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Birth weight and asthma in young adults of a Brazilian birth cohort

Peso ao nascer e asma em adultos jovens de um coorte brasileiro de nascimentos

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Abstract *This article aims to evaluate the association between birth weight and asthma in adulthood, estimated by employing structural equation modeling. Cohort study with 1,958 participants aged 23-25 years from Ribeirão Preto, São Paulo, Brazil. Standardized questionnaires were applied and pulmonary function evaluated, including bronchial reactivity with methacholine. A theoretical model was proposed to explore the effects of birth weight and asthma in adulthood. Asthma, socioeconomic status at birth (Birth SES), and current socioeconomic status (Adult SES) were obtained by constructs. Maternal age, sex, skin color, body mass index (BMI), smoking, parental asthma history, history of respiratory infection before five years old, history of hospitalization for lung disease before two years old, and atopy were the studied variables. 14.1% of participants were diagnosed with asthma. Birth weight was associated with asthma (Standardized Coefficient - SC_{total}=-0.110; p=0.030), and an indirect effect was also observed ($SC_{indirect}$=-0.220; p=0.037), mediated by hospitalization before two years and respiratory infection before five years. Lower birth weight showed an increased risk of asthma in adulthood and the SES Birth and Adult SES variables underlie this association.*

Key words *Birth weight, Cohort studies, Asthma, Hospitalization, Infections*

Resumo *O objetivo deste artigo é avaliar associação entre peso ao nascer e asma na vida adulta pela análise de equações estruturais. Estudo de coorte com 1.958 participantes de 23-25 anos, residentes em Ribeirão Preto, São Paulo, Brasil. Foram aplicados questionários padronizados e avaliado a função pulmonar, incluindo hiper-reatividade brônquica com metacolina. O modelo teórico foi proposto para explorar os efeitos do peso ao nascer e asma na vida adulta. Asma, status socioeconômico ao nascimento (SES Nascimento) e status socioeconômico adulto (SES adulto) foram obtidos por um construto. Variáveis estudadas: idade materna, idade, sexo, cor da pele, índice de massa corporal (IMC), tabagismo, história de asma dos pais, história de infecção respiratória antes dos cinco anos, história de internação por doença pulmonar antes dos dois anos e atopia. 14,1% dos participantes foram diagnosticados com asma. Peso ao nascer foi associado com asma (Coeficiente Padronizado - CP_{total}=-0,110; p=0,030), e foi observado efeito indireto ($CP_{indireto}$=-0,220; p=0,037), mediado por internação antes dos dois anos e infecção respiratória antes dos 5 anos. Menor peso ao nascer aumentou o risco para asma na vida adulta e as variáveis SES Nascimento e SES adulto foram subjacentes a esta associação.*

Palavras-chave *Peso ao nascer, Estudo de coorte, Asma, Internação, Infecção*

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Introduction

Asthma is a chronic disease and the major cause of childhood morbidity and mortality, with increased prevalence in recent decades in several countries[1-3]. It affects 300 million people all over the world and its prevalence increases by 50% every decade[4].

Epidemiological studies have shown several risk factors for the development of asthma: respiratory infections[5], socioeconomic factors[6], air pollution[7], lower body mass index (BMI), atopy, maternal smoking during pregnancy, and adult smoking[3,8,9]. In addition, fetal life, intrauterine nutrition, and environmental exposures can modify the structure, physiology, and metabolism of the body during growth and influence long-term health, increasing the risk of the development of non-communicable chronic diseases (NCCD), including asthma[8,10].

Studies have shown impaired respiratory infections in early childhood in adult lung function[5]. These infections are more often in newborns with low birth weight (LBW, <2500 g) compared to those born with adequate birth weight (≥3000 g)[11]. It is unknown whether this association occurs: between birth weight and childhood respiratory infection or birth weight and lung size, a decrease in growth, and incomplete formation of airways in intrauterine life[9,12,13].

LBW and preterm birth (gestational age <37 weeks) are strongly associated with an increased risk of disease in adulthood. Perinatal risk factors of asthma are not well known and show inconsistent results in the literature. However, simultaneous exposure to these factors with other risk factors, such as cesarean delivery, respiratory distress syndrome, and meconium aspiration can impact the development of asthma[14].

