Review Article

Asthma in adolescents: what did ERICA study show us?

Asma em adolescentes: o que o estudo ERICA nos mostrou?

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ABSTRACT

Asthma is a heterogeneous disease characterized by a history of respiratory symptoms that vary in intensity and over time. Due to its high prevalence, asthma is considered a global public health problem affecting all age groups, especially children and adolescents. This study aimed to analyze scientific papers on asthma based on the Study of Cardiovascular Risks in Adolescents (ERICA). We provide a narrative review of original articles on asthma based on ERICA data published in indexed journals in English and Portuguese. ERICA was a national multicenter study conducted in 2013 and 2014 that investigated the prevalence of asthma and cardiovascular risk factors, including obesity, diabetes mellitus, systemic arterial hypertension, dyslipidemia, smoking, sedentary lifestyle, and inadequate eating habits, and the association between these factors in adolescents aged 12 to 17 years, students from public and private schools in Brazilian cities of more than 100,000 population. In the 5 selected studies, the prevalence of asthma was significantly higher in female adolescents in all capitals and macro-regions of Brazil, occurring predominantly in the southeast region of the country. In addition, asthma was strongly associated with smoking (passive and active) as well as with short sleep duration, but not with serum vitamin D levels. Regarding metabolic parameters, metabolic syndrome and some of its components, such as waist circumference, were significantly associated with severe asthma in Brazilian adolescents.

Keywords: Asthma, adolescent, smoking, metabolic syndrome, sleep.

RESUMO

A asma é uma doença heterogênea caracterizada pela história de sintomas respiratórios que variam de intensidade e ao longo do tempo. Devido à sua alta prevalência, constitui um problema mundial de saúde pública, atingindo todas as faixas etárias, em especial crianças e adolescentes. O objetivo deste artigo foi analisar as produções científicas sobre asma baseadas no Estudo de Riscos Cardiovasculares em Adolescentes (ERICA). Trata-se de uma revisão narrativa incluindo os artigos originais sobre asma baseados nos dados do ERICA, publicados em periódicos indexados em inglês e português. O ERICA foi um estudo multicêntrico nacional realizado em 2013 e 2014, que investigou a prevalência de asma e fatores de risco cardiovascular, incluindo obesidade, *diabetes mellitus*, hipertensão arterial sistêmica, dislipidemia, tabagismo, sedentarismo, hábitos alimentares inadequados, e a associação entre esses fatores, em adolescentes de 12 a 17 anos, estudantes de escolas públicas e privadas de municípios brasileiros com mais de 100.000 habitantes. Nos cinco estudos selecionados, foi possível demonstrar que a prevalência de asma foi significativamente maior entre adolescentes do sexo feminino em todas as capitais e macrorregiões do Brasil, com predomínio da doença na região Sudeste do nosso país. Além disso, a asma esteve fortemente associada ao tabagismo (passivo e ativo) e foi associada à duração curta do sono. Por outro lado, não esteve associada com os níveis séricos de vitamina D. Em relação aos parâmetros metabólicos, foi observado que a síndrome metabólica e alguns de seus componentes, como a circunferência abdominal, estiveram significativamente associados à asma grave em adolescentes brasileiros.

Descritores: Asma, adolescente, tabagismo, síndrome metabólica, sono.

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Introduction

Asthma is a heterogeneous disease characterized by a history of respiratory symptoms that vary in intensity and over time.[1] Variable obstruction of pulmonary airflow occurs, which can become persistent.[1] It is usually associated with bronchial hyperresponsiveness and airway inflammation.[1]

Due to its high prevalence, asthma is considered a global public health problem affecting all age groups, especially children and adolescents.[2] It is a complex disease with several potential determinants, from genetic to environmental factors, including lifestyle.[3] Epidemiological studies have shown that smoking, air pollution, urban lifestyle, obesity, fast food, and low antioxidant content are associated with asthma in children and adolescents.[3]

Furthermore, in low- and middle-income countries such as Brazil, people with asthma have a disproportionately high morbidity and mortality rate, suggesting that socioeconomic factors may influence these rates, either due to overall poorer living conditions or limited access to treatment.[4]

