Acta Medica Okayama

Volume 63, *Issue* 1 2009 *Article* 7

FEBRUARY 2009

Impact of Breastfeeding on Body Weight of Preschool Children in a Rural Area of Japan: Population-based Cross-sectional Study

Hirokazu Komatsu* Takashi Yorifuji† Toshihide Iwase‡

Ayako Sasaki** Soshi Takao†† Hiroyuki Doi‡‡

*Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, hkomatsu@minos.ocn.ne.jp

†Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,

‡Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,

**Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,

††Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,

‡‡Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,

Impact of Breastfeeding on Body Weight of Preschool Children in a Rural Area of Japan: Population-based Cross-sectional Study

Hirokazu Komatsu, Takashi Yorifuji, Toshihide Iwase, Ayako Sasaki, Soshi Takao, and Hiroyuki Doi

Abstract

To investigate the effect of exclusive breastfeeding on the likelihood of Japanese preschool children being overweight, population-based cross-sectional survey data from M town in Japan were used. Using the population registry of this town, all 616 preschool children were identified, and a self-administered questionnaire was sent to their parents. The exposure variable of interest was exclusive breastfeeding from birth to 6 months, and the outcome variable of interest was the children being overweight at preschool age. Statistical analyses used included logistic regression and sensitivity analyses. In the final analyses, we included 448 preschool children. Although all point estimates indicated a protective effect, logistic regression analyses showed no significant reduction in being overweight due to exclusive breastfeeding in the unadjusted model (odds ratio (OR)0.70, 95% confidence intervals:0.30-1.64), the model adjusted for birth weight (OR0.70, 95% CI:0.30-1.63), the model adjusted for child lifestyle (OR0.71, 95% CI:0.30-1.67), or the model adjusted for parental factors (OR0.46, 95% CI:0.15-1.37). In sensitivity analyses, point estimates were not significant, but a protective effect was observed. In conclusion, our results suggest that breastfeeding might have a protective effect on Japanese preschool children against being overweight, although statistical significance was not observed due to the limitation of the statistical power of the findings.

KEYWORDS: breastfeeding, overweight, preschool children

Acta Med. Okayama, 2009
Vol. 63, No. 1, pp. 49–55

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

Impact of Breastfeeding on Body Weight of Preschool Children in a Rural Area of Japan: Population-based Cross-sectional Study

Hirokazu Komatsu*, Takashi Yorifuji, Toshihide Iwase, Ayako Sasaki, Soshi Takao, and Hiroyuki Doi

Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700–8558, Japan

To investigate the effect of exclusive breastfeeding on the likelihood of Japanese preschool children being overweight, population-based cross-sectional survey data from M town in Japan were used. Using the population registry of this town, all 616 preschool children were identified, and a self-administered questionnaire was sent to their parents. The exposure variable of interest was exclusive breastfeeding from birth to 6 months, and the outcome variable of interest was the children being overweight at preschool age. Statistical analyses used included logistic regression and sensitivity analyses. In the final analyses, we included 448 preschool children. Although all point estimates indicated a protective effect, logistic regression analyses showed no significant reduction in being overweight due to exclusive breastfeeding in the unadjusted model (odds ratio (OR) = 0.70, 95% confidence intervals: 0.30–1.64), the model adjusted for birth weight (OR = 0.70, 95% CI: 0.30–1.63), the model adjusted for child lifestyle (OR = 0.71, 95% CI: 0.30–1.67), or the model adjusted for parental factors (OR = 0.46, 95% CI: 0.15–1.37). In sensitivity analyses, point estimates were not significant, but a protective effect was observed. In conclusion, our results suggest that breastfeeding might have a protective effect on Japanese preschool children against being overweight, although statistical significance was not observed due to the limitation of the statistical power of the findings.

Key words: breastfeeding, overweight, preschool children

The protective effect of breastfeeding and the dose-dependent effect of breastfeeding duration on the likelihood of children becoming overweight have been reported [1, 2]. Indeed, recent meta-analyses suggest a 10–20% reduced risk of obesity in breastfed infants [3, 4], and a further 4% reduction in obesity risk for each additional month of breastfeeding [5]. While not breastfeeding is not the only cause of the obesity epidemic, increasing breastfeeding rates might be one way to attenuate the epidemic of children becoming overweight [6]. Thus the World Health Organization and the United Nations Children's Fund have recommended exclusive breastfeeding during the first 6 months of life in both developed and developing countries [7].

