Anthropometry, Glucose Tolerance, and Insulin Concentrations in Indian Children

Relationships to maternal glucose and insulin concentrations during pregnancy

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OBJECTIVE — The purpose of this study was to test the hypothesis that the environment experienced by fetuses of mothers with gestational diabetes mellitus (GDM) and mothers with higher glucose concentrations that are in the normal range causes increased adiposity and altered glucose/insulin metabolism in childhood.

RESEARCH DESIGN AND METHODS — Children (n = 630) whose mothers were tested for glucose tolerance during pregnancy had detailed anthropometry performed at birth and annually thereafter. At 5 years, plasma glucose and insulin concentrations were measured in the children (2-h oral glucose tolerance test) and their fathers (fasting samples only).

RESULTS — Newborns of diabetic mothers (n = 41) were larger in all body measurements than control newborns (babies with nondiabetic parents). At 1 year, these differences had diminished and were not statistically significant. At 5 years, female offspring of diabetic mothers had larger subscapular and triceps skinfold thicknesses (P = 0.01) and higher 30- and 120-min insulin concentrations ($P < 0.05$) than control children. Offspring of diabetic fathers (n = 41) were lighter at birth than control children ($P < 0.001$); they showed no differences in anthropometry at 5 years. In control children, skinfold thickness and 30-min insulin concentrations were positively related to maternal insulin area under the curve, and skinfold thicknesses were related to paternal fasting insulin concentrations independently of the parents' skinfold thickness and socioeconomic status.

CONCLUSIONS — Maternal GDM is associated with adiposity and higher glucose and insulin concentrations in female offspring at 5 years. The absence of similar associations in offspring of diabetic fathers suggests a programming effect in the diabetic intrauterine environment. More research is needed to determine whether higher maternal glucose concentrations in the nondiabetic range have similar effects.

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The prevalence of type 2 diabetes is escalating in developing countries undergoing the "epidemiologic transition." India is predicted to have 79 million people with type 2 diabetes by the year 2030 (32 million in 2000) (1). Studies in western populations, predominantly among the Pima Indian communities of North America, have shown that individuals whose mothers were diabetic when they were in utero have an increased risk of early obesity and impaired glucose tolerance (IGT) and type 2 diabetes in adult life (2–4). The risk is increased compared with offspring of diabetic fathers and siblings born before the onset of maternal diabetes (3,5), suggesting that it results from the fetal environment in gestational diabetes mellitus (GDM) rather than from genes. Even in nondiabetic pregnancies, variations within the normal range of maternal fasting glucose concentrations are associated with altered neonatal adiposity (6). It is not known whether this is associated with changes in later body size and glucose/insulin concentrations in the offspring.

There are few data from India on the prevalence of GDM and none on the follow-up of the offspring of diabetic mothers (ODM). We measured glucose tolerance in a cohort of pregnant South Indian women (7). The prevalence of GDM was 6.2% (n = 49), considerably higher than that reported in a previous Indian study (8). The ODM were bigger, especially in body fat (skinfold thickness), skeletal size (length), and muscle mass (mid–upper arm circumference), compared with neonates of nondiabetic mothers (7). Even the offspring of nondiabetic mothers (ONDM) with higher fasting glucose concentrations had higher birth weight. The children have been followed-up to the age of 5 years to observe the long-term associations of various degrees of maternal glucose and insulin concentrations on childhood anthropometry and glucose/insulin metabolism. At 5 years, fasting plasma glucose and insulin concentrations were also measured in the children's fathers, enabling us to comment on whether associations were due to the maternal environment or to genes.

RESEARCH DESIGN AND METHODS

— During 1997–1998, women (n = 830) booking consecutively into the antenatal clinic of the Holdsworth Memorial Hospital (HMH) in Mysore, India, had a 100-g, 3-h oral glucose tolerance test (OGTT) at 30 ± 2 weeks' gestation. Their plasma glucose and insulin concentrations were measured as pre-

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Abbreviations: GAUC, glucose area under the curve; GDM, gestational diabetes mellitus; HMH, Holdsworth Memorial Hospital; HOMA, homeostasis model assessment equation; IAUC, insulin area under the curve; IGT, impaired glucose tolerance; ODM, offspring of diabetic mothers; OGTT, oral glucose tolerance test; ONDM, offspring of nondiabetic mothers.

