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Dairy food, calcium, and vitamin D intake in pregnancy and wheeze and eczema in infants

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ABSTRACT:

The present prospective study examined the association between maternal consumption of dairy products, calcium, and vitamin D during pregnancy and the risk of wheeze and eczema in the infants aged 16-24 months.

Subjects were 763 Japanese mother-child pairs. Data on maternal intake during pregnancy were assessed with a diet history questionnaire. Symptoms of wheeze and eczema were based on criteria of the International Study of Asthma and Allergies in Childhood.

Higher maternal intake of total dairy products, milk, cheese, and calcium during pregnancy was significantly related to a decreased risk of infantile wheeze, but not eczema (adjusted odds ratios [ORs] between extreme quartiles [95% confidence intervals [CIs]] = 0.45 [0.25-0.79], 0.50 [0.28-0.87], 0.51 [0.31-0.85], and 0.57 [0.32-0.99], respectively). When maternal vitamin D consumption during pregnancy was categorized into 2 groups using a cut-off point at the 25th percentile, children whose mothers had consumed $4.309 \mu \text{g/day}$ or more had a significantly reduced risk of wheeze and eczema (adjusted ORs [95% CIs] = 0.64 [0.43-0.97] and 0.63 [0.41-0.98], respectively).

Higher consumption of calcium and dairy foods other than yogurt during pregnancy may reduce the risk of infantile wheeze. Higher vitamin D intake during pregnancy may be protective against childhood wheeze and eczema.

KEYWORDS: Calcium, dairy, eczema, pregnancy, vitamin D, wheeze

Epidemiological studies of the relationship of intake of dairy products with asthma, wheeze, and/or eczema have provided mixed results [1-8]. Some studies found a protective relationship between dairy food intake and any symptoms of such conditions [1-3] whereas others reported a null association [4-7]. Only one cross-sectional study of young Australian adults showed a significant positive association between intake of dairy products other than milk and the prevalence of asthma [8].

The role of intrauterine exposure in the development of allergic disorders has gained interest. A birth cohort study in Germany showed no associations between maternal intake of milk, yogurt, or cheese during pregnancy and the risk of doctor-diagnosed eczema in the children at 2 years of age [9]. In a birth cohort study in the Netherlands, maternal dairy intake (average of milk and milk product consumption) during pregnancy was not related to the risk of childhood wheeze during the first 8 years of life [10]. A significant inverse exposure-response relationship between maternal vitamin D intake during pregnancy and the risk of recurrent wheeze, but not eczema, was found in 3-year-old children in the US [11]. A prospective study in the UK found that higher maternal vitamin D consumption during pregnancy was significantly associated with a decreased risk of wheeze in children aged 5 years whereas such an inverse association was not observed in children at 2 years of age [12]. Prenatal deficiency of vitamin D may affect fetal lung and immune system development [13]. Dairy foods are a rich source of calcium. To our knowledge, no epidemiological study has investigated the association between maternal calcium intake during pregnancy and the risk of childhood allergic disorders.

In this investigation, we examined the association between maternal consumption of dairy products, calcium, and vitamin D during pregnancy and the risk of wheeze and eczema in Japanese children at 16-24 months of age using data from the Osaka Maternal and Child Health Study (OMCHS).

METHODS

Study population

The OMCHS is a prospective cohort study. Details of the OMCHS have been described elsewhere [14]. We recruited pregnant women at baseline. Neyagawa City is one of the 43 municipalities in Osaka Prefecture, a metropolis in Japan. Of the 3639 eligible subjects in Neyagawa City, 627 women (17.2%) participated in the OMCHS between November 2001 and March 2003. In order to increase the sample size, pregnant women living in municipalities other than Neyagawa City were also recruited. Eight pregnant females who lived in municipalities adjacent to Neyagawa City and who had become aware of the OMCHS at an obstetric clinic before August 2002 decided by themselves to participate in the OMCHS. Also, there were 77 participants who received explanations of the OMCHS from public health nurses in 6 other municipalities from August 2002 to March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and 3 obstetric hospitals in 3 other municipalities.

