Nutrition, Metabolism & Cardiovascular Diseases (2016) **26**, 706–712

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Predictors of blood pressure at 7–13 years: The "new millennium baby" study

P. Brambilla [a,*], G. Bedogni [b], A. Pietrobelli [c,d], S. Cianfarani [e,f], C. Agostoni [g]

[a] *Azienda Sanitaria Locale 2, Melegnano, Milan, Italy*
[b] *Liver Research Center, Basovizza, Trieste, Italy*
[c] *Verona University Medical School, Verona, Italy*
[d] *Pennington Biomedical Research Center, Baton Rouge, LA, USA*
[e] *D.P.U.O. "Bambino Gesù" Children's Hospital – "Tor Vergata" University, Rome, Italy*
[f] *Department of Women's and Children's Health, Karolinska Instituten, Stockholm, Sweden*
[g] *Pediatric Clinics, DISCCO, University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

Received 1 November 2014; received in revised form 4 November 2015; accepted 5 November 2015
Available online 1 December 2015

KEYWORDS
Blood pressure;
Body mass index;
Breast-feeding;
Complementary feeding;
Family history;
Lifestyle

Abstract *Background and aims:* The purpose of this study is to evaluate the association between blood pressure (BP) at 7–13 years of age and body mass index (BMI), early feeding, lifestyle indicators, and parental characteristics.
Methods and results: Retrospective plus cross-sectional cohort study was started in 1294 children born in 2000–2004, right from their birth in primary care settings. Early feeding was estimated by measuring breast-feeding (BF) duration, complementary feeding (CF) introduction time, and lifestyle indicators such as daily screen time and weekly extracurricular sports activity time. Parental education, smoking, and obesity-related diseases were also considered. Multivariable linear regression and mediation analysis were used.

CF introduction at 5–6 months of age was a negative predictor of systolic and diastolic BP (mean systolic BP-standard deviation score (SDS) −0.38 [95% CI: −0.47, −0.29] ($p < 0.001$); mean diastolic BP-SDS −0.32 [95% CI: −0.40, −0.24]) ($p < 0.001$); BMI was a positive predictor of systolic and diastolic BP ($p < 0.001$); and parental hypertension was a positive predictor of diastolic BP ($p < 0.05$). Predictors of mean BMI-SDS at 7–13 years of age were birth weight, screen time, and parental obesity and smoking ($p < 0.001$). BF had no effect on BP or BMI. Mediation analysis showed virtually no indication of the effect of CF on BP mediated by BMI.
Conclusions: CF introduction between 5 and 6 months of age could be associated with low BP at 7–13 years. The effect of CF on BP seems to be independent of BMI. Low screen time is associated with low BMI. CF time may play a role in the occurrence of surrogates of noncommunicable disorders in future.

Introduction

Identification of predictors of childhood obesity has been the topic of several studies in recent years, and some longitudinal birth cohort studies have described the role played by prenatal/natal factors and early feeding [1–3]. In this context, particular effort should be made to evaluate modifiable variables, such as breast-feeding (BF) duration and complementary feeding (CF) introduction time [4–9].

* Corresponding author. Via Parada 32, 20854 Vedano al Lambro, Italy. Tel.: +39 3392238772; fax: +39 0295158603.
E-mail addresses: paolo.brambilla3@gmail.com (P. Brambilla), giorgiobedogni@gmail.com (G. Bedogni), angpie@tin.it (A. Pietrobelli), stefano.cianfarani@opbg.net (S. Cianfarani), carlo.agostoni@unimi.it (C. Agostoni).

http://dx.doi.org/10.1016/j.numecd.2015.11.005
0939-4753/

The effects of early nutrition on blood pressure (BP) in childhood is another topic that is worth discussing [10–12]. Moreover, it is difficult to disentangle the individual effects of early feeding and body mass index (BMI) on BP, considering the association between BMI and BP [13].

In order to explore these associations, we included children from the Italian Health System Organization, who are taken care of by family pediatricians (FP), providing longitudinal data collected for 10 scheduled health checks from their birth to 14 years of age, in this study.

The aims of this study were to evaluate: a) predictors of BMI; b) predictors of BP; and c) the potential role of BMI (both final BMI value and BMI trajectories) as mediator to find the association between early feeding and BP in a cohort of children of age 7–13 years, who are assessed from birth by FPs via a standard routine care. The influences of parental characteristics and lifestyle indices of the children were also considered.

