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Early rapid weight gain, parental body mass index and the association with an increased waist-to-height ratio at 5 years of age

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Abstract

Background/Objectives

Obesity-related adverse health consequences are closely associated with abdominal obesity. Risk factors for overweight and obesity have been studied but there is a lack of information regarding risk factors for abdominal obesity, especially in the preschool population. The aim of the present study was to examine early life risk factors for an increased waist-to-height ratio (WHtR) in children at five years of age and, in addition, to investigate if these risk factors also were associated with overweight or obesity.

Subjects/Methods

The study population comprised 1,540 children from a population-based longitudinal birth cohort study that included 2,666 Swedish children. The children were included if they had complete growth data for the analyses used in this study. Children were classified as having WHtR standard deviation scores (SDS) $\geq$ 1 or < 1 at five years of age, according to Swedish reference values, and as having body mass index standard deviation scores (BMI_{SDS}) for overweight/obesity, or normal weight/underweight according to the International Obesity Task Force criteria. Associations between child-related, socioeconomic status-related, parental health-related and nutrition- and feeding practice-related factors during the first two years and a $WHtR_{SDS} \geq 1$ or a BMI_{SDS} for overweight/obesity at five years were investigated with logistic regression analyses.

Results

At five years of age, 15% of the children had $WHtR_{SDS} \geq 1$ and 11% had overweight or obesity. In multivariable analyses, rapid weight gain (RWG) during 0–6 months (OR: 1.90, 95% CI: 1.23–2.95, p = 0.004), maternal pre-pregnancy BMI (1.06, 1.01–1.11, p = 0.019) and

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paternal BMI (1.11, 1.01–1.21, p = 0.028) were associated with $WHtR_{SDS \geq}$ 1. RWG during
0–6 months (2.53, 1.53–4.20, p<0.001), 6–12 months (2.82, 1.37–5.79, p = 0.005), and
maternal pre-pregnancy BMI (1.11, 1.06–1.17, p<0.001) were associated with overweight
or obesity.

Conclusions

Early risk factors, including rapid weight gain, are associated with increased $WHtR_{SDS}$ and
overweight or obesity at 5 years of age. Preventive interventions should target early RWG
and parental overweight and obesity.

Introduction

Rates of overweight and obesity in children have increased during the last decades, suggesting
future global health challenges. In 1990, 32 million children below 5 years of age had over-
weight or obesity and in 2016 this number had increased to over 41 million [1]. Excess weight
in childhood is associated with adverse health consequences later in life, such as metabolic syn-
drome, diabetes, hypertension and cardiovascular diseases [2]. In both adults and children,
obesity-related adverse health consequences are closely associated with abdominal obesity [3,
4], and although these associations need to be further investigated in the preschool population,
early signs of metabolic syndrome have been identified as early as during the preschool years
[5, 6].

There is no consensus regarding the best measure to identify abdominal obesity in pre-
school children, but waist-to-height ratio (WHtR) and waist circumference (WC) are two
anthropometric measures that have been suggested as good surrogate measures of abdominal
obesity and associated cardiometabolic risk in children and adolescents [7–9]. Both methods
are easy to perform without any advanced equipment [10, 11].

Although a significant number of studies have examined early life risk factors for over-
weight and obesity in both childhood and adulthood [12–16], few have investigated risk factors
for abdominal obesity, especially in children below six years of age. Given that abdominal obe-
sity has been identified as an important metabolic risk factor, and because these risk factors
are increasingly observed in children at younger ages [5, 6], the field needs to be further
investigated.

Previous research focusing on abdominal obesity in older children has shown that rapid
weight gain (RWG) during the first two years of a child's life has been associated with both
abdominal obesity in adults [17] and overweight or obesity later in life [12, 16, 18]. The reasons
for this accelerated weight gain are somewhat unclear, but it is known that breastfed infants
have a slower weight-gain trajectory than formula-fed infants, at least in Western settings [19].
One suggested reason for this is differences in milk composition between formula milk and
breast milk; for example, protein intake associated with formula milk feeding has been shown
to promote RWG [19]. Added sugars in infant formula have also been associated with RWG
[20]. In previous research, we have shown that bottle feeding at birth, 3–4 and at six months
and night-time meals containing formula milk at 3–4 months were associated with RWG
between 0 and six months [21]. Additionally, bottle size, risk of over-feeding, infant-initiated
bottle emptying [22] and feeding on schedule [23] have been suggested as possible antecedents
of RWG. The relationship between RWG and either gut microbiome or sleep-wake cycles are
also being investigated [24].

In addition to RWG, other risk factors for abdominal obesity have been examined; low birth weight has been associated with abdominal obesity, measured by WHtR, in children 3–16 years of age [25], and maternal gestational weight gain has been associated with abdominal obesity in children aged 2–9 [26]. In children aged 8 to 18 years, maternal pre-pregnancy body mass index (BMI) has been associated with abdominal obesity, measured by WC [27]. Female sex is another factor that has been associated with abdominal obesity. Griffiths *et al.* found that 5-year-old UK girls born at the beginning of the millennium had marginally higher waist circumference than boys, and that the girls' waist circumference had risen more steeply, when compared to children born in the 1970s and 1980s [28].

Regarding risk factors for overweight or obesity other than RWG, higher birth weight [29, 30], maternal pre-pregnancy BMI [12, 29] and maternal gestational weight gain [31, 32] have all been associated with later overweight or obesity in children. Infant nutrition, such as consumption of infant formula [19, 33], milk cereal drink (MCD), a complementary product often served from a bottle and recommended from the age of six months in Sweden, [34] and feeding practices from feeding bottles [22], have all been associated with overweight or obesity later in life. Socioeconomic factors, such as maternal low educational level and smoking have been associated with poorer eating habits [35], and more television watching [36], both of these may lead to excess weight in children. The impact of paternal influences on childhood overweight have been studied, but their effects are still unclear [12].

Given the associations between abdominal obesity and cardiometabolic risk factors in children, and the knowledge gap regarding risk factors for abdominal obesity in the preschool population, the aim of the present study was to examine early risk factors for an increased WHtR at five years of age, in a cohort of Swedish preschool children. A second aim was to investigate if these risk factors also were associated with overweight or obesity at the same age, as measured by BMI.