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

viously described (7). Two pregestational diabetic women were excluded. GDM was diagnosed using the criteria of Carpenter and Coustan (9): two or more plasma glucose concentrations ≥5.3 (fasting), ≥10.0 (60 min), ≥8.7 (120 min), and ≥7.8 mmol/l (180 min). This was the established test in clinical use at HMH. Each woman's own consultant obstetrician managed her further clinical care. For the 674 women who delivered at HMH, 639 had complete OGTT data and 41 were diabetic; 12 of these were treated with insulin.

Of the 639 babies, 630 were born alive without major congenital anomalies. Mean ± SD gestation was 39.0 ± 1.75 weeks, and 49 babies (7.7%) were delivered preterm (<37 weeks). Seventy babies (11.0%) were small for gestational age (gestation-adjusted birth weight <2,500 g). Babies were measured by one of four trained observers within 72 h of birth using standardized techniques. Weight was measured using a digital weighing scale (Seca, Hamburg, Germany), and crown-heel length was measured using a Harpenden neonatal stadiometer (CMS Instruments, London, U.K.). Head, chest (xiphisternum), and mid–upper arm circumferences were measured with a blank tape, marked, and measured against a fixed ruler. Skinfold thicknesses (triceps and subscapular) were measured using Harpenden calipers (CMS Instruments).

Follow-up at 1-year was on the child's first birthday (±4 weeks) for children born at term and on the anniversary of the expected date of delivery (±4 weeks) for preterm children. Subsequent follow-ups were on the child's birthday (±4 weeks) for all. Measurement techniques were similar to those at birth. At 5 years anthropometry was performed on the child and both parents. Circumferences were measured using graduated anthropometric tapes. Height was measured using a wall-mounted stadiometer (Microtoise, CMS Instruments). Measures were standardized by regular intra- and interobserver variation studies. Seven children with medical conditions that could affect growth (mental retardation [$n = 4$], congenital heart disease [$n = 1$], hydrocephalus [$n = 1$], and hereditary spherocytosis [$n = 1$]) were excluded from the analysis after birth.

At 5 years, a 2-h OGTT (World Health Organization protocol) was administered to all children after an overnight fast (10). An intravenous cannula was inserted after the skin was anesthetized with EMLA cream. Blood samples were collected for measurement of HbA_{1c} (A1C) and plasma glucose and insulin concentrations (fasting and 30 and 120 min after a 1.75 g/kg body wt load of anhydrous glucose in 150 ml water). Fasting blood samples were taken for glucose/insulin concentrations from willing fathers ($n = 482$). Glucose and insulin assays were carried out at the Diabetes Research Centre, KEM Hospital, Pune, India, whose laboratory is a member of the U.K. National External Quality Assessment Service program for insulin assays. Glucose was analyzed by the glucose oxidase–peroxidase method using an Auto-Analyzer (Abbott Laboratories, Chicago, IL), and insulin was analyzed by a time-resolved, fluoroimmunoassay (DELFIA) method. Intra- and interassay coefficients of variations were <5 and <10%, respectively. Samples were stored at −80°C (maximum 4 months) until transfer to Pune. A1C was measured at the MV Diabetes Specialities Centre, Chennai, India, by the Variant A1C program (BioRad Laboratories, Hercules, CA).

The hospital ethical committee approved the study. Informed verbal consent was obtained from the parents and children.