Some studies showed an inverse association between birth weight and asthma symptoms in young adults (20 to 24 years of age)[12] and birth weight can increase the risk of asthma twice as well in young adults 26 years of age[13].

Although several factors are involved in the association studied, they are interrelated in determining asthma, either as confounding factors or as mediators of the causal chain.

The complex temporal relation in this association between birth weight and asthma involves other causality variables, such as childhood respiratory infections, socioeconomic status, and maternal and adult smoking. Thus, birth weight may be a *mediating factor* in the causal chain or an *independent risk factor* for asthma. This can be explored using structural equation modeling (SEM), a useful tool to investigate these relationships in multicausal epidemiological studies.

Thus, this study aimed to evaluate the association between birth weight and asthma in adulthood.

Methods

Sample

This study use data from the fourth phase of the study "From perinatal health to the health of young adults: a study of a cohort born from June 1, 1978, to 31 May 1979 in the hospitals of Ribeirão Preto, SP". This longitudinal prospective cohort evaluated 9,067 mothers and their respective newborns, corresponding to 98% of births in Ribeirão Preto-SP. The proportion of mothers discharged from the hospital before being interviewed was 2.5% and less than 1% refused the interview. Infants born to mothers who did not reside in the municipality (2,173) and twins (146) were excluded from the study. Thus, 6,748 remained in the study, 257 died during the first year of life, and 86 died by 20 years of age[15].

This cohort had four waves of follow-up: at school age in 1987/89, male conscripts aged 18 years in 1996/97, young adults aged 23-25 years in 2002/04 and adults aged 37-39 years in 2016/17. The present study involved subjects evaluated at birth and in 2002/04, aged 23-25, to determine the relative importance of events from the prenatal period to the beginning of adult life for physical growth and the determination of the risk profile for NCCD, with emphasis on cardiovascular disease, asthma, and allergy[15].

The subjects were 23 to 25 years old and 2013 young adults is evaluated and 145 were excluded because they did not undergo the bronchial provocation test, totaling 1958 participants in the final sample.

Questions related to socioeconomic status, age, education, smoking, parity, type of delivery, duration of pregnancy, gender, date of birth and occurrence of death were record and the newborns were weighed naked on scales calibrated weekly with a precision of 10 grams.

Variables

Latent variables

Latent variables result from the combination of various observed variables to explain the cor-

relations between them, with a better statistical estimate by representing the theoretical concepts more appropriately.

Then, to explain correlations between some variables, the following constructs were elaborate: socioeconomic status at birth (Birth SES), adult socioeconomic status (Adult SES), and asthma.

Exposure variable: Birth weight and low birth weight

The exposure variable birth weight was categorized as low birth weight (LBW. <2500 g); insufficient weight (2500-2999 g); adequate weight (3000-3999 g) and high birth weight (≥4000 g).

The exposure variable low birth weight was categorized as low birth weight <2500 g (yes: <2500 g or no: ≥2500 g).

Outcome variable: Asthma

Variable asthma consisted of the following variables:

At least one of the following *disease symptoms*: wheezing (yes or no), tightness in the chest (yes or no), shortness of breath at rest during the day in the last 12 months, and/or night waking with shortness of breath in the last 12 months (yes or no), questions obtained from European Community Respiratory Health Survey (ECRHS)[16]. The presence of at least one of the symptoms was to improve the accuracy of the diagnosis of asthma.

Diagnosis of asthma (yes or no): Measurement of bronchial hyperresponsiveness with methacholine, categorized as concentration provocative of 20% (PC20) decrease in forced expiratory volume in the first second (VEF_1), PC20≤4 mg/ml, indicating bronchial hyperresponsiveness or obstructive pattern, and PC20>4 mg/ml, absence of bronchial hyperresponsiveness, according to the American Thoracic Society[17].