Subjects and methods

Study participants and design

This study is part of the longitudinal and population-based birth cohort study, the Halland Health and Growth Study (H^2GS). H^2GS included at baseline 2,666 children– 1,349 males and 1,317 females–born between October 1, 2007 and December 31, 2008 in the county of Halland, in the south-western part of Sweden. During the data collection period, there were 3,860 births in the county. All children were eligible to take part in the study, without any exclusions, and 69% of the families agreed to participate. The families were recruited when they visited child health care centres (CHCCs) for the first time. The coverage for CHCCs in Sweden is approximately 98.4% of children below six years of age. Weight, height and WC were measured on nine occasions during the first five years, with the first measurement point between 0 and 45 days after birth. In conjunction with each measurement point, the parents filled in questionnaires regarding their child's nutrition, health and lifestyle, along with background data on the family. The study protocol, recruitment process and the representativeness of the sample have been reported in detail elsewhere [37]. In the current study, 1,540 of the 2,666 children were selected, based on if they had complete growth data for the analyses used in this study. This study was approved by the regional ethical review board in Lund, Sweden (Study no.: 299/2007). Written informed consent was obtained from the parents of all the participating children.

Only children with measurements of weight, length and WC at five years of age and information regarding maternal gestational age were included in this study, and those without that information (437 males and 385 females) were excluded. We also excluded children measured
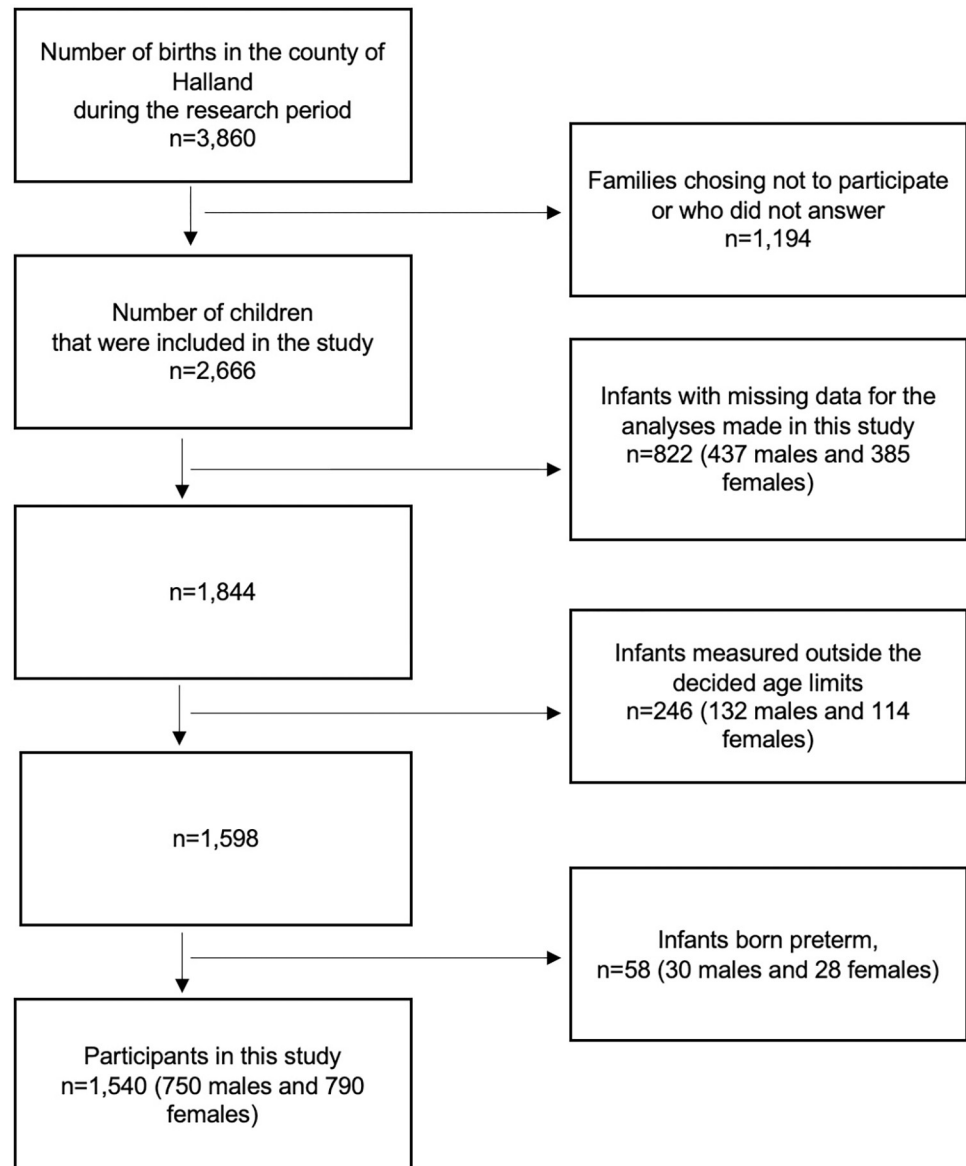
Fig 1. Flowchart of the participants in the study.

outside our set age limit of ± 1.5 months below 12 months of age (except at 0–1 month, where 0–45 days was used instead) and ± 2.5 months thereafter (132 males and 114 females). Additionally, children born preterm (30 males and 28 females) were excluded. The total remaining study population consisted of 750 males and 790 females (Fig 1). A slightly higher proportion of the excluded children (1,126) were male, 53% versus 49%, and had a slightly lower birth weight, 3,495 g versus 3,580 g.

