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Original Article

Effects of maternal smoking during pregnancy on body composition in offspring

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Abstract ***Background***: The aim of the present cross-sectional study was to use objective methods to assess the association between maternal smoking and body composition in offspring.

Methods: A total of 2508 grade 4 school children were enrolled; all underwent lifestyle disease and passive smoking screening. Children were classified into four groups according to their urinary cotinine level and maternal smoking status during or before pregnancy. Items measured on lifestyle disease screening were compared among the four groups.

Results: Only degree of obesity (DO) and body mass index (BMI) were significantly associated with maternal smoking during pregnancy. The prevalence of both DO >20% and DO >30%, and BMI >22% and BMI >25% was highest in children of mothers who smoked during pregnancy. These children had a tendency toward shorter height and increased weight although it was not statistically significant. There were no significant differences between maternal smoking status and lipid profile among groups. Confounders such as food, exercise and sleep were able to be eliminated

Conclusion: Maternal smoking during pregnancy may be an independent risk factor of changing body composition in offspring, that is, shorter height and increased weight.

Key words body composition, lifestyle, maternal smoking, passive smoking, screening.

Obesity is a major health problem in Japan and in other developed nations and the incidence has more than doubled over the past 10 years.[1,2] Bjørge *et al*. recently reported that obesity in adolescence might be related to increased mortality due to ischemic heart disease, colon cancer and pulmonary disease in adulthood.[3] There are three critical time periods for the development of obesity: the prenatal period, the period of adiposity rebound (around 4 years old), and adolescence.[4] The importance of these critical periods on the prevalence of adult obesity, however, remains unclear.[5] Barker *et al*. proposed the so-called fetal origin of adult disease hypothesis, in which the onset of adult lifestyle diseases such as cardiovascular disease and metabolic syndrome might originate during the prenatal period.[6,7] In fact, birthweight per se is important, because both high and low birthweights have been shown to be associated with increased obesity.[8,9] Furthermore, subsequent analyses have highlighted the strong associations between early measures of growth and subsequent obesity, indicating that rapid growth during infancy may also be a critical determinant of obesity risk. Many investigations have previously identified a number of genetic, intrauterine, environmental and lifestyle factors that may be associated with childhood obesity.[10–12] Interestingly, mothers who smoke during pregnancy have been shown to have an increased likelihood of having overweight or obese offspring.[13–20] To our knowledge, no studies have used objective methods to assess the association between maternal smoking and obesity in offspring. Cotinine, a metabolite of nicotine, is considered to be the most reliable biomarker of secondhand smoke, and was recommended by the National Research Council.[21] Recently, this has been used to study tobacco smoke exposure in population studies.

We have recently started a passive smoking screening program using a combination of measurements of urinary cotinine and questionnaires for parents of school children in grade 4.[22] Furthermore, a lifestyle screening examination is also under way in school children of the same age in Japan. Therefore, we investigated the relationship between maternal smoking during pregnancy and offspring body composition and lipid profile using an objective method of cotinine measurement.

Methods

Subjects

In Kumagaya city there were 3609 school children in grade 4 during the 2 years 2007–2008 (1810 children in 2007 and 1799 children in 2008). Of the 3609 children, 3454 (95.7%) were enrolled in the lifestyle disease screening program and 2604

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Table 1 Lifestyle disease and passive smoking screening questionnaire

Lifestyle disease screening	Passive smoking screening
Items	Items
Food(breakfast/dinner)	Smoking status
*Have breakfast?	*Is mother smoking?
*Breakfast with family?	*Is father smoking?
*Eat between meals?	*If above question is "yes", How many?
*Dinner with family?	Mother (cigarettes/day)
*Drinking after dinner?	Father (cigarettes/day)
*Try to have a vegetable?	*When did your smoking start?
*Which do you like?	*Where do you smoke usually? Check next
*Meat, fish, vegetable	*(living, own room, dining room, bedroom, under a ventilation fun , outside window)
*Dine out last 3 days?	
	*Are you smoking at place where your child is?
Play	*Was mother smoking during pregnancy?
*How long play outside after school?	*If above question is "yes" or "no", Check next. (never smoke, stop smoking before pregnancy, smoking during 1–3 months, 3–6 months, throughout pregnancy)
Weighing scale	
*Have a weighing scale?	
	*How many cigarettes during pregnancy?
Exercise	mother (cigarettes/day)
*Physical activity at school	father (cigarettes/day)
*Do you like a exercise?	*Is there anyone other than parents smoking at home
*Do you play sports after school?	*If yes, who is smoking? ( )
Watching TV	Disease status
*Watching TV at dinner?	*Have a significant past history of disease?
*How long watching TV?	*If yes, what kinds of disease?
Sleep	
*Sleeping duration	

