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

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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 lower 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].

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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 newly scheduled health check, according to their actual age. Of the remaining unmeasured 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 (m²). 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. Prehypertensive 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).
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 −0.01, \( p < 0.05 \)); 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 \( \geq 12 \) 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...
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

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

<table>
<thead>
<tr>
<th>Breast-feeding</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>243</td>
<td>18.8</td>
</tr>
<tr>
<td>Mixed</td>
<td>241</td>
<td>18.6</td>
</tr>
<tr>
<td>≥3 and &lt;6 months</td>
<td>164</td>
<td>12.7</td>
</tr>
<tr>
<td>≥6 and &lt;9 months</td>
<td>263</td>
<td>20.3</td>
</tr>
<tr>
<td>≥9 and &lt;12 months</td>
<td>171</td>
<td>13.2</td>
</tr>
<tr>
<td>≥12 months</td>
<td>212</td>
<td>16.4</td>
</tr>
</tbody>
</table>

**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 obesity | 224 | 17.3 |
| Parental hypertension | 219 | 16.9 |
| Parental early CVD | 178 | 13.8 |
| Parental diabetes | 39  | 3.0  |

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**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).
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 Frietita, Giuseppe Lietti, Paola Manzoni, Valeria Mazzoleni, Marcella Petrone, Patrizia Picco, Ambrogina Pirolo, and Ferdinando Ragazzon.

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