Auxology and classifications

For gestational age at birth, the date of the mother's last menstrual period, confirmed by antenatal ultrasound reports, was used. Information regarding birth weight, birth length, sex and gestational age was collected from the Swedish National Medical Birth Register. Birth length

was reported to the nearest half centimeter and birth weight was reported to the nearest gram. Anthropometric measurements were performed during the first 45 days after birth, and then at 3–4, 6, 12, 18, 24, 36, 48 and 60 months, by trained child health care nurses at the CHCCs. Infants below 15 kg were weighed without clothes, in a supine position on baby scales. Children above 15 kg were weighed on mechanical or electronic step scales in a standing position without shoes and wearing underwear. Stadiometers were used to measure height. In children below two years of age, height was measured in a supine position and, after two years of age, height was measured in a standing position without shoes. WC was measured without clothes and midway between the lowest rib and the top of the iliac crest, at the end of a gentle expiration. For children below two years of age, WC was measured in a supine position and in a standing position for children two years of age and above. Crude WHtR values were calculated as WC (cm)/height (cm) and were then transformed to sex- and age-specific standard deviation scores (SDS) using the estimated mean and SD functions, based on Swedish reference data [38]. Within the framework of this project, the intra- and inter-operator reliability for WC were studied in children predominantly younger than 24 months. The intraclass correlation coefficients were 0.98, both within and between those who made the measurements, although one of the persons had no experience, apart from a short introduction. Classification of children as having a $WHtR_{SDS} \geq 1$ or <1 was made at the age of five. The children were classified as: small for gestational age (SGA), defined as birth weight or birth length ≤ -2 SDS; appropriate for gestational age (AGA); or large for gestational age (LGA), defined as birth weight or birth length for gestational age ≥ 2 SDS based on Swedish reference values [39]. RWG was defined as a change $> +0.67$ in weight SDS, as described by Ong *et al.* [18, 40]. In our study, this change was examined during 0–6 or 6–12 months. This increase in SDS represents the distance between two adjacent centile lines in standard weight growth charts.

Crude BMI values were calculated as weight (kg)/height^2 (m^2) and were thereafter transformed to sex- and age-specific SDS, using the estimated mean and standard deviation (SD) functions based on Swedish reference data [41]. The classifications of children as either having overweight/obesity or normal weight/underweight were made at the age of five years and were based on crude BMI cut-off values by the International Obesity Task Force (IOTF) [42]. Crude BMI values were transformed to corresponding BMI_{SDS}: 1.26 and 1.20 for overweight and 2.44 and 2.22 for obesity, in males and females, respectively. Corresponding SDS for underweight, the second grade of thinness (the equivalent of BMI <17 at 18 years), were –2.44 and –2.22 for males and females, respectively. Conversion of crude BMI and WHtR values to SDS values was made in MATLAB (v.9.0.0.341360R2016a; The MathWorks, Natick, Massachusetts, USA).

Risk factors for an increased WHtR at five years of age

The selection of risk factors was based on previous research regarding risk factors for abdominal obesity or overweight/obesity, and available data in this infant cohort [12, 16, 18, 25–28, 43]. The investigated child-related risk factors were sex, birth weight and RWG between 0–6 and 6–12 months. Birth weight and sex were collected from the Swedish National Medical Birth Register, and RWG was calculated based on measurements from the CHCCs. The investigated nutrition- and feeding practice-related risk factors were breastfeeding and bottle feeding at 0–1, 3–4, 6, 12, 18 and 24 months, together with MCD consumption at 6, 12,18 and 24 months. Breastfeeding was reported at every measurement point and divided into predominant, partial or no breastfeeding, based on answers from the questionnaire responses. At each time point, the parents were asked if the child was breastfed or not. The parents who answered yes were asked how many times per day, with three response alternatives: 1–5 times/day, 6–10

times/day or more than 10 times/day. Infants who were breastfed 6–10 times/day or more were considered predominantly breastfed, while the ones breastfed 1–5 times/day were considered partly breastfed. Bottle feeding was reported at every measurement point, and the parents responded as to whether their infant was fed by a bottle or not. The use of MCD was reported from six months of age. Investigated socioeconomic status-related risk factors were parental educational level (with upper secondary school as reference) and parental smoking, both of which were based on answers from the questionnaire responses. Parental health-related risk factors were pre-pregnancy BMI, maternal gestational weight gain, and paternal BMI, all of them were collected from answers from the questionnaire responses.

Statistics

Unadjusted logistic regression analyses were performed to examine associations between each of the risk factors and $WHtR_{SDS} \geq 1$ or overweight/obesity at five years of age. Variables that showed associations that were considered significant at the < 0.05 level in the univariable logistic regressions were used in the final multivariable models. The dependent variables were children with a $WHtR_{SDS} \geq 1$ versus children with a $WHtR_{SDS} < 1$, or children with overweight/obesity versus children with normal weight/underweight. Variables for maternal pre-pregnancy BMI, maternal gestational weight gain and paternal BMI were used as continuous variables in the analyses. IBM SPSS statistics (v.25.0; IBM Corp, Armonk, New York, USA) was used in all statistical analyses.

Results

Study population

When the 1,540 children were classified according to $WHtR_{SDS} \geq 1$ or <1, 15% had $WHtR_{SDS} \geq 1$ and 85% had $WHtR_{SDS} < 1$ at five years of age (Table 1). When they were classified according to BMI_{SDS} for overweight/obesity or normal weight/underweight, 2% (n = 34) had underweight, 87% (n = 1334) had normal weight, 9% (n = 141) had overweight and 2% (n = 31) had obesity, according to the IOTF BMI cut-off values. Regarding birth size, 3% were born SGA, 93% AGA and 4% LGA.

Associations between risk factors and increased $WHtR_{SDS}$ at five years of age

On examining associations between the risk factors and a $WHtR_{SDS} \geq 1$ at five years of age with univariable logistic regressions, odds ratios (OR) and 95% confidence intervals (CT) showed that, among the child-related risk factors, RWG during 0–6 and 6–12 months was significantly associated with a $WHtR_{SDS} \geq 1$ (Table 2). No associations were found for socioeconomic status-related risk factors. Parental health-related risk factors that showed significant positive associations with an increased $WHtR_{SDS}$ were maternal pre-pregnancy BMI and paternal BMI. The nutrition- and feeding practice-related risk factors MCD consumption at 24 months and bottle feeding at 12 and 24 months were significantly positively associated with an increased $WHtR_{SDS}$ at five years of age.

On examining associations between risk factors and an elevated $WHtR_{SDS}$ at five years of age with multivariable logistic regression, where all variables were controlled for each other, OR and 95% CI showed that RWG between 0–6 months, maternal pre-pregnancy BMI and paternal BMI were significantly positively associated with an increased $WHtR_{SDS}$ at five years of age (Table 3).

Table 1. Characteristics of the study population classified by WHtR$_{SDS}$ and BMI$_{SDS}$.