Observed variables at birth

Maternal age (until 19 years, 20-34 years, ≥35 years); Maternal smoking during pregnancy (yes or no); Socioeconomic status at birth construct (Birth SES), consisted of the following variables: maternal schooling years (0 to 4, 5 to 8, 9 to 11, and ≥12), maternal occupation (unskilled manual worker and semi-skilled, skilled manual worker and non-manual worker), according to International Standard Classification of Occupation[18] and monthly family income based on Brazilian national minimum wage in force during the 1978/79 period, categorized as 0 to 1.9 minimum wages, 2 to 2.9 minimum wages, 3 to 4.9 minimum wages, and 5 or more minimum wages.

Observed variables in adult life

Adult current socioeconomic status construct (Adult SES), consisted of the following variables: adult schooling (0 to 4 years, 5 to 8 years, 9 to 11 years, and 12 years or more), adult occupation (unskilled manual worker and semi-skilled, skilled manual worker and non-manual worker) and monthly family income based on the Brazilian national minimum wage in force during the 2002/04 period, categorized as less than 1 minimum wages, 1 to 2.9 minimum wages, 3 to 4.9 minimum wages, 5 to 9.9 minimum wages, and 10 or more minimum wages; Gender (male, female); Skin color (white, not white); Birth order (first son or not); Body mass index (BMI), categorized in: thinness (BMI<18.5 Kg/m²), normal weight (BMI between 18.5 and 24.9 Kg/m²), overweight (BMI between 25 and 29.9 Kg/m²) and obesity (BMI≥30 Kg/m²)[19]; Adult smoking (yes or no); Parental asthma history (yes or no); History of respiratory infection before five years old (yes or no); History of hospitalization for lung disease before two years old (yes or no); Atopy (yes or no).

Statistical Analysis

Proposed theoretical model

The contributing variables to the development of asthma were: maternal age, maternal smoking, skin color, history of respiratory infection before five years old, history of hospitalization for lung disease before two years, birth SES, adult SES, birth order, gender BMI, atopy, adult smoking, and parental asthma history. A direct acyclic graph was designed (Figure 1) to delineate causal pathways between birth weight and asthma employing Directed Acyclic Graph (DAG - DAGitty 3.0)[20].

Structural equation modeling (SEM)

Structural equation modeling (SEM) is an epidemiological tool used to test hypotheses on relationships between latent variables (not observed variables) and observed variables, permitting the analyses of a set of structural equations[21]. Through this method, it is also possible to test the direct and indirect effects (mediation), exploring pathways and mechanisms of these effects and testing the association between LBW and asthma. Analyzes were performed using Mplus software version 6.0, considering the level of significance set at 5%.

Exploratory factor analyses (EFA) were elaborated to determine the number of variables