Finally, a total of 1,002 women between the 5th and 39th week of pregnancy gave their fully informed consent in writing and completed the baseline survey. Of the 1,002 women, 867 mother-child pairs participated in the second survey from 2 to 9 months postpartum. Of the 867 mother-child pairs, 763 participated in the third survey from 16 to 24 months postpartum and were included in the present analysis. The OMCHS was approved by the ethics committee of the Osaka City University School of Medicine.

Measurements

Baseline assessment of the OMCHS included a set of 2 self-administered questionnaires. Also, a self-administered questionnaire was used in both the second and third survey. Participants mailed the answered questionnaires to the data management center at the time of each survey. Research technicians completed missing or illogical data by telephone interview.

One of the self-administered questionnaires at baseline was a semi-quantitative, comprehensive, diet history questionnaire (DHQ) that assesses dietary habits during the preceding month [15, 16]. Estimates of daily intake of foods (150 items in total), energy, and selected nutrients were calculated using an ad hoc computer algorithm for the DHQ [15, 16], based on the Standard Tables of Food Composition in Japan [17, 18]. Total dairy product intake was considered as the sum of milk, yogurt, and cheese. Information on dietary supplements was not used because only a small number of participants used calcium (5.5%) and multivitamin (4.2%) supplements at least once a week. According to a validation study of 92 women aged 31-69 years, Pearson's correlation coefficients between the DHQ and 16-day weighed dietary records were 0.51 for calcium and 0.47 for vitamin D (Sasaki S, unpublished data, 2004). Energy-adjusted intake by the residual method was used for the analyses [19].

A second questionnaire at baseline asked about maternal age, gestation, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, and changes in diet in the previous one month. A paternal or maternal history of asthma, atopic eczema, and allergic rhinitis was defined as positive if the respective parent had been treated with medications for any of these allergic disorders at some time prior to the start of the baseline survey.

A self-administered questionnaire in the second survey elicited information on the baby's sex, birth weight, and date of birth, number of baby's older siblings, maternal smoking during pregnancy, and smoking in the household. A self-administered questionnaire in the third survey included questions on breastfeeding duration in months and symptoms of wheeze and eczema based on the International Study of Asthma and Allergies in Childhood (ISAAC) phase-I questionnaire [20, 21]. Wheeze was defined as present if the mother answered "yes" to the question "Has your child had wheezing or whistling in the chest in the last 12 months?". For eczema, affirmative answers to the following three questions were required: "Has your child ever had an itchy rash which was coming and going for at least 6 months?", "Has your child had this itchy rash at any time in the last 12 months?" and "Has this itchy rash at any time affected any of the following places: the folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?"

Statistical analysis

Intake of dietary factors under study was categorized at quartile points based on the distribution in 763 subjects. Maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in the same room as the infant, breastfeeding duration, and age of infant at the third survey were *a priori* selected as potential confounding factors.

Estimations of crude odds ratios (ORs) and their 95% confidence intervals (CIs) of wheeze and eczema for each category of dietary intake under study in comparison with the lowest intake category were made by means of logistic regression analysis. Multiple logistic regression analysis was used to adjust for potential confounding factors. Trend of association was assessed by a logistic regression model assigning consecutive integers (1 to 4) to the quartiles of the exposure variables. All computations were performed using the SAS software package version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

In the third survey, the prevalence of wheeze and eczema based on the ISAAC criteria was 22.1% and 18.6%, respectively, among 763 infants. About 75% of infants had been breastfed for 6 months or longer (table 1). Slight or substantial changes in diet in the previous 1 month were reported by 551 mothers due to nausea gravidarum (n = 453), maternal and fetal health (n = 89), and other reasons (n = 9). Maternal mean daily total energy consumption and energy-adjusted intake of total dairy products, calcium, and vitamin D during pregnancy were 7628.6 kJ, 168.8 g, 542.3 mg, and 6.2 µg, respectively (table 2).