	WHtR$_{SDS}$		BMI$_{SDS}$	
	≥1 SD	<1 SD	Overweight/obesity	Normal weight
	(n = 231)	(n = 1309)	(175)	(1365)
At birth				
MBW ± SD (g)	3605 ± 458	3575 ± 482 p = 0.539	3785 ± 420	3553 ± 479 p<0,001
Missing (n)	11	62	7	66
Size for gestational age[a]				
SGA (n)	8	40	4	44
AGA (n)	214	1211	160	1265
LGA (n)	7	57	10	54
Missing (n)	2	1	1	2
Gestational age				
37^0–37^6 (n)	13	56	8	61
38^0–40^6 (n)	168	958	127	999
41^0–43^5 (n)	50	295	40	305
Missing (n)	0	0	0	0
Maternal age				
<25 (n)	21	129	16	134
25–35 (n)	156	865	115	906
≥35 (n)	51	303	43	311
Missing (n)	3	12	1	14
Maternal pre-pregnancy BMI				
<18.5 (n)	0	43	1	43
18.5–24.9 (n)	142	920	93	969
25–29.9 (n)	53	202	47	208
≥30 (n)	25	100	29	96
Missing (n)	11	44	5	49
Maternal gestational weight gain				
Less than adequate (n)	38	256	25	269
Adequate (n)	83	443	48	478
Excessive (n)	88	514	86	516
Missing (n)	22	96	16	102
Paternal BMI				
<18.5 (n)	5	44	5	44
18.5–24.9 (n)	146	965	121	990
24.9–29.9 (n)	49	196	26	219
≥30 (n)	1	3	0	4
Missing (n)	30	101	23	108
At 5 years, mean ± SD				
WHtR	0.53 ± 0.0	0.47 ± 0.0 p<0,001	0.52 ± 0.0	0.48 ± 0.0 p<0,001
WHtR$_{SDS}$	1.57 ± 0.5	-0.32 ± 0.8 p<0,001	1.23 ± 0.9	-0.20 ± 0.9 p<0,001
BMI (kg/m^2)	17.36 ± 1.6	15.35 ± 1.1 p<0,001	18.37 ± 1.2	
BMI$_{SDS}$	1.16 ± 1.0	-0.31 ± 1.0 p<0,001	1.82 ± 0.6	15.30 ± 1.0 p<0,001

(*Continued*)

Table 1. (Continued)

	WHtR$_{SDS}$		BMI$_{SDS}$	
	≥1 SD	<1 SD	Overweight/obesity	Normal weight
	(n = 231)	(n = 1309)	(175)	(1365)
				-0.33 ± 0.9 p< 0,001

[a]Classification of size for gestational age was based on values of birth weight and/or birth length. For mean values in birth weight, WHtR, WHtR$_{SDS}$, BMI and BMI$_{SDS}$, the group with WHtR$_{SDS}$ ≥1 was compared with the group with <1 and the group with overweight/obesity according to BMI$_{SDS}$ was compared with the group with normal weight/underweight. Maternal gestational weight gain categories were based on the institute of Medicine (IOM) guidelines by BMI status [44].

MBW, mean birth weight; SD, standard deviation; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; 37^0–37^6, 37 weeks and 0 days– 37 weeks and 6 days; 38^0–40^6, 38 weeks and 0 days– 40 weeks and 6 days; 41^0–43^5, 41 weeks and 0 days– 43 weeks and 5 days; WHtR$_{SDS}$, waist-to-height ratio standard deviation scores; BMI$_{SDS}$, body mass index standard deviation scores.

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Associations between risk factors and overweight or obesity at five years of age

On examining the variables that were positively associated with a WHtR$_{SDS}$ ≥1 at five years of age, regarding their association with overweight or obesity at age five with univariable logistic regression analyses, OR and 95% CI showed that three of them, RWG between 0–6 months, RWG between 6–12 months and maternal pre-pregnancy BMI were significantly positively associated with overweight or obesity (Table 4).

In the multivariable model, the same variables, RWG during 0–6 months, RWG during 6–12 months and maternal pre-pregnancy BMI were significantly positively associated with overweight or obesity at five years of age. None of the nutrition- and feeding practice-related risk factors showed significant associations with overweight or obesity at five years of age.

Discussion

In this longitudinal birth cohort study, 15% of the children had a WHtR$_{SDS}$ ≥1 at five years of age, and three risk factors were significantly positively associated with this increased WHtR$_{SDS}$: RWG during 0–6 months, maternal pre-pregnancy BMI and paternal BMI. Regarding the second aim, which was to investigate if these risk factors also were associated with overweight or obesity, as measured by BMI at five years of age, 9% of the children had overweight and 2% had obesity. RWG between 0–6 months, between 6–12 months and maternal pre-pregnancy BMI were significantly positively associated with this excess weight in the children.

RWG during 0–6 months was positively associated with both an increased WHtR$_{SDS}$ and overweight or obesity at five years of age and RWG during 6–12 months was associated with overweight or obesity. In a number of previous studies, RWG during the first two years of life has been associated with childhood overweight or obesity later in life [12, 16, 18]. The number of studies examining associations between RWG and abdominal obesity are fewer, but these associations have been found in two-year-old children [45]. In a recent review by Zheng *et al.*, regarding associations between RWG and health risks later in life, the authors hypothesised that abdominal obesity potentially may be the factor linking RWG and later health risks [16]. Our results regarding early RWG as a risk factor for an increased WHtR$_{SDS}$ are concordant with this hypothesis and indicate that the first six months of life is a crucial period that needs further examination regarding these associations. This period of life is also associated with a large accumulation of fat mass in the growing child [46]. Children have predominantly subcutaneous fat during their first months, but Moreno *et al.* showed by sonography that in the second year of life, there was a pronounced increase in pre-peritoneal fat thickness, a proxy for

Table 2. Odds ratios and 95% confidence intervals for risk factors for an elevated WHtR$_{SDS}$ at five years of age.