The Study of Cardiovascular Risks in Adolescents (ERICA, for the acronym in Portuguese) was a national multicenter study that aimed to estimate the prevalence of cardiovascular risk factors, including obesity, diabetes mellitus, systemic arterial hypertension, dyslipidemia, passive and active smoking, sedentary lifestyle, inadequate eating habits, and the association between these factors in adolescents aged 12 to 17 years, students from public and private schools in Brazilian cities of more than 100,000 population.[5] In this survey, conducted in 2013 and 2014, adolescents also answered a standardized written asthma questionnaire from the International Study of Asthma and Allergies in Childhood (ISAAC) to estimate the prevalence of asthma in this population.[6,7]

Several studies have been based on ERICA data, studying the prevalence of asthma and possible associated factors in Brazilian adolescents.[8-12] The aim of this article was to analyze published studies on asthma based on ERICA results.

Methods

This is a narrative review of original articles on asthma based on ERICA data published in indexed journals in English and Portuguese. The MEDLINE (National Center for Biotechnology Information, Bethesda, MD) and LILACS (Latin American and Caribbean Health Science Literature Database) databases were searched using the following keywords: "asthma" AND "adolescent" OR "adolescence" AND "ERICA," from 2016 (when the first ERICA article on asthma was published) to the present day. We added 1 article that was not found through this search, despite being within the inclusion criteria.

The ISAAC standardized written asthma module questionnaire for the age group 13 to 14 years, validated and translated into Portuguese, was used for the diagnosis and classification of asthma severity in ERICA. The presence of active asthma was obtained as the percentage of positive answers to the question "Have you had wheezing in the last 12 months?".[6,7] Adolescents with ≥ 4 wheezing attacks in the last 12 months were considered to have severe asthma.[13] The presence of asthma diagnosed by a doctor was defined as the percentage of positive answers to the question: "Has a doctor told you that you have asthma?".[6,7]

Results

We included 5 studies on adolescent asthma based on ERICA data. Their main findings are described below.

ERICA: prevalence of asthma in Brazilian adolescents (2016)

This article aimed to describe the prevalence of active asthma and medical diagnosis of asthma in Brazilian adolescents.[8] Data from 74,589 adolescents participating in ERICA were used. The overall prevalence of active asthma was 13.1%, significantly higher in female (14.8%; 95% CI 13.7-16.0) than in male (11.2%; 95% CI 10.3-12.2) adolescents, and among students from private schools (15.9%; 95% CI 14.2-17.7) than public schools (12.4%; 95% CI 11.4-13.4). The overall prevalence of a medical diagnosis of asthma was 8.7% (95% CI 8.2-9.1), with no significant differences between sex, age group, or skin color.[8] Table 1 shows the prevalence of active asthma in macro-regions and in public and private schools.

The geographical distribution of the prevalence of active asthma in the country was highest in the Southeast (14.5%; 95% CI 12.9-16.1) and in São Paulo (16.7%; 95% CI 14.7-18.7), Belo Horizonte (15.8%; 95% CI 13.9-17.7), and Goiânia (15.4%; 95% CI 13.1-17.7). The North region had the lowest prevalence among the macro-regions (9.7%; 95% CI 9.7-10.5), as well as Teresina (6.3%; 95% CI 4.9-7.7),

São Luís (7.4%; 95% CI 6.0-8.8), and João Pessoa (7.8%; 95% CI 6.4-9.2). The prevalence of active asthma was higher among female adolescents in all Brazilian capitals and regions. As for the medical diagnosis of asthma, the highest prevalence was found in the North (13.5%; 95% CI 12.7-14.2) and in Porto Alegre (19.8%; 95% CI 17.5-22.3), Belém (15.7%; 95% CI 13.5-17.8), and Vitória (15.5%; 95% CI 12.6-18.3). On the other hand, the Midwest region had the lowest prevalence among the macro-regions (6.9%; 95% CI 6.0-7.8), as well as Cuiabá (4.8%; 95% CI 3.8-5.9), Campo Grande (5.4%; 95% CI 4.2-6.6), and João Pessoa (6.5%; 95% CI 5.2-7.7).[8]

Severe asthma is associated with metabolic syndrome in Brazilian adolescents (2018)

