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Pathways in the association between sugar sweetened beverages and child asthma traits in the 2nd year of life: Findings from the BRISA cohort

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Abstract

Studies on the exposure of children to sugar-sweetened beverages (SSBs) at an early age may contribute to better understand the common causes and the temporal order of the relationships between obesity and asthma in early childhood. The objective of this study was to estimate the association between SSB and child asthma traits in the 2nd year of life, modeling direct and indirect pathways mediated by the highest BMI-z of the child and allergic inflammation. Data from the BRISA cohort, São Luís-MA, Brazil (n = 1140), were obtained from the baseline and from the follow-up performed at the 2nd year of life. The main explanatory variable was the calories from added sugars in SSBs as a percentage of the total daily energy intake. The outcome child asthma traits was a latent variable deduced from four indicators: medical diagnosis of asthma, wheezing, emergency visit due to intense wheezing, and medical diagnosis of rhinitis. A high percentage of daily calories from sugars added to SSBs was directly associated with higher values of child asthma traits (standardized coefficient (SC = 0.073; $P = .030$)). High levels of eosinophils were also directly associated with child asthma traits (SC = 0.118; $P = .049$). No mediation pathways were observed via greater BMI-z or eosinophil counts. Therefore, early exposure of children to SSB may contribute to increased risk of childhood asthma, preceding the link between sugar consumption and overweight/obesity, not yet evident in children in the first 2 years of life.

KEYWORDS

asthma, child, structural equation modeling, sugar-sweetened beverages

1 | INTRODUCTION

Asthma is the most prevalent chronic inflammatory disease in childhood. About 5%-10% of the world population has asthma.¹ Although an association between childhood obesity and asthma has been consistently demonstrated, the temporal order of the relationship and the causal pathways between them are not well understood.² Inflammatory mechanisms seem to play a role in both obesity and asthma,³ with inflammation being a common finding in all asthmatic patients.⁴ Additionally, obesity and asthma seem to share common causes, as, for example, the Western diet.⁵

Soft drinks and other sugar-sweetened beverages (SSB) are the primary source of added sugars and the main source of discretionary calories (the difference between total energy requirements and the energy consumed to meet recommended nutrient intakes) in the Western diet.⁶ SSB has been consistently associated with excess weight, also among children.⁷ Sugar-containing beverages (some including a 100% fruit juice), SSB, and especially soft drink consumption were associated with increased odds of asthma in a systematic review ($n = 19$ studies),⁸ including children older than 2 years of age.⁹⁻¹¹ Studies of children exposure to SSB even at earlier ages may contribute to better understand the role of SSB as a common cause of obesity and asthma and also to elucidate the temporal order of these relationships.

Obesity increases eosinophil activity in asthmatic children,³ while sugar consumption seems implicated in susceptibility to allergic inflammation of the airways and activation of the innate immune system.¹² Thus, both obesity and cellular immune response may be part of the causal chain between the SSB exposure and asthma and thus act as mediators.

Structural equation modeling is a statistical tool that allows us to test a hypothetical causal structure of multiple variables in the association between the exposure and the outcome, including direct and indirect pathways.¹³ Therefore, the objective of the present study was to estimate the association between exposure to SSB and the latent variable child asthma traits in the 2nd year of life, modeling indirect pathways mediated by the highest BMI-z and the cellular immune response.

2 | METHODS

This study, which is a part of a larger project "Etiological factors of preterm birth and consequences of perinatal factors on the child's health: birth cohorts in two Brazilian cities, Ribeirão Preto and São Luís (BRISA)," Brazil, used data available from São Luís, a city located in the northeast of Brazil.

The BRISA prenatal cohort study (baseline) involved a sample consisting of pregnant women ($n = 1447$). The first follow-up of the cohort occurred at birth. A second follow-up of the cohort was conducted during the 2nd year of life of the children. The final sample consisted of 1140 mothers and their children (78.78% of the original sample). Details of BRISA cohorts are published in Silva et al.¹⁴

Key Message

The consumption of added sugars by very young children seems implicated in asthma; preceding the link between sugar consumption to overweight/obesity, not yet evident in children up to 2 years of age. Moreover, exclusive breastfeeding is clearly protective to asthma in this study and the wider literature. Ours results supports early policy interventions for diets of young children, that may result in lifelong impact on asthma as also as obesity in future.

The following data from the baseline study collected with questionnaire were used: maternal age (years); birthweight (kilograms), obtained from the newborn's medical record; monthly household income (minimum wages); maternal education level (years of schooling); occupation of household head (unskilled manual, semi-skilled manual, and skilled manual work, office functions, top-level professional, administrator/manager/director/owner), and economic class according to the Economic Classification Criteria-Brazil¹⁵ (classes A and B, class C, and classes D and E), categorized as upper class (classes A and B), middle class (C), or lower class (D and E).