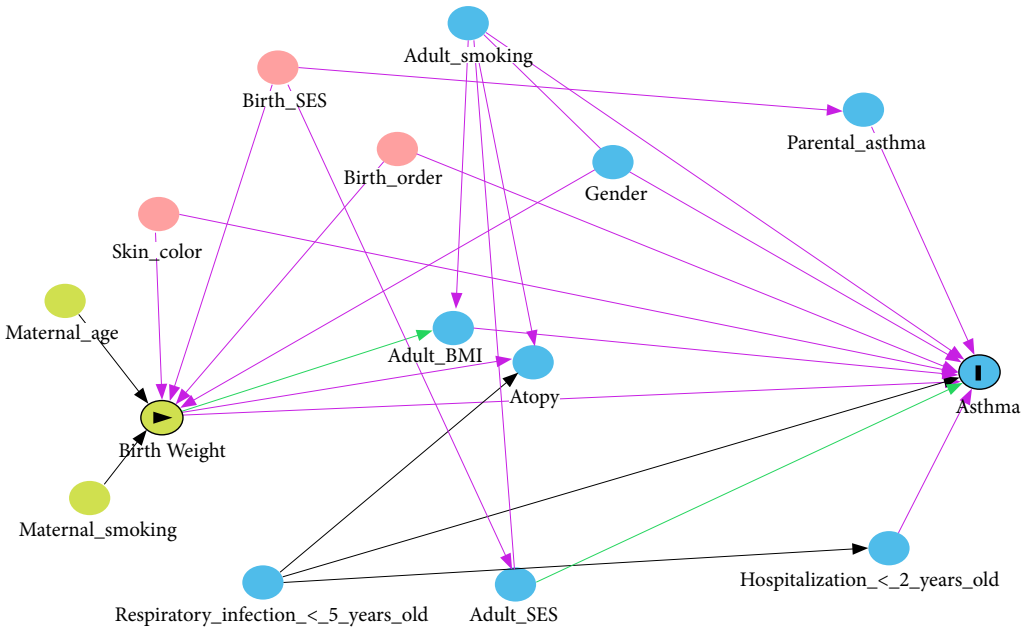

Figure 1. Directed Acyclic Graph (DAG). Birth Cohort of Ribeirão Preto 1978/79.

Source: Authors.

needed to explain the correlation between a set of observed variables. The indicators for all latent variables were selected based on convergent loadings (>0.50). Then, confirmatory factorial analyses (CFA) were elaborate to verify the factors previously determined by EFA[22]. Model fit was assessed based on the following fit indices: a) p-value<0.05 in the chi-square test (χ^2); b) p>0.05 and upper 90% confidence interval limit <0.08 for the Root Mean Square Error of Approximation (RMSEA); c) Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI) values >0.95; d) Weighted Least Square Mean and Variance Adjusted (WLSMV) value <1[23]. Mod-indices (modification index) command was used to obtain suggestions of changes in the proposed variables constructs[22].

The study was approved by the Research Ethics Committee of the Hospital das Clínicas and of the Ribeirão Preto School of Medicine, University of São Paulo, on 02/02/2000, HCRP process No. 7606/99. All participants received and signed the consent form.

Results

The characteristics of the population at birth and at 23/25 years of age are listed in Table 1. The prevalence of LBW was 6.8% (n=133), parental asthma history 9.8% (n=192) and maternal smoking 25.4% (n=488), adult smoking 17.4% (n=340), history of respiratory infection before five years old 19.2% (n=325), history of hospitalization for lung disease before two years old 11.4% (n=198) and atopy 44.4% (n=843) (Table 1).

The factor loads of each construct "Birth SES", "Adult SES" and "Asthma" were above 0.50 and p-values <0.001 (Table 2). The latent variable asthma showed convergent loads higher than 0.50 for the following indicators: PC20 (0.753), wheezing in the last 12 months (0.681), and diagnosis of asthma (0.552).

Lower birth weight values were associated with asthma (Standardized Coefficient - SC_{total}=-0.110; p=0.030) and "birth SES" (SC_{total}=-0.142; p=0.001) (Table 3).

Higher adult smoking values (SC_{total}=0.205; p<0.001, SC_{direct}=0.205; p<0.001), and history of respiratory infection before five years old (SC_{total}=1.366; p<0.001, SC_{direct} =1.327; p=0.001) had a

Table 1. Characteristics of participants at birth and young adult. Ribeirão Preto, São Paulo, Brazil, 1978/79-2002/04.

Characteristics	N	%
Birth weight		
Adequate	1.286	65.7
Low birth weight	133	6.8
Insufficient weight	401	20.5
High birth weight	138	7
Parental asthma history		
No	1.766	90.2
Yes	192	9.8
Maternal age (anos)		
<20	234	12
20-34	1.549	79.1
≥35	163	8.3
Maternal smoking		
No	1.432	73.1
Yes	488	25
Gender		
Male	962	49.1
Female	996	50.9
Birth order		
First son	757	38.8
Not the first	1.194	61.2
Skin color		
White	1.296	66.2
Not white	662	33.8
Smoking		
Yes	340	17.4
No	1.618	82.6
BMI		
Thinness	161	8.2
Normal weight	1.085	55.5
Overweight	475	24.3
Obesity	233	11.7
Respiratory infection before five years		
No	1.371	80.8
Yes	325	19.2
Hospitalization for ling disease before two years		
No	1.543	88.6
Yes	198	11.4
Atopy		
No	1.055	55.6
Yes	843	44.4

BMI = Body Mass Index; Asthma = Medical diagnosis of asthma, one of the symptoms: wheezing, tightness in the chest, shortness of breath at rest during the day, shortness of breath at night for at least 12 months, and bronchial hyperresponsiveness.

