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The Effect of Breastfeeding on Weight Gain in Infants: Results of a Birth Cohort Study

H. Kalies[1], J. Heinrich[2], M. Borte[3,4], B. Schaaf[5], A. von Berg[5], R. von Kries[1], H.-E. Wichmann[2,6], G. Bolte[2,7,8] for the LISA Study Group*

[1]Department of Epidemiology, Institute of Social Pediatrics and Adolescent Medicine, Ludwig-Maximilian-University Munich,
[2]Institute of Epidemiology, GSF National Research Center for Environment and Health, Neuherberg,
[3]Department of Pediatrics, University of Leipzig,
[4]Department of Pediatrics, Municipal Hospital "St. Georg" Leipzig,
[5]Department of Pediatrics, Marien-Hospital Wesel,
[6]Chair of Epidemiology, Institute of Medical Data Management, Biometrics and Epidemiology, Ludwig-Maximilian-University Munich,
[7]Department of Epidemiology, University of Ulm,
[8]Department of Environmental Health, Bavarian Health and Food Safety Authority, Oberscheissheim,
Germany

Abstract: The objective of this study was to examine whether duration of exclusive breastfeeding is associated with elevated weight gain in infants during the first two years of life. In this prospective cohort study 2624 healthy term neonates were followed from birth to age 2 years in 4 German study centres. Data on breastfeeding and potential confounders were gathered by questionnaires. Data on anthropometric measures at birth and age 2 years were obtained from routine standardised medical check up documentation. Odds ratios for the association between breastfeeding and weight gain until age 2 years ($\geq 90^{th}$ sex-specific percentile of the cohort) were calculated by logistic regression, adjusting for age at introduction and composition of solid food, maternal BMI, maternal smoking during pregnancy, socioeconomic status, study centre, birth order and, in unstratified analysis, sex. Children exclusively breastfed for less than 6 months had a greater risk of elevated weight gain at the age of 2 years than children breastfed for 6 months and more (OR [95% CI]: 1.65 [1.17, 2.30]). Duration of exclusive breastfeeding was inversely associated with the risk of elevated weight gain in a strongly duration-dependent way. Those infants who were exclusively breastfed 1 month at the most had twice as often elevated weight gain (OR [95% CI]: 1.99 [1.34, 2.97]) compared to infants breastfed at least 6 months. Our data show that exclusive breastfeeding protects against elevated weight gain during infancy which may be the first step on the pathway of obesity development.

Key words: overweight, children, breast feeding, weight gain, birth cohort study, risk factor

Introduction

Rising prevalences of childhood obesity are becoming a major public health problem in most industrialized countries [5, 14, 22, 25, 28, 32]. Overweight in childhood leads to severe psychological and health problems and predisposes to overweight in adulthood with all its known adverse health outcomes [18, 29, 30, 36]. Since effective therapeutic interventions are both expensive and far from satisfactory [4], the identification of risk factors for childhood obesity and the best time point for preventive strategies is a great public health issue.

Recent studies focussed on early-acting risk factors for later obesity in childhood [31, 33, 37]. Promoting breastfeeding in the context of preventing later overweight would be challenging as breastfeeding is known to offer ideal nutrition and to confer unique immunologic, psychological, growth, and developmental benefits [1]. There are several publications studying the effect of breastfeeding on the development of later overweight [9, 16, 17, 21, 31, 41, 42]. They were mostly derived from cross-sectional studies and some were limited by insufficient consideration of confounders. Recently, a report of a birth cohort study showed an association of breast-feeding and overweight in children