Compared with maternal total dairy product intake during pregnancy in the first quartile, consumption of that in the fourth quartile was significantly associated with a decreased risk of wheeze in the offspring, showing a clear inverse exposure-response relationship: the adjusted OR for comparison of the highest with the lowest quartile was 0.45 (95% CI: 0.25-0.79, p for trend = 0.007) (table 3). Likewise, higher maternal intake of milk and cheese during pregnancy was independently related to a reduced risk of wheeze in the children: the adjusted ORs for the highest vs. lowest quartiles were 0.50 (95% CI: 0.28-0.87, p for trend = 0.02) and 0.51 (95% CI: 0.31-0.85, p for trend = 0.02), respectively. With regard to different types of milk, maternal consumption of full-fat, but not low-fat, milk was significantly inversely related to the risk of infantile wheeze. No evident relationship was observed between maternal yogurt consumption during pregnancy and the risk of wheeze in the offspring. Maternal calcium intake during pregnancy was independently inversely associated with the risk of wheeze: the adjusted OR between extreme quartiles was 0.57 (95% CI: 0.32-0.99, p for trend = 0.04). Compared with maternal vitamin D intake during pregnancy in the first quartile, only its consumption in the second quartile was independently related to a decreased risk of wheeze in the children.

Maternal intake of total dairy products, milk, yogurt, cheese, and calcium during pregnancy was not measurably associated with the risk of eczema in the offspring. There was an inverted J-shaped association between maternal vitamin D intake during pregnancy and the risk of eczema in the children although adjusted ORs for the second and third quartiles were of borderline significance.

Because all adjusted ORs for infantile wheeze and eczema associated with maternal vitamin D intake during pregnancy in the second, third, and fourth quartiles were below unity, maternal vitamin D consumption during pregnancy was categorized into 2 groups using a cut-off point at the 25th percentile (< 4.309 and \geq 4.309 µg/day). Its consumption of 4.309 µg/day (172.4 IU/day) or more was significantly associated with a decreased risk of both wheeze and eczema in the offspring: the adjusted ORs were 0.64 (95% CI: 0.43–0.97) and 0.63 (95% CI: 0.41–0.98), respectively. No interaction was found in the association of maternal calcium intake during pregnancy with infantile wheeze between children whose mothers had consumed 4.309 µg or more of vitamin D daily during pregnancy and those whose mothers had consumed less than 4.309 µg daily (p = 0.77 for homogeneity of OR for the highest quartile).

Maternal intake of total dairy products, milk, and cheese was correlated with maternal calcium consumption: Pearson's correlation coefficients were 0.85 (p < 0.0001), 0.74 (p < 0.0001), and 0.39 (p < 0.0001), respectively. The significant inverse relationships between maternal consumption of total dairy products, milk, and cheese in the highest quartile and the risk of wheeze in the children were completely attenuated by further adjustment for maternal calcium intake during pregnancy as a continuous variable: the further adjusted ORs were 0.68 (95% CI: 0.30–1.53), 0.74 (95% CI: 0.36–1.50), and 0.63 (95% CI: 0.37–1.07), respectively.