From the 2nd year of life, the following variables were used: child's age (months); sex; medical diagnosis of asthma; episodes of wheezing some time in their life; medical emergency visit due to intense wheezing; medical diagnosis of rhinitis; exclusive breastfeeding; dietary intake; eosinophil count; and weight and height of the child.

Exclusive breastfeeding was defined based on the answer to the following question: "Up to what age was your baby exclusively breastfed (baby received only breast milk, no other liquids or solids were given – not even water, tea, other types of milk, other beverages or foods)?"

The weight of the child was measured with a digital scale to the nearest 0.1 kg (Tanita®). Height was measured with a portable stadiometer to the nearest 0.1 cm (Altuxata®), following recommended techniques.¹⁶ The children's dietary history was assessed enquiring their mothers, using a 24-hour dietary recall, a valid assessment tool to analyze usual intake of nutrients, as showed in a previous study using the same population sample.¹⁷

Peripheral blood eosinophil count is potentially useful as a marker of eosinophilic airway inflammation and was determined in venous blood containing the anticoagulant EDTA.¹⁴

Maternal age and birthweight were used as discrete numerical variables in the model. Exclusive breastfeeding was treated as a dichotomous categorical variable: <6 and ≥6 months. Child's sex was used as a dichotomous variable (male = 1, female = 2). Child's age was a discrete numerical variable, analyzed in months. Child's body mass index (BMI) z-score according to age and sex was calculated based on the growth curves of the World Health Organization¹⁸ and used as a continuous variable. BMI z-scores have been used successfully in early life to predict mid-childhood adiposity¹⁹; advantageously, it

may be used throughout the life course. Eosinophil count (cells/mL) was categorized into tertiles (first, second, and third).

The main explanatory variable was the calories from added sugars in SSBs as a percentage of the total daily energy intake by children around the 2nd year of life. To compose this variable, the percentage of calories from sugars added to SSBs were derived from soft drinks, industrialized fruit juice with added sugars (not included 100% fruit juice), and ready-made chocolate drinks. The amount of sugar in these products was treated as a continuous variable measured in grams (g) and the percentage of daily calories from sugars added to SSBs in relation to total calories consumed by the child was calculated and used as a continuous variable.

2.1 | Latent variables

Latent variables result from the combination of observed variables or indicator variables. In a latent variable, only common variance shared by different indicators persists, resulting in the estimate of effects free from the bias originated by measurement errors.¹³

The latent variable socioeconomic status (SES), already validated in a previous study of the BRISA cohort,²⁰ made up of the following variables: (a) maternal education level; (b) occupation of household head; (c) monthly household income, and (d) economic class.

Childhood asthma symptoms as a latent variable have already been tested by confirmatory factor analysis in a previous study from our group.²¹ In this paper, a new nomenclature child asthma traits was adopted to better represent its continuous scale, ranging from normal (without asthma) to the more severe disease. The variable "child asthma traits" was based on four indicators abstracted from the second-year follow-up questionnaire: (1) medical diagnosis of

medical; (2) medical diagnosis of rhinitis; and (3) use of emergency service due to wheezing. All these three indicators were used as dichotomous variables (no or yes) and 4) number of wheezing episodes categorized as no wheezing, <3, 3-6, and >6 episodes. These indicators individually did not measure asthma well. However, using them together allowed us to better measure asthma²¹ as a continuous variable named child asthma traits and thus reduce its measurement error²² in a structural equation model.

Figure 1 presents the proposed theoretical model constructed to analyze the association between early exposure to SSB and the latent variable child asthma traits in the 2nd year of life. The highest BMI-z and cellular immune response (eosinophil counts) were tested as mediators since they may be part of the causal chain between SSB exposure and child asthma traits. As potential confounders, the latent SES was considered a more distal determinant of the exposure SSB and the latent child asthma traits, and SES may also have effects on other variables. Maternal age may influence the choice and supply of food to the child. High birthweight is a determinant of childhood obesity²³; meanwhile, there is evidence that both low birthweight²⁴ and high birthweight may increase childhood asthma risk.²⁵ Exclusive breastfeeding may also have a protective effect on child's BMI z-score and on asthma.²¹

2.2 | Statistical analysis

Given the occurrence of losses to follow-up, all variables were compared by the chi-squared test between children who were seen for the second follow-up and those who were not. It was observed that only children born at lower gestational ages were less frequently seen for the second follow-up. Weighting of the sample