LISA Study Group:
GSF - National Research Center for Environment and Health, Institute of Epidemiology, Neuherberg (Wichmann HE, Heinrich J, Bolte G, Belcredi P, Jacob B, Schoetzau A, Mosetter M, Schindler J, Höhnke A); University of Leipzig, Department of Pediatrics (Borte M, Schulz R, Sierig G, Mirow K, Gebauer C, Schulze B, Hainich J), Institute of Clinical Immunology and Transfusion Medicine (Sack U, Emmrich F); Marien-Hospital Wesel, Department of Pediatrics (von Berg A, Schaaf B, Scholten C, Bollrath C); UFZ - Centre for Environmental Research Leipzig-Halle Ltd., Department of Human Exposure Research and Epidemiology (Herbarth O, Diez U, Lehmann I, Rehwagen M, Schlink U); Ludwig-Maximilian-University Munich, Dr von Haunersches Kinderspital, Division of Pediatric Infectious Diseases and Immunology (Weiss M, Albert M); Friedrich-Schiller-University Jena, Institute of Clinical Immunology (Fahlbusch B), Institute of Occupational, Social and Environmental Medicine (Bischof W, Koch A)

aged 6 years, but it did not investigate dose-response effects [3].

The first two years of life seem to constitute a critical period for the development of obesity in young adults born at full term. Here, the evaluation of overweight in infants by measures such as body mass index might not always be valid since the length of an infant is difficult to assess and may comprise a huge amount of measurement error [11]. In contrast, weight is easier and more reliable to measure and rapid weight gain in early infancy is strongly associated with overweight not only in childhood [12, 33, 37] but also in young adulthood [38].

We therefore analysed elevated weight gain from birth to 2 years as a potential pathway for obesity development later in life. Our objective was to determine if breastfeeding and its duration are associated with a reduced risk of elevated weight gain in infants during the first two years of life using data of a birth cohort with detailed evaluation of breastfeeding and associated risk factors.

Subjects and Methods

Subjects and Data Sources

In the prospective birth cohort study 'LISA' (Influences of life-style factors on the immune system and the development of allergies in childhood), 3097 healthy neonates were enrolled between November 1997 and January 1999 in four German cities (Munich, Leipzig, Wesel, Bad Honnef). Mothers were contacted shortly after the birth of their child in 14 birth clinics. Exclusion criteria of this study were: preterm birth (maturity < 37 gestational weeks), low birthweight (< 2500 g), congenital malformation, symptomatic neonatal infection, antibiotic medication, hospitalisation or intensive medical care during neonatal period and other than German nationality. Moreover, those neonates whose mothers had an immune-related disease (autoimmune disorders, diabetes, hepatitis B), were on long-term medication or abused drugs and/or alcohol were excluded.

From birth until the age of 2 years, data on infants' health, living conditions, and socio-demographic characteristics were gathered at regular time intervals using parental-completed questionnaires and monthly protocols. Data on breastfeeding and the supply of bottle milk and additional food were assessed on a monthly scale in the first year of life. Birthweight and birthlength were obtained from the 'Mutterpass', a standardised preventive medical check up documentation for pregnant women in Germany. Height and weight of the infants at age 3-10 days (U2), 4-6 weeks (U3), 3-4 months (U4), 6-7 months (U5), 10-12 months (U6), and 21-24 months (U7) were recorded at preventive medical check-ups in the well-baby check-up books and were given by the parents in the questionnaires. At age 2 years, height and weight of those infants who did not have data of the U7 were measured during a medical examination. Participation rate at two years of follow-up was 86% (N=2664).

The study was approved by the local ethic committees and carried out in accordance with the institutional guidelines for the protection of human subjects. Written informed consent was obtained from all parents of participating infants.

The study population of this analysis comprised those infants with a follow-up until age 2 years and complete data on breastfeeding and anthropometric measures (N = 2624; 85% of the initial cohort).

Description of Variables

Weight gain at age 2 years was calculated as difference in kilogram between weight at birth and weight at the U7-examination or the study examination divided by age in months at this examination, multiplied with 24 to account for measurements reported before or after the age of exactly 24 months. Elevated weight gain was defined as a weight gain greater or equal than the 90th sex-specific percentile of this cohort.

Duration of exclusive breastfeeding was defined as the number of months breastfed without concomitant feeding of infant's formulas (conventional cow's milk-based or others) and classified a priori in two categories (< 6 months, ≥ 6 months), and for dose-response-analysis in the categories: 0-1 months, 2-3 months, 4-5 months, ≥ 6 months. The composition and timing of the introduction of solid foods was considered separately.