Maternal intake of calcium and vitamin D was correlated with maternal consumption of docosahexaenoic acid and vitamin E (table 4). Our previous findings using data from the OMCHS showed significant inverse associations between maternal intake of α-linolenic acid, docosahexaenoic acid [22], and vitamin E (Miyake Y, et al., submitted) during pregnancy and the risk of wheeze in the infants aged 16-24 months. Additional adjustment for maternal intake of α -linolenic acid, docosahexaenoic acid, or vitamin E during pregnancy did not materially alter the significant inverse relationships between maternal intake of total dairy products, milk, and cheese during pregnancy and the risk of wheeze in children. However, the inverse associations between maternal intake of calcium in the highest quartile and 4.309 µg/day or more of vitamin D and infantile wheeze were not statistically significant after further control for maternal intake of docosahexaenoic acid (further adjusted ORs [95% CIs] = 0.60 [0.34-1.04] and 0.76 [0.47-1.25], respectively) or vitamin E (further adjusted ORs [95% CIs] = 0.62[0.35–1.08] and 0.71 [0.47–1.08], respectively) whereas the significant inverse associations remained after additional adjustment for maternal α -linolenic acid intake. According to our previous findings regarding eczema, additional adjustment for maternal intake of n-6 polyunsaturated fatty acids [22], green and yellow vegetables, citrus fruit, or β -carotene (Miyake Y, et al., submitted) did not materially change the significant inverse association between maternal intake of 4.309 μ g/day or more of vitamin D and infantile eczema whereas the inverse association had disappeared after further control for maternal vitamin E intake (further adjusted OR [95% CI] = 0.68[0.44 - 1.06]).

DISCUSSION

On the other hand, no material associations were observed between maternal consumption of total dairy products, milk, yogurt, cheese, and calcium during pregnancy and the risk of eczema in the offspring. Children whose mother had consumed daily

4.309 μ g or more of vitamin D during pregnancy had a significantly reduced risk of wheeze and eczema, suggesting a threshold effect rather than a monotonic trend. The potential protective effects of maternal consumption of total dairy products, milk, and cheese during pregnancy on wheeze in infants essentially disappeared when we additionally controlled for maternal calcium intake during pregnancy in this study. Thus, the beneficial associations with dairy foods might be attributable to some extent to calcium or unmeasured constituents associated with calcium. Unknown factors in yogurt might have interfered with the expected benefit of maternal calcium intake during pregnancy in the development of wheeze in the offspring in our population. All calcium in bodily fluids, whether in blood, in interstitial spaces or within the cell cytosol or organelles, originates from the diet [23]. Several routes of Ca²⁺ influx may be implemented at various stages of the development and maturation of lymphocytes [24]. However, no association was found between maternal calcium intake during pregnancy and the risk of eczema in infants in the current study.

The average vitamin D intake by pregnant women participating in a previously cited UK birth cohort study and in a US birth cohort study was 137 IU/day and 548 IU/day, respectively [11, 12]. The corresponding figure for the current study was 248 IU/day. Milk fortified with vitamin D is the main source of vitamin D intake in the American diet [11]. Fish and eggs are major sources of vitamin D intake among Japanese. An inverse relationship between maternal vitamin D intake during pregnancy and the risk of childhood wheeze was observed in the 3 different populations regardless of the amount of vitamin D intake. The main source of vitamin D is the cutaneous synthesis induced by sunlight exposure irrespective of populations [26]. The two previous birth cohort studies [11, 12] and our study did not take sunlight exposure status into consideration. Another UK prospective study reported that children whose mothers had higher serum concentrations of 25 (OH)-vitamin D in late pregnancy had a significantly increased risk of visible eczema on examination at 9 months and asthma at age 9 years [27]. The effects

of vitamin D on allergic disorders might depend on the timing of vitamin D exposure. In a birth cohort study in Finland, subjects who had received vitamin D supplementation regularly during the first year compared to others had a marginally significantly increased risk of asthma at age 31 years [28]. Higher vitamin D intake at 5 months of age was significantly positively related to the risk of eczema at the age of 6 years in Swedish children [29].

The present study had methodological strengths. Study subjects were homogeneous in terms of having the same residential background. We incorporated extensive information on potential confounding factors. The prospective design was likely to reduce the possibility of recall bias. The definition of wheeze and eczema was based on the ISAAC questions although validation tests of the ISAAC questions have not been performed for Japanese infants. No attempt was made to ascertain outcome status through reviews of medical records. Moreover, the outcomes under study were measured at varying ages between 16 and 24 months and additionally wheeze in infancy is known not to be a good predictor of asthma over the longer term. These disadvantages could bias the magnitude of the observed effects towards the null.