In Japan, the proportion of breastfed infants has gradually decreased [8], whereas the prevalence of Japanese children who are overweight has rapidly increased in the last 2 decades [9]. Therefore, much

Received October 14, 2008; accepted November 21, 2008.
*Corresponding author. Phone: +81–86–223–7151 (ex. 7175); Fax: +81–86–235–7178
E-mail: hkomatsu@minos.ocn.ne.jp (H. Komatsu)

attention has been given to the effect of exclusive breastfeeding on preventing children from becoming overweight as a population strategy [10].

Although one previous study investigated the prevalence of exclusive breastfeeding and the factors associated with breastfeeding in Japan, no study has examined the effect of breastfeeding on the body weight of Japanese children [11]. Therefore, in the present study, we used population-based cross-sectional survey data from M town to verify the research hypothesis that breastfeeding had a protective effect which prevented Japanese preschool children from becoming overweight.

Materials and Methods

Study design and participants. In February 2008, M town conducted a population-based cross-sectional survey to investigate the descriptive features of this town related to maternal and child health. M town is a rural area in Okayama prefecture, Japan, and has a population of about 15,000. In the present study, using the February 2008 population registry of this town, all 616 preschool children aged 2–6 years and their parents were chosen as a target population. A self-administered questionnaire was sent to the parents by staff from the municipal office of M town. Parents filled in their children's basic characteristics and lifestyle factors and their own characteristics, and returned the questionnaire by mail. In order to increase the follow-up rate, municipal office staff reminded the parents to return the completed questionnaire. It was considered that the return of the questionnaire indicated that informed consent had been given. We then used this descriptive survey data to investigate the effect of exclusive breastfeeding on the prevalence of preschool children being overweight.

Measurements. Our exposure variable of interest was the infant feeding pattern from birth to 6 months. We asked the parents the following question: "What form of infant feeding did you use during the first 6 months of life?" This question was answered using a 5-category scale: exclusive breastfeeding; more breastfeeding than infant formula; both equally; more infant formula than breastfeeding; exclusive infant formula. The validity of maternal recall of their children's infant feeding habits was examined in previous studies [12, 13] which suggested that this type of questionnaire has high validity.

Our outcome variable of interest was whether each preschool child was overweight. Height and weight were collected by parents as part of the self-administered questionnaire, and were reported to the nearest 0.1 cm and 0.1 kg, respectively. Although these measurements were self-administered, recent data suggest that such measurements have high validity among children and adolescents [14, 15]. Body mass index (BMI) was calculated as weight in kg divided by the square of height in m. Then the age and sex-specific criteria of the International Obesity Task Force (IOTF) were used to determine if each child was overweight [16].

Using information from previous studies [1, 17, 18], we considered the following variables as potential confounders: children's basic characteristics (birth weight), children's lifestyle factors (breakfast habits, snack consumption, sleep duration, television watching time), and parents' characteristics (overweight (BMI $\geq 25 kg/m^2$) and educational attainment). Birth weight was transcribed by the parent from the Maternal and Child Health Handbook to the questionnaire.

Statistical analysis. In our study, infant feeding variables were dichotomized into 2 categories: "exclusive breastfeeding", and "others", the latter of which encompassed the more breastfeeding than infant formula/both equally/more infant formula than breastfeeding/exclusive infant formula feeding patterns. The "others" category was used as a reference for comparison with "exclusive breastfeeding". All other potential confounders were also dichotomized: birth weight ($\geq 2,500$ g, $< 2,500$ g); breakfast habits (eats every day, does not eat every day); snack consumption (≥ 4 days per week, < 4 days per week); sleep duration (≥ 9 h, < 9 h), television watching time (≥ 2 h per day, < 2 h per day); parental body weight (at least one overweight parent, both parents not overweight); paternal and maternal educational attainment (secondary school or high school, other levels of education), respectively.

We first examined the prevalence of overweight preschool children separated by infant feeding category, and conducted a chi-square test to determine the proportion who were overweight. Then we investigated the difference between the 2 dichotomized infant feeding categories, using a chi-square test for the

proportion and a *t*-test for the mean of each basic characteristic.

Secondly, we used multivariate logistic regression to estimate the effect of exclusive breastfeeding on preschool children becoming overweight. We constructed 4 models. Model 1 was a crude model. In order to adjust for children's basic characteristics, model 2 included birth weight plus model 1. In model 3, we adjusted for children's lifestyle factors such as breakfast habits, snack consumption, sleep duration, and television watching time plus model 2. Finally, in model 4, we included parental body weight and paternal educational attainment plus model 3 to adjust for parental factors. Paternal educational attainment was used as a marker of the socio-economic status of the family.

