SD score value regressed on earlier SD score values. The continuous outcome variables were normalized so that *B* (regression coefficient) values for the associations with SD scores at birth and changes in early life indicate the SD change in the outcome per SD change in the predictor. All analyses are adjusted for age, sex, and lifestyle factors: alcohol consumption (four levels from none to heavy), physical activity (continuous measure estimated from reported activity levels, transformed, and expressed as a sex-specific SD score), tobacco use (categorized into never, ex-user, and current user), socioeconomic status in childhood based on father's occupation (ranging from 1 [low class] to 6 [high class]), socioeconomic status in adult life derived from education level, household possessions and occupation (ranging from 1 [low class] to 17 [high class]), and family history of any of high blood pressure, angina, myocardial infarction, stroke, or diabetes in a first-degree relative.

We thank the participants and field and laboratory staff. We acknowledge Dr. Shanti Ghosh and I.M. Moriyama who initiated the cohort study with Dr. Bhargava, Vinod Kapani for technical input, and Rajeshwari Verma and Bhaskar Singh for maintaining liaison with the cohort.

References

1. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, Rao PV, Yajnik CS, Prasanna Kumar KM, Nair JD: High prevalence of diabetes and impaired glucose tolerance in India; National Urban Diabetes Survey. *Diabetologia* 44:1094–1101, 2001
2. Prabhakaran D, Shah P, Chaturvedi V, Ramakrishnan L, Manhapra A, Reddy KS: Cardiovascular risk factor prevalence among men in a large industry of northern India. *Natl Med J India* 18:59–65, 2005
3. 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
4. Ghaffar A, Reddy KS, Singhi M: Burden of non-communicable diseases in South Asia. *Br Med J* 328:807–810, 2004
5. Newsome CA, Shiell AW, Fall CHD, Phillips DIW, Shier R, Law CM: Is birthweight related to later glucose and insulin metabolism? A systematic review. *Diabet Med* 23:339–348, 2003
6. Huxley R, Owen CG, Whincup PH, Cook DG, Rich-Edwards J, Smith GD, Collins R: Is birth weight a risk factor for ischemic heart disease in later life? *Am J Clin Nutr* 85:1244–1250, 2007
7. Barker DJP, Osmond C, Forsen TJ, Kajantie E, Eriksson JG: Trajectories of growth among children who have coronary events as adults. *N Engl J Med* 353:1802–1809, 2005
8. Eriksson JG, Forsen T, Tuomilehto J, Osmond C, Barker DJ: Early adiposity rebound in childhood and risk of type 2 diabetes in adult life. *Diabetologia* 46: 190–194, 2003
9. Hales CN, Barker DJP, Clark PMS, Cox LJ, Fall CHD, Osmond C: Fetal and infant growth and impaired glucose tolerance at age 64 years. *Br Med J* 303:1019–1022, 1991
10. Singhal A, Lucas A: Early origins of cardiovascular disease: is there a unifying hypothesis? *Lancet* 363:1642–1645, 2004
11. Stettler N, Zemel BS, Kumanyika S, Stallings VA: Infant weight gain and childhood overweight status in a multicenter cohort study. *Pediatrics* 109:194–199, 2002
12. Bhargava SK, Sachdev HPS, Fall CHD, Osmond C, Lakshmy R, Barker DJP, Biswas SKD, Ramji S, Prabhakaran D, Reddy KS: Relation of serial changes in childhood body mass index to impaired glucose tolerance in young adulthood. *N Engl J Med* 350:865–875, 2004
13. Sachdev HPS, Fall CHD, Osmond C, Lakshmy R, Dey Biswas SK, Leary SD, Reddy KS, Barker DJP, Bhargava SK: Anthropometric indicators of body composition in young adults: relation to size at birth and serial measurements of body mass index in childhood; the New Delhi birth cohort. *Am J Clin Nutr* 82:456–466, 2005
14. World Health Organization: *Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications: Report of a WHO Consultation.* Geneva, World Health Organization, WHO/NCD/NCS/99.2, 1999
15. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults: Third report of the National Cholesterol Education Program (NCEP) (Adult Treatment Panel III). *JAMA* 285: 2486–2497, 2001
16. Grundy S: Metabolic syndrome scientific statement by the American Heart Association and the National Heart, Lung, and Blood Institute. *Arterioscler Thromb Vasc Biol* 25:2243–2244, 2005
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and β-cell function from fasting glucose and insulin concentrations in man. *Diabetologia* 28:412–419, 1985
18. National Center for Health Statistics: 2000 growth charts: United States [article online]. Available at: http://www.cdc.gov/growthcharts/. Accessed 1 July 2007
19. Ramadhani MK, Grobbee DE, Bots ML, Castro Cabezas M, Vos LE, Oren A, Uiterwaal CS: Lower birthweight predicts metabolic syndrome in young adults: the Atherosclerosis Risk in Young Adults (ARYA) study. *Atherosclerosis* 184:21–27, 2006
20. Yajnik CS, Fall CHD, Coyaji KJ, Hirve SS, Rao S, Barker DJ, Joglekar C, Kellingray S: Neonatal anthropometry: the thin-fat Indian baby, the Pune Maternal Nutrition Study. *Int J Obes* 26:173–180, 2003
21. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C: Being big or growing fast; a systematic review of size and growth in infancy and later obesity. *BMJ* 331:929–931, 2005
22. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HPS: Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 371:340–357, 2008
23. Stettler N: Growing up optimally in societies undergoing the nutritional transition, public health and research challenges. *Int J Epidemiol* 36:558–559, 2007
24. Stein AD, Wang M, Ramirez-Zia M, Flores R, Grajeda R, Melgar P, Ramakrishnan U, Martorell R: Exposure to a nutrition supplementation intervention in early childhood and risk factors for cardiovascular disease in adulthood: evidence from Guatemala. *Am J Epidemiol* 164:1160–1170, 2006
25. Misra A, Vikram NK, Arya S, Pandey RM, Dhingra V, Chatterjee A, Dwivedi M, Sharma R, Luthra K, Guleria R, Talwar KK: High prevalence of insulin resistance in postpubertal Asian Indian children is associated with adverse truncal body fat patterning, abdominal obesity and excess body fat. *Int J Obes Relat Metab Disord* 28: 1217–1226, 2004