Risk factors	WHtR≥1 SDS	WHtR <1 SDS	Univariable logistic regressions[a]		
			OR	95% CI	p
Child-related risk factors					
Gender					
Male	99	651	1	Ref	
Female	132	658	1.32	1.00–1.75	0.054
Birth weight in kilograms	n/a	n/a	1.14	0.85–1.54	0.392
Rapid weight gain 0–6 months					
No	74	588	1	Ref	
Yes	105	473	1.76	1.28–2.43	**0.001**
Rapid weight gain 6–12 months					
No	157	983	1	Ref	
Yes	22	78	1.77	1.07–2.92	**0.026**
Nutrition-and feeding practice-related risk factors					
Milk cereal drink consumption					
24 months					
No	60	281	1	Ref	
Yes	105	718	1.46	1.03–2.06	**0.032**
Bottle feeding					
12 months					
No	27	103	1	Ref	
Yes	165	1007	1.60	1.02–2.52	**0.043**
Bottle feeding 24 months					
No	60	268	1	Ref	
Yes	110	748	1.52	1.08–2.15	**0.017**
Socioeconomic status-related risk factors					
Maternal educational level					
Upper secondary school	100	520	1	Ref	
Elementary school	67	16	1.24	0.69–2.23	0.469
University	102	650	0.82	0.61–1.10	0.182
Other	10	60	0.87	0.43–1.75	0.690
Paternal educational level					
Upper secondary school	118	693	1	Ref	
Elementary school	13	69	1.10	0.59–2.07	0.751
University	68	419	0.95	0.69–1.32	0.770
Other	11	55	1.18	0.60–2.31	0.641
Maternal smoking					
No	214	1226	1	Ref	
Yes	14	69	1.16	0.64–2.10	0.619
Paternal smoking					
No	118	1116	1	Ref	
Yes	25	113	0.20	0.85–2.14	0.202
Parental health-related risk factors					
Maternal pre-pregnancy BMI	n/a	n/a	1.07	1.03–1.10	**<0.001**
Maternal gestational weight gain	n/a	n/a	1.00	0.97–1.03	0.930

(Continued)

Table 2. (Continued)

Risk factors	WHtR$\geq$1 SDS	WHtR $<$1 SDS	Univariable logistic regressions[a]		
			OR	95% CI	p
Paternal BMI	n/a	n/a	1.09	1.02–1.16	**0.007**

[a]The logistic regressions included each of the independent variables separately. Among risk factors related to nutrition- and feeding practices, breastfeeding and bottle feeding at 0–1, 3–4, 6, 12, 18 and 24 months and milk cereal drink consumption at 6, 12, 18 and 24 months were investigated, but significant associations with an elevated WHtR$_{SDS}$ at five years of age were only found for milk cereal drink consumption at 24 months and bottle feeding at 12 and 24 months. A p-value <0.05 was considered significant.

OR, odds ratios; 95% CI, 95% confidence intervals; p, p value; WHtR, waist-to-height ratio; SDS, standard deviation scores; BMI, body mass index.

abdominal visceral fat, in copmarison with subcutaneous fat thickness that only increased to a smaller extent [47]. It has also been shown that children with RWG during their first two years had increased pre-peritoneal fat mass [45]. In older children, 6–14.9 years, it has been suggested that increased adiposity is associated with increased fat deposition in the abdominal area [48].

Maternal pre-pregnancy BMI was another risk factor that was positively associated in our current study with an increased WHtR$_{SDS}$ and with overweight or obesity. Associations between maternal pre-pregnancy BMI and overweight or obesity in children have been reported in previous studies [12, 29], but the number of studies examining its effect on abdominal obesity are limited. However, the association has been found in older children, aged 8 to 18 [27]. Another study, with 10-year-old children from the Netherlands, also found associations between maternal pre-pregnancy BMI and abdominal fat [49]. The underlying mechanisms behind these associations are still unclear and have mainly been investigated in small human studies and animal studies [50]. This indicates that more studies regarding the mechanisms behind maternal pre-pregnancy BMI and an increased WHtR$_{SDS}$ in preschool children and in older children are needed.

Regarding paternal BMI and its association with an increased WHtR$_{SDS}$ in children, it has been shown that fathers with obesity or abdominal obesity (WC >102 centimeters) were more

Table 3. Odds ratios and 95% confidence intervals for risk factors for an elevated WHtR$_{SDS}$ in children at five years of age.

Risk factors	Multivariable logistic regressions[a]		
	OR	(95% CI)	P
WHtR$_{SDS}$ $\geq$1—WHtR$_{SDS}$ <1[b]			
Rapid weight gain 0-6m	1.90	(1.23–2.95)	**0.004**
Rapid weight gain 6-12m	1.85	(0.93–3.69)	0.081
Maternal pre-pregnancy BMI	1.06	(1.01–1.11)	**0.019**
Paternal BMI	1.11	(1.01–1.21)	**0.028**
Milk cereal drink 24m	1.17	(0.52–2.62)	0.713
Bottle feeding 12m	1.17	(0.57–2.42)	0.668
Bottle feeding 24m	1.54	(0.67–3.55)	0.308

[a]In the logistic regressions, the variables were all controlled for each other. No other variables were included in the models, besides those presented in the table.

[b]The children were classified as having waist-to-height ratio standard deviation scores (WHtR$_{SDS}$) $\geq$1 or <1 according to Swedish reference values (38). OR, odds ratios; 95% CI, 95% confidence interval; p, p value; m, months; BMI, body mass index. A p-value <0.05 was considered significant.

Table 4. Odds ratios and 95% confidence intervals for risk factors for overweight or obesity in children at five years of age.

Risk factors	Univariable logistic regressions[a]			Multivariable logistic regressions[b]		
	OR	(95% CI)	p	OR	(95% CI)	p
Ow/Ob- Nw/Uw[c]						
Rapid weight gain 0-6m	1.95	(1.36–2.81)	**<0.001**	2.53	(1.53–4.20)	**<0.001**
Rapid weight gain 6-12m	2.03	(1.19–3.47)	**0.009**	2.82	(1.37–5.79)	**0.005**
Maternal pre-pregnancy BMI	1.12	(1.09–1.16)	**<0.001**	1.11	(1.06–1.17)	**<0.001**
Milk cereal drink 24m	1.17	(0.78–1.75)	0.454	2.23	(0.96–5.21)	0.064
Bottle feeding 12m	1.26	(0.73–2.17)	0.404	1.91	(0.85–4.26)	0.116
Bottle feeding 24m	0.87	(0.57–1.33)	0.512	0.48	(0.19–1.22)	0.124

[a]The univariable logistic regressions included each of the independent variables separately, and in the

[b]multivariable logistic regressions they were all controlled for each other. No other variables were included in the models besides those presented in the table.