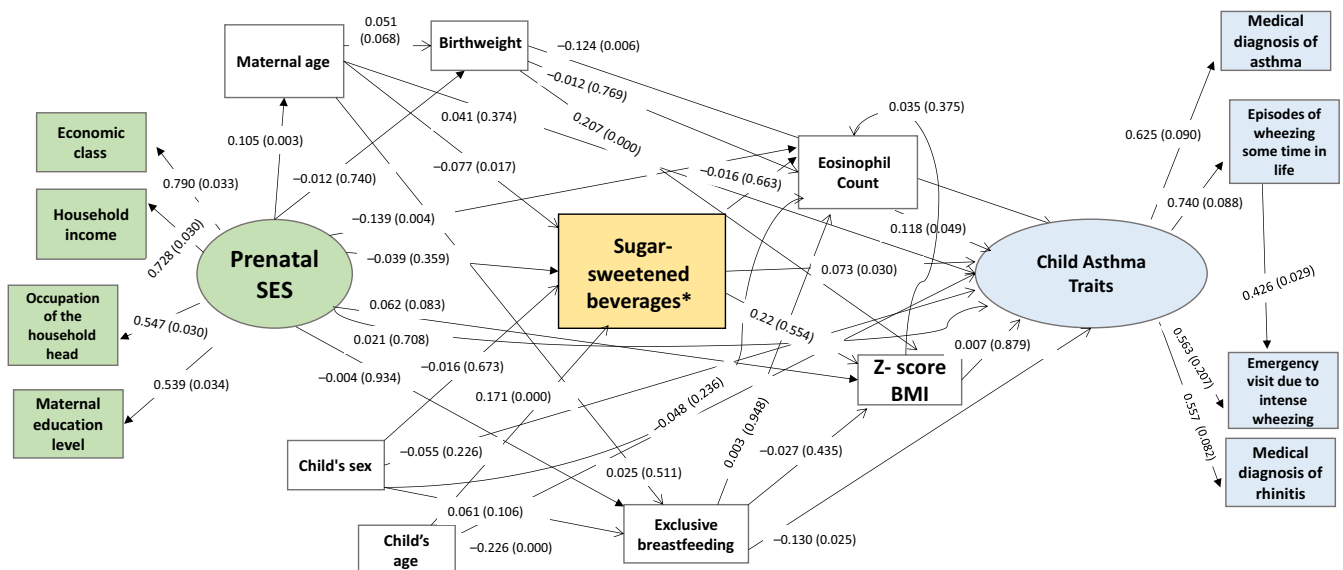


FIGURE 1 Proposed theoretical model to analyze the association between early exposure to sugar-sweetened beverages and "child asthma traits" in the 2nd year of life, mediated by BMI-z and by the number of eosinophils (BRISA prenatal cohort, São Luís-MA, 2010-2013).

*Calories from added sugars in SSBs as a percentage of the total daily energy intake. The values shown in Figure 1 are the standardized coefficient with their respective P-values

was therefore performed by calculating the probability of the child attending the second follow-up visit as a function of gestational age using a logistic regression model. The inverse of the probability of selection was then calculated in order to minimize spurious associations arising from sampling losses and used to weight the structural equation model estimates.

The initial statistical analyses and construction of the weighting variable were performed using the Stata® 14.0 software, and the Mplus® 7.0 software was used for structural equation modeling.

In structural equation modeling, weighted least-squares mean and variance-adjusted (WLSMV) estimation was carried out. The previous described fit indices were considered to determine whether the model showed good fit¹³ (Table 2).

The modindices command was used in the structural equation modeling¹³ to identify new pathways which if included would result in a better fitting model. Suggestions of modification whose values were >10 were added if they were considered plausible from a theoretical perspective. Total, direct, and indirect effects of the observed variables on the latent variant child asthma traits were estimated using standardized coefficients (SC). The effect was considered significant when $P < .05$.

Firstly, SSB exposure and all variables disposed in the theoretical model were analyzed in association with child asthma traits by structural equation modeling. Subsequently, other components of the unhealthy diet (sugared yogurts, popsicles, ice creams, and industrialized baby foods; sugared cakes and cookies; saturated fat and sodium) and healthy diet components (total fiber; Brazilian staple foods: rice, bean, meat, and milk; fruits and vegetables) were also tested replacing SSB in the theoretical model and analyzed by structural equation modeling (Supplementary Material).

2.3 | Ethical aspects

The study was approved by the Research Ethics of the Hospital of the Federal University of Maranhão, Brazil (protocol 4771/2008-30). Written informed consent was obtained from all pregnant women.

3 | RESULTS

The characteristics of the mothers and children studied are shown in Tables 1 and 2. The prevalence of a medical diagnosis of asthma was 2.8%, 4.6% of the children had 3–6 episodes of wheezing, 14.0% required an emergency visit due to intense wheezing, and 6.4% had a medical diagnosis of rhinitis (Table 2).

The details regarding food consumption of children from the BRISA cohort at the 2nd year of life are depicted in Table 3. The mean of the calories from added sugars in SSBs as a percentage of the total daily energy intake by children was 7.4% and the median was 5.7%.