Methods

Participation of FPs

The new millennium baby study was a retrospective plus cross-sectional one conducted in 2011, whose participants were a principal investigator (PB) and 13 other FPs working in Lombardia since January 2000 using the same pediatric software (Junior Bit, So.Se.Pe.Srl, Padua, Italy). The FPs were selected based on their experience in data collection for scientific purposes.

Population pathway

Selection, evaluation, and analysis are the three steps involved in population pathway.

Data were automatically extracted from FPs' computers in 2011 according to the following inclusion criteria of children: 1) born at term (≥37 weeks of gestation) and singleton between January 2000 and December 2004; 2) age ≥6.0 and ≤11.0 years; and 3) to have completed the entire set of planned health check with the same FP. Children whose parents had poor Italian-speaking skills were excluded from the study. A total of 2639 children represented the selected population.

Between July 2012 and December 2013 (evaluation period), FPs collected, in selected children and during the next health check, a new measure of height and weight and information via a standard form (BP, pubertal status, lifestyle habits, and feeding modalities during the first year of life), together with parental information (ethnic origin, cardiovascular disease-related history, age, and education level). All the aforementioned child and parental data were collected.

Of the 2639 selected children, 1860 were evaluated in 2012–2013 during a new scheduled health check, according to their actual age. Of the remaining unevaluated 779 children, the actual age was out of the range for a specific health check for 545 (70%) children, 206 (26%) shifted to a general practitioner for health check or changed their residence, and 28 (4%) children did not participate in the planned health check.

A total of 1294 Caucasian children represented the final analyzed sample, after excluding non-Caucasian children ($n = 61$), those with at least one mandatory data missing ($n = 472$), those with a chronic disease that can affect growth and nutrition during the entire period ($n = 21$), and 12 outliers (age out of the range of 7–13 years (9), birth weight <3 standard deviation score (SDS) (2), and actual weight <4 SDS (1)).

A written informed consent was obtained from all parents by FPs. This study was approved by Ethical Committee of University of Milan, Italy.

Anthropometric measures

Weight and height of the children were measured the FPs following standard anthropometric procedures [14]. Weight was measured using an approved scale with a precision of 50 g and periodic calibration, which requires weighing them with minimal dress; height was measured using a stadiometer with a precision of 0.1 cm by removing shoes. The collected anthropometric data were then standardized. BMI was calculated as weight (kg)/height (m^2). BMI-SDS and birth weight-SDS were calculated in accordance with World Health Organization (WHO) reference tables [15].

Systolic and diastolic blood pressures (SBP and DBP) were calculated using standard procedure in accordance with the National Health Blood Pressure Education Program (NHBPEP) [16]. Values of SBP and DBP were measured in triplicate using manual sphygmomanometers, and their mean values were converted to SDS [16].

Pubertal status

During clinical examination, the children were classified into prepubertal (stage 1) and pubertal (stage 2–5) categories according to Tanner [17]. Data on age at menarche were collected in menstruated girls.

Early feeding modalities

Data on feeding practices, recorded in computers as collected in real time during the first 18 months of life, were classified by the same FP according to standardized categories by means of a questionnaire following instructions received during 2011 training. The children were subdivided into six groups based on BF duration: BF ≥12 months, BF ≥9 and <12 months, BF ≥6 and <9 months, BF ≥3 and <6 months, mixed (BF <3 months and infant formula associated), and no BF. CF introduction time was defined as the time of introduction of regular solid food, which was classified into four groups: before 5 months, ≥5 and <6 months, ≥6 and <7 months, and ≥7 months.

Parental history

The following parental information were collected by means of a standardized questionnaire: a) birth year, ethnic origin, and education level of both parents and b) smoking habits, obesity, hypertension, type 2 diabetes mellitus, dyslipidemia, and early cardiovascular disease (<55 years) of at least one of the parents.

Lifestyle indices

Parents were asked to quantify mean daily hours spent by the child on screen-based activities (TV, videogames, PC, etc.) and mean weekly hours spent in extracurricular physical activities, following instructions received during 2011 training. Both activities were reported to last for 0.5–1 h.

Definitions

The International Obesity Task Force BMI cutoff points were used to categorize participants as underweight, normal weight, overweight, or obese [18,19].