This study aimed to evaluate the association between asthma and metabolic alterations in Brazilian adolescents participating in the ERICA study.[9] A total of 37,410 participants were included and completed the questionnaire, biochemical determinations, anthropometric, and blood pressure measurements. The definition of metabolic syndrome (MS) considered increased waist circumference (WC) and the presence of 2 or more risk factors: high triglycerides ≥ 150 mg/dL and/or high blood glucose ≥ 100 mg/dL and/or reduced HDL-cholesterol

Table 1

Prevalence (%) of asthma and physician-diagnosed asthma among Brazilian adolescents. ERICA, 2013-2014

Variable	Sample	Active asthma		Physician-diagnosed asthma	
		%	95% CI	%	95% CI
Macro-regions					
North	15073	9.7	9.0-10.5	13.5	12.7-14.2
Northeast	23167	10.1	8.8-11.4	9.0	8.1-9.9
Midwest	9727	13.6	11.9-15.3	6.9	6.0-7.8
Southeast	17080	14.5	12.9-16.1	7.6	6.8-8.3
South	9542	13.9	12.5-15.3	10.4	8.9-11.9
Sex					
Women	41225	14.8	13.7-16.0	8.5	7.8-9.1
Men	33364	11.2	10.3-12.2	8.9	8.2-9.5
Age (years)					
12-14	34141	12.6	11.3-13.9	8.9	8.3-9.5
15-17	40448	13.4	12.3-14.6	8.4	7.7-9.1
Types of school					
Private	15882	15.9	14.2-17.7	9.6	8.7-10.5
Public	58707	12.4	11.4-13.4	8.5	7.9-9.0
Brazil	74589	13.1	12.1-13.9	8.7	8.2-9.1

95% CI = 95% confidence interval.
Adapted from Kuschnir FC, et al.[8].

< 40 mg/dL or < 50 mg/dL in young girls aged 16-17 years old and/or high blood pressure ≥ 130/85 mm Hg.[9] The prevalence of active asthma and severe asthma were 13.8% (95% CI 12.4-15.2) and 2.09% (95% CI 1.95-2.24), respectively. The prevalence of MS was 2.3% (95% CI 2.14-2.45). Active asthma was associated with high WC (prevalence ratio - PR 1.19; 95% CI 1.00-1.43) and high LDL-cholesterol (PR 1.28; 95% CI 1.08-1.48), but not MS (PR 0.94; 95% CI 0.67-1.13) in this sample. On the other hand, severe asthma was associated with MS (PR 2.43; 95% CI 1.39-4.27), and this association remained significant after adjusting for age, sex, active smoking, and body mass index (BMI) - (PR 1.71; 95% CI 1.03-2.82). In addition, significant associations were observed between severe asthma and obesity (PR 1.28; 95% CI 1.02-1.62), high WC (PR 1.74; 95% CI 1.16-2.61), hyperglycemia (PR 1.78; 95% CI 1.05-2.98), and hyperinsulinemia (PR 1.55; 95% CI 1.03-2.33), which are known components of MS.[9]

ERICA: smoking is associated with more severe asthma in Brazilian adolescents (2019)

This study investigated the association between smoking and asthma.[10] A total of 66,394 ERICA participants were included with complete questionnaires on asthma, smoking, lifestyle, and social and demographic variables. The variables relating to smoking were defined as "experimentation" (adolescents who had tried cigarettes at least once in their lives); "current smoking" (those who had smoked cigarettes for at least 1 day in the last 30 days); "frequent smoking" (having smoked cigarettes for at least 7 days in a row in the last 30 days), and "passive smoking" (participants whose household had at least 1 smoker).[10]

The prevalence of active asthma and severe asthma were 13.2% (95% CI: 12.9-13.5) and 2.4% (95% CI: 2.3-2.5), respectively. The prevalence of active asthma was significantly higher among female students, of white/other skin color and from private schools. As for smoking, 18.2% (95% CI: 17.3-19.1) of adolescents had tried cigarettes. Of these, 25.3% were classified as "current smokers" and 11.8% as "frequent smokers." The prevalence of adolescents with at least 1 household smoker was 27.5% (95% CI: 26.6-28.3). The prevalence of active asthma and severe asthma was significantly higher in adolescents exposed to: experimentation (active asthma: PR 1.78; 95% CI 1.51-2.09; severe asthma: PR 2.01; 95% CI