The following potential confounders of the association between duration of breastfeeding and elevated weight gain were considered. Each of these have previously been described as risk factors for childhood overweight or elevated weight gain [3, 21, 40-43]: the age at introduction of solid food was categorised in 1-3 months, 4-6 months and > 6 months. Composition of solid food was obtained in the categories self-made, ready-made or a mixture from both. Self-reported height and weight of the mother before pregnancy were assessed to calculate body mass index (kg/m^2) of the mother. The body mass index of the mother was included in the analysis as a continuous variable. Self-reported maternal smoking during pregnancy was assessed by trimesters and dichotomised in never vs. ever. Birth order of the child in the family was dichotomised in first vs. not first child. Socioeconomic status of the child was obtained by the level of parental education, which was defined by a combination of the highest school degree and professional training. It was dichotomised in low/medium (up to 10 years of schooling and completed apprenticeship at the most) and high/very high (at least 12 years of schooling in combination with an apprenticeship or a university degree). In addition, sex and location of the study centre were considered for the analyses.

Statistical Analysis

The data were described with their median, 10th and 90th percentiles or proportions with 95% confidence intervals. Crude and adjusted odds ratios and their respective confidence intervals were calculated using logistic regression analysis. To receive valid point estimators for the association between breastfeeding and elevated weight gain, potential confounding factors were included in the regression model based on a priori

considerations and after excluding multicollinearity. Interaction terms between the potential confounders (age of introduction of solid food, composition of solid food, maternal smoking during pregnancy, birth order in family, socioeconomic status) and exposure (breastfeeding) were tested by implementing them in the adjusted model. Because of missing values in the potential confounding factors and to facilitate comparisons, incidences and odds ratios were calculated only for those 2377 infants with complete data on all covariates considered in the regression models. Taking the present-day recommendations for the duration of breastfeeding into account, exclusive breastfeeding for 6 months or longer was considered as 'reference' group [46]. Significance of a dose-response trend between duration of exclusive breastfeeding and elevated weight gain was tested by including exclusive breastfeeding as ordinal variable into the regression model. For sensitivity analyses, the alteration of the point estimates by excluding twins (N = 49, 2% of the study population), those infants who had ever been in a hospital during the first two years of life (N = 149, 6%) and infants with low/medium socioeconomic status (N = 649, 25%), respectively, were assessed.

All calculations were carried out with the software package SAS version 8.2 (SAS Institute, Cary, NC).

Results

Characteristics of the Study Subjects

Of all 2624 infants in the study sample, 1347 were boys (51%) and 1277 girls (49%). Median age (10th-90th percentile) at the examination was 24.3 months (23.1-25.0). The characteristics of breastfeeding and all other categorical covariables are given in Table 1.

In total, 24.4% of all infants were exclusively breastfed for the first 0-1 month, 16.3% for 2-3 months, 20.8% for 4-5 months and 38.6% for 6 months or longer. The first category includes those infants never breastfed at all (N = 177; 6.8% of all infants, boys: N = 80, 5.9%, girls: N = 97, 7.6%). The timing of introduction of solid foods was for the most part consistent with the recommendations of the American Academy of Paediatrics for infant feeding [1] with only 9.5% of the infants being fed solid food in the first three months of life. 15.7% of the mothers smoked at