BP was classified into SBP-SDS and DBP-SDS, as well as normotensive, pre-hypertensive, and hypertensive BP. Pre-hypertensive children had mean SBP and/or DBP between ≥90th and <95th percentile for age, gender, and height, whereas hypertensive children had mean SBP and/or DBP ≥95th percentile [16].

Statistical analysis

Most continuous variables had non-Gaussian distributions and are reported in percentiles.

The association between early feeding and outcomes of interest (e.g., BMI, SBP, and DBP) was evaluated using multivariable linear regression [20]. Heteroscedasticity and multicollinearity were identified by standard methods. Robust confidence interval was calculated for all models because of the evidence of heteroscedasticity. Model fit was assessed by standard methods. Multivariable linear regression models with BMI-SDS as outcome had the following predictors: 1) sex (0 = female; 1 = male); 2) age (years); 3) birth weight (SDS); 4) BF (0 = no, partial, or <6 months; 1 = exclusive for ≥6 months); 5) CF (0 = not started between 5 and 6 months; 1 = started between 5 and 6 months); 6) extracurricular physical activity (hours/weeks); 7) screen time (hours/days); 8) mother's school degree (0 = elementary or middle; 1 = high school or university); 9) smoking parent (0 = no; 1 = yes); and 10) obese parent (0 = no; 1 = yes). Multivariable linear regression models with SBP-SDS and DBP-SDS as outcomes had the following two additional predictors: 11) BMI-SDS; and 12) hypertensive parent (0 = no; 1 = yes).

We tested whether the effect of early feeding on BP is mediated by BMI using the general counterfactual-based approach developed for the analysis of causal mediation by Imai [21]. The following three measures of BMI as mediators were used: 1) BMI calculated during the same visit when BP was measured (present BMI); 2) mean BMI, calculated as the mean of all repeated measures of BMI available between 0 years of age and study visit; and 3) slope of BMI, calculated as the child-specific slope of a BMI–age regression line using repeated measures of BMI available between 0 years of age and study visit. The theoretical advantage of the mean BMI and the slope of BMI over the present BMI is that they provide information on the stability of BMI over time.

Statistical analysis was performed using Stata version 13.1, together with the user-written command *medsens* [22].

Results

Table 1 reports the general features and Table 2 the feeding modalities, lifestyle, and parental characteristics of the 1294 studied children. Mean combined weight and height measures of each child ranged from 12.1 to 19.2 among FPs, with measures being always ≥10 for all children. Of the total 1294 children, 72.3% were in their prepubertal stage at the time of study, 36 (2.8%) obese, 226 overweight (17.5%), 93 underweight (7.2%), 63 (4.9%) pre-hypertensive, and 27 (2.1%) were hypertensive.

None of the children were introduced CF before 4 or after 8 months. Screen time and extracurricular sports activity time were inversely proportional (r −0.12, $p < 0.001$). The majority of parents had educational levels of high school or university degree (77.9% of mothers and 68.2% of fathers).

Figure 1 shows a plot of regression coefficients obtained at multivariable linear regression of BMI-SDS, SBP-SDS, and DBP-SDS against the predictors of interest.

Predictors of BMI (panel 1 Fig. 1)

An increase of 1 year of age was associated with a decrease of 0.05 (95% CI −0.09 to −0.01, $p < 0.05$) SDS of BMI; an increase of 1 SDS of birth weight was associated with an increase of 0.12 SDS (0.05–0.18, $p < 0.001$); an increase of 1 h/day of screen time was associated with an increase of 0.11 SDS (0.05–0.18, $p < 0.001$); having a smoking parent was associated with an increase of 0.24 SDS (0.11–0.37, $p < 0.001$); and having an obese parent was associated with an increase of 0.69 SDS of BMI (0.53–0.85, $p < 0.001$).

Predictors of SBP (panel 2 Fig. 1)

An increase of 1 SDS of birth weight was associated with a decrease of 0.06 (95% CI −0.11 to −0.01, $p < 0.05$) SDS of SBP; an increase of 1 SDS of BMI was associated with an increase of 0.17 SDS (0.12–0.21, $p < 0.001$); having introduced CF between 5 and 6 months was associated with a decrease of 0.38 SDS (−0.47 to −0.29, $p < 0.001$); and having a mother with low education was associated with a decrease of 0.13 SDS of SBP (−0.24 to −0.01, $p < 0.05$).