1.35-2.98); active smoking (active asthma: PR 2.08; 95% CI 1.65-2.64; severe asthma: PR 2.29; 95% CI 1.38-3.82); frequent smoking (active asthma: PR 2.25; 95% CI 1.64-3.07; severe asthma: PR 2.41; 95% CI 1.23-4.73); and passive smoking (active asthma: PR 1.47; 95% CI 1.27-1.67; severe asthma: PR 1.66; 95% CI 1.19-2.32). These associations remained significant after adjustments.[10] In addition, a dose-response relationship was observed: the higher the number of smokers in the household, the higher the prevalence of asthma, as shown in Figure 1.[10]

Association between asthma and sleep hours in Brazilian adolescents: ERICA (2021)

This study aimed to investigate the association between asthma and bedtime in adolescents participating in ERICA.[11] Short sleep duration (SSD) was considered as sleeping < 7 hours per night, which has already been used in other national studies. The prevalence of common mental disorders (CMD), which correspond to non-psychotic mental disorders, primarily associated with symptoms of depression, anxiety, and nonspecific and somatic complaints, was also assessed as a possible confounding factor in the asthma-sleep association, using the General Health Questionnaire, 12-item version (GHQ-12), validated for the Brazilian population. Those with a score ≥ 3 were classified as CMD cases.[11]

A total of 59,442 participants with complete data were included. The prevalence of active asthma was significantly higher in students with SSD (PR: 1.17; 95% CI: 1.01-1.35; p = 0.034). On the other hand, there was no association between active asthma and age group. The association between asthma and SSD remained significant even after adjusting for sex, age group, type of school, weight status, and CMD.[11]

Asthma and vitamin D in Brazilian adolescents: Study of Cardiovascular Risks in Adolescents (ERICA) (2021)

This study aimed to analyze the association between asthma and serum vitamin D levels in Brazilian adolescents.[12] Serum concentrations of 25-hydroxyvitamin D were dichotomized into: sufficient levels (≥ 20 ng/mL) or insufficient/deficient levels (< 20 ng/mL). A total of 1,053 adolescents from 4 Brazilian state capitals (Fortaleza, Brasília, Rio de Janeiro, and Porto Alegre) were assessed. The prevalence of active asthma was 15.4%, and vitamin insufficiency/
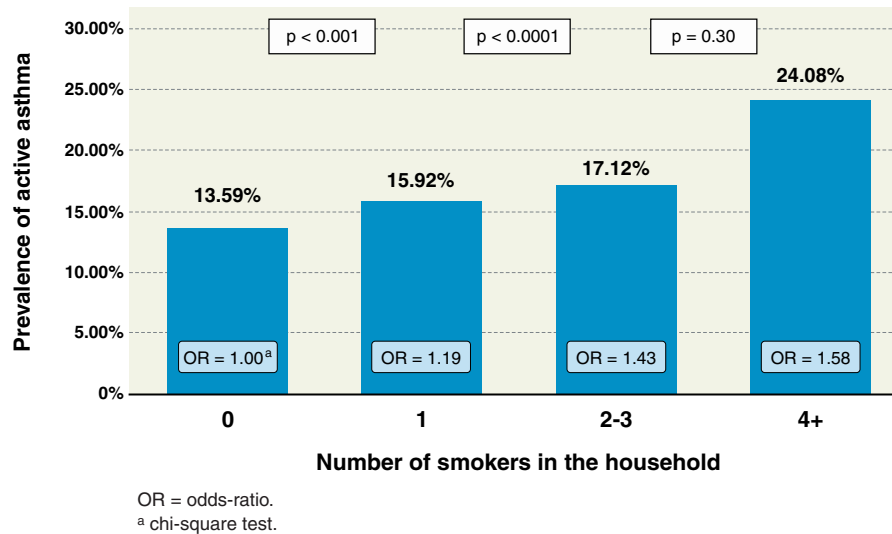
Figure 1