Table 1. Characteristics of the subjects: Exposure of interest and covariables

	All		Boys		Girls	
	N	%	N	%	N	%
Exclusive breastfeeding duration (n = 2624)						
0-1 month	639	24.4	323	24.0	316	24.7
2-3 months	427	16.3	230	17.1	197	15.4
4-5 months	545	20.8	270	20.0	275	21.5
≥ 6 months	1013	38.6	524	38.9	489	38.3
Introduction of solid food (n = 2605)						
1st – 3rd month	248	9.5	120	9.0	128	10.1
4th – 6th month	1795	68.9	930	69.6	865	68.2
> 6th month	562	21.6	286	21.4	276	21.7
Composition of solid food (n = 2554)						
Self made	824	32.3	454	34.4	370	30.0
Ready-made	759	29.7	387	29.3	372	30.2
Mixture	971	38.0	480	36.3	491	39.8
Maternal smoking during pregnancy (n = 2528)						
No	2130	84.3	1108	85.2	1022	83.3
Yes	398	15.7	193	14.8	205	16.7
Birth order in family (n = 2618)						
First child	1480	56.5	767	57.1	713	55.9
Not first child	1138	43.5	576	42.9	562	44.1
Study centre (n = 2624)						
Munich	1307	49.8	690	51.2	617	48.3
Leipzig	785	29.9	377	28.0	408	31.9
Wesel	265	10.1	147	10.9	118	9.2
Bad Honnef	267	10.2	133	9.9	134	10.5
Socioeconomic status (n = 2595)						
Low / medium	649	25.0	311	23.3	338	26.8
High / very high	1946	75.0	1023	76.7	923	73.2

Table 2. Characteristics of the subjects: Weight gain at 24 months.

	All		Boys		Girls	
	median	10th-90th percentile	median	10th-90th percentile	median	10th-90th percentile
Weight at birth (kg) (N = 2624)	3.45	2.91-4.06	3.52	3.00-4.12	3.39	2.87-3.99
Weight at 24 months (kg) (N=2624)	12.30	10.70-14.20	12.70	11.10-14.60	12.00	10.50-13.60
Weight gain at 24 months (kg) (N=2624)	8.78	7.29-10.58	9.09	7.62-10.91	8.45	7.08-10.07

any time during pregnancy and the median BMI (10^{th}-90th percentile) before pregnancy of all 2563 mothers with known body mass index was 21.7 kg/m^2 (19.0-27.3).

Median weight at birth (10^{th}-90^{th} percentile) was 3.5 kg (2.9-4.1) and 12.3 kg (10.7-14.2) at the U7-examination, with girls being slightly lighter than boys. Median weight gain (10^{th}-90^{th} percentile) at 24 months was 8.8 kg (7.3-10.6) (Table 2). There was no association between birthweight and duration of breastfeeding, timing of introduction of solid food, and elevated weight gain at age 24 months. Therefore birthweight was not considered as potential confounder in multivariable analysis. Furthermore, birthlength was not related to weight gain (data not shown).

Risk of Elevated Weight Gain by Duration of Breastfeeding

Crude odds ratio [95% CI] for children being exclusively breastfed for less than 6 months was 1.94 [1.43, 2.63]. After adjustment for all a priori selected potential confounding factors the odds ratio was only slightly lower at 1.65 [1.17, 2.30] (Table 3). Additional adjustment for birthlength, birthweight or gestational age at birth did not change the estimate more than 10%.

The only effect modifier which reached a p-value of less than 0.1 was the interaction term between sex and breastfeeding (p=0.088). But stratification of the analysis by sex revealed that the effect of exclusive breast-

Table 3. Crude and adjusted[a] odds ratios [95% CI] for risk of elevated weight gain at age 24 months (N = 2377).

	Crude odds ratio	Adjusted odds ratio
Exclusive breastfeeding < 6 months	1.94 [1.43, 2.63]	1.65 [1.17, 2.30]
Introduction of solid food		
1 - 3 month	2.02 [1.16, 3.53]	1.31 [0.71, 2.42]
4 - 6 month	2.00 [1.35, 2.97]	1.49 [0.97, 2.28]
> 6 month	1.00 (reference)	1.00 (reference)
Composition of solid food		
self made	1.00 (reference)	1.00 (reference)
ready-made	0.84 [0.62, 1.14]	0.56 [0.39, 0.81]
mixture	0.60 [0.42, 0.85]	0.77 [0.56, 1.06]
Sex female	0.97 [0.74, 1.26]	0.99 [0.75, 1.30]
Maternal BMI	1.04 [1.01, 1.08]	1.03 [1.00, 1.07]
Maternal smoking during pregnancy	1.57 [1.12, 2.19]	1.31 [0.92, 1.86]
Birth order in family: not first child	0.78 [0.59, 1.03]	0.77 [0.58, 1.02]
Study centre		
Munich	1.00 (reference)	1.00 (reference)
Leipzig	0.99 [0.71, 1.37]	0.92 [0.66, 1.30]
Wesel	1.82 [1.21, 2.74]	1.50 [0.98, 2.29]
Bad Honnef	1.23 [0.79, 1.92]	1.05 [0.67, 1.66]
High/very high socio-economic status	0.75 [0.56, 1.01]	1.00 [0.72, 1.38]