(72.2%) in the passive smoking screening program. Finally, 2508 children had complete blood test, urinary cotinine measurement and lifestyle disease and passive smoking questionnaire data.

The age of these 2508 children ranged from 9 to s10 years and the ratio of male to female was 1.0:1.03 (1235/1273). In lifestyle disease screening, bodyweight and length, blood test and lifestyle questionnaire were recorded. Degree of obesity (DO) and body mass index (BMI) were calculated according to the formulas (weight − reference mean weight in Japan)/reference mean weight (%), and weight (kg)/length (m^2), respectively.[23] In the present study, obesity was defined as BMI >25 and/or DO >30%, and overweight was also defined as BMI >22 and/or DO >20%. The definition was different from that for adults because of imbalance of weight and height in this age group. Blood tests included measurements of white blood cells, red blood cells, hemoglobin, hematocrit, as well as aspartate aminotransferase and alanine aminotransferase liver function tests, and lipid profiles of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C). Atherosclerotic index was also calculated according to the formula (TC − HDL-C)/HDL-C. In addition, detailed information regarding food intake, sleep and exercise were obtained, as shown in Table 1.

Furthermore, the passive smoking screening program was carried out in the same group over the same period. The passive smoking screening program included urinary cotinine measurement and a questionnaire (Table 1) completed by their parents.

Questionnaire survey

In lifestyle disease screening, parents responded to 17 items about food, exercise and watching television. Of the 17 items, 11 were food-related questions, three were exercise related and the remaining three were television- and sleep-related questions. Three of the 11 food-related questions, however, were excluded from statistical analysis because they reported dietary factors in great detail, leaving 16 items included in the statistical analysis as shown in Table 1.

In the passive smoking screening program, 13 items on smoking status were completed by the mother, father and any other person living in the same house. In addition, parents completed questions on children's past history of passive smoking-related diseases such as asthma, otitis media, shortened height, caries and allergies.

Cotinine measurement

Urine samples of the first morning void were collected from all children and stored at −40°C. Urinary cotinine levels were analyzed with the enzyme immunoassay method using a monoclonal antibody kit (Cosmic, Tokyo, Japan). In this analysis, the value obtained was the total cotinine level. Total cotinine included cotinine, norcotinine, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine and *trans*-3'-hydroxycotinine-O-glucuronide.[24] The measurement limit of total cotinine was 1.3 ng/mL in this analysis.

Using data from the passive smoking screening program, urinary cotinine >10 ng/mL was indicative of passive smoking.

This could be further categorized as: >40 ng/mL, high passive smoking; 25–39.9 ng/mL, moderate passive smoking; and 10–24.9 ng/mL, mild passive smoking. Parents were informed of these values. These cut-offs could be inadequate and are higher than those of previous reports. We considered, however, that a cut-off of 5 ng/mL would have too strong a psychological impact on parents in the community.

Study design

The information regarding maternal and paternal smoking during pregnancy was obtained from questionnaires. A retrospective cohort study was then performed according to maternal smoking during pregnancy and children's urinary cotinine level. Children were classified into four groups: group A, children of mothers who smoked during pregnancy; group B, children of mothers who stopped smoking immediately on confirmation of pregnancy; group C, children of mothers who never smoked but who had detectable cotinine levels; and group D, children of mothers who never smoked and who had undetectable cotinine levels. Body composition (weight, height and BMI) and blood test results (including lipid profile) were then compared among these four groups.

Potential confounding factors

Several confounding factors were identified, the most important of which were childhood diet, and physical activity. Mothers were asked to report the frequency of their child's consumption of fast food, salad and soft drinks, and the amount of time their child spent watching television and the amount of time their child spent engaging in sports or exercise. Information regarding weight, feeding pattern (breast-feeding or bottle feeding) immediately after delivery, and children's birthweight, however, could not be obtained.