Association between the number of smokers in the household and the prevalence of active asthma in Brazilian adolescents. ERICA, 2013-2014

Adapted from Jordão EAOC et al, 2019.[10]

deficiency was 21%. There was no statistically significant association between active asthma and hypovitaminosis D. The prevalence of active asthma and hypovitaminosis D were, respectively, 2.34 (95% CI 1.28-4.30) and 3.22 (95% CI 1.75-5.95) times higher in Porto Alegre than in Rio de Janeiro, regardless of possible confounding factors. However, there were no significant associations between the prevalence of active asthma and variables related to vitamin D in any of the cities studied.[12]

Discussion

Studies on asthma using ERICA data have shown that the prevalence of asthma was significantly higher among female adolescents in all Brazilian capitals and macro-regions, with a predominance of the disease in Southeastern Brazil.[8] Furthermore, asthma was strongly associated with smoking (passive and active)[10] and short sleep duration.[11] On the other hand, it was not associated with serum vitamin D levels.[12] In relation to metabolic parameters, it was observed that MS and some of its components, such as WC, were significantly associated with severe asthma in Brazilian adolescents.[9]

ISAAC was one of the key global studies designed to investigate the epidemiology of asthma in children and adolescents. It is a multicenter study that evaluated the prevalence of asthma, allergic rhinoconjunctivitis, and atopic eczema in children (6 to 7 years old) and adolescents (13 to 14 years old).[6] The first phase of ISAAC was completed in 1996 and involved around 450,000 adolescents from 155 centers located in 56 countries.[14] The global prevalence of asthma in adolescents, defined as the presence of wheezing in the last 12 months, was 13.2%. In Brazil, the prevalence was 19.5%.[14] ISAAC phase III was conducted 7 years after phase I and involved almost 1 million adolescents from 233 centers in 97 countries.[15,16] The global prevalence of asthma increased to 13.7%. In Brazil, the prevalence of active asthma in ISAAC phase III was 19%, ranging from 11.8%-30.5%.[15,16]

The Brazil's National Survey of School Health (*Pesquisa Nacional em Saúde do Escolar* - PeNSE), another cross-sectional study conducted nationwide in 2012, involved 109,104 Brazilian adolescents, 9th grade students from public and private schools, the majority (86%) aged between 13 to 15 years.[17] The self-report ISAAC questionnaire was used to estimate

the prevalence of asthma, and found rates of 23.2% and 12.4% for asthma symptoms and physician-diagnosed asthma, respectively.[17] When compared to the results found by ISAAC in 5 Brazilian state capitals, the prevalence of asthma increased in São Paulo, Curitiba, and Porto Alegre, whereas it decreased in Salvador.[17]

When comparing ERICA with other studies based on the ISAAC questionnaire in different locations in Brazil, ERICA showed lower prevalence rates for active asthma and physician-diagnosed asthma.[8,17,18] The 2012 PeNSE showed rates of 23.2% and 12.4%, respectively, for active asthma and physician-diagnosed asthma in adolescents aged 13 to 15 years.[17] Similarly to our results, the highest percentages of active asthma (24.9% vs 14.5%) were observed in the Southeast region and of physician-diagnosed asthma (18.4% vs 13.5%) in the North region. Another similar result was the higher prevalence of active asthma in girls compared to boys.[17] Solé et al. assessed the prevalence of asthma in adolescents aged 13 to 14 in 7 Brazilian cities participating in the ISAAC phase III in 2003 and its temporal trend after 9 years of study.[18] The mean prevalence of active asthma decreased over this period (19.5% vs 17.5%), and the prevalence of physician-diagnosed asthma increased (14.3% vs 17.6%), both rates higher than those found in ERICA.[18] The prevalence of physician-diagnosed asthma found in ERICA was also lower when compared to the ISAAC and PeNSE results.[8,17,18]

As for the prevalence of active asthma among students from public and private schools, PeNSE[17] found no significant differences. ERICA found a higher percentage of active asthma among adolescents from private schools.[8] This result can be explained since adolescents from private schools are more likely to have better family financial conditions and consequently greater access to health services.[8]