The initial structural equation model presented a good fit, except for the square test value ($P < .001$), which was not considered due to its sensitivity to the large sample size. Changes to the model based on modification indices were not considered plausible

TABLE 1 Sociodemographic characteristics of the women

Variable		
Maternal age (y)	Mean	SD
	26.1	5.6
	Median	Percentiles 25-75
	26.0	22.0-30.0
Education level (years of schooling)	N	%
	0-4	1.5
	5-8	10.0
	9-11	77.0
	12 or more	11.1
	No information ^a	0.4
Occupation of the household head		
Unskilled manual	308	27.0
Semi-skilled manual	463	40.6
Skilled manual	51	4.5
Office functions	162	14.2
Top-level professional	58	5.1
Administrator/manager/director/owner	37	3.2
No information ^a	61	5.4
Household income (minimum wages) ^b		
<1	12	1.1
1-2	527	46.2
3-4	362	31.8
≥5	208	18.2
No information ^a	31	2.7
Economic class ^c		
A-B	170	14.9
C	746	65.4
D-E	172	15.1
No information ^a	52	4.6
Total	1140	100.0

Note: Mean, SD: standard deviation, median, and percentiles. BRISA prenatal cohort, São Luís, Brazil, 2010-2013.

^aValues unknown or not informed.

^bHousehold income expressed as times the national minimum wage effective in 2010/2013.

^cEconomic class according to the Economic Classification Criteria-Brazil, categorized into A/B, C, and D/E.

theoretically, so the initially proposed model was also the final one (Supplementary Material).

In the final model, each indicator of the latent variables Prenatal SES and child asthma traits had factor loadings ≥ 0.50 , and all indicators of these variables had significant P -values ($P < .001$) (Table 4; Figure 1).

A high percentage of daily calories from the sugars added to the SSBs consumed was associated with higher values of child asthma traits (SC = 0.073; $P = .030$). Furthermore, a small indirect effect of SSB via higher child's age on child asthma traits was also observed

TABLE 2 Demographic and health-related data of the children

Variable		
Birthweight (kilograms)	Mean	SD
	3.3	0.5
	Median	Percentiles 25-75
	3.3	3.0-3.6
Child's age (mo)	Mean	SD
	15.9	2.1
	Median	Percentiles 25-75
	15.0	14.0-17.0
Body mass index z-score ^a	Mean	SD
	0.6	1.3
	Median	Percentiles 25-75
	0.6	-0.2-1.4
Exclusive breastfeeding (mo)	N	%
<6	503	44.1
6 or more	616	54.0
No information ^b	21	1.8
Child's sex		
Male	571	50.1
Female	564	49.5
No information ^b	5	0.4
Medical diagnosis of asthma		
No	1108	97.2
Yes	32	2.8
Episodes of wheezing some time in life		
None	802	70.3
<3 episodes	256	22.5
3-6 episodes	52	4.6
>6 episodes	20	1.7
No information ^b	10	0.9
Emergency visit due to intense wheezing		
No	976	85.6
Yes	159	14.0
No information ^b	5	0.4
Medical diagnosis of rhinitis		
No	1,062	93.2
Yes	73	6.4
No information ^b	5	0.4
Eosinophil count (tertile)		
1st tertile (54-318 cells/mL)	255	22.4
2nd tertile (319-580 cells/mL)	257	22.5
3rd tertile (>580 cells/mL)	254	22.3
No information ^b	374	32.8
Total	1140	100.00

Note: Mean, SD: standard deviation, median, and percentiles. BRISA prenatal cohort, São Luís, Brazil, 2010-2013.

^az-score of BMI for age and sex.

^bValues unknown or not informed.

(SC = 0.012, SE; $P = .039$) (Table 5). Mediation pathways in the association between SSB and child asthma traits were not observed either via greater BMI-z or via eosinophil counts (data not shown in tables). High levels of eosinophils were directly associated with child asthma traits (SC = 0.118; $P = .049$).

As secondary findings in the proposed model analyzed by structural equation modeling, birthweight (SC = -0.124; $P = .006$), child's age (SC = -0.226; $P = <.001$), and exclusive breastfeeding ≥ 6 months were associated with lower values of child asthma traits (SC = -0.130; $P = .025$) (Table 5).

Finally, other components of unhealthy diet (except SSB) or of a healthy diet were not associated with child asthma traits ($P > .05$) (Supplementary Material). Overall, the weighted estimates taking losses to follow-up into account were similar to unweighted ones, and all associations were maintained when the weighting factor was applied to the structural equation model (Supplementary Material).

4 | DISCUSSION

A high percentage of daily calories from the sugars added to the SSBs consumed was associated with higher child asthma traits values in children up to 2 years old; however, no mediating pathway was observed by greater BMI-z or by cellular immune response.