Statistical analysis

Group characteristics were analyzed using analysis of variance (ANOVA) for variables with a normal distribution. Wilcoxon's test was used for variables with a non-normal distribution and the χ^2 test was used for categorical variables. Student's *t*-test was used for comparison of height and bodyweight between groups A and D. Multiple regression analyses were used to control for possible confounders. $P<0.05$ was considered significant.

Results

A total of 2508 grade 4 school children were enrolled in the present study. The children ranged from 9 to 10 years of age. For approximately half of these children, passive smoking and lifestyle disease screenings were performed in 2007, and for the remaining half in 2008. The participation rates in lifestyle disease and passive smoking screening programs were 95.3% and 71.2%, respectively. According to mother's smoking status, 263 children were classified into group A, 493 into group B, 633 into group C and 1044 into group D.

Baseline lifestyle data

Comparison of lifestyle questionnaire responses showed that "breakfast with family", "drinking after dinner", "playing outside after school", "exercise" and "watching television" were significantly associated with the risk of obesity (Table 2). Responses to each item varied from group A to group D. For example, the

Table 2 Baseline lifestyle and maternal smoking status: Analysis of variance

	Group A	Group B	Group C	Group D	*P*-value
	n = 263 % yes	*n* = 493 % yes	*n* = 633 % yes	*n* = 1044 % yes	
Food(breakfast/dinner)					
Have a breakfast?	97.5	98.4	99.7	99.1	0.12 (NS)
Breakfast with family?	76.2	84.1	87.6	89.1	0.0019
Eat between meals?	90.9	85	88.7	89.5	0.25 (NS)
Dinner with family?	97.5	99.2	98.7	99.3	0.35 (NS)
Drinking after dinner?	64.8	54.4	56.1	50.9	0.048
Try to have a vegetable?	88.2	90	88.3	91.9	0.051 (NS)
Which do you like?					
Meat, fish, vegetable	66.1	63.6	64	66.5	0.833 (NS)
Dine out last 3 days?	19.2	15.8	12.8	9.9	0.0022
Play					
*How long play outside after school? less than 2 hours? (yes, no)	68.6	68.4	62.2	57.3	0.001
Weighing scale					
Have a weighing scale?	89.3	93	94.8	94.7	0.139 (NS)
Exercise					
Physical activity at school	51.8	54.2	47.5	51.3	0.438 (NS)
Do you like exercise?	88.3	88.3	87.9	89.8	0.84 (NS)
Do you play sports after school?	60	68.1	71.4	69.3	0.0059
Watching TV					
Watching TV at dinner?	81.8	75.7	76	67.4	0.002
How long watching TV? Less than 2 hours? (yes, no)	55.5	62.7	69.3	69.3	0.012
Sleep					
Sleep duration <6 h?	5.1	5	5.5	2.3	0.112 (NS)

Table 3 Baseline smoking status: Analysis of variance

	Group A n = 263 % yes	Group B n = 493 % yes	Group C n = 633 % yes	Group D n = 1044 % yes	*P*-value
Smoking status					
*Is mother smoking?	77.8	58.6	9.5	1.6	<0.0001
*Is father smoking?	65.2	66	72.2	39.2	<0.0001
*If above question is "yes", How many?					
†Mother (cigarettes/day)	18	8.1	4.8	5.8	0.0076
†Father (cigarettes/day)	42.4	33.8	43.8	29.1	<0.001
*When did your smoking start?(years old)	19.5	20.1	None	None	
*Where do you smoke usually? Check next.					
*(living, own room, dinning room, bedroom, under a ventilation fun , outside window)	NS	N.S	None	None	
*Are you smoking at place where your child is?					
Mother	69.9	50.3	36.5	13	<0.0001
Father	72.1	53.5	58.6	25.8	<0.0001
*How many cigarettes during pregnancy?					
†Mother (cigarettes/day)	9	None	None	None	
†Father (cigarettes/day)	35.4	23.5	26.3	19.7	
*Is there anyone other than parents smoking at home					
*If yes, who is smoking? ( )					
Disease status					
*Have a significant past history of disease?	NS	NS	NS	NS	
*If yes, what kinds of disease?	(–)	(–)	(–)	(–)	
Urinary cotinine concentration (ng/mL)	12.3 ± 330	8.9 ± 269	7.6 ± 115	0.6 ± 0.4	0.0001

†Percentage who smoked >20 cigarettes per day. Several mothers started to smoke after they gave birth

percentage who reported "yes" to the question of "breakfast with family" was lowest in group A and highest in group D. Namely, group D reported the best lifestyle and group A the worst.