There are other limitations in this study that deserve recognition. Our DHQ could only approximate consumption although the correlation between the DHQ and dietary records was reasonable, as described above. The consequence would have been an underestimation of values in our results. Our DHQ was designed to assess recent dietary intake, i.e. for 1 month prior to completing the questionnaire. This disadvantage is likely to be alleviated after adjustment for the season when data were collected, however. Changes in diet in the past 1 month were controlled for because pregnant females are likely to change their diet. The observed inverse associations with maternal intake of calcium and 4.309 μ g/day or more of vitamin D were attenuated by further adjustment for maternal consumption of docosahexaenoic acid or vitamin E. Thus, maternal

consumption of docosahexaenoic acid or vitamin E might have confounded the inverse associations. Although we adjusted for a variety of potential confounders, we cannot eliminate the possibility that the observed inverse associations are a consequence of residual confounding by uncontrolled dietary or nondietary factors.

The follow-up rate was not good. Of the 1002 participants at baseline, 239 mother-child pairs did not take part in the third survey. There were no material differences between the 239 non-participants and the 763 participants in the third survey with regard to distribution of maternal age, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, and maternal intake of total energy, milk, yogurt, cheese, and calcium. Compared with non-participants in the third survey, participants were less likely to report low family income and a low maternal and paternal educational level and were more likely to have a high intake of vitamin D. Moreover, at baseline, the participation rate in Neyagawa City was only 17.2% and in other areas the participation rate could not be calculated because the exact number of eligible subjects among the sources from which participants were recruited was not available. Thus, the mother-child pairs in this study were likely not representative of Japanese mother-child pairs in the general population. In fact, educational levels were higher in the mothers in our study than in the general population. According to the 2000 population census of Japan, the proportions of females aged 30 to 34 years in Osaka Prefecture with years of education of < 13, 13–14, 15+, and unknown were 49.2, 32.3, 13.6, and 4.9%, respectively [30]. The present population might have had a greater awareness about health than the general population.

In summary, findings from this prospective study suggest that higher maternal consumption of total dairy products, milk, cheese, calcium, and vitamin D during pregnancy may reduce the risk of infantile wheeze. Also, higher maternal vitamin D intake during pregnancy may be protective against eczema in the children. Our data,

however, did not provide evidence that yogurt intake during pregnancy is preventive against infantile wheeze and eczema. Because of lack of inverse relationships between maternal intake of total dairy products, milk, cheese, and calcium during pregnancy and the risk of infantile eczema, we cannot rule out the possibility that such intake might be preventive against respiratory infections rather than atopy. Further confirmation of these findings is required.

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| Variable | n (%) or mean (SD) |
|---|--------------------|
| Baseline characteristics | |
| Maternal age (years) | 30.0 (4.0) |
| Gestational age at baseline (weeks) | 17.7 (6.7) |
| Residential municipality (%) | |
| Neyagawa City | 457 (59.9) |
| Other than Neyagawa City | 306 (40.1) |
| Family income (% yen/year) | |
| < 4,000,000 | 211 (27.7) |
| 4,000,000-5,999,999 | 313 (41.0) |
| \geq 6,000,000 | 239 (31.3) |
| Maternal education (% years) | |
| < 13 | 212 (27.8) |
| 13–14 | 329 (43.1) |
| ≥15 | 222 (29.1) |
| Paternal education (% years) | |
| < 13 | 289 (37.9) |
| 13–14 | 127 (16.6) |
| ≥15 | 347 (45.5) |
| Maternal history of asthma (%) | 80 (10.5) |
| Maternal history of atopic eczema (%) | 120 (15.7) |
| Maternal history of allergic rhinitis (%) | 256 (33.6) |
| Paternal history of asthma (%) | 64 (8.4) |
| Paternal history of atopic eczema (%) | 72 (9.4) |
| Paternal history of allergic rhinitis (%) | 143 (18.7) |
| Changes in diet in the previous 1 month (%) | |
| None or seldom | 212 (27.8) |
| | |