Finally, we conducted sensitivity analyses changing the grouping of infant feeding categories to investigate the stability of the effect estimate of "exclusive breastfeeding". First, we combined the last 2 infant feeding categories, "more infant formula than breastfeeding/exclusive infant formula", as a reference to estimate the effect of "exclusive breastfeeding". Next we used the last infant feeding category, "exclusive infant formula", as a reference. We also conducted further sensitivity analyses controlling for maternal educational attainment instead of paternal educational attainment, and controlling for both maternal and paternal educational attainment in model 4.

We reported odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was defined at two-sided *p* values less than the 0.05 level. All analyses were conducted using the statistical software package SPSS 15.0J (SPSS Japan Inc. Tokyo, Japan).

Results

Questionnaires were returned by parents of 476 of the 616 preschool children (77.3%). We excluded those who had no identification number (n=2), those who had no information about breastfeeding (n=3), and those who had no information about height and weight (n=23). Therefore, we included 448 preschool children in the final analyses.

In descriptive analyses of the 5 feeding categories (Table 1), the proportion of exclusive breastfeeding was 24.6%, while the proportion of exclusive infant formula was 3.8%. The prevalence of overweight children was 6.4% in the exclusive breastfeeding category, while the prevalence of overweight children in the exclusive infant formula category was 11.8%. However, there was no significant difference in the prevalence of being overweight among the five categories. Moreover, when categories were dichotomized into the "exclusive breastfeeding" category and the "others" category (Table 2), there were no differences in children's basic characteristics, children's lifestyle factors, parental characteristics, or missing values. There were a few missing values among the children's factors, while 8.9–21.9% of parental characteristics were missing.

From the results of logistic regression analyses (Table 3), there was no significant reduction in the prevalence of being overweight in the exclusive breastfeeding group either in the unadjusted model (OR=0.70, 95% CI: 0.30–1.64 (model 1)) or the adjusted models (OR=0.70, 95% CI: 0.30–1.63 (model 2); OR=0.71, 95% CI: 0. 30–1.67 (model 3); OR=0.46, 95% CI: 0.15–1.37 (model 4)) when compared with a reference category. However, all point estimates indicated a protective effect of exclusive breastfeeding against becoming overweight.

In sensitivity analyses, the ORs (95% CIs) of

Table 1 Prevalence of overweight preschool children, according to infant feeding categories (n=448)

	N (Total=448)	number of overweight preschool children	(%)
Exclusive breastfeeding	110	7	6.4
More breastfeeding than infant formula	97	11	11.3
Both equally	75	7	9.3
More infant formula than breastfeeding	149	10	6.7
Exclusive infant formula	17	2	11.8

Table 2 Basic characteristics of children's factors and parental factors according to the dichotomized infant feeding categories

	Exclusive breastfeeding n = 110	Others* n = 338	*p* value
Children's basic characteristics			
Sex Male (%)	49 (44.5)	176 (52.1)	0.17
Female (%)	61 (55.5)	162 (47.9)	
Mean age (SD)	4.4 (1.4)	4.6 (1.4)	0.30
Birth weight; ≥2,500 g (%)	101 (91.8)†	306 (90.5)†	0.55
Children's lifestyle factors			
Breakfast habit; everyday (%)	101 (91.8)	313 (92.6)	0.79
Snack consumption; ≥4 days per week (%)	39 (35.5)	120 (35.5)†	0.98
Sleep duration; ≥9 h per day (%)	63 (57.3)	180 (53.3)	0.46
Television watching time; ≥2 h per day (%)	23 (20.9)	98 (29.0)	0.10
Parental factors			
Parental body weight; at least one overweight parent (%)	24 (21.8)	82 (24.3)	0.47
Missing values (%)	21 (19.1)	74 (21.9)	
Paternal education; secondary or high school (%)	52 (47.3)	155 (45.9)	0.70
Missing values (%)	11 (10.0)	30 (8.9)	

Abbreviation: SD represents standard deviation.
*"Others" includes the following 4 infant feeding categories: more breastfeeding than infant formula; both equally; more infant formula than breastfeeding; exclusive infant formula.
†These categories have one missing value. There were no missing values in the other categories of children's basic characteristics and lifestyle factors.