[a] adjusted for introduction and composition of solid food, maternal BMI, maternal smoking during pregnancy, socioeconomic status, study centre, birth order and sex.

Table 4. Incidence, crude and adjusted[a] odds ratios [95% CI] for risk of elevated weight gain at age 24 months by duration of exclusive breastfeeding (N = 2377).

		Incidence (%)	Crude odds ratio	Adjusted odds ratio
All				
	0-1 month	14.1 [11.5, 17.0]	2.37 [1.67, 3.36]	1.99 [1.34, 2.97]
	2-3 months	11.9 [9.0, 15.4]	1.85 [1.23, 2.78]	1.61 [1.04, 2.50]
	4-5 months	10.1 [7.7, 12.9]	1.55 [1.05, 2.29]	1.40 [0.93, 2.11]
	≥ 6 months	6.7 [5.3, 8.4]	1.00 (reference)	1.00 (reference)
Boys				
	0-1 month	12.4 [9.0, 16.5]	2.00 [1.22, 3.28]	1.76 [1.01, 3.06]
	2-3 months	12.2 [8.2, 17.1]	1.98 [1.15, 3.41]	1.78 [1.00, 3.19]
	4-5 months	11.9 [8.2, 16.3]	1.79 [1.06, 3.01]	1.60 [0.92, 2.79]
	≥ 6 months	6.7 [4.7, 9.2]	1.00 (reference)	1.00 (reference)
Girls				
	0-1 month	15.8 [12.0, 20.3]	2.80 [1.70, 4.60]	2.35 [1.31, 4.21]
	2-3 months	11.7 [7.5, 17.0]	1.66 [0.89, 3.12]	1.50 [0.77, 2.92]
	4-5 months	8.4 [5.4, 12.3]	1.32 [0.74, 2.37]	1.20 [0.65, 2.23]
	≥ 6 months	6.7 [4.7, 9.3]	1.00 (reference)	1.00 (reference)

[a] adjusted for introduction and composition of solid food, maternal BMI, maternal smoking during pregnancy, socioeconomic status, study centre, birth order and, in unstratified analysis, sex.

feeding on elevated weight gain had the same direction for both sexes, the odds ratios differed only marginally (boys: 1.70 [1.08, 2.69], girls: 1.61 [0.98, 2.67]).

With increasing duration of exclusive breastfeeding a reduction in the incidence of having elevated weight gain at 24 months was observed (Table 4; first column).

Crude and adjusted odds ratios showed a clear dose-dependent effect of the duration of breastfeeding on the risk of having elevated weight gain at 24 months (Table 4). Compared with the reference group comprising subjects who had been exclusively breastfed 6 months or longer, categories of shorter duration were associated with higher odds of elevated weight gain. Adjustment for all a priori selected potential confounding factors slightly reduced this effect. Nevertheless, the dose-response trend remained highly significant ($p < 0.001$). Infants who were exclusively breastfed for 0-1 months only had a 99% higher odds of having elevated weight gain at 24 months; for infants exclusively breastfed 2-3 months and 4-5 months, the risk of having elevated weight gain at 24 months was 61% and 40% higher than for the reference group. The association was more pronounced in girls: stratification of the confounder-adjusted model by sex showed that girls who were exclusively breastfed for 0-1 months only were at a 135% higher risk of having elevated weight gain at 24 months, compared with a 76% higher risk for boys.