Baseline smoking status data

Comparison of smoking status showed that most items were significantly different among the four groups (Table 3). The smoking rates of parents of children in groups A and B (mother smoked during or before pregnancy) were higher than in parents of children in groups C and D (mother never smoked). Furthermore, more than half of parents of children whose mother smoked during or before pregnancy, smoked at the place where their child was. The smoking status of groups A and B were worse than that of groups C and D. Comparison of groups C and D showed no significant difference in smoking status.

Urinary cotinine levels of school children were clearly different among the four groups ($P = 0.0001$). Children in group A whose mother smoked during pregnancy had a 20-fold greater mean urinary cotinine level than children in group D, and children in group B had a 15-fold greater level than those in group D. There was no significant difference in cotinine level between groups B and C. In addition, a past history of disease was not significantly different among the four groups.

Maternal smoking status and lifestyle items

Table 4 lists analysis of variance results for characteristics of the four groups classified by maternal smoking status. Only DO and BMI were significantly different among the groups. Neither height nor weight was significantly different among the groups. Comparisons between groups C and D showed that neither DO nor BMI was significantly different ($P = 0.08$, $P = 0.062$, respectively). Furthermore, prevalence of both DO >20–30% and BMI >22–25 was the highest in group A (Fig. 1). In contrast, there were no significant differences between maternal smoking status and lipid profile among the four groups.

Potential confounders

As shown in Table 2, six lifestyle factors relating to television watching, sports and food were considered potential confounders affecting DO and BMI. Therefore, a statistical adjustment was attempted to exclude the effects of these six confounders. Table 5 lists DO and BMI in the four groups after adjustment for potential confounders. In all subjects, significant differences were found among the four groups, and DO and BMI were not changed after adjustment. As a result, maternal smoking during pregnancy was considered an independent risk factor of changing body composition in offspring. This change of body composition might be related to shorter height and increased weight.

Discussion

The present study shows that DO and BMI were increased in the offspring of mothers who smoked during and before pregnancy compared with offspring of mothers who never smoked. This body composition change may be the result of increased weight and decreased height, even though these were not significantly different. These factors remained significant after adjustment for lifestyle factors. It has been previously reported that the children of mothers who smoked during pregnancy were more likely to be overweight or obese. And there have been two meta-analyses regarding the relationship between maternal smoking during pregnancy and offspring obesity.[25,26] Cotinine and nicotine,

Table 4 Subject characteristics vs maternal smoking status in 2508 schoolchildren: Analysis of variance