Table 3 Odds ratios (ORs) and 95% confidence intervals (CIs) for exclusive breastfeeding associated with overweight preschool children, according to 4 logistic regression models

	Model 1 n = 448		Model 2 n = 446		Model 3 n = 445		Model 4 n = 351	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Exclusive breastfeeding	0.70	0.30–1.64	0.70	0.30–1.63	0.71	0.30–1.67	0.46	0.15– 1.37
Others*	1.00		1.00		1.00		1.00	
Birth weight (≥2,500 g/<2,500 g)†			1.77	0.41–7.65	1.75	0.40–7.62	1.22	0.27– 5.61
Breakfast habit (everyday/not everyday)†					1.37	0.30–6.14	1.72	0.21–13.82
Snack consumption (≥4 days/<4 days)†					0.65	0.30–1.42	0.42	0.17– 1.05
Sleep duration (≥9 h/<9 h)†					0.86	0.44–1.70	0.82	0.37– 1.79
Television watching time (≥2 h/<2 h)†					1.13	0.52–2.48	1.26	0.50– 3.20
Parental body weight (at least one overweight parent/both parents not overweight)†							0.97	0.42– 2.27
Paternal educational attainment (secondary or high school/other level of education)†							0.40	0.17– 0.92

*"Others" includes the following 4 infant feeding categories: more breastfeeding than infant formula; both equally; more infant formula than breastfeeding; exclusive infant formula.
†Latter category was used as a reference.

exclusive breastfeeding were 0.56 (0.17–1.92) when we used the last 2 infant feeding categories combined as a reference category in model 4 and 0.15 (0.02–1.01) when we used the last infant feeding category as a reference category in model 4. Both point estimates indicated a protective effect of breastfeeding against becoming overweight, but this result was not statistically significant. Moreover, when we controlled for maternal educational attainment instead of paternal educational attainment in model 4, the adjusted OR of exclusive breastfeeding was almost the same as in model 4 (data not shown). Even when we adjusted for both paternal and maternal educational attainment together, the adjusted OR still remained almost the same (data not shown).

Discussion

In the present study, although no significant effect of exclusive breastfeeding on the likelihood of preschool children being overweight was found, all point estimates indicated a protective effect of exclusive breastfeeding on body weight. The results of sensitivity analyses were consistent with this finding. Therefore, these findings suggest that exclusive breastfeeding may reduce the likelihood of preschool children in Japan becoming overweight.

The point estimate of exclusive breastfeeding in this study is comparable with previous studies [19]. It is possible that no significant effect of exclusive breastfeeding was found because the study did not have enough statistical power (type two error). This survey was originally designed to investigate the prevalence of maternal and child health characteristics, and consequently the number of participants and the prevalence of overweight preschool children may have been too small to investigate the association between exclusive breastfeeding and preschool children being overweight. If we had used a larger number of participants and conducted the study in an area with a higher prevalence of overweight preschool children, we might have observed a significant protective effect of breastfeeding. Our results are consistent with previous studies that also failed to find an association between breastfeeding and being overweight [20].

At least 2 possible mechanisms have been proposed to explain the protective effect of breastfeeding. One possible mechanism is behavioral. Infants naturally regulate their energy intake, but their parent's behavior can override their appetite signs. During infancy, while bottle feeding is usually conducted by their parents according to a regular schedule, regardless of infants' signals of hunger and satiety, mothers who are breastfeeding may be more responsive to infants' signals regarding the frequency and volume of feeding [21]. Therefore, compared with bottle feeding, the act of breastfeeding may promote maternal feeding styles that are less controlling and more responsive to infant cues of hunger and satiety, thereby allowing infants greater self-regulation of energy intake growing up [6, 22].

Another possible mechanism is through the metabolic consequences of ingesting breast milk, and through the biologic activity of components of breast milk. Higher plasma-insulin concentrations were observed in bottle-fed infants than in breastfed infants, and higher plasma insulin concentrations stimulate fat deposition and lead to early development of adipocytes [23]. Moreover, breastfed infants may have a lower protein intake [24], and higher protein intake early in life might increase the risk of becoming overweight in later life [25]. Bioactive factors contained in breast milk may modulate growth factors which inhibit adipocyte differentiation *in vitro* [26, 27]. Although the mechanisms of the protective effect of breastfeeding against becoming overweight in later life have not yet been fully clarified, neonatal life may be a critical period in determining the long-term effects of feeding. It is possible that infant breastfeeding has a long-term effect on the metabolic programming of glucose metabolism and body composition in later life in humans, as has been found in animal studies [28, 29]. In terms of the fetal origin of adult disease hypothesis, which focuses primarily on the prenatal period and infancy as determinants of long-term health [30], our results might also suggest protective effects of breastfeeding not only against adulthood obesity but also against chronic diseases that can be consequences of adulthood obesity.