Source: Authors.

total and direct effect on asthma. The history of hospitalization for lung disease before two years (SC_{total}=0.398; p<0.001) had a total effect on asthma (Table 3).

Lower maternal smoking values (SC_{direct}=-0.147; p=0.044) and a history of hospitalization for lung disease before two years (SC_{direct}=-0.862; p=0.031) had a direct effect on asthma (Table 3).

Birth weight was also indirectly associated with asthma with this effect being mediated by hospitalization for lung disease before two years old and a history of respiratory infection before five years old ($SC_{indirect}$=-0.220; p=0.037) (Table 3).

Some exposure variables showed an indirect effect on asthma: Birth SES mediated by adult smoking ($SC_{indirect}$=0.061; p=0,002) and by the history of respiratory infection before five years old and ($SC_{indirect}$=0,164; p=0.039); lower Adult SES values mediated by adult smoking ($SC_{indirect}$=-0.050; p=0.002); higher maternal smoking values mediated by adult smoking ($SC_{indirect}$=0.040; p=0.004) and higher hospitalization for lung disease before two years old values mediated by history of respiratory infection before five years old ($SC_{indirect}$=1.257; p=0.001) (Table 3).

In another analysis where LBW was the exposure variable and preterm birth was excluded, any association between LBW and asthma was found. However, LBW was indirectly associated with asthma mediated by Adult SES and adult smoking. Some variables were indirectly associated with asthma too, mediated by LBW: Birth SES (mediated by LBW, Adult SES, and adult smoking), maternal age (mediated by maternal smoking, LBW, Adult SES, and adult smoking), and maternal smoking (mediated by LBW, Adult SES and smoking adult) (Table 4).

Discussion

Main findings

In the present study, lower birth weight values were associated with adult asthma at Birth Cohort 1978/79.

Higher adult smoking, hospitalization for lung disease before two years, and respiratory infection before five years values had a total and direct effect on asthma. Maternal smoking had a direct and indirect (mediated by adult smoking) on asthma. Hospitalization for lung disease before two years had also an indirect effect on asthma mediated by respiratory infection before

Table 2. Factorial loading, standard error, and p-value for the final latent variables of Birth SES, Adult SES, and Asthma, by structural equation modeling (SEM). Ribeirão Preto, São Paulo, Brazil, 1978-2002/04.

Constructs	Factorial loading	Standard error	p-value
Birth SES			
Family income	0.793	0.017	p<0.001
Maternal schooling	0.860	0.015	p<0.001
Maternal occupation	0.778	0.023	p<0.001
Adult SES			
Family income	0.875	0.036	p<0.001
Adult´s schooling	0.964	0.039	p<0.001
Current adult´s occupation	0.498	0.026	p<0.001
Asma			
PC20	0.547	0.042	p<0.001
Medical diagnosis of asthma	0.983	0.067	p<0.001
Wheezing	0.711	0.062	p<0.001

SES: socioeconomic status; Birth SES: Latent variable of the socioeconomic status of the family; Adult SES: Latent variable of the socioeconomic status of the adult; Asthma: Latent variable using the variables PC20 (measurement of bronchial hyperresponsiveness with methacholine in mg/dL, considering positive when causing a 20% decrease in FEV1), medical diagnosis of asthma, and wheezing at least 12 months.

Source: Authors.

Table 3. Effects of birth weight and observed variables on adult asthma. Ribeirão Preto, São Paulo, Brazil, 1978/79-2002/04.