	Group A n = 263 (Mean ± variance)	Group B n = 493 (Mean ± variance)	Group C n = 633 (Mean ± variance)	Group D n = 1044 (Mean ± variance)	*P*-value
Age (years)	9.2 ± 0.15	9.2 ± 0.16	9.2 ± 0.15	9.2 ± 0.16	0.91 (NS)
M/F					
Height (cm)	133 ± 39	134 ± 32	133 ± 36	134 ± 35	0.19 (NS)
Weight (kg)	31.1 ± 51.4	30.7 ± 39.9	30.5 ± 45.1	30.3 ± 40.5	0.4 (NS)
BMI (kg/m^2)	17.4 ± 9.0	17.1 ± 7.0	17.0 ± 7.1	16.9 ± 6.9	0.029
Degree of obesity	4.9 ± 292	2.0 ± 220	2.2 ± 211	1.1 ± 211	0.002
Blood cell count					
White blood cell	6629 ± 271	6793 ± 298	6754 ± 266	6778 ± 277	0.96 (NS)
Red blood cell	465 ± 780	464 ± 725	464 ± 876	467 ± 790	0.27 (NS)
Hb (g/dL)	13 ± 0.59	13 ± 0.56	13 ± 0.52	13 ± 0.47	0.11 (NS)
Platelet	29.4 ± 25.6	28.9 ± 28.9	28.6 ± 27.0	28.6 ± 28.6	0.4 (NS)
Liver function test					
AST	26 ± 20	26 ± 16	26 ± 16	26 ± 23	0.6 (NS)
ALT	14 ± 40	14 ± 30	14 ± 33	14 ± 44	0.89 (NS)
Lipid profile					
Total cholesterol	170	168	169	169	0.86 (NS)
HDL-C	62 ± 147	63 ± 144	64 ± 167	64 ± 147	0.44 (NS)
Atherosclerotic index	1.69 ± 0.29	1.68 ± 0.25	1.69 ± 0.35	1.65 ± 0.24	0.3 (NS)
Blood pressure (mmHg)					
Systolic	109 ± 138	110 ± 103	109 ± 93	111 ± 102	0.17 (NS)
Diastolic	59 ± 78	58 ± 73	59 ± 67	59 ± 76	0.06 (NS)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Hb, hemoglobin; HDL-C, high-density lipoprotein cholesterol.

however, have not been evaluated in any previous studies. In the present study the difference between groups C and D on cotinine-based classification of passive smoking was due mainly to smoking by the father. Nicotine has a vasoconstriction effect on the vessels of the placenta and fetus.[27] Subsequently, the fetus is smaller and born lighter. In comparison between groups C and D, DO and BMI were only slightly different. Groups C and D included children of mothers who had never smoked (group D), and children who had been exposed to secondhand smoke from their father (group C). Therefore, increased levels of both indices are not thought to be due to an effect of recent passive smoking.