Table 1 Measurements of the children.

	Girls				Boys				All			
	N	P_{50}	P_{25}	P_{75}	N	P_{50}	P_{25}	P_{75}	N	P_{50}	P_{25}	P_{75}
Age (years)	655	9.8	8.6	11.0	639	9.8	8.5	10.9	1294	9.8	8.5	11.0
Gestational age (months)	655	39.9	38.5	40.0	639	40.0	39.0	40.0	1294	40.0	38.7	40.0
Birth weight (kg)	655	3.2	3.0	3.5	639	3.4	3.1	3.6	1294	3.3	3.0	3.6
Birth weight (SDS)	655	−0.02	−0.54	0.67	639	0.03	−0.52	0.60	1294	0.01	−0.52	0.62
Weight (kg)	655	33.3	28.0	40.1	639	33.0	28.0	40.0	1294	33.0	28.0	40.0
Height (m)	655	1.38	1.31	1.47	639	1.39	1.31	1.46	1294	1.38	1.31	1.46
Height (SDS)	655	0.22	−0.46	0.90	639	0.37	−0.29	1.04	1294	0.28	−0.36	0.95
BMI (kg/m^2)	655	17.4	15.6	19.4	639	17.1	15.8	19.1	1294	17.3	15.7	19.2
BMI (SDS)	655	0.31	−0.40	1.14	639	0.41	−0.31	1.28	1294	0.38	−0.36	1.21
Waist (cm)	655	61.0	57.0	67.0	639	62.0	58.0	66.0	1294	61.5	57.0	66.5
Waist/height (cm/cm)	655	0.45	0.42	0.48	639	0.44	0.42	0.47	1294	0.44	0.42	0.47
SBP (mmHg)	655	104.0	95.0	110.0	639	102.0	98.0	110.0	1294	104.0	95.0	110.0
SBP (SDS)	655	0.08	−0.48	0.68	639	0.06	−0.50	0.60	1294	0.06	−0.48	0.65
DBP (mmHg)	655	60.0	55.0	66.0	639	60.0	55.0	66.0	1294	60.0	55.0	66.0
DBP (SDS)	655	−0.05	−0.46	0.50	639	−0.06	−0.44	0.53	1294	−0.06	−0.46	0.51
Age at menarche (years)	40	11.0	10.7	11.4	0	–	–	–	40	11.0	10.7	11.4
Father's age (years)	655	34.6	31.8	37.3	639	34.5	31.6	37.2	1294	34.5	31.8	37.2
Mother's age (years)	655	31.9	29.5	34.9	639	32.1	29.3	34.7	1294	32.0	29.4	34.8

Abbreviations: BMI = body mass index; DBP = diastolic blood pressure; N = number of children; P_{25} = 25th percentile; P_{50} = 50th percentile; P_{75} = 75th percentile; SBP = systolic blood pressure; SDS = standard deviation scores.

Predictors of DBP (panel 3 Fig. 1)

An increase of 1 SDS of age was associated with an increase of 0.04 (95% CI 0.01–0.07, $p < 0.01$) SDS of DBP; an increase of 1 SDS of BMI was associated with an increase of 0.10 SDS (0.06–0.14, $p < 0.001$); having introduced CF between 5 and 6 months was associated with a decrease of 0.32 SDS (−0.40 to −0.24, $p < 0.001$); having a mother with low education was associated with a decrease of 0.12 SDS (−0.22 to −0.02, $p < 0.05$); an increase of 1 SDS of birth weight was associated with a decrease of 0.05 SDS (95% CI −0.09 to −0.001, $p < 0.05$); and having an hypertensive parent was associated with an increase of 0.11 SDS of DBP (0.01–0.22, $p < 0.05$).

BF duration did not show association with any outcome even when other BF categorizations were compared, or when children with BF ≥12 months were compared with those of no BF (data not provided).

Mediation analysis

The general mediation model used to check whether BMI (M) mediates the effect of early feeding practices (X) on BP (Y) is depicted in Fig. 2.