Variables	Effect	Factor loading	Standard error	p-value
Birth weight	Total	-0.110	-2.168	0.030
	Direct	-0.103	-1.361	0.174
	Indirect (1)	-0.220	-2.089	0.037
Birth SES	Total	-0.142	-3.275	0.001
	Direct	-0.190	-1.561	0.118
	Indirect (2)	0.061	3.111	0.002
	Indirect (3)	0.164	2.065	0.039
Adult SES	Total	-0.140	-1.600	0.110
	Direct	-0.091	-1.025	0.305
	Indirect (4)	-0.050	-3.087	0.002
Maternal Smoking	Total	0.016	0.360	0.719
	Direct	-0.147	-2.011	0.044
	Indirect (5)	0.040	2.916	0.004
Adult smoking	Total	0.205	4.199	p<0.001
	Direct	0.205	4.197	p<0.001
Respiratory infection before five years	Total	1.366	3.639	p<0.001
	Direct	1.327	3.477	0.001
Hospitalization for lung disease before two years	Total	0.398	7.295	p<0.001
	Direct	-0.862	-2.152	0.031
	Indirect (6)	1.257	3.322	0.001

1 - Mediated by hospitalization for lung disease before two years and respiratory infection before five years; 2 - Mediated by adult smoking; 3 - Mediated by respiratory infection before five years; 4 - Mediated by adult smoking; 5 - Mediated by adult smoking; 6 - Mediated by respiratory infection before five years.

Source: Authors.

Table 4. Effects of LBW and observed variables on adult asthma. Ribeirão Preto, São Paulo, Brazil, 1978/79-2002/04.

Variables	Effect	Factor loading	Standard error	p-value
LBW	Total	0.116	1.329	0.184
	Direct	0.092	0.612	0.540
	Indirect (1)	0.019	2.328	0.020
Birth SES	Total	-0.139	-3.179	0.001
	Direct	-0.025	-0.166	0.868
	Indirect (2)	-0.004	-2.017	0.044
Adult SES	Total	-0.314	-1.985	0.047
	Direct	-0.229	-1.405	0.160
Maternal age	Total	0.003	0.115	0.909
	Direct	-	-	-
	Indirect (3)	-0.001	-1.972	0.049
Maternal smoking	Total	0.020	0.418	0.676
	Direct	-0.136	-1.578	0.115
	Indirect (4)	0.006	2.152	0.031
Adulto smoking	Total	0.229	3.676	0.000
	Direct	0.230	3.688	0.000
Respiratory infection before five years	Total	1.219	2.433	0.015
	Direct	1.175	2.307	0.021
Hospitalization for lung disease before two years	Total	0.437	7.082	0.000
	Direct	-0.678	-1.268	0.205

1 - Mediated by Adult SES and adult smoking; 2 - Mediated by LBW, Adult SES and adult smoking; 3 - Mediated by maternal smoking, LBW, Adult SES and adult smoking; 4 - Mediated by LBW, Adult SES and smoking adult.

Source: Authors.

five years. Also, this study showed associations between asthma and Birth SES and Adult SES.

This association between LBW and asthma could be explained by mechanisms of early adaptation in response to adverse exposures during fetal life and childhood, such as impaired lung growth, and decreased airways and lung volume[2]. Therefore, LBW may have a direct and indirect effect on other variables for the development of asthma.

In a subanalysis, some variables were indirectly associated with asthma, mediated by LBW: Birth SES (mediated by LBW, Adult SES, and adult smoking), maternal age (mediated by maternal smoking, LBW, Adult SES, and adult smoking), and maternal smoking (mediated by LBW, Adult SES and smoking adult).

These three pathways showed that LBW indirectly influences the development of asthma. This result may be an explanation for the controversial results in the literature; adult SES and adult smoking were present in these three pathways, as well as in the indirect association between birth weight and asthma. Therefore, the association between birth weight and asthma may depend on the sample characteristics and adequate control of the observed variables.

Characteristics

Children born with LBW can have an increased risk of asthma symptoms during childhood and adulthood, however, this risk may not be related only to poor intrauterine nutrition,

fetal growth, and perinatal conditions. Environmental factors in childhood, such as low socioeconomic status and smoking seem to present a greater impact on the development of asthma in adulthood[12,21], and similar results were observed in this study. Lower Adult SES value had an indirect effect on asthma mediated by adult smoking. Maternal smoking, hospitalization for lung disease before two years, and respiratory infection before five years have a total and direct effect on asthma.