TABLE 1 Distribution of selected characteristics of 763 parent-child pairs

| Slight | 336 (44.0) |
|---|----------------|
| Substantial | 215 (28.2) |
| Season when data were collected (%) | |
| Spring | 241 (31.6) |
| Summer | 127 (16.6) |
| Fall | 167 (21.9) |
| Winter | 228 (29.9) |
| Characteristics at the postnatal assessment | |
| Maternal smoking during pregnancy (%) | 97 (12.7) |
| Baby's older siblings (% 1 or more) | 381 (49.9) |
| Baby's sex (% male) | 403 (52.8) |
| Baby's birth weight (g) | 3071.0 (415.5) |
| Household smoking in same room as infant | 195 (25.6) |
| Breastfeeding duration (% months) | |
| < 6 | 189 (24.8) |
| ≥ 6 | 574 (75.2) |
| Age of infant at third survey (% months) | |
| 16–19 | 263 (34.5) |
| 20 | 370 (48.5) |
| 21–24 | 130 (17.0) |

SD: standard deviation.

| Variable [#] | Mean (SD) | |
|--------------------------|-----------------|--|
| Total energy (kJ) | 7628.6 (1924.1) | |
| Total dairy products (g) | 168.8 (119.7) | |
| Milk (g) | 122.6 (108.8) | |
| Yogurt (g) | 40.5 (39.8) | |
| Cheese (g) | 5.7 (8.5) | |
| Calcium (mg) | 542.3 (170.7) | |
| Vitamin D (µg) | 6.2 (3.7) | |

TABLE 2 Distribution of daily intake of dairy products, calcium, and vitamin D in 763pregnant women at baseline

SD: standard deviation. [#]: Nutrient and food intake were adjusted for total energy intake using the residual method.

| | Wheeze | | | Eczema | | |
|-----------------------|-----------|-------------------|-----------------------------------|-----------|-------------------|-----------------------------------|
| Variable [#] | No. cases | Crude OR (95% CI) | Adjusted OR (95% CI) [¶] | No. cases | Crude OR (95% CI) | Adjusted OR (95% CI) [¶] |
| Total dairy products | ducts | | | | | |
| Q1 (43.6) | 50 | 1.00 | 1.00 | 43 | 1.00 | 1.00 |
| Q2 (120.8) | 50 | 0.99 (0.63–1.57) | 1.04(0.64-1.70) | 22 | 0.45 (0.25–0.77) | 0.45 (0.25–0.81) |
| Q3 (184.5) | 44 | 0.84 (0.52–1.34) | 0.85 (0.52–1.40) | 38 | 0.85 (0.52–1.39) | 0.94 (0.55–1.59) |
| Q4 (280.7) | 25 | 0.42 (0.25–0.71) | 0.45 (0.25–0.79) | 39 | 0.88 (0.54–1.43) | 1.01 (0.59–1.73) |
| p for trend | | 0.002 | 0.007 | | 0.89 | 0.50 |
| Milk | | | | | | |
| Q1 (16.1) | 46 | 1.00 | 1.00 | 37 | 1.00 | 1.00 |
| Q2 (77.9) | 51 | 1.14 (0.72–1.81) | 1.28 (0.79–2.10) | 33 | 0.86 (0.51–1.45) | 0.94 (0.54–1.63) |
| Q3 (144.7) | 47 | 1.02(0.64 - 1.63) | 1.10 (0.67–1.82) | 35 | 0.93 (0.55–1.55) | 1.12 (0.65–1.94) |
| Q4 (194.0) | 25 | 0.47 (0.27–0.80) | 0.50 (0.28–0.87) | 37 | 0.99 (0.60–1.65) | 1.19 (0.69–2.06) |
| p for trend | | 0.009 | 0.02 | | 0.95 | 0.44 |
| Yogurt | | | | | | |
| Q1 (4.4) | 39 | 1.00 | 1.00 | 41 | 1.00 | 1.00 |