Statistical methods

Insulin resistance was estimated using the homeostasis model assessment equation (HOMA) (11). The insulin increment (a measure of insulin secretion) was derived using the formula: (30-min insulin − fasting insulin)/30-min glucose (12). Maternal plasma glucose (GAUCs) and insulin (IAUCs) areas under the curve were calculated using the trapezoid rule (13). IGT was defined as a fasting glucose concentration <7.0 and 120-min glucose ≥7.8 but <11.1 mmol/l. Fathers were defined as diabetic if they were already known to have diabetes or if their fasting glucose concentration was ≥7.0 mmol/l (10). The children born to non-GDM mothers and nondiabetic fathers were designated control subjects. Skinfold measurements, insulin concentrations, HOMA, and insulin increments were log transformed to normality. Birth measurements were adjusted to 40 weeks of gestation, with sexes separate, using linear regression. Sex-specific within-cohort SD scores for all anthropometric measurements were derived as [(observed value − cohort mean)/cohort SD]. Differences between ODM and control offspring were assessed using *t* tests. Trends in outcome variables with the parents' glucose and insulin concentrations were assessed in the control offspring using multiple linear regression.

RESULTS — Of the 630 children, 25 (4.0%) were known to have died between birth and 5 years (1 ODM). At 1 year, 542 of the surviving children (90%, 36 ODM) were studied, and at 5 years 555 children (92%, 36 ODM) were studied, of whom 542 completed the OGTT (98%). Of those followed-up at 1 year, 85% of babies were breast fed for a minimum of 3 months. The infant feeding pattern was similar in ODM and control babies. Children lost to follow-up were lighter at birth than those who attended the clinic (2,828 vs. 2,999 g, $P = 0.1$). There were no significant differences in maternal weight, GDM percentage, or the babies' sex ratio.

ODM

At birth, ODM of both sexes were significantly larger than ONDM and control babies in all anthropometric measurements (Table 1, Fig. 1). The differences diminished during the first year of life (Table 1, Fig. 1); female, but not male, ODM remained larger than control children in most body measurements, but the differences were not statistically significant.

At 2 years, ODM had larger mid–upper arm circumferences ($P = 0.03$) and triceps skinfold thicknesses ($P = 0.04$) than the control children. At 5 years they had larger BMI, mid–upper arm circumference, and triceps and subscapular skinfold thicknesses (Table 1). These differences were statistically significant only in girls (Fig. 1) (interaction term, sex × maternal GDM status significant for subscapular skinfold thickness, $P = 0.04$). The differences persisted for skinfold thickness and mid–upper arm circumference in female ODM even after adjusting for maternal BMI or skinfold measurements ($P < 0.05$).

Overall, girls had higher insulin concentrations than boys (Table 2). Thirty- and 120-min insulin concentrations and 30-min insulin increment were higher in female ODM than in control offspring. Differences remained significant for 120-min insulin concentrations after adjusting for maternal BMI ($P = 0.04$) and borderline significant after adjusting for maternal skinfold measurements ($P = 0.08$). There were no differences in boys. Glucose concentrations and A1C were similar in both groups. Twenty-two children (12 boys and 10 girls, 4.1%) had IGT. Of

Table 1—*Characteristics of ODM, offspring of diabetic fathers, and control children*