The present study provides further evidence on the issue, by showing that exposure to SSB, even at ages earlier than those that have been studied, increases the risk of child asthma traits. A previous study, focusing on sugar-containing beverages, showed that high consumption of sugar-containing beverages (>21.5 cups/week) was associated with asthma in older children (11-year-olds). In that study, asthma was based on parents' report of wheezing, medical prescription of inhaled corticosteroids in the last 12 months, and medical diagnosis.⁹ Another study showed that a high frequency of beverages containing excess free fructose consumption (≥ 5 times/week) was associated with asthma in children (2-9 years), based on parents' report of current or past asthma.¹⁰ In another one, child (median age, 3.3 years) intake of SSB (quartile 4 $\times$ quartile 1) was also associated with asthma in mid-childhood (7 years), based on doctor's diagnosis of asthma, plus either report of wheezing or asthma medication use in the past 12 months.¹¹ In our study, the approach we used to measure asthma was advantageous, since an accurate diagnosis of asthma is difficult in children up to 5 years of age. Thus, the use of a cluster of four indicators of child asthma traits,²¹ treated as a continuous latent variable, reduced measurement error, as well as possible errors in the association between SSB and asthma.

High BMI was not a mediator of the association between SSBs and child asthma traits. This result was similar to one of a previous study that analyzed the association between sugar-containing beverages and asthma in 11-year-old children, which found no evidence of mediation by BMI.⁹ Other studies also showed that the association between beverages containing excess free fructose²⁶ or SSB¹¹ and asthma was independent of BMI adjustment.

TABLE 3 Food consumption data of the children (daily)

Variable	Mean	SD	Median	Percentiles 25-75
Consumption of sugar-sweetened beverages (%) ^a :	7.4	5.6	5.7	3.3-9.8
Chocolate milk (Kcal) ^b	86.3	56.7	80.0	40.1-120.0
Soft drinks (Kcal) ^b	56.9	27.3	52.0	40.0-70.8
Industrialized Juices (Kcal) ^b	73.3	48.7	63.0	43.0-82.2
Sugared pasty products (%) ^a :	7.3	4.6	6.3	4.1-8.7
Dairy drinks (Kcal) ^b	77.8	46.5	79.0	39.5-79.0
Popsicles and ice cream (Kcal) ^b	81.4	30.9	91.6	44.0-97.2
Industrialized baby food (Kcal) ^b	71.2	13.9	76.0	64.0-76.0
Sugared solids (%) ^a :	4.8	3.3	3.8	2.6-6.6
Cakes (Kcal) ^b	82.1	63.7	66.2	33.1-125.8
Cookies (Kcal) ^b	54.9	42.7	43.5	29.0-58.0
Staple foods ^c	459.8	293.2	407.1	250.1-590.2
Rice (Kcal) ^c	115.0	69.7	112.2	62.4-138.7
Bean (Kcal) ^c	51.3	84.7	31.1	20.7-53.2
Meat (Kcal) ^c	158.2	113.7	127.5	85.8-214.3
Milk (Kcal) ^c	360.6	264.3	316.8	158.7-475.2
Saturated fat (grams)	11.9	9.8	9.6	5.0-16.7
Total fiber (grams)	7.9	6.0	6.7	3.6-10.6
Staple foods (tertile) ^c		n	%	
1st tertile (19.8-316.7 Kcal)		431	37.9	
2nd tertile (316.8-515.7 kcal)		324	28.5	
3rd tertile (>515.7 Kcal)		381	33.6	
Fruits (tertile)		n	%	
1st tertile (1.6-12.9 grams)		278	38.0	
2nd tertile (12.9-22.7 grams)		211	28.9	
3rd tertile (>22.7 grams)		242	33.1	
Vegetables (tertile)		n	%	
1st tertile (0.3-15.7 grams)		306	41.9	
2nd tertile (15.8-31.2 grams)		183	25.0	
3rd tertile (> 31.2 grams)		242	33.1	
Sodium (tertile)		n	%	
1st tertile (0.3-545.0 milligrams)		244	33.9	
2nd tertile (545.1-907.4 milligrams)		244	33.9	
3rd tertile (>907.4 milligrams)		243	33.2	

Note: Mean, SD: standard deviation, median, and percentiles. BRISA prenatal cohort, São Luís, Brazil, 2010-2013.

^aCalories from added sugars as a percentage of the total daily energy intake.

^bTotal energy of sugars.

^cDaily energy.

Analyzing in detail pathways related to obesity by structural equation modeling, SSB consumption was not associated with high BMI (data not shown in table). Possibly the effect of these beverages on BMI may be observed later, since a systematic review has shown an association between SSB consumption and obesity risk, but in children older than those of our sample.²⁷ Additionally, the pathway from high BMI to child asthma traits was also not significant (data not shown in table). This last finding was contrary to our expectations, since a meta-analysis

showed an association between high BMI and childhood wheezing disorders, including children under 5 years.² A possible explanation for these distinct results may be the low prevalence of overweight (8.7%) and obesity (2.7%) in our sample of toddlers 1-2 years (data not shown in table). Together, these results suggest that the association between SSB and asthma temporally precedes the relationship between obesity and asthma. Thus, mechanisms other than obesity may be behind the association showed between SSB and child asthma traits.