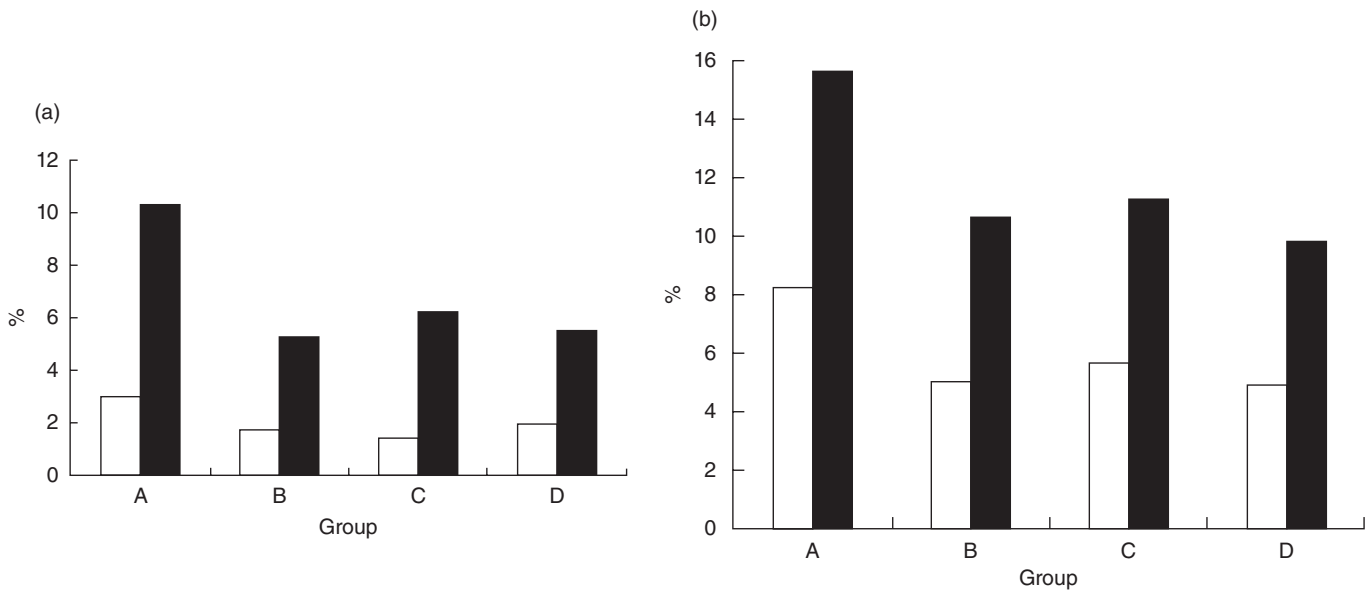

Fig. 1 Prevalence of (a) high body mass index (BMI: □, BMI ≥ 25; ■, BMI ≥ 22) and (b) high degree of obesity (DO: □, DO ≥ 30%; ■, DO ≥ 20%) in offspring versus level of maternal smoking. Group A, children of mothers who smoked during pregnancy; group B, children of mothers who stopped smoking immediately on confirmation of pregnancy; group C, children of mothers who never smoked but who had detectable cotinine levels; and group D, children of mothers who never smoked and who had undetectable cotinine levels.

Table 5 Effects of potential confounders on BMI and obesity index

	Group A (Mean ± variance)	Group B (Mean ± variance)	Group C (Mean ± variance)	Group D (Mean ± variance)	*P*-value
Potential confounders					
Breakfast with family? Only "yes"					
BMI	17.5 ± 10.3	17.1 ± 5.8	17.0 ± 7.1	16.7 ± 6.7	0.04
Degree of obesity	5.1 ± 341	2.1 ± 178	2.1 ± 216	0.1 ± 206	0.02
Drinking after dinner? Only "no"					
BMI	17.5 ± 8.9	17.0 ± 6.2	16.9 ± 7.0	16.6 ± 5.9	0.05
Degree of obesity	5.5 ± 305	1.9 ± 194	1.4 ± 210	–0.5 ± 234	0.04
Dine out last 3 days? Only "no"					
BMI	17.8 ± 9.3	17.2 ± 6.7	17.0 ± 7.2	16.4 ± 6.8	0.04
Degree of obesity	6.3 ± 542	2.1 ± 168	2.0 ± 255	–0.1 ± 253	0.03
How long play outside after school? Only "no"					
BMI	17.2 ± 10.8	17.0 ± 4.6	16.8 ± 5.8	16.1 ± 7.4	0.03
Degree of obesity	5.4 ± 344	2.2 ± 212	1.9 ± 310	0.1 ± 198	0.03
Do you play sports after school? Only "yes"					
BMI	17.5 ± 9.2	17.1 ± 6.5	17.0 ± 6.8	16.7 ± 5.5	0.04
Degree of obesity	5.9 ± 458	2.3 ± 139	2.0 ± 223	0.1 ± 211	0.04
Watching TV at dinner? Only "no"					
BMI	17.4 ± 10.4	17.1 ± 3.9	16.9 ± 7.2	16.4 ± 6.9	0.03
Degree of obesity	5.2 ± 311	2.2 ± 158	1.9 ± 206	0.1 ± 245	0.02
How long watching TV? Only "<2 h"					
BMI	17.9 ± 8.8	17.1 ± 5.9	16.9 ± 7.1	16.6 ± 6.1	0.02
Degree of obesity	6.4 ± 465	2.1 ± 176	2.0 ± 205	0.1 ± 301	0.03

BMI, body mass index

In the present study, with regard to smoking status, there was a high level of cotinine and high smoking rate in the parents of children whose mother smoked during pregnancy. In addition, the lifestyle of children in the groups in which mothers smoked during pregnancy was also worse. Socioeconomic status and educational level were considered to be relatively low in this group, so children might have an unhealthy lifestyle and poor environmental status including passive smoking.[28] Nevertheless, DO and BMI remained high in group A after adjustment for lifestyle. These data may indicate that maternal smoking during pregnancy is an independent risk factor of changing body composition in offspring.

Jaddoe *et al*. recently reported that HDL-C and low-density lipoprotein cholesterol levels were low in the offspring of mothers who smoked during pregnancy.[29] In the present study, HDL-C was slightly low in children of group A, and HDL-C was negatively correlated with BMI, although these differences were not significant, which is consistent with previous reports. A significant difference may be found in a prospective cohort study using a larger subject group.