	ODM	*P**	Control children	*P*†	Offspring of diabetic fathers
n	41		548		41
Mothers					
Age (years)	28.8 ± 4.6	<0.001	23.5 ± 4.0	0.03	24.9 ± 4.1
Height (cm)	153.6 ± 6.7	0.2	154.8 ± 5.4	0.4	154.0 ± 6.4
BMI (kg/m^2)	26.9 ± 4.1	<0.001	23.3 ± 3.4	0.4	23.9 ± 3.7
Offspring					
Birth					
Gestational age (weeks)	39.1 ± 1.2	0.8	39.0 ± 1.8	0.9	39.1 ± 1.2
Preterm births	1 (2.9)	0.2	46 (8.4)	0.4	2 (4.9)
Weight (g)	3344 ± 421	<0.001	2973 ± 408	0.05	2869 ± 305
SGA	0 (0)	0.02	64 (11.7)	0.6	6 (14.6)
Crown-heel length (cm)	50.5 ± 2.3	<0.001	49.2 ± 2.1	0.4	48.9 ± 1.9
Ponderal index (kg/m^3)	26.0 ± 2.5	0.01	24.9 ± 2.7	0.3	24.5 ± 1.8
MUAC (cm)	11.3 ± 0.8	<0.001	10.5 ± 0.9	0.03	10.2 ± 0.7
Triceps skinfold (mm)	5.1 (4.6–6.1)	<0.001	4.2 (3.7–4.9)	0.06	4.0 (3.6–4.4)
Subscapular skinfold (mm)	5.3 (4.7–6.2)	<0.001	4.4 (4.0–5.0)	0.053	4.2 (3.8–4.6)
1 year					
Weight (kg)	8.5 ± 1.2	0.8	8.4 ± 1.1	0.5	8.3 ± 1.0
Crown-heel length (cm)	73.5 ± 2.5	0.6	73.3 ± 2.9	0.3	72.8 ± 2.6
BMI (kg/m^2)	15.6 ± 1.7	0.9	15.7 ± 1.4	0.9	15.6 ± 1.5
MUAC (cm)	14.3 ± 1.1	0.2	14.1 ± 1.1	0.8	14.1 ± 1.3
Triceps skinfold (mm)	7.8 (6.9–9.5)	0.7	7.7 (6.8–8.9)	0.995	7.8 (6.6–8.8)
Subscapular skinfold (mm)	6.5 (5.3–7.9)	0.8	6.4 (5.5–7.3)	0.7	6.4 (5.6–7.1)
5 years					
Weight (kg)	15.8 ± 2.1	0.09	15.2 ± 2.0	0.96	15.2 ± 1.9
Crown-heel length (cm)	106.0 ± 4.5	0.6	105.6 ± 4.4	0.6	106.0 ± 4.3
BMI (kg/m^2)	14.0 ± 1.2	0.03	13.6 ± 1.1	0.7	13.5 ± 1.0
MUAC (cm)	15.9 ± 1.3	0.006	15.3 ± 1.2	0.96	15.3 ± 1.2
Triceps skinfold (mm)	8.5 (6.7–10.3)	0.01	7.7 (6.5–8.9)	0.2	8.0 (7.1–8.9)
Subscapular skinfold (mm)	6.6 (5.2–8.3)	0.01	5.9 (4.9–6.9)	0.4	6.1 (5.1–7.1)

Data are means ± SD, *n* (%), or geometric mean (interquartile range). **P* for the difference between ODM and control children; †*P* for the difference between offspring of diabetic fathers and control children. MUAC, mid–upper arm circumference; SGA, small for gestational age.

these, 4 (all girls) were born to mothers with GDM (11.4 vs. 3.2% in the control children, odds ratio 4.0 [95% CI 1.2–13.2], $P = 0.02$ adjusting for sex and BMI).

Offspring of diabetic fathers

At 5-year follow-up, 41 fathers (8.5%) had diabetes (17 previously diagnosed and 24 diagnosed from fasting blood samples). Their offspring had lower birth weights and smaller mid–upper arm circumferences than control children (Table 1). There were no differences in anthropometric measurements between offspring of diabetic fathers and control children between 1 and 5 years. They had significantly lower 120-min insulin and glucose concentrations (Table 2). Girls had a higher prevalence of IGT. There were no differences between offspring of diabetic fathers and control children in other glucose and insulin variables or A1C.

Control children

In the control children at 5 years, maternal IAUC was positively related to offspring anthropometry, 30-min insulin concentrations, and insulin increment (Table 3). The strength of the associations with offspring anthropometry was reduced after adjusting for maternal skinfold measurements and socioeconomic status (Table 3). U-shaped associations were observed between maternal GAUC and offspring skinfold measurements. No significant associations were seen with IGT or A1C concentrations. Findings were similar in both sexes. Positive associations were also observed among father's fasting insulin and offspring anthropometry, insulin concentrations, and insulin increment at 5 years (Table 3). These associations were not significant after adjustment for father's skinfold measurements and socioeconomic status, except for a U-shaped association between paternal fasting insulin and subscapular skinfolds.