TABLE 4 Factor loading, standard error, and *P*-value of the latent variables Prenatal Socioeconomic Status and child asthma traits

Latent variable	Factor loading ^a	Standard error	<i>P</i> -value
Prenatal SES ^b			
Maternal education level	0.539	0.034	<.001
Occupation of household head	0.547	0.030	<.001
Household income	0.728	0.033	<.001
Economic class ^c	0.790	0.033	<.001
"child asthma traits" ^d			
Medical diagnosis of asthma	0.625	0.090	<.001
Wheezing episodes (≥3)	0.740	0.088	<.001
Medical emergency due to intense wheezing	0.563	0.207	<.007
Rhinitis	0.557	0.082	<.001

Note: BRISA prenatal cohort, São Luís, Brazil, 2010-2013.

^aExpected load greater than 0.5.

^bLatent variable of prenatal socioeconomic status.

^cEconomic class according to the Economic Classification Criteria-Brazil, categorized into A/B, C, and D/E.

^dLatent variable of asthma.

Likewise, the other mediating pathway tested in our study, the eosinophils were also not in the chain linking SSB to child asthma traits. In a mice model, sugar consumption had an effect in the susceptibility to allergic inflammation of the airways and activation of the innate immune system.¹² In our results, a high eosinophil count was directly associated with higher child asthma traits values, characterizing that this outcome also included allergic cases, which might be triggered by other exposures, such as aeroallergens.²⁸

Alternatively, the inflammatory mechanisms induced by the formation of advanced glycation endproducts (AGE),²⁹ especially from free fructose, on the gut (enFruAGE) may explain the association between excess free fructose consumption and childhood asthma.¹⁰ In addition, the harmful effect of high free fructose may underlie the association that has been shown between higher intake of free sugar³⁰ and especially SSB consumption^{11,21} in the gestational period and offspring asthma.

Diet has a determinant role in gut microbiota composition and diversity, affecting the mucosal immunity and influencing lung immune response.³¹ The gut-lung axis has been studied as a mechanism linked to asthma.³² Moreover, dietary exposure in early life has a crucial role in the modulation of human microbiome, since its major plasticity is observed at the first 2 years of life.³³ An animal model study has shown that early life sugar consumption, simulating SSB exposure by humans, resulted in lower diversity of the intestinal microbiome.³⁴ Thus, early life SSB exposure, as observed in the present study, may result in a dysbiotic gut microbiota and asthma. This hypothesis, however, needs to be confirmed in future human studies.

SSB intake is associated with consumption of other components of an unhealthy diet and also with low intake of fruits and vegetables,³⁵ which may confound the association between SSB and asthma. However, components of the unhealthy diet or of a healthy diet were not associated with child asthma traits in our study, providing further evidence of the role of SSB in asthma etiology. As a secondary

finding in our analysis, exclusive breastfeeding (≥6 months) was associated with reduced child asthma traits values. This finding reinforces the results of a systematic review, which showed a strong association between exclusive breastfeeding and reduced risk of asthma in children 0-2 years of age, which decreased with age, but remained significant at 7 years or more.³⁶ The subjacent protective mechanism to explain the association between breastfeeding and asthma remains uncertain, but may involve immune response and/or reduced exposure to potential diet allergens while the baby was exclusively breastfed,³⁶ including SSB.

Among the study limitations, no allergy tests were performed, which would have permitted better characterization of the sample in terms of the child's allergic status. However, sensitization tests are expensive, so they would be infeasible due to the large sample size of our study. As an indicator of the allergic response, immune system cells were evaluated and higher tertiles of eosinophil count were found to be associated with higher child asthma traits values. Although SSB exposure and asthma indicators were enquired at the same time, the mean age of the children was only 16 months (12-24 months), so the measure of exposure was taken as early as possible, perhaps too early to allow the first asthma traits to appear.

As a strength of this study, structural equation modeling allowed us to explore the association between SSB consumption on child asthma traits, analyzing direct and indirect pathways mediated by BMI and by the cellular immune response. Advantageously, child asthma traits measured as a latent variable reduced the measurement error of this complex syndrome in small children.²¹ Besides SSB, no other unhealthy dietary exposures in the 2nd year of life tested in our study were associated with child asthma traits, adding new evidence regarding the association between SSB and increased risk of asthma.