[c]The children were classified as having overweight or obesity or as having normal weight or underweight according to BMI cut-off values by the International Obesity Task Force [42].

OR, odds ratios; 95% CI, 95% confidence interval; p, p value; Ow/Ob, overweight/obesity; Nw/Uw, normal weight/underweight; BMI, body mass index.

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likely to have children born SGA [51], and several studies have shown that children born SGA are more prone to RWG, abdominal obesity and insulin resistance [52]. Due to the population-based design of this study, only a few percent of the children included were born SGA, and therefore it was not possible to examine if a similar association existed in the current study. There are also conflicting results. A study in six-year-old children from the Netherlands showed no association between paternal BMI and subcutaneous or pre-peritoneal abdominal fat [53].

There were significantly positive associations between MCD consumption at 24 months, as well as bottle feeding at 12 and 24 months, and an increased WHtR$_{SDS}$ in the univariable analyses; however, these associations were not found in the multivariable analyses. Regarding overweight or obesity, there were no associations with the nutrition- and feeding practice-related risk factors. In other studies, both bottle feeding [12] and the consumption of MCD have been associated with overweight or obesity in children [34], and bottle feeding has been associated with RWG during the first year [54]; however, our results indicate that early RWG and parental overweight are more important risk factors for increased WHtR$_{SDS}$ and overweight or obesity at five years than are nutrition and feeding-practice-related factors. However, associations between bottle feeding and formula feeding-practices with RWG [22, 54], suggests that such factors may have an indirect effect. Furthermore, follow-up studies in this population may reveal whether early nutrition and feeding practices are associated with abdominal obesity, overweight or obesity later in life.

A limitation of the current study was that we had to exclude children because of missing growth data at five years of age, or because they were measured outside our set age limit. The main reason for this exclusion was because we wanted to include only measurements close to the measurement points, and wider limits for this would have affected precision. We made multiple independent assessments of associations; this represents a risk factor for overstating associations, and could be considered a limitation. The p-values in our results must therefore be considered with caution. An additional limitation was that our study was based on Swedish children, and this must be considered when generalising the results to populations with another ethnic composition and different impact of socioeconomic factors. The main strengths of this study were the population-based longitudinal design, following a large birth cohort over time, and that all measurements were made by trained child health care nurses.

Conclusion

We found that rapid weight gain during 0–6 months and parental BMI were positively associated with a $WHtR_{SDS} \geq 1$ at five years of age. Rapid weight gain during both 0–6 months and 6–12 months and maternal pre-pregnancy BMI were associated with overweight or obesity at the same age. Preventive interventions regarding abdominal obesity and childhood excess weight should target early rapid weight gain, parental overweight and parental obesity. Further research is required to uncover whether these risk factors are associated with subsequent abdominal obesity, overweight or obesity in older children and adolescents.

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References

1. WHO. Report of the Comission on Ending Childhood Obesity. World Health Organization; 2016. Accessed 1 March 2022. Available from https://apps.who.int/iris/bitstream/handle/10665/204176/9789241510066_eng.pdf

2. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. International journal of obesity. 2011; 35 (7):891–8. https://doi.org/10.1038/ijo.2010.222 PMID: 20975725

3. Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. Pediatrics. 2004; 114(2):e198–205. https://doi.org/10.1542/peds.114.2.e198 PMID: 15286257

4. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. The American journal of clinical nutrition. 2004; 79(3):379–84. https://doi.org/10.1093/ajcn/79.3.379 PMID: 14985210

5. Shashaj B, Bedogni G, Graziani MP, Tozzi AE, DiCorpo ML, Morano D, et al. Origin of cardiovascular risk in overweight preschool children: a cohort study of cardiometabolic risk factors at the onset of obesity. JAMA pediatrics. 2014; 168(10):917–24. https://doi.org/10.1001/jamapediatrics.2014.900 PMID: 25111132

6. Kjellberg E, Roswall J, Bergman S, Almqvist-Tangen G, Alm B, Dahlgren J. Longitudinal birth cohort study found that a significant proportion of children had abnormal metabolic profiles and insulin

resistance at 6 years of age. Acta paediatrica (Oslo, Norway: 1992). 2018. https://doi.org/10.1111/apa.14599 PMID: 30328152

7. McCarthy HD, Ashwell M. A study of central fatness using waist-to-height ratios in UK children and adolescents over two decades supports the simple message—'keep your waist circumference to less than half your height'. International journal of obesity. 2006; 30(6):988–92. https://doi.org/10.1038/sj.ijo.0803226 PMID: 16432546

8. Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. International journal of obesity and related metabolic disorders: journal of the International Association for the Study of Obesity. 2000; 24(11):1453–8. https://doi.org/10.1038/sj.ijo.0801401 PMID: 11126342

9. Yoo EG. Waist-to-height ratio as a screening tool for obesity and cardiometabolic risk. Korean journal of pediatrics. 2016; 59(11):425–31. https://doi.org/10.3345/kjp.2016.59.11.425 PMID: 27895689

10. Power C, Lake JK, Cole TJ. Measurement and long-term health risks of child and adolescent fatness. International journal of obesity and related metabolic disorders: journal of the International Association for the Study of Obesity. 1997; 21(7):507–26. https://doi.org/10.1038/sj.ijo.0800454 PMID: 9226480

11. Nambiar S, Truby H, Davies PS, Baxter K. Use of the waist-height ratio to predict metabolic syndrome in obese children and adolescents. Journal of paediatrics and child health. 2013; 49(4):E281–7. https://doi.org/10.1111/jpc.12147 PMID: 23521181

12. Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk Factors for Childhood Obesity in the First 1,000 Days: A Systematic Review. American journal of preventive medicine. 2016; 50(6):761–79. https://doi.org/10.1016/j.amepre.2015.11.012 PMID: 26916261

13. Aris IM, Bernard JY, Chen LW, Tint MT, Pang WW, Soh SE, et al. Modifiable risk factors in the first 1000 days for subsequent risk of childhood overweight in an Asian cohort: significance of parental overweight status. International journal of obesity. 2018; 42(1):44–51. https://doi.org/10.1038/ijo.2017.178 PMID: 28751763