CONCLUSIONS — This study showed that the increased body size observed at birth in offspring born to Indian mothers with GDM diminished in the 1st postnatal year, reappeared in female children by 2 years, and persisted until at least 5 years. Female ODM had an increased risk of IGT at 5 years and increased 30- and 120-min insulin concentrations. These differences were independent of maternal adiposity. In contrast, offspring of diabetic fathers were lighter at birth than control children, showed no difference in body size from control children at 5 years, and had lower insulin concentrations.

Macrosomia in newborns of diabetic mothers is thought to be caused by chronic fetal hyperinsulinemia (14,15). Freinkel (16) postulated that GDM imparts long-term metabolic effects in the offspring ("fuel-mediated teratogenesis").

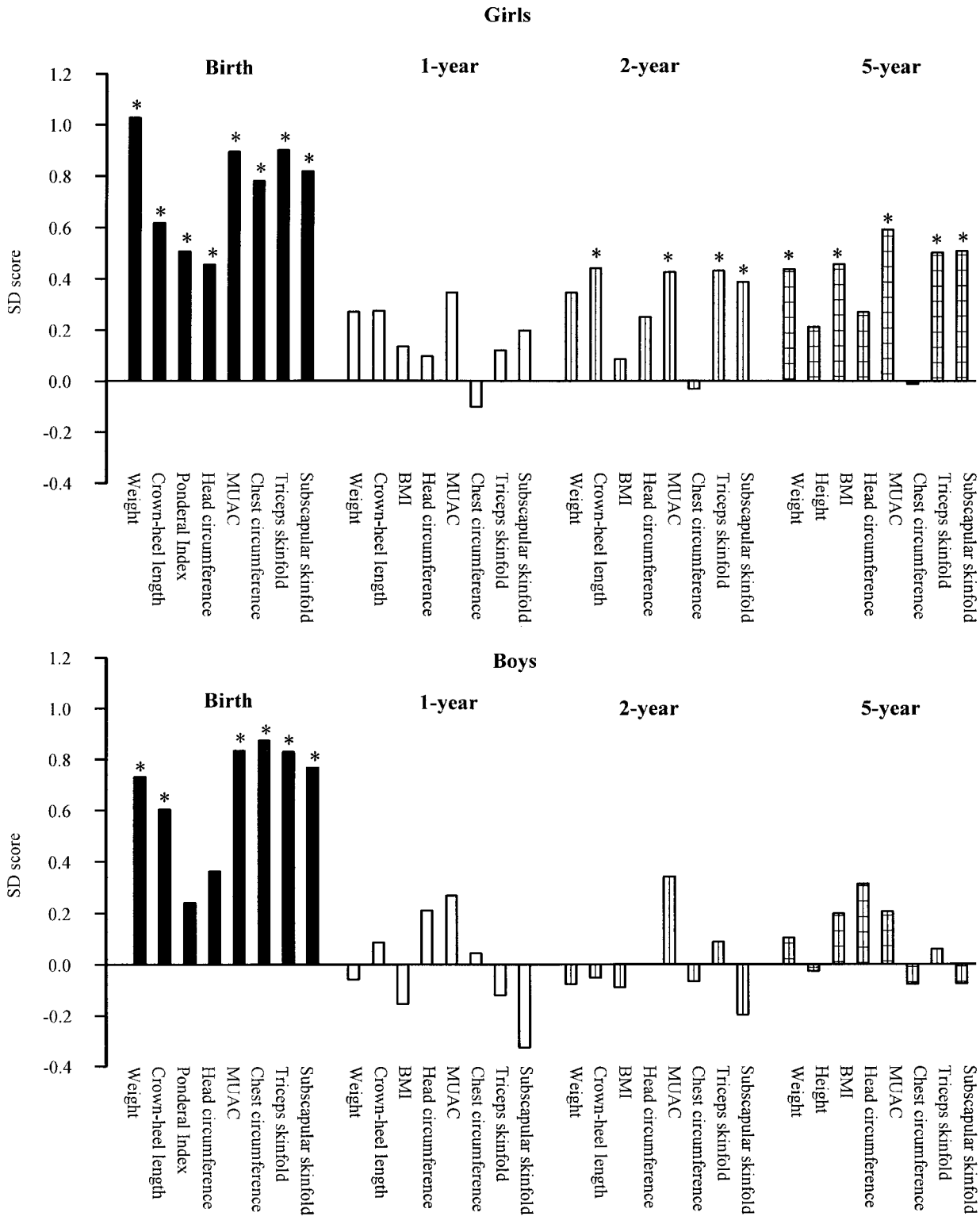

Figure 1—*Mean SD scores for anthropometry at birth, 1, 2, and 5 years for ODM relative to the whole cohort (represented by zero). *Difference between measurements for ODM and ONDM statistically significant ($P < 0.05$). MUAC, mid–upper arm circumference.*

Studies have since shown that ODM exhibit early obesity (relative weight) and increased incidence of adult IGT and type 2 diabetes (2,3,17). Changes have also been observed in childhood. Silverman et al. (4) observed that macrosomia resolved during infancy, as in the Mysore children, and recurred gradually thereafter. The children became heavier and taller than average from 5–7 years onward and had higher insulin concentrations and a higher incidence of IGT (4). A recent study showed increased insulin secretion and reduced insulin sensitivity in ODM (18).