TABLE 3 Odds ratios and 95% confidence intervals for wheeze and eczema in 763 children aged 16-24 months by quartiles of maternal

| Q2 (16.9) | 39 | 0.99 (0.60–1.64) | 1.01 (0.60–1.70) | 33 | 0.76 (0.45–1.26) | 0.72 (0.42–1.23) |
|-------------|----|------------------|------------------|----|------------------|------------------|
| Q3 (40.3) | 51 | 1.41 (0.88–2.28) | 1.76 (1.05–2.98) | 33 | 0.76 (0.45–1.26) | 0.73 (0.42–1.27) |
| Q4 (94.6) | 40 | 1.03 (0.62–1.69) | 1.26 (0.74–2.16) | 35 | 0.82 (0.49–1.35) | 0.79 (0.46–1.37) |
| p for trend | | 0.58 | 0.15 | | 0.44 | 0.41 |
| Cheese | | | | | | |
| Q1 (0.0) | 58 | 1.00 | 1.00 | 41 | 1.00 | 1.00 |
| Q2 (2.2) | 33 | 0.48 (0.29–0.77) | 0.47 (0.28–0.78) | 38 | 0.90 (0.55–1.48) | 0.79 (0.46–1.34) |
| Q3 (4.5) | 43 | 0.66 (0.42–1.04) | 0.61 (0.37–1.00) | 33 | 0.76 (0.45–1.26) | 0.74 (0.43–1.29) |
| Q4 (12.5) | 35 | 0.51 (0.31–0.82) | 0.51 (0.31–0.85) | 30 | 0.68(0.40-1.14) | 0.67 (0.38–1.16) |
| p for trend | | 0.02 | 0.02 | | 0.11 | 0.16 |
| Calcium | | | | | | |
| Q1 (364.8) | 46 | 1.00 | 1.00 | 40 | 1.00 | 1.00 |
| Q2 (481.3) | 51 | 1.14 (0.72–1.81) | 1.23 (0.75–2.03) | 35 | 0.84 (0.51–1.40) | 0.89 (0.52–1.53) |
| Q3 (571.1) | 42 | 0.88 (0.55–1.42) | 1.01 (0.60–1.70) | 27 | 0.62 (0.36–1.05) | 0.66 (0.37–1.18) |
| Q4 (714.4) | 30 | 0.58 (0.35–0.97) | 0.57 (0.32–0.99) | 40 | 0.99 (0.61–1.63) | 1.08 (0.63–1.86) |
| p for trend | | 0.02 | 0.04 | | 0.72 | 0.99 |
| Vitamin D | | | | | | |
| Q1 (3.5) | 53 | 1.00 | 1.00 | 46 | 1.00 | 1.00 |