Further sensitivity analyses, where the analyses were confined to the study population without twins, to infants who never were in a hospital after birth, and to families with a high or very high socioeconomic status, respectively, did not show relevant changes of the effect estimates (data not shown).

Discussion

Early infancy is supposed to be an important period for the development of obesity in later childhood and adulthood. New etiologic hypotheses about critical periods or pathways for obesity development are under investigation to find the best and earliest starting points for prevention of this prevalent health problem. In early infancy, the valid length of an infant may be difficult to assess [11], which might in particular be true when using data of regular preventive medical check-up books. Weight is easier to measure and has been shown to be a strong determinant of later obesity [12, 33, 37, 38]. In addition, rapid early weight gain has also been linked to increased risks of adulthood type 2 diabetes and cardiovascular disease as well as for cancer [2, 6, 10, 13, 15].

By analysing data of a large prospective birth cohort study in Germany we could show that breastfeeding reduced the risk of elevated weight gain at the age of 2 years. This association was strongly dose-dependent, e.g. with infants never or only 1 month exclusively breastfed having more than twice as often elevated weight gain at 2 years than infants who were exclusively breastfed for 6 months or longer. Other studies have also shown significant differences in weight or weight gain between breast-fed and formula-fed infants, but were limited to the first year of life and did not consider other confounding factors, were small in size, and did not report dose-response effects or relative risks [7]. The protective effect of breastfeeding on the development of later overweight has been shown in cross-sectional studies [17, 21, 26, 41, 42], and recently in a cohort study [3]. The latter showed that breastfeeding for 3 months or more lowered the adjusted risk for overweight and obesity at the age of 6 years significantly by about 50%. However, no dose-response effect of breastfeeding on overweight was calculated.

The strength of our data is that information on exposure and confounding factors was collected close to its origination and in the case of breastfeeding on a

monthly scale, ensuring a high validity and precision of the data. Recall bias will not constitute a problem. Misclassification on weight, however, may be assumed to be random and therefore should not result in systematic errors. After two years of follow-up participation rate was still high (85%), but losses to follow-up at 2 years were unequally distributed and higher among parents of lower socioeconomic status. The effect that the willingness to participate positively correlates with increasing socioeconomic status is also known from other cohort studies [39]. In our study, sensitivity analyses indicated that this did not bias the results.

Early infancy is physiologically a period of very rapid weight gain, with the birthweight doubling in the first 4 to 6 months. It might therefore be a critical period for the development of obesity and the underlying energy regulation mechanisms. Epidemiological studies and animal models describe life-long changes in the appetite regulating centres and in the insulin secretion of rats overfed for short periods after birth [34, 44, 38]. The nonlinear intake during breastfeeding, a lower energy density of human milk compared with formula milk, and a better self control of food consumption in breast-fed children are possible explanations for the observed effect of breast-feeding on weight gain [8, 19, 23, 45]. In addition, breast milk contains bioactive factors that may regulate fat deposition and appetite control [20, 27, 35].

It has been suggested that the inverse association between breastfeeding and growth is likely to be due to reverse causation [24]: differences in weight gain might cause differences in the duration of exclusive breastfeeding, if infants who gain weight faster are supplemented earlier in response to their avid feeding. We controlled for the introduction of solid food in our study with no significant effect on weight gain at 24 months. However, the observational design of our study does not allow to refute this hypothesis.

In summary, the clear duration-dependent effect of breastfeeding on elevated weight gain at 2 years in this prospective study has shown an additional argument for the promotion of exclusive breastfeeding in Germany; further observation of this cohort will fill the gap on the long term impact of early weight gain on overweight in childhood and early adulthood.

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Address for correspondence:
Dr. Joachim Heinrich
GSF National Research Center for Environment and Health
Institute of Epidemiology
Ingolstaedter Landstr. 1
D-85764 Neuherberg, Germany
Tel. +49-89-31874150
Fax +49-89-31873380
Email joachim.heinrich@gsf.de