The 12 mediation models (M1–M12) used to evaluate such association are presented in Table 3. Even the statistically significant direct effect of BF on BP was very small. The direct effect was higher for CF than for BF, with an inverse association between BP and CF, as expected from multivariable linear analyses. However, the proportion of the effect of CF on BP mediated by BMI was extremely low and negligible on biological grounds. Thus, no convincing evidence of mediation of BF or CF on BP via BMI was found. This finding was consistent across three different measures of BMI.

Discussion

This study demonstrates the effects of birth weight, parental obesity, and parental smoking on BMI in childhood, together with the effect of screen time. Studies related to this topic can be found elsewhere [23,24]. Screen time is a key-point for an intervention aimed to reduce sedentary behavior. Because of the difficulty in scoring, independent associations of extracurricular physical activity with BMI, reported by other studies [25], were not found. However, in our study population, screen time and physical activity were inversely correlated.

Concerning predictors of BP, our data confirm the crucial role played by BMI on both SBP and DBP, as found elsewhere [13]. An independent effect of parental hypertension on DBP was detected in our study population. On the contrary, we did not find any association between BF duration and childhood BP. The collected data are reliable, as information on early feeding were obtained in real time and categorized by a standardized procedure. The composition of cohorts of this study was closer to breast milk (particularly protein content and fat quality) when compared with those of the previous studies [10,26]. A protective effect of BF could have been more easily detected in children from lower social classes. As breast milk has many other important benefits for both infant and mother, it should be supported in any case.

A new finding from the study is the possible protective role found for CF introduction between 5 and 6 months. Children with CF introduction within this range had mean SBP and DBP lowered by 0.38 and 0.32 SDS, respectively, regardless of BF duration. This finding could suggest a possible ideal window for CF introduction associated with BP in childhood. It is intriguing that both early and late CF

Table 2 Feeding modalities, lifestyle habits, and parental history of disease.

Breast-feeding	*n*	%
Never	243	18.8
Mixed	241	18.6
≥3 and <6 months	164	12.7
≥6 and <9 months	263	20.3
≥9 and <12 months	171	13.2
≥12 months	212	16.4
Complementary feeding introduction		
≥4 and <5 months	64	5.0
≥5 and <6 months	751	58.0
≥6 and <7 months	425	32.8
≥7 and <8 months	54	4.2
Mother's school degree		
Elementary	2	0.2
Middle	284	21.9
High	761	58.8
University	247	19.1
Father's school degree		
Elementary	10	0.8
Middle	401	31.0
High	654	50.5
University	229	17.7
Screen time		
<1 h/day	18	1.4
≥1 and <2 h/day	360	27.8
≥2 and <3 h/day	600	46.4
≥3 and <4 h/day	216	16.7
>4 h/day	100	7.7
Extracurricular physical activity		
None	113	8.7
<1 h/week	132	10.2
≥1 and <2 h/week	346	26.7
≥2 and <3 h/week	252	19.5
≥3 and <4 h/week	229	17.7
≥4 h/week	222	17.2
Parental smoking	416	32.1
Parental dyslipidemia	224	17.3
Parental obesity	219	16.9
Parental hypertension	178	13.8
Parental early CVD	39	3.0
Parental diabetes	16	1.2

introduction might be a risk factor for hypertension, a U-shaped association.

The mediation analysis conducted in our study population showed no evidence of mediation of CF introduction time on BP via BMI. This indicates that the association between CF introduction time and BP in childhood is only minimally mediated by an effect on BMI. Other possibly implicated mechanisms were sodium intake and effects on appetite and food choice during childhood and more. Finally, the life-course effects may progressively follow the earlier programming effects through the "accumulation of risk" phenomena [27].

Limitations

The new millennium baby study was conducted to facilitate ideal follow-up of children by their FP and implement multiple preventive counseling sessions. As the proportion of parents included in this study had a higher rate of school degrees than national rates, it is clear that an