When adjusted for parental factors, the results also suggested that there was a protective effect of exclusive breastfeeding against the likelihood of preschool children becoming overweight, but this finding was not statistically significant. It is possible that this protective effect of breastfeeding was overestimated by selection bias because 8.9–21.9% of the values for

parental factors were missing. However, taking into account the protective point estimates in other models which are almost the same as in previous studies [3, 4], it is unlikely that the direction of the association was changed by the bias due to these missing values.

The strengths of our study are as follows. This is the first study in Japan which verified the research hypothesis that exclusive breastfeeding reduces the likelihood of preschool children becoming overweight. Moreover, this is a population-based study with a high follow-up rate. A further strength is the fact that birth weight, which is an important confounder of child body weight, was transcribed from the Maternal and Child Health Handbook.

However, there are also some limitations in our study. First, it is possible that parents who had overweight children remembered more bottle feeding than breastfeeding. Our results may be overestimated due to recall bias; however, it is unlikely that the bias completely changes the direction of the association, because it is not well known among ordinary parents in Japan that bottle-fed infants become overweight more often than breastfed infants. Secondly, there may be a generalizability problem. When applying our findings to other populations, it may be necessary to take into account the low prevalence of overweight children and the basic characteristics of this study population. However, because the effect of exclusive breastfeeding is unlikely to be different in urban and rural areas according to the possible mechanisms described above, the advantage of a population-based study may partly overcome this generalizability problem. Thirdly, we have no data on the physical activity of the children studied. Therefore, although we measured television watching time as a surrogate measure for physical activity, there are still residual confoundings. Fourthly, we could not disentangle the effect of gestational age at birth on preschool children becoming overweight. Finally, we also have no data on the duration of breastfeeding, so we could not estimate the effect of the duration of breastfeeding.

In conclusion, our results suggest that breastfeeding might have a protective effect, acting to prevent Japanese preschool children from becoming overweight, although statistical significance was not observed due to the limitation of the statistical power of the study. In future studies, the effect of breastfeeding on the prevalence of overweight adolescents and adults needs to be verified by a large-sample longitudinal design in Japan.

Acknowledgments. We gratefully acknowledge the support provided by the municipal office staff and preschool staff of M town.

References

1. Gillman MW, Rifas-Shiman SL, Camargo CA, Jr, Berkey CS, Frazier AL, Rockett HR, Field AE and Colditz GA: Risk of overweight among adolescents who were breastfed as infants. JAMA (2001) 285: 2461–2467.
2. von Kries R, Koletzko B, Sauerwald T, von Mutius E, Barnert D, Grunert V and von Voss H: Breast feeding and obesity: cross sectional study. BMJ (1999) 319: 147–150.
3. Arenz S, Ruckerl R, Koletzko B and von Kries R: Breast-feeding and childhood obesity--a systematic review. Int J Obes Relat Metab Disord (2004) 28: 1247–1256.
4. Owen CG, Martin RM, Whincup PH, Smith GD and Cook DG: Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. Pediatrics (2005) 115: 1367–1377.
5. Harder T, Bergmann R, Kallischnigg G and Plagemann A: Duration of breastfeeding and risk of overweight: a meta-analysis. Am J Epidemiol (2005) 162: 397–403.
6. Gillman MW and Mantzoros CS: Breast-feeding, adipokines, and childhood obesity. Epidemiology (2007) 18: 730–732.
7. World Health Organization: Nutrient adequacy of exclusive breastfeeding for the term infant during the first six months of life. WHO, Geneva (Switzerland) (2001).
8. Equal Employment Children and Families Bureau, Maternal and Child Health Division: Maternal and child health statistics of Japan. Mother and child health organization, Tokyo (1998) (in Japanese).
9. Matsushita Y, Yoshiike N, Kaneda F, Yoshita K and Takimoto H: Trends in childhood obesity in Japan over the last 25 years from the national nutrition survey. Obes Res (2004) 12: 205–214.
10. Equal Employment Children and Families Bureau, Maternal and Child Health Division: Interim Report of Sukoyaka Oyako 21. Ministry of Health, Labour and Welfare, Tokyo (2006) (in Japanese).
11. Kaneko A, Kaneita Y, Yokoyama E, Miyake T, Harano S, Suzuki K, Ibuka E, Tsutsui T, Yuko Yamamoto and Ohida T: Factors associated with exclusive breast-feeding in Japan: for activities to support child-rearing with breast-feeding. J Epidemiol (2006) 16: 57–63.
12. Vobecky JS, Vobecky J and Froda S: The reliability of the maternal memory in a retrospective assessment of nutritional status. J Clin Epidemiol (1988) 41: 261–265.
13. Kark JD, Troya G, Friedlander Y, Slater PE and Stein Y: Validity of maternal reporting of breast feeding history and the association with blood lipids in 17 year olds in Jerusalem. J Epidemiol Community Health (1984) 38: 218–225.
14. Shannon B, Smiciklas-Wright H and Wang MQ: Inaccuracies in self-reported weights and heights of a sample of sixth-grade children. J Am Diet Assoc (1991) 91: 675–678.
15. Strauss RS: Comparison of measured and self-reported weight and height in a cross-sectional sample of young adolescents. Int J