Children of mothers who smoked during pregnancy have been found to be born smaller and may grow rapidly in infancy, and subsequently become overweight or obese.[30] The mechanism of this weight gain remains unclear. Two possible mechanisms have been proposed, however, to explain the development of obesity in offspring of mothers who smoked. One involves hypothalamic function and the other involves abnormalities in fat cells.[31,32] Experimental studies in rats have shown that gestational starvation of the mother is associated with offspring obesity. A series of studies in rats found larger retroperitoneal and parametrial fat pads in the offspring rather than increased total bodyweight.[33] These findings indicate that obesity in the offspring of mothers who were starved during early gestation is due to altered hypothalamic regulatory mechanisms of energy intake and expenditure rather than to abnormalities of the adipocytes. A similar mechanism may be involved in the offspring of mothers who smoked during gestation because nicotine induces maternal starvation or reduced appetite. Furthermore, vasoconstriction induced by nicotine and hypoxemia induced by carbon monoxide may occur in the hypothalamus of the fetus. In addition, fetal exposure to nicotine has been shown to cause abnormal cell proliferation, differentiation and synaptic activity in the brain and the peripheral autonomic pathways.[34] If these explanations regarding the two mechanisms are correct, fetal exposure to nicotine may lead to permanent changes in hypothalamic regulation of food intake and energy expenditure.

Study limitations

As noted earlier, birthweight, mother's weight and socioeconomic status were also major risk factors for offspring obesity. We were not able to evaluate these data in the present study, and therefore could not completely eliminate the effects of these factors. The design of the present investigation was cross-sectional, and abnormal subjects such as very low-birthweight infants, and those with chromosomal abnormalities and metabolic diseases were excluded. Although the present study was performed in a small area of one city in Japan, recent socioeconomic level, race and parent's education level were relatively heterogeneous. Therefore, these confounders should be investigated in the next step. Offspring obesity is induced by multiple factors. Nevertheless, we believe that, together with the results of previous studies, the present results show that maternal smoking

during pregnancy is a major risk factor for changing body composition in offspring aged 9–10 years.