Table 2—*Glucose and insulin concentrations according to maternal GDM and paternal diabetes status*

	ODM			*P**		Control children			*P*†			Offspring of diabetic fathers		
	Total	Girls	Boys	Total	Girls	Boys	Total	Girls	Boys	Total	Girls	Boys	Total	Girls	Boys
n	35	22	13				474	243	231				41	21	20
Plasma glucose (mmol/l)															
Fasting	4.8 ± 0.5	4.7 ± 0.6	4.9 ± 0.4	0.8	0.5	0.5	4.8 ± 0.5	4.8 ± 0.5	4.8 ± 0.5	0.9	0.7	0.8	4.8 ± 0.5	4.8 ± 0.4	4.8 ± 0.5
30 min	7.5 ± 1.4	7.7 ± 1.6	7.3 ± 0.9	0.3	0.3	0.8	7.3 ± 1.4	7.3 ± 1.4	7.2 ± 1.5	0.5	0.5	0.2	7.1 ± 1.3	7.5 ± 1.3	6.7 ± 1.6
120 min	6.1 ± 1.1	6.2 ± 1.3	5.9 ± 0.7	0.3	0.2	0.8	5.9 ± 1.0	5.8 ± 0.9	6.0 ± 1.0	0.4	0.1	0.007	5.7 ± 1.2	6.1 ± 1.1	5.3 ± 1.1
A1C (%)	5.6 ± 0.9	5.7 ± 1.0	5.4 ± 0.4	0.6	0.5	0.5	5.5 ± 0.5	5.5 ± 0.5	5.6 ± 0.5	0.4	0.5	0.6	5.6 ± 0.4	5.6 ± 0.3	5.6 ± 0.5
IGT	4 (11.4)	4 (18.3)	—	0.01	<0.001	0.4	15 (3.2)	4 (1.7)	11 (4.8)	0.1	0.01	0.97	3 (7.7)	2 (10.5)	1 (5)
Plasma insulin (pmol/l)															
Fasting	23 (14–35)	25 (17–36)	20 (11–32)	0.1	0.4	0.3	19 (12–29)	22 (14–32)	17 (11–27)	0.2	0.7	0.1	22 (14–34)	23 (18–32)	21 (12–36)
30 min	172 (123–275)	210 (141–291)	123 (79–241)	0.1	0.05	0.97	136 (87–225)	152 (103–242)	122 (73–213)	0.96	0.5	0.6	136 (104–252)	136 (103–242)	135 (88–254)
120 min	105 (73–150)	122 (74–171)	82 (52–142)	0.03	0.04	0.7	82 (57–127)	90 (62–131)	76 (52–121)	0.04	0.5	0.008	63 (29–125)	81 (62–131)	49 (25–79)
Other insulin variables															
HOMA	0.8 (0.5–1.3)	0.9 (0.6–1.3)	0.7 (0.3–1.0)	0.2	0.5	0.3	0.7 (0.4–1.1)	0.8 (0.5–1.2)	0.6 (0.4–1.0)	0.2	0.7	0.2	0.8 (0.5–1.3)	0.8 (0.5–1.2)	0.8 (0.4–1.3)
Insulin increment (pmol/mmol)	36 (20–47)	44 (27–54)	26 (12–38)	0.1	0.04	0.8	29 (14–40)	32 (16–44)	27 (12–38)	0.7	0.8	0.4	31 (16–46)	30 (16–44)	31 (15–48)