14. Rolland-Cachera MF, Deheeger M, Bellisle F, Sempe M, Guilloud-Bataille M, Patois E. Adiposity rebound in children: a simple indicator for predicting obesity. The American journal of clinical nutrition. 1984; 39(1):129–35. https://doi.org/10.1093/ajcn/39.1.129 PMID: 6691287

15. Ong KK. Size at birth, postnatal growth and risk of obesity. Hormone research. 2006; 65 Suppl 3:65–9. https://doi.org/10.1159/000091508 PMID: 16612116

16. Zheng M, Lamb KE, Grimes C, Laws R, Bolton K, Ong KK, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. Obesity reviews: an official journal of the International Association for the Study of Obesity. 2018; 19(3):321–32. https://doi.org/10.1111/obr.12632 PMID: 29052309

17. Demerath EW, Reed D, Choh AC, Soloway L, Lee M, Czerwinski SA, et al. Rapid postnatal weight gain and visceral adiposity in adulthood: the Fels Longitudinal Study. Obesity. 2009; 17(11):2060–6. https://doi.org/10.1038/oby.2009.105 PMID: 19373221

18. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. Acta paediatrica (Oslo, Norway: 1992). 2006; 95(8):904–8. https://doi.org/10.1080/08035250600719754 PMID: 16882560

19. Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. Energy and protein intakes of breastfed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. Am J Clin Nutr. 1993; 58(2):152–61. https://doi.org/10.1093/ajcn/58.2.152 PMID: 8338041

20. Kong KL, Burgess B, Morris KS, Re T, Hull HR, Sullivan DK, et al. Association Between Added Sugars from Infant Formulas and Rapid Weight Gain in US Infants and Toddlers. The Journal of nutrition. 2021; 151(6):1572–80. https://doi.org/10.1093/jn/nxab044 PMID: 33880550

21. Lindholm A, Bergman S, Alm B, Bremander A, Dahlgren J, Roswall J, et al. Nutrition- and feeding practice-related risk factors for rapid weight gain during the first year of life: a population-based birth cohort study. BMC pediatrics. 2020; 20(1):507. https://doi.org/10.1186/s12887-020-02391-4 PMID: 33148198

22. Appleton J, Russell CG, Laws R, Fowler C, Campbell K, Denney-Wilson E. Infant formula feeding practices associated with rapid weight gain: A systematic review. Maternal & child nutrition. 2018:e12602. https://doi.org/10.1111/mcn.12602 PMID: 29655200

23. Mihrshahi S, Battistutta D, Magarey A, Daniels LA. Determinants of rapid weight gain during infancy: baseline results from the NOURISH randomised controlled trial. BMC pediatrics. 2011; 11:99. https://doi.org/10.1186/1471-2431-11-99 PMID: 22054415

24. Petrov ME, Jiao N, Panchanathan SS, Reifsnider E, Coonrod DV, Liu L, et al. Protocol of the Snuggle Bug/Acurrucadito Study: a longitudinal study investigating the influences of sleep-wake patterns and

gut microbiome development in infancy on rapid weight gain, an early risk factor for obesity. BMC pediatrics. 2021; 21(1):374. https://doi.org/10.1186/s12887-021-02832-8 PMID: 34465311

25. Sokolovic N, Kuriyan R, Kurpad AV, Thomas T. Sleep and birthweight predict visceral adiposity in overweight/obese children. Pediatric obesity. 2013; 8(3):e41–4. https://doi.org/10.1111/j.2047-6310.2012.00142.x PMID: 23512928

26. Dello Russo M, Ahrens W, De Vriendt T, Marild S, Molnar D, Moreno LA, et al. Gestational weight gain and adiposity, fat distribution, metabolic profile, and blood pressure in offspring: the IDEFICS project. International journal of obesity. 2013; 37(7):914–9. https://doi.org/10.1038/ijo.2013.35 PMID: 23567926

27. Tan HC, Roberts J, Catov J, Krishnamurthy R, Shypailo R, Bacha F. Mother's pre-pregnancy BMI is an important determinant of adverse cardiometabolic risk in childhood. Pediatric diabetes. 2015; 16 (6):419–26. https://doi.org/10.1111/pedi.12273 PMID: 25800542

28. Griffiths LJ, Dezateux C, Cole TJ. Sex and ethnic differences in the waist circumference of 5-year-old children: findings from the Millennium Cohort Study. International journal of pediatric obesity: IJPO: an official journal of the International Association for the Study of Obesity. 2011; 6(2–2):e196–8. https://doi.org/10.3109/17477166.2010.526224 PMID: 21073404

29. Heppe DH, Kiefte-de Jong JC, Durmus B, Moll HA, Raat H, Hofman A, et al. Parental, fetal, and infant risk factors for preschool overweight: the Generation R Study. Pediatric research. 2013; 73(1):120–7. https://doi.org/10.1038/pr.2012.145 PMID: 23138398

30. Sacco MR, de Castro NP, Euclydes VL, Souza JM, Rondo PH. Birth weight, rapid weight gain in infancy and markers of overweight and obesity in childhood. European journal of clinical nutrition. 2013; 67 (11):1147–53. https://doi.org/10.1038/ejcn.2013.183 PMID: 24084514

31. Gaillard R, Steegers EA, Franco OH, Hofman A, Jaddoe VW. Maternal weight gain in different periods of pregnancy and childhood cardio-metabolic outcomes. The Generation R Study. International journal of obesity. 2015; 39(4):677–85.

32. Durmus B, Arends LR, Ay L, Hokken-Koelega AC, Raat H, Hofman A, et al. Parental anthropometrics, early growth and the risk of overweight in pre-school children: the Generation R Study. Pediatric obesity. 2013; 8(5):339–50. https://doi.org/10.1111/j.2047-6310.2012.00114.x PMID: 23239588

33. Koletzko B, Demmelmair H, Grote V, Prell C, Weber M. High protein intake in young children and increased weight gain and obesity risk. The American journal of clinical nutrition. 2016; 103(2):303–4. https://doi.org/10.3945/ajcn.115.128009 PMID: 26791192

34. Almquist-Tangen G, Bergman S, Dahlgren J, Lindholm A, Roswall J, Alm B. Consuming milk cereal drinks at one year of age was associated with a twofold risk of being overweight at the age of five. Acta paediatrica (Oslo, Norway: 1992). 2019; 108(6):1115–21.