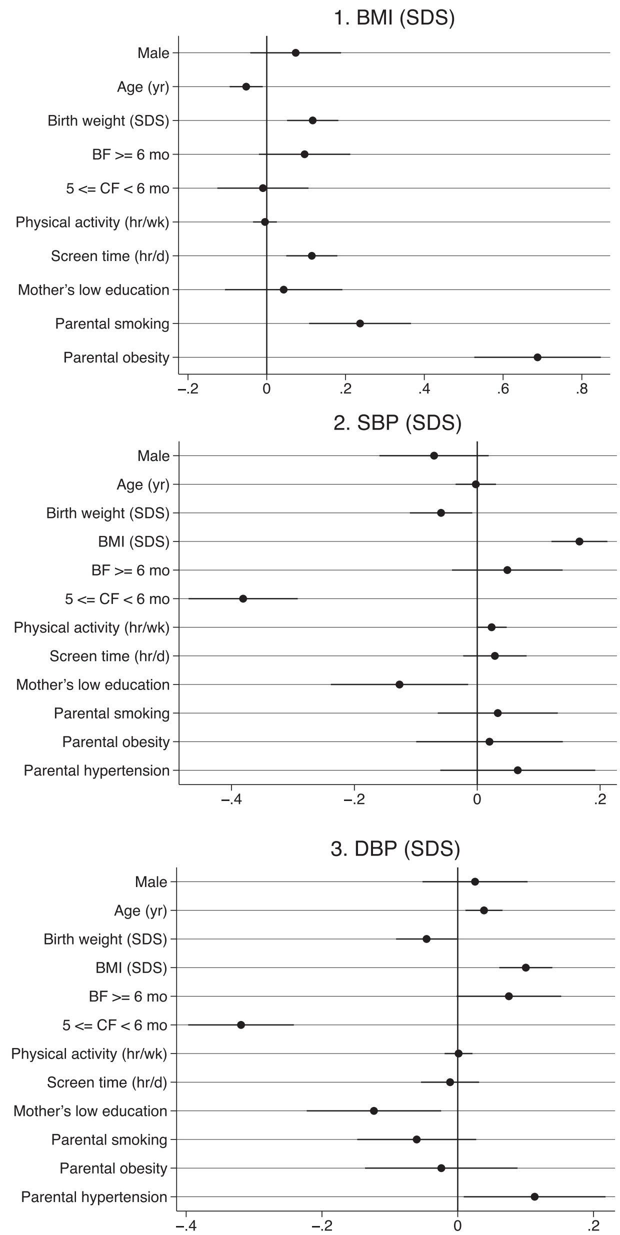

Figure 1 Regression coefficients and robust 95% confidence intervals of BMI-SDS (panel 1), SBP-SDS (panel 2), and DBP-SDS (panel 3) versus predictors of interest, from multivariable linear regression.

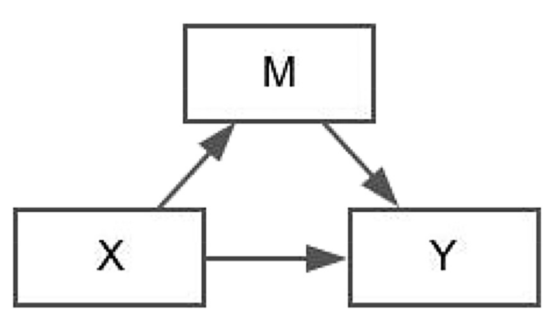

Figure 2 The general mediation model used to test whether BMI (M) mediates the effect of early feeding practices (X) on BP (Y).

Table 3 Mediation analysis of the effects of early feeding on Blood Pressure via Body Mass Index (see Fig. 2 for the graphical depiction of the mediation model and see Statistical analysis for details).