Comparison with existing literature

In a systematic review of 41 articles, 26 observed an association between LBW and asthma[3], whereas some studies did not find this association[24,25].

Studies stated that the mechanisms of this association are not yet fully understood[2,13], and the influence of risk factors is not well established, although simultaneous exposures of perinatal factors with the risk factors can impact the development of asthma[14].

Some studies show decreased lung function in childhood in children born with LBW and a higher prevalence of respiratory symptoms[3]; also, similar results were found in this study: birth weight values were indirectly associated with asthma mediated by hospitalization for lung disease before two years and respiratory infection before five years.

In the first years of life, a respiratory disease associated with wheezing is a frequent cause of hospitalizations and morbidity and is associated with a higher risk of asthma in school-age children[26].

Infections during the preschool period can contribute to the onset and persistence of wheezing, therefore, this symptom tends to disappear in the early school years when not atopic and with normal lung function. In these cases, wheezing is associated with infection, without dyspnea[27].

Regarding socioeconomic status, this study shows that Birth SES had an indirect effect on asthma mediated by adult smoking and respiratory infection before five years. Several studies constantly show lower Birth SES as a risk factor for asthma incidence, control, and exacerbation[28], because they have worse hygiene habits, difficult access to health care and emergency medication, greater exposure to smoking and pollution, and higher BMI[29].

Adult SES had also an indirect effect on asthma mediated by adult smoking. Some studies show a higher prevalence of asthma symptoms throughout life in affluent societies. The diagnosis of asthma can be considered an explanation for this result, because this diagnosis can be adopted earlier by families with higher status socioeconomic, with higher education, more information, and better access to health care and medication. Symptoms of asthma may be underreported in those with lower socioeconomic status[29].

Several authors suggest that maternal smoking can influence the development of the newborn respiratory system, pulmonary function, and LBW risk[25], contributing to increasing the risk of asthma during childhood. Other studies show that maternal smoking is associated with LBW and lower socioeconomic status and both contribute to the development of asthma[30].

Strengths and limitations

The *strength* of this study is the prospective follow-up of more than 2,000 participants, and the use of the bronchoprovocation test as a tool to compose the diagnosis of asthma. New statistical tools, such as structural equation modeling, allow the creation of latent variables and a greater understanding of the contribution of LBW in the development of asthma.

A *limitation* of this study was the diagnosis of asthma made only in the fourth phase of the Cohort follow-up, when the participants were between 23 and 25 years of age, not being possible to obtain the diagnosis of asthma during childhood.

Another limitation is the lack of detailed information related to pregnancy and early childhood. Information on hospitalizations and respiratory infections in childhood was obtained during an interview with young adults, therefore, memory bias needs to be considered. Finally, the reproducibility of the ECRHS questionnaire used in the Brazilian population was also not studied[17].

There is a complex relationship between the risk factors that influence the development of asthma. In cohort studies, researchers have endeavored the risk factors for asthma and NCCD in adulthood, from the earliest stages of life. Cohort studies are considered very important, because they allow the long-term follow-up of the individual, contributing to the understanding of transitions from childhood to adulthood and the development of chronic diseases in adults[15].

This study makes a valuable contribution to the study of asthma by being able to demonstrate the effects of birth weight on the causal pathway

of asthma, reinforcing the importance of the life cycle for these issues.

In conclusion, lower birth weight values increase the risk of asthma in adulthood and the pathways of these associations passed through factors from early childhood, mediated by hospitalization for lung disease before two years and respiratory infection before five years. The present study makes a valuable contribution to the study of asthma demonstrating the effects that birth weight generates on the pathway of asthma and analyzing variables that demonstrate contradictory results in the literature, such as SES[26]. Birth SES and Adult SES were variables underlying asthma association with birth weight, mediated by adult smoking and respiratory infection before five years in the former, and adult smoking in the latter.

Collaboratioins

FP Vitti and VC Cardoso designed the study, were involved in the analyses, and wrote the article. LL Padilha and CCC Ribeiro helped in the analysis with Structural Equation Modeling. C Grandi, H Bettiol, MA Barbieri and EO Vianna were involved in writing and editing the article.

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