Regarding the association between asthma, MS and its components, active asthma was associated with high WC and high LDL-cholesterol, but ERICA found no association with MS.[9] On the other hand, severe asthma was associated with MS and several of its components (obesity, high WC, hyperglycemia, and hyperinsulinemia).[9] Most of the epidemiological data published worldwide on the relationship between asthma and MS and/or its components come from studies conducted in adults.[19,20] A Spanish study with 85,555 workers showed that high WC or BMI, high triglycerides or low HDL-cholesterol were

significantly associated with wheezing.[19] Another study with 121,965 Parisian adults showed an association between altered lung function and MS, and the best predictor of this outcome was obesity, with similar results both in men and women.[20] In the adolescent population, Forno et al. observed in a sample with 1,429 Americans that insulin resistance was associated with changes in lung function (reduced values of forced expiratory volume in the first second [FEV_1] and forced vital capacity [FVC]), and MS was associated with a lower FEV_1/FVC ratio.[21] ERICA did not analyze lung function, although stronger and more significant associations were found between the components of MS and severe asthma, compared to active asthma.[9] Thus, the relationship between asthma and MS may vary according to asthma severity, and this association may be reflected in altered lung function in adolescents with abnormalities in glucose and lipid metabolism.

In a longitudinal study evaluating 2 German cohorts (GINIplus and LISAplus), researchers investigated early life events, as well as environmental and lifestyle factors, and correlated them with lung function in adolescents at the age of 15.[22] It was observed that lung infections in early life were early events associated with airflow limitation and FEF_{25-75} (intermediate forced expiratory flow, between 25 and 75%). The environmental factors associated with lung function at the age of 15 were: passive smoking, vitamin D concentration, BMI, and asthma diagnosis.[22] Although ERICA did not assess lung function and it was a cross-sectional study, we observed more significant associations between severe asthma and smoking, compared to active asthma.[10] Similarly, we found stronger associations between metabolic alterations, such as increased BMI and severe asthma.[9] On the other hand, we found no significant associations between active or severe asthma and hypovitaminosis D.[12]

PeNSE assessed aspects other than prevalence related to asthma in Brazilian adolescents. One study looked at socioeconomic, environmental, psychosocial, family-related and lifestyle factors associated with asthma in Brazilian adolescents.[23] Data from 109,104 PeNSE participants was evaluated and found that exposure to violence (feeling unsafe at school, bullying, exposure to firearms) and physical aggression perpetrated by an adult in the family were environmental factors most strongly associated with asthma.[23] As for mental health indicators, feelings of loneliness and sleeping problems were the most

significant factors.[23] Among behavioral factors, the strongest association was with smoking.[23] ERICA also found associations between asthma and short sleep duration[11] and, more significantly, with smoking.[10] However, no data were collected on violence, so no further studies could be conducted on this subject.

Another study based on PeNSE data assessed asthma-related factors in adolescents[24] and analyzed data from 106,983 participants. The prevalence of asthma was 23.2% and factors were found to be independently associated with asthma.[24] These include: women (OR=1.17); age < 14 years (OR=1.17); more days consuming ultra-processed foods (OR=1.16); active smoking (OR=1.36); alcohol consumption (OR=1.37); use of illicit drugs (OR=1.37); and having sought health care in the last year (OR=1.67).[24] Similarly, ERICA found an association with women[8] and active smoking.[10] No analysis was conducted on the consumption of ultra-processed foods and alcoholic beverages, but these data have already been collected and could be evaluated in future studies.

This article has limitations, including the fact that it is a review based on secondary data from only a few studies. In addition, ERICA was a cross-sectional study and no causal relationships could be established between the factors assessed and asthma. On the other hand, ERICA was a nationwide multicenter study with a representative sample of Brazilian adolescents using the ISAAC questionnaire, standardized worldwide and validated for our context. It was therefore possible to build up an extensive overview on asthma and some of its determinants.

In conclusion, asthma is still a very prevalent disease in the Brazilian adolescent population and is an important public health problem in this age group. It is multifactorial in nature and is associated with various factors such as smoking, metabolic alterations, and sleep disorders. The study of different environmental and lifestyle factors associated with asthma could broaden our understanding of the disease and, consequently, improve its control and management.

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