35. Rogers I, Emmett P. The effect of maternal smoking status, educational level and age on food and nutrient intakes in preschool children: results from the Avon Longitudinal Study of Parents and Children. European journal of clinical nutrition. 2003; 57(7):854–64. https://doi.org/10.1038/sj.ejcn.1601619 PMID: 12821885

36. Burke V, Gracey MP, Milligan RA, Thompson C, Taggart AC, Beilin LJ. Parental smoking and risk factors for cardiovascular disease in 10- to 12-year-old children. The Journal of pediatrics. 1998; 133 (2):206–13. https://doi.org/10.1016/s0022-3476(98)70221-5 PMID: 9709707

37. Gerd AT, Bergman S, Dahlgren J, Roswall J, Alm B. Factors associated with discontinuation of breastfeeding before 1 month of age. Acta paediatrica (Oslo, Norway: 1992). 2012; 101(1):55–60. https://doi.org/10.1111/j.1651-2227.2011.02405.x PMID: 21767302

38. Roswall J, Bergman S, Almqvist-Tangen G, Alm B, Niklasson A, Nierop AF, et al. Population-based waist circumference and waist-to-height ratio reference values in preschool children. Acta paediatrica (Oslo, Norway: 1992). 2009; 98(10):1632–6. https://doi.org/10.1111/j.1651-2227.2009.01430.x PMID: 19604174

39. Niklasson A, Ericson A, Fryer JG, Karlberg J, Lawrence C, Karlberg P. An update of the Swedish reference standards for weight, length and head circumference at birth for given gestational age (1977–1981). Acta paediatrica Scandinavica. 1991; 80(8–9):756–62. https://doi.org/10.1111/j.1651-2227.1991.tb11945.x PMID: 1957592

40. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. BMJ (Clinical research ed). 2000; 320 (7240):967–71. https://doi.org/10.1136/bmj.320.7240.967 PMID: 10753147

41. Karlberg J, Luo ZC, Albertsson-Wikland K. Body mass index reference values (mean and SD) for Swedish children. Acta paediatrica (Oslo, Norway: 1992). 2001; 90(12):1427–34. https://doi.org/10.1080/08035250152708851 PMID: 11853342

42. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatric obesity. 2012; 7(4):284–94. https://doi.org/10.1111/j.2047-6310.2012.00064.x PMID: 22715120

43. Kruithof CJ, Gishti O, Hofman A, Gaillard R, Jaddoe VW. Infant weight growth velocity patterns and general and abdominal adiposity in school-age children. The Generation R Study. European journal of clinical nutrition. 2016; 70(10):1144–50.

44. Institute of Medicine, National Research Council. Weight gain during pregnancy; reexamining the guidelines. Washington, DC, The National Academies Press, 2009. Accessed 11 March 2022. Available from https://www.nap.edu/catalog/12584/weight-gain-during-pregnancy-reexamining-the -guidelines

45. Durmus B, Mook-Kanamori DO, Holzhauer S, Hofman A, van der Beek EM, Boehm G, et al. Growth in foetal life and infancy is associated with abdominal adiposity at the age of 2 years: the generation R study. Clinical endocrinology. 2010; 72(5):633–40. https://doi.org/10.1111/j.1365-2265.2009.03708.x PMID: 19769622

46. Veldhuis JD, Roemmich JN, Richmond EJ, Rogol AD, Lovejoy JC, Sheffield-Moore M, et al. Endocrine control of body composition in infancy, childhood, and puberty. Endocrine reviews. 2005; 26(1):114–46. https://doi.org/10.1210/er.2003-0038 PMID: 15689575

47. Holzhauer S, Zwijsen RM, Jaddoe VW, Boehm G, Moll HA, Mulder PG, et al. Sonographic assessment of abdominal fat distribution in infancy. European journal of epidemiology. 2009; 24(9):521–9. https://doi.org/10.1007/s10654-009-9368-1 PMID: 19639387

48. Moreno LA, Fleta J, Mur L, Sarría A, Bueno M. Fat distribution in obese and nonobese children and adolescents. Journal of pediatric gastroenterology and nutrition. 1998; 27(2):176–80. https://doi.org/10.1097/00005176-199808000-00009 PMID: 9702649

49. Santos S, Monnereau C, Felix JF, Duijts L, Gaillard R, Jaddoe VWV. Maternal body mass index, gestational weight gain, and childhood abdominal, pericardial, and liver fat assessed by magnetic resonance imaging. International journal of obesity. 2019; 43(3):581–93. https://doi.org/10.1038/s41366-018-0186-y PMID: 30232419

50. Gaillard R, Santos S, Duijts L, Felix JF. Childhood Health Consequences of Maternal Obesity during Pregnancy: A Narrative Review. Annals of nutrition & metabolism. 2016; 69(3–4):171–80. https://doi.org/10.1159/000453077 PMID: 27855382

51. McCowan LM, North RA, Kho EM, Black MA, Chan EH, Dekker GA, et al. Paternal contribution to small for gestational age babies: a multicenter prospective study. Obesity. 2011; 19(5):1035–9. https://doi.org/10.1038/oby.2010.279 PMID: 21127471

52. Ong KK. Catch-up growth in small for gestational age babies: good or bad? Current opinion in endocrinology, diabetes, and obesity. 2007; 14(1):30–4. https://doi.org/10.1097/MED.0b013e328013da6c PMID: 17940416

53. Gaillard R, Steegers EA, Duijts L, Felix JF, Hofman A, Franco OH, et al. Childhood cardiometabolic outcomes of maternal obesity during pregnancy: the Generation R Study. Hypertension (Dallas, Tex: 1979). 2014; 63(4):683–91. https://doi.org/10.1161/HYPERTENSIONAHA.113.02671 PMID: 24379180

54. Li R, Magadia J, Fein SB, Grummer-Strawn LM. Risk of bottle-feeding for rapid weight gain during the first year of life. Archives of pediatrics & adolescent medicine. 2012; 166(5):431–6. https://doi.org/10.1001/archpediatrics.2011.1665 PMID: 22566543