Data are means ± SD, *n* (%), or geometric mean (interquartile range). **P* for the difference between ODM control children. †*P* for the difference between offspring of diabetic fathers and control children.

Genes are thought to play a major role in the etiology of type 2 diabetes. Among the Pima Indians, offspring of diabetic fathers had more type 2 diabetes than those of nondiabetic fathers (3). However, offspring exposed to diabetes in utero had a higher prevalence of obesity and type 2 diabetes than their siblings born before diabetes was diagnosed in their mothers, suggesting that this finding was attributable to the intrauterine environment (5). Our data showing increased adiposity and insulin concentrations in ODM but not in offspring of diabetic fathers are consistent with this conclusion. Long-term effects on adiposity and glucose metabolism in ODM have been ascribed to early islet cell activation. Induction of diabetes in pregnant rats caused overexhaustion and a subsequent reduction of β-cell activity in the offspring (19). In addition, hyperinsulinemia and/or leptin resistance in ODM may modify hypothalamic appetite regulation, causing hyperphagia (20,21).

There is good evidence that the increased relative weight of ODM is due mainly to increased adiposity (22). Effects on lean tissue are debated. In our study, female ODM had larger skinfold thicknesses than control children. Hunter et al. (18), using bioimpedance, observed a higher percentage of body fat but not lean mass in a small study comparing offspring of pregestational type 2 diabetic mothers with ONDM. Durnwald et al. (22) observed reduced lean mass in large-for-gestational-age ODM. In another study, large-for-gestational-age ODM had larger arm circumferences as well as skinfold thicknesses at 7 years than control children (23). Larger arm circumferences in our female ODM may be due to subcutaneous fat or may reflect a positive influence of maternal GDM on lean tissue growth.

Because our ODM group was small, apparently greater effects in female subjects may be a chance finding. Alternatively, there may be differences between the sexes. An earlier study suggested that girls contributed most to the differences observed in ODM during early childhood (24). We can only speculate about the causes of any sex difference. They could be metabolic/endocrine or behavioral. We believe girls are less physically active than boys in this population, although we have no data to support this theory. Additionally, the closeness of girls to their mothers may have further behavioral effects, as women with GDM may exercise

Table 3—*Anthropometry, insulin concentrations, and HOMA at 5 years in the control children according to quartiles of maternal insulin (IAUC), glucose (GAUC), and paternal insulin*