This study warns that even in early life, exposure to SSB would be a risk factor for child asthma traits. The average proportion of calories derived from added sugars consumed by the children was

TABLE 5 Standardized coefficient, standard error, and P-value of the total and direct effects analyzing exposure variables and “child asthma traits” at 2nd year of life

“child asthma traits” ^a	Total effect			Direct effect		
	Standardized coefficients	Standard error	P-value	Standardized coefficients	Standard error	P-value
Prenatal SES ^b	−0.035	0.056	.527	−0.021	0.057	.708
Maternal age (y)	0.026	0.046	.564	0.041	0.046	.374
Birthweight (kilograms)	−0.124	0.044	.005	−0.124	0.045	.006
Child's sex						
Male	Ref.					
Female	−0.070	0.045	.124	−0.055	0.045	.226
Exclusive breastfeeding						
< 6 mo	Ref.					
6 or more mo	−0.129	0.058	.025	−0.130	0.058	.025
Child's age (mo)	−0.214	0.047	<.001	−0.226	0.048	<.001
Percent SSB ^c	0.071	0.033	.030	0.073	0.033	.030
Child's body mass index z-score ^d	0.011	0.043	.803	0.007	0.044	.879
Tertile of eosinophil count (cells/mL)						
1st tertile	Ref.					
3rd tertile	0.118	0.060	.049	0.118	0.060	.049

Note: BRISA prenatal cohort, São Luís, Brazil, 2010–2013.

Indirect effect of children's age on asthma via SSB (standardized coefficients: 0.012, standard error: 0.006, $P = .039$).

^aLatent variable of asthma.

^bLatent variable of prenatal socioeconomic status.

^cCalories from added sugars in SSBs as a percentage of the total daily energy intake.

^dZ-score of BMI for age and sex.

The values in bold represent statistical significance ($P < .05$).

higher than 5% that has been recommended by the World Health Organization for the prevention of obesity.³⁷ The American Heart Association also recommends that the consumption of added sugars be avoided by children up to 2 years to reduce the future cardiovascular risk.³⁸ Asthma, as a non-communicable disease, has been consistently associated with both obesity^{39,40} and cardiovascular risk in the future.⁴¹

5 | CONCLUSION

This study adds to a growing body evidence that consumption of added sugars by very young children seems implicated in asthma, preceding the link between sugar consumption and overweight/obesity, not yet evident in children in the first 2 years of life. In our sample, the introduction of SSB was too early and also excessive, since the median of added sugar intake from SSB was above 5% of total daily calories, warning to increasing risks of obesity and cardiovascular diseases in the future. Taken together, our results support early policy interventions to enhance diets of young children that may help reduce the lifelong impacts of unhealthy diets on asthma and other non-communicable diseases.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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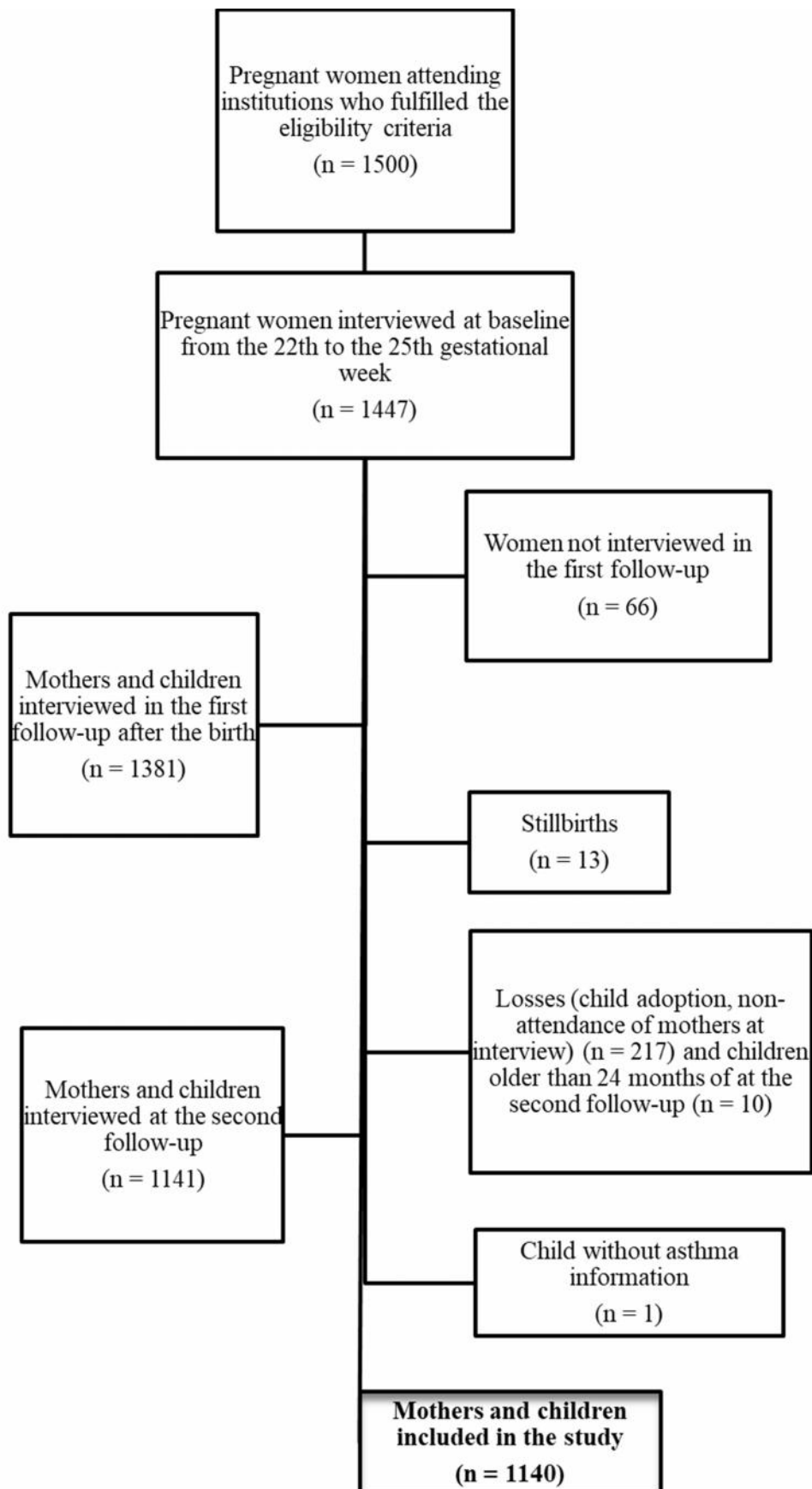
SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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Supplementary Material