| Q3 (6.4)44 $0.77(0.49-1.23)$ $0.80(0.49-1.31)$ 29 $0.56(0.33-0.93)$ $0.59(0.34-1.02)$ Q4 (9.1)42 $0.73(0.46-1.16)$ $0.69(0.42-1.14)$ 36 $0.73(0.44-1.19)$ $0.67(0.39-1.13)$ p for trend 0.44 0.39 $0.69(0.42-1.14)$ 36 $0.73(0.44-1.19)$ $0.67(0.39-1.13)$ P for trend 0.44 0.39 $0.69(0.42)$ $0.69(0.42)$ $0.69(0.42)$ $0.67(0.39)$ OR: odds ratio; CI: confidence interval. #: 0.44 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 OR: odds ratio; CI: confidence interval. #: 0.39 0.39 0.18 $0.73(0.44)$ Interval ratio; CI: confidence interval. #: 0.39 0.39 0.18 0.13 Interval ratio; CI: confidence interval. #: 0.39 0.39 0.18 <th>Q2 (5.1)</th> <th>30</th> <th>0.48 (0.29–0.79)</th> <th>0.48(0.28-0.80)</th> <th>31</th> <th>0.61 (0.36–1.004)</th> <th>0.63 (0.37–1.09)</th> | Q2 (5.1) | 30 | 0.48 (0.29–0.79) | 0.48(0.28-0.80) | 31 | 0.61 (0.36–1.004) | 0.63 (0.37–1.09) |
|---|--------------|----------------|------------------------------|---|-----------------|---------------------------------|-------------------|
| 42 $0.73 (0.46-1.16)$ $0.69 (0.42-1.14)$ 36 $0.73 (0.44-1.19)$ 0.44 0.39 $0.69 (0.42-1.14)$ 36 $0.73 (0.44-1.19)$ Ids ratio; CI: confidence interval. #: Quartile medians in g/day (except for calcium [mg/day] and vitamin D [µg/day]intake using the residual method are given in parentheses; 1: Adjustment for maternal age, gestation at baseline, respanity at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic of thinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal sr ncy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding infant at third survey. | Q3 (6.4) | 44 | 0.77 (0.49–1.23) | 0.80 (0.49–1.31) | 29 | 0.56 (0.33-0.93) | 0.59 (0.34–1.02) |
| 0.44 Ids ratio; CI: confidence interval. [#] : Quartil intake using the residual method are giver pality at baseline, family income, maternal c rhinitis, changes in maternal diet in the pr ncy, baby's older siblings, baby's sex, baby infant at third survey. | Q4 (9.1) | 42 | 0.73 (0.46–1.16) | $0.69\ (0.42 - 1.14)$ | 36 | 0.73 (0.44–1.19) | 0.67 (0.39–1.13) |
| OR: odds ratio; CI: confidence interval. [#] : Quartile medians in g/day (except for calcium [mg/day] and vitamin D [µg/day]) adjusted energy intake using the residual method are given in parentheses; [¶] : Adjustment for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration, and age of infant at third survey. | p for trend | | 0.44 | 0.39 | | 0.18 | 0.13 |
| energy intake using the residual method are given in parentheses; ¹ : Adjustment for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration, and age of infant at third survey. | OR: odds r | atio; CI: con | fidence interval. #: Quartil | e medians in g/day (except for | calcium [mg/ | /day] and vitamin D [$\mu g/d$ | ay]) adjusted |
| municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration, and age of infant at third survey. | energy inta | ake using the | residual method are given | in parentheses; [¶] . Adjustment | for maternal | age, gestation at baseline, | residential |
| allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration, and age of infant at third survey. | municipali | ty at baseline | e, family income, maternal | and paternal education, materr | nal and paterr | al history of asthma, atop | ic eczema, and |
| pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration, and age of infant at third survey. | allergic rhi | initis, change | s in maternal diet in the pr | evious 1 month, season when d | lata at baselin | le were collected, materna | l smoking during |
| age of infant at third survey. | pregnancy, | , baby's oldeı | r siblings, baby's sex, baby | 's birth weight, household smo | oking in same | room as infant, breastfeed | ing duration, and |
| | age of infa | nt at third su | rvey. | | | | |

| | P | Pearson's correlation coefficients (p-value) | nts (p-value) |
|---------------------------------|----------------------|--|-----------------|
| Variable [#] | Total dairy products | Calcium | Vitamin D |
| a-Linolenic acid | -0.15 (< 0.0001) | -0.10 (0.004) | -0.01 (0.70) |
| Docosahexaenoic acid | -0.04 (0.25) | 0.14 (0.0002) | 0.69 (< 0.0001) |
| n-6 Polyunsaturated fatty acids | -0.16 (< 0.0001) | -0.09 (0.02) | 0.004~(0.91) |
| Green and yellow vegetables | 0.07 (0.06) | 0.24 (< 0.0001) | 0.14 (< 0.0001) |
| Citrus fruit | -0.04(0.24) | 0.05 (0.17) | 0.12 (0.001) |
| Vitamin E | -0.03 (0.47) | 0.19 (< 0.0001) | 0.30 (< 0.0001) |
| β-Carotene | 0.09(0.01) | 0.38 (< 0.0001) | 0.23 (< 0.0001) |