	Outcome (Y)	Predictor (X)	Mediator (M)	Direct effect			Total effect			Proportion of total effect mediated		
				EST	LCI95	UCI95	EST	LCI95	UCI95	EST	LCI95	UCI95
M1	SBP (SDS)	BF ≥ 6 months	BMI (SDS)	0.094	0.002	0.185	0.099	0.005	0.194	0.047	0.020	0.267
M2	SBP (SDS)	BF ≥ 6 months	mBMI (SDS)	0.090	−0.006	0.179	0.098	0.001	0.186	0.076	0.030	0.392
M3	SBP (SDS)	BF ≥ 6 months	sBMI (SDS)	0.101	0.007	0.194	0.100	0.006	0.193	−0.012	−0.076	−0.006
M4	DBP (SDS)	BF ≥ 6 months	BMI (SDS)	0.120	0.041	0.199	0.123	0.041	0.204	0.021	0.012	0.056
M5	DBP (SDS)	BF ≥ 6 months	mBMI (SDS)	0.119	0.038	0.198	0.123	0.043	0.204	0.034	0.020	0.094
M6	DBP (SDS)	BF ≥ 6 months	sBMI (SDS)	0.123	0.043	0.203	0.123	0.044	0.203	−0.005	−0.013	−0.003
M7	SBP (SDS)	5 ≤ CF < 6 months	BMI (SDS)	−0.384	−0.475	−0.295	−0.387	−0.480	−0.293	0.008	0.006	0.010
M8	SBP (SDS)	5 ≤ CF < 6 months	mBMI (SDS)	−0.380	−0.472	−0.288	−0.388	−0.481	−0.295	0.021	0.017	0.028
M9	SBP (SDS)	5 ≤ CF < 6 months	sBMI (SDS)	−0.388	−0.481	−0.296	−0.389	−0.482	−0.297	0.003	0.002	0.004
M10	DBP (SDS)	5 ≤ CF < 6 months	BMI (SDS)	−0.326	−0.405	−0.248	−0.328	−0.409	−0.248	0.005	0.004	0.007
M11	DBP (SDS)	5 ≤ CF < 6 months	mBMI (SDS)	−0.324	−0.404	−0.246	−0.328	−0.407	−0.249	0.013	0.010	0.017
M12	DBP (SDS)	5 ≤ CF < 6 months	sBMI (SDS)	−0.328	−0.408	−0.249	−0.328	−0.407	−0.249	0.002	0.001	0.002

Abbreviations: BF = breast-feeding; BMI = body mass index; CF = complementary feeding; DBP = diastolic blood pressure; EST = point estimate of the effect; LCI95 = 95% lower confidence interval of the effect; mBMI = mean of the repeated measures of BMI collected between the age of 0 years and age at the study time; sBMI = slope of the BMI—age regression line calculated using the repeated measures of BMI collected between the age of 0 years and age at the study time; SBP = systolic blood pressure; SDS = standard deviation score; UCI95 = 95% upper confidence limit of the effect. M1—12 = Model number.

economically privileged sector was selected as the study population. Consequently, some families with poor compliance to recommendations were automatically excluded, and our findings cannot be generalized. This selection bias is probably the main reason for the lack of association found for some predictors, as opposed to other studies [28], and an explanation for the low prevalence of obesity and hypertension was found in the sample. The fact that some associations could be present in less-advanced conditions cannot be ignored.

Another limitation is the lack of information concerning nutritional intake for the rest of the pediatric ages. A protective effect of BF on adult obesity could be found only when nutritional data at 2 years of age were available [29].

Conclusions

CF introduction between 5 and 6 months was associated with lower BP values. This association was minimally mediated by BMI. BF duration was not associated with both BMI and BP. These data suggest that nutrition habits in the first year need to be reassessed for future metabolic consequences.

Screen time and CF introduction between 5 and 6 months of age seem to be important for preventing obesity and hypertension.

Source of funding or sponsor

None.

Conflict of interest

The authors have no conflict of interest to disclose.

Acknowledgments

The authors thank the following members of the new millennium baby study group: Gigliola Biondelli, Monica Bosco, Lorenza Crippa, Riccardo De Angelis, Alessandra Florioli, Lorenzo Fraietta, Giuseppe Lietti, Paola Manzoni, Valeria Mazzoleni, Marcella Petrone, Patrizia Picco, Ambrogina Pirola, and Ferdinando Ragazzon.

References

[1] Rudolf M. Predicting babies' risk of obesity. Arch Dis Child 2011; 96(11):995—7.

[2] Fraser A, Macdonald-Wallis C, Tilling K, Boyd A, Golding J, Davey Smith G, et al. Cohort profile: the Avon longitudinal study of parents and children: ALSPAC mothers cohort. Int J Epidemiol 2013;42(1):97—110.

[3] Center for Longitudinal Studies. Millennium cohort study (MCS). 2010. http://www.cls.ioe.ac.uk/studies.asp?section=000100020001 [accessed April 2015].

[4] Casazza K, Fontaine KR, Astrup A, Birch LL, Brown AW, Bohan Brown MM, et al. Myths, presumptions, and facts about obesity. NEJM 2013;368(5):446—54.