	n	BMI (kg/m^2)	Height (cm)	MUAC (cm)	Skinfold thickness (mm)		30-min insulin (pmol/l)	HOMA	Insulin increment (pmol/mmol)
					Triceps	Subscapular			
Maternal IAUC									
1 (lowest)	123	13.5	105.5	15.3	7.8	6.1	152	1.0	26
2	113	13.5	105.5	15.2	7.7	6.0	161	0.9	29
3	124	13.5	105.5	15.2	7.6	5.9	187	0.8	34
4 (highest)	101	13.9	106.0	15.7	8.7	6.6	224	0.9	42
*P**		0.02	0.4	0.007	0.002	0.06	<0.001	0.998	<0.001
P†		0.04	0.5	0.1	0.02	0.08	<0.001‡	0.2‡	<0.001‡
Maternal GAUC									
1 (lowest)	127	13.6	105.4	15.3	8.1	6.4	160	0.9	28
2	141	13.5	105.4	15.3	7.7	6.0	182	0.9	33
3	116	13.6	105.8	15.4	7.6	5.8	183	0.8	33
4 (highest)	94	13.6	106.0	15.4	8.4	6.4	196	0.9	36
*P**		0.05§	0.5	0.4	0.001§	<0.001§	0.04	0.6	0.06
P†		0.01§	0.2	0.9	0.001§	<0.001§	0.3‡	0.2‡	0.4‡
Paternal fasting insulin									
1 (lowest)	110	13.5	105.4	15.2	7.6	6.1	151	0.8	27
2	107	13.6	105.9	15.3	7.9	5.9	176	0.9	32
3	97	13.5	105.6	15.4	8.0	6.1	197	1.0	35
4 (highest)	95	13.6	105.9	15.4	8.1	6.2	201	0.9	36
*P**		0.4	0.1	0.07	0.004	0.07	0.04	0.02	0.01
P‖		0.6	0.6	0.97	0.08	0.002§	0.6¶	0.4¶	0.3¶

P values were derived by multiple linear regressions, using all variables as continuous. *Adjusted for sex. †Adjusted for sex, maternal sum of skinfold measurements, and socioeconomic status. ‡Adjusted for sex, maternal sum of skinfold measurements, child's sum of skinfold measurements at 5 years, and socioeconomic status. §Quadratic association. ‖Adjusted for sex, paternal sum of skinfold measurements, and socioeconomic status. ¶*P* adjusted for sex, paternal sum of skinfold measurements, child's sum of skinfold measurements at 5 years, and socioeconomic status. MUAC, mid–upper arm circumference.

less or have unhealthy diets. If the impact is, indeed, greater in girls, this is of concern as they may go on to develop GDM themselves, perpetuating an intergenerational cycle.

A starting hypothesis in our study was that maternal glucose concentrations even in the nondiabetic range may alter the fetal environment sufficiently to induce long-term metabolic changes in offspring. Our study does not provide conclusive evidence for this hypothesis. We found positive associations in the control children, independent of maternal BMI and skinfold measurements, between maternal IAUC values during pregnancy and offspring skinfold measurements and 30-min insulin concentrations. However, there were similar, albeit weaker, findings in relation to paternal insulin concentrations. Weaker trends for fathers could be seen because their insulin profile was less completely characterized than that for mothers. Our data are equally compatible with genetic transmission of adiposity and/or insulin resistance from either parent, and this issue needs further research. In the only previous study of these outcomes in ONDM, associations were observed in the Pima Indians between maternal glucose concentrations and the offspring's fasting insulin and postload glucose concentrations in childhood (2). We have not found any comparable data for fathers.

Our study showed that neonates of diabetic fathers were lighter than control newborns. Several recent studies have described this phenomenon (25–27). This finding is relevant to the well-described association between low birth weight and later insulin resistance and type 2 diabetes (28), for which two main explanations have been proposed. The "thrifty phenotype" hypothesis proposes that it reflects programming by undernutrition during the critical stages of fetal development (29). The "fetal insulin" hypothesis proposes that both low birth weight and type 2 diabetes result from common genes conferring insulin resistance (30). Our data suggest that such genes could, at least partly, explain the low birth weight–type 2 diabetes link.

In summary, our study signals maternal GDM as a risk factor for increased adiposity, IGT, and altered insulin secretion in early childhood and as a potentially important factor contributing to the burden of type 2 diabetes in India. Our findings are striking, given that our children have a low BMI by international standards (31). There is some evidence that good metabolic control during pregnancy prevents these outcomes (24). Unfortunately, we cannot comment on the glycemic control in our mothers because specialist diabetes clinics are not generally available for pregnant women in India. Further follow-up of our children and similar cohorts will determine whether a greater emphasis on diabetes control is required.

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