Supplemental Figure 1. Flow chart of the participants of the BRISA prenatal cohort study, São Luís, Brazil.



Supplemental Table 1 Fit indices of weighted and unweighted structural equation models analysing the association between exposure to sugar-sweetened beverages and “child asthma traits” in the 2nd year of life. BRISA Prenatal Cohort, São Luís, Brazil, 2010-2013.

Fit indices	Values	Weighted Model	Unweighted Model
Chi-squared test	-	146.593	147.300
Degrees of freedom	-	81	81
p-value χ^2	-	< 0.001	< 0.001
RMSEA †	<0.05	0.027	0.027
90% confidence interval	< 0.08 (upper limit)	0.020 - 0.034	0.020 - 0.034
Comparative Fit Index	> 0.95	0.975	0.975
Tucker-Lewis Index	> 0.95	0.964	0.964
Weighted root mean square residual	< 1.00	0.921	0.922

† RMSEA: root mean square error of approximation.

29 **Supplemental Table 2** Standardized coefficients, standard errors and p-values of the unweighted
 30 model of the total and direct effects analysing the association between the exposure variables and
 31 “child asthma traits” in the 2nd year of life. BRISA Prenatal Cohort, São Luís, Brazil, 2010-2013.
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“Child asthma traits” †	Total effect			Direct effect		
	Standardized coefficient	Standard error	p-value	Standardized coefficient	Standard error	p-value
Prenatal SES ‡	-0.039	0.055	0.479	-0.024	0.057	0.670
Maternal age (years)	0.025	0.046	0.584	0.041	0.046	0.380
Birth weight (kilos)	-0.123	0.043	0.005	-0.123	0.045	0.007
Child’s sex						
Male	Ref.					
Female	-0.070	0.045	0.125	-0.055	0.046	0.228
Exclusive breastfeeding						
< 6 months	Ref.					
6 or more months	-0.134	0.058	0.020	-0.134	0.058	0.020
Child’s age (months)	-0.215	0.047	<0.001	-0.227	0.048	<0.001
Percent SSB §	0.074	0.033	0.026	0.076	0.034	0.026
Child’s body mass index z-score ¶	0.011	0.044	0.802	0.007	0.044	0.877
Tertile of eosinophil count (cells/ml)						
1 rd tertile	Ref.					
3 rd tertile	0.121	0.060	0.044	0.121	0.060	0.044

33 † Latent variable of asthma. .
 34 ‡ Latent variable of prenatal socioeconomic status. .
 35 § Calories from added sugars in SSBs as a percentage of the total daily energy intake
 36 ¶ Z-score of BMI for age and sex.
 37 Indirect effect of children's age on asthma via SSB (Standardized coefficients: 0.013, Standard error: 0.006, p =
 38 0.035).
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51 **Supplemental Table 3** Standardized coefficients, standard errors and p-values of direct effects
 52 analysing the association between food consumption variables and “child asthma traits” in the 2nd
 53 year of life. BRISA Prenatal Cohort, São Luís, Brazil, 2010-2013.

Variable	Direct effect in “child asthma traits”		
	Standardized coefficient	Standard error	p-value
Consumption of sugar sweetened beverages (unweighted) (%) †	0.076	0.034	0.026
Sugared pasty products (%) †	0.045	0.057	0.432
Sugared Solids (%) †	-0.112	0.067	0.096
Staple foods (tertile) ‡	-0.031	0.048	0.521
Saturated fat (grams)	-0.022	0.038	0.559
Total fiber (grams)	0.042	0.052	0.420
Fruits (tertile)	-0.043	0.062	0.488
Vegetables (tertile)	0.093	0.064	0.146
Sodium (tertile)	0.019	0.063	0.760

† Calories from added sugars as a percentage of the total daily energy intake.

‡ Daily energy.