[5] Kramer MS, Fombonne E, Igumnov S, Vanilovic I, Matush L, Mironova E, et al. Effects of prolonged and exclusive breastfeeding on child behavior and maternal adjustment: evidence from a large, randomized trial. Promotion of breastfeeding intervention trial (PROBIT) study group. Pediatrics 2008;121(3):e435—40.

[6] Yan J, Liu L, Zhu Y, Huang G, Wang PP. The association between breastfeeding and childhood obesity: a meta-analysis. BMC Public Health 2014;14:1267.

[7] Fewtrell MS, Lucas A, Morgan JB. Factors associated with weaning in full term and preterm infants. Arch Dis Child Fetal Neonatal Ed 2003;88(4):F296—301.

[8] Schack-Nielsen L, Sørensen TI, Mortensen EL, Michaelsen KF. Late introduction of complementary feeding, rather than duration of breastfeeding, may protect against adult overweight. Am J Clin Nutr 2010;91(3):619—27.

[9] Baker JL, Michaelsen KF, Rasmussen KM, Sørensen TI. Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. Am J Clin Nutr 2004;80(6):1579—88.

[10] Martin RM, Gunnell D, Smith GD. Breastfeeding in infancy and blood pressure in later life: systematic review and meta-analysis. Am J Epidemiol 2005;161(1):15–26.
[11] Kramer MS, Matush L, Vanilovich I, Platt RW, Bogdanovich N, Sevkovskaya Z, et al. Effects of prolonged and exclusive breast-feeding on child height, weight, adiposity, and blood pressure at age 6.5 y: evidence from a large randomized trial. Am J Clin Nutr 2007;86(6):1717–21.
[12] Kwok MK, Leung GM, Schooling CM. Breastfeeding and adolescent blood pressure: evidence from Hong Kong's "children of 1997" birth cohort. Am J Epidemiol 2013;178(6):928–36.
[13] Sorof JM, Lai D, Turner J, Poffenbarger T, Portman RJ. Overweight, ethnicity, and the prevalence of hypertension in school-aged children. Pediatrics 2004;113(3 pt 1):475–82.
[14] Lohman TG, Roche AF, Martorell R. In: Lohman, Roche, Martorell, editors. Anthropometric standardization reference manual. Champaign IL Human Kinetics Books; 1988.
[15] http://www.who.int/childgrowth/ [accessed July 2015].
[16] National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555–76.
[17] Tanner JM. Growth and maturation during adolescence. Nutr Rev 1981;39(2):43–55.
[18] Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition of child overweight and obesity worldwide: international survey. BMI 2000;320(7244):1–6.
[19] Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. BMJ 2007;335(7612):194 [Epub 2007 Jun 25].
[20] Weisberg S. Applied linear regression. Hoboken, NJ: Wiley-Interscience; 2005.
[21] Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. Psychol Methods 2010;15:309–34.
[22] Hicks R, Tingley D. Causal mediation analysis. Stata J 2011;11: 605–19.
[23] Griffiths LJ, Hawkins SS, Cole TJ, Dezateux C, Millennium Cohort Study Child Health Group. Risk factors for rapid weight gain in preschool children: findings from a UK-wide prospective study. Int J Obes 2010;34(4):624–32.
[24] Birbilis M, Moschonis G, Mougios V, Manios Y, Healthy Growth Study Group. Obesity in adolescence is associated with perinatal risk factors, parental BMI and sociodemographic characteristics. Eur J Clin Nutr 2013;67(1):115–21.
[25] Ekelund U, Brage S, Froberg K, Harro M, Anderssen SA, Sardinha LB, et al. TV viewing and physical activity are independently associated with metabolic risk in children: the European Youth Heart Study. PLoS Med 2006;3(12):e488.
[26] Owen CG, Whincup PH, Gilg JA, Cook DG. Effect of breast feeding in infancy on blood pressure in later life: systematic review and meta-analysis. BMJ 2003;327(7425):1189–95.
[27] Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. J Epidemiol Community Health 2003;57:778–83.
[28] Pei Z, Flexeder C, Fuertes E, Thiering E, Koletzko B, Cramer C, et al. Early life risk factors of being overweight at 10 years of age: results of the German birth cohorts GINIplus and LISAplus Study Group. Eur J Clin Nutr 2013;67(8):855–62.
[29] Peneau S, Hercberg S, Rolland-Cachera MF. Breastfeeding, early nutrition, and adult body fat. J Pediatr 2014;164:1363–8.