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References

1 Kokubo Y, Okamura T, Yoshimasa Y *et al*. Impact of metabolic syndrome components on the incidence of cardiovascular disease in a general urban Japanese population: The Suita study. *Hypertens. Res.* 2008; **31**: 2027–35.
2 Chinn S, Rhona RJ. Prevalence and trends in overweight and obesity in three cross-sectional studies of British children, 1974–94. *Br. Med. J.* 2001; **322**: 24–6.
3 Bjørge T, Engeland A, Tverdal A, Smith GD. Body mass index in adolescence in relation to cause-specific mortality: A follow-up of 230,000 Norwegian adolescents. *Am. J. Epidemiol.* 2008; **168**: 30–37.
4 Dietz WH. Critical periods in childhood for the development of obesity. *Am. J. Clin. Nutr.* 1994; **59**: 955–9.
5 Dietz WH, Gortmaker SL. Preventing obesity in children and adolescents. *Ann. Rev. Public Health* 2001; **22**: 337–53.
6 Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. *Lancet* 1989; **2**: 577–80.
7 Oken E, Gillman MW. Fetal origins of obesity. *Obes. Res.* 2003; **11**: 496–506.
8 Rogers I, EURO-BLCS Study Group. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int. J. Obes.* 2003; **27**: 755–77.
9 Reilly JJ, Armstrong J, Dorosty AR *et al*. ALSPAC Study Team. Early life risk factors for obesity in childhood: Cohort study. *BMJ* 2005. doi: 10.1136/bmj.38470.670903.E0
10 Sowen NA, Stember ML. Parental risk factors for infant obesity. *MCN Am. J. Matern. Child Nurs.* 2000; **25**: 234–40.
11 Leary S, Ness A, Emmett P, Davey Smith G, ALSPAC Study Team. Maternal diet in pregnancy and offspring height, sitting height and leg length. *J. Epidemiol. Community Health* 2005; **59**: 467–72.
12 McMillen IC, Rattanatray L, Duffield JA *et al*. The early origins of later obesity: Pathways and mechanisms. *Adv. Exp. Med. Biol.* 2009; **646**: 71–81.
13 Vik T, Jacobsen G, Vatten L, Bakketeig LS. Pre- and post-natal growth in children of women who smoked during pregnancy. *Early Hum. Dev.* 1996; **45**: 245–5.
14 Toschke AM, Koletzko B, Slikker W, Hermann M, von Kries R. Childhood obesity is associated with maternal smoking in pregnancy. *Eur. J. Pediatr.* 2002; **161**: 445–8.
15 Von Kries R, Toschke AM, Koletzko B, Slikker W. Maternal smoking during pregnancy and childhood obesity. *Am. J. Epidemiol.* 2002; **156**: 954–61.
16 Power C, Jefferis BJMH. Fetal environment and subsequent obesity: A study of maternal smoking. *Int. J. Epidemiol.* 2002; **31**: 413–19.
17 Bergmann KE, Bergmann RL, von Kries R *et al*. Early determinants of childhood overweight and adiposity in a birth cohort study: Role of breastfeeding. *Int. J. Obes.* 2003; **27**: 162–72.
18 Wideroe M, Vik T, Jacobsen G, Bakketeig LS. Does maternal smoking during pregnancy cause childhood overweight? *Paediatr. Perinat. Epidemiol.* 2003; **17**: 171–9.
19 Toschke AM, Montgomery SM, Pfeiffer U, von Kries R. Early intrauterine exposure to tobacco-inhaled products and obesity. *Am. J. Epidemiol.* 2003; **158**: 1068–70.
20 Adams AK, Harvey HE, Prince RJ. Association of maternal smoking with overweight at age 3y in American Indian children. *Am. J. Clin. Nutr.* 2005; **82**: 393–8.
21 Benowitz NL. Biomarkers of environmental tobacco smoke exposure. *Environ. Health Perspect.* 1999; **107**(Suppl 2): 349–55.
22 Ino T. A passive smoking screening program for children. *Prev. Med.* 2006; **42**: 427–9.
23 Amemiya S, Dobashi K, Urakami T, Sugihara S, Ohzeki T, Tajima N. Metabolic syndrome in youths. *Pediatr. Diabetes* 2007; **8**(Suppl 9): 48–54.
24 Park S, Lee DH, Park JG, Lee YT, Chung J. A sensitive enzyme immunoassay for measuring cotinine in passive smokers. *Clin. Chim. Acta* 2010; **411**: 1238–42.
25 Ino T. Maternal smoking during pregnancy and offspring obesity: Meta-analysis. *Pediatr. Int.* 2010; **52**: 94–9.
26 Oken E, Levitan EB, Gillman MW. Maternal smoking during pregnancy and child overweight: Systematic review and meta-analysis. *Int. J. Obes.* 2008; **32**: 201–10.
27 Benowitz NL. Nicotine addiction. *Prim. Care* 1999; **26**: 611–31.
28 Rogers I, Emmett PM, ALSPAC Study Team. The effect of maternal smoking status, educational level and age on food and nutrient intakes in preschool children: Results from the Avon Longitudinal Study of Parents and Children. *Eur. J. Clin. Nutr.* 2003; **57**: 854–64.
29 Jaddoe VW, de Ridder MA, van den Elzen AP, Hofman A, Uiterwaal CS, Witteman JC. Maternal smoking in pregnancy is associated with cholesterol development in the offspring: A 27-years follow-up study. *Atherosclerosis* 2008; **196**: 42–8.
30 Ong KKL, Preece MA, Emmett PM, Ahmed ML, Dunger DB, ALSPAC Study Team. Size at birth and early childhood growth in relation to maternal smoking, parity and infant breast-feeding: Longitudinal birth cohort study and analysis. *Pediatr. Res.* 2002; **52**: 863–7.
31 van der Meulen J. Commentary: Maternal smoking during pregnancy and obesity in the offspring. *Int. J. Epidemiol.* 2002; **31**: 420–21.
32 Anguita RM, Sigulem DM, Sawaya AL. Intrauterine food restriction is associated with obesity in young rats. *J. Nutr.* 1993; **123**: 1421–28.
33 Jones AP, Simon EL, Friedman MI. Gestational undernutrition and the development of obesity in rats. *J. Nutr.* 1984; **11**: 1484–92.
34 Jauniaux E, Burton GJ. Morphological and biological effects of maternal exposure to tobacco smoke on the feto-placental units. *Early Hum. Dev.* 2007; **83**: 699–706.