Obes Relat Metab Disord (1999) 23: 904–908.
16. Cole TJ, Bellizzi MC, Flegal KM and Dietz WH: Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ (2000) 320: 1240–1243.
17. Reilly JJ, Armstrong J, Dorosty AR, Emmett PM, Ness A, Rogers I, Steer C and Sherriff A; Avon Longitudinal Study of Parents and Children Study Team: Early life risk factors for obesity in childhood: cohort study. BMJ (2005) 330: 1357.
18. Grummer-Strawn LM and Mei Z; Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System: Does breastfeeding protect against pediatric overweight? Analysis of longitudinal data from the Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System. Pediatrics (2004) 113: e81–86.
19. Hediger ML, Overpeck MD, Kuczmarski RJ and Ruan WJ: Association between infant breastfeeding and overweight in young children. JAMA (2001) 285: 2453–2460.
20. Hediger ML, Overpeck MD, Ruan WJ and Troendle JF: Early infant feeding and growth status of US-born infants and children aged 4–71 mo: analyses from the third National Health and Nutrition Examination Survey, 1988–1994. Am J Clin Nutr (2000) 72: 159–167.
21. Fomon SJ, Filmer LJ, Jr, Thomas LN, Anderson TA and Nelson SE: Influence of formula concentration on caloric intake and growth of normal infants. Acta Paediatr Scand (1975) 64: 172–181.
22. Taveras EM, Rifas-Shiman SL, Scanlon KS, Grummer-Strawn LM, Sherry B and Gillman MW: To what extent is the protective effect of breastfeeding on future overweight explained by decreased maternal feeding restriction? Pediatrics (2006) 118: 2341–2348.
23. Lucas A, Sarson DL, Blackburn AM, Adrian TE, Aynsley-Green A and Bloom SR: Breast vs bottle: endocrine responses are different with formula feeding. Lancet (1980) 1: 1267–1269.
24. Whitehead RG: For how long is exclusive breast-feeding adequate to satisfy the dietary energy needs of the average young baby? Pediatr Res (1995) 37: 239–243.
25. Rolland-Cachera MF, Deheeger M, Akrout M and Bellisle F: Influence of macronutrients on adiposity development: a follow up study of nutrition and growth from 10 months to 8 years of age. Int J Obes Relat Metab Disord (1995) 19: 573–578.
26. Hauner H, Rohrig K and Petruschke T: Effects of epidermal growth factor (EGF), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) on human adipocyte development and function. Eur J Clin Invest (1995) 25: 90–96.
27. Petruschke T, Rohrig K and Hauner H: Transforming growth factor beta (TGF-beta) inhibits the differentiation of human adipocyte precursor cells in primary culture. Int J Obes Relat Metab Disord (1994) 18: 532–536.
28. Desai M and Hales CN: Role of fetal and infant growth in programming metabolism in later life. Biol Rev Camb Philos Soc (1997) 72: 329–348.
29. Burns SP, Desai M, Cohen RD, Hales CN, Iles RA, Germain JP, Going TC and Bailey RA: Gluconeogenesis, glucose handling, and structural changes in livers of the adult offspring of rats partially deprived of protein during pregnancy and lactation. J Clin Invest (1997) 100: 1768–1774.
30. Gluckman P and Hanson M: Developmental Origins of Health and Disease. 1st Ed, Cambridge University Press, New York (2006).