



ORIGINAL ARTICLE

OPEN ACCESS 

Study on the association between cesarean section birth and asthma risk in the pediatric population of the health area of Palencia between 1993 and 2020

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Received 23 January 2024; Accepted 14 May 2024

Available online 1 July 2024

KEYWORDS

cesarean birth;
asthma risk;
pediatric population

Abstract

Introduction and Objectives: Both asthma prevalence and the percentage of cesarean sections have increased in parallel in recent years. Research studies suggest an increased risk of developing atopic diseases and asthma after cesarean section birth compared to vaginal delivery. The main objective of this study is to analyze the risk of asthma admission after cesarean section birth compared to vaginal delivery in the pediatric population.

Population and Methods: Retrospective observational analytical case-control study from 1993 to 2020. The cases include all admitted patients to our health area hospital, for patients aged 7 to 16 diagnosed with asthma. For each case, a control without a diagnosis of asthma is selected with the same age, and that has also caused an episode of admission.

Results: A total of 290 admission episodes with a diagnosis of asthma were obtained, caused by 155 patients. Out of these, 145 cases with documented delivery types were selected. For cases, 155 controls were selected. The historical proportion of cesarean sections in the asthmatic group is 18.6%, compared to 14.2% in the non-asthmatic group. There is a statistically non-significant difference of 4.4% more cesarean sections in the asthmatic group compared to the control group.

Discussion: We have not demonstrated a statistically significant association between being born by cesarean section and an increased risk of asthma admission. Based on this finding, we cannot conclude that there is an association between being born by cesarean section and a higher risk of suffering from asthma, unlike what has been postulated in other research studies.

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<https://doi.org/10.15586/aei.v52i4.1084>

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Introduction

Asthma is a heterogeneous disease characterized by clinical findings reflecting the presence of chronic, diffuse, fluctuating, or reversible lower airway obstruction, generally of an inflammatory nature.^{1,2}

Approximately 235 million people worldwide have asthma, with a prevalence varying significantly among different countries, ranging from 2% in Tartu (Estonia) to 11.9% in Melbourne (Australia).³ In Spain, asthma is approximately 4.9%, and in our health area, the prevalence is around 3.5%.⁴

Regarding the pediatric population, the International Study of Asthma and Allergies in Childhood (ISAAC), in its phase III, confirms wide variations in asthma prevalence in children worldwide. This study examines asthma prevalence in children aged 6-7 and 13-14. The prevalence of asthma varies with rates ranging from 3.4% to 29.2% in the 6-7 age group and from 5.1% to 22% in the 13-14 age group among the countries studied.^{5,6} In the pediatric population of our country, Spain, the overall prevalence of asthma is 10%, similar to the European Union prevalence.^{7,8} By age group, it is 10% in children aged 6-7 and 9% in children aged 13-14.⁵

Although prevalence variability can be attributed to different definitions, diagnostic methods, and genetics, it can also be caused by other environmental risk factors, which vary in each country.³ Also, considering each country's different populations, higher asthma rates are concentrated in the lower socioeconomic strata of wealthy countries.⁹

On the other hand, not only is there variability in the prevalence of asthma in different countries, but there is also an increasing trend of asthma and atopy prevalence worldwide in the last 30 years.¹⁰ Regarding to pediatric population in our country, the prevalence of asthma has remained constant in Spanish children aged 13-14, while it has increased from 7% to 10% in children aged 6-7.^{5,11}

The causes of this increase in prevalence are not well defined, showing differences, as said before, between countries and within the same country.⁹

The rise in asthma prevalence seems to be parallel to the increase in allergic diseases, and asthma also increases among patients with non-asthmatic allergic diseases, such as rhinitis.⁹ When stratifying by asthma phenotype, the increased prevalence is attributed to allergic asthma, with stabilization of non-allergic asthma.^{6,7}

Factors related to the increase in asthma in the allergic population can be divided into three groups:⁹ First, lifestyle changes, such as increased indoor time, sedentary behavior, resulting in obesity, and vitamin D deficiency due to reduced intake and little sun exposure. Second, there is an increase in indoor allergens. Third, changes in hygiene, including a decrease in infections and parasitism and the use of broad-spectrum antibiotics. The hygiene hypothesis has been proposed as one of the causes behind the increase in allergic diseases, including asthma. This hypothesis suggests that reduced exposure to environmental infectious agents in early life, due to current hygiene practices, could lead to immunity toward the allergic phenotype.¹² The mechanism would be that exposure to infectious agents in early life would favor the proper maturation

of the intestinal flora. On the contrary, reduced exposure to environmental infectious agents could affect its development. Finally, the alteration of intestinal flora maturation has been associated with the development of allergic diseases.¹³

On the other hand, some studies have observed an association between cesarean section birth and altered development of the child's intestinal flora.¹⁴ In line with this possible risk factor, a meta-analysis of studies investigating the association between cesarean section and asthma development suggests a 20% increase in asthma risk after cesarean birth compared to vaginal birth.¹⁵ Based on this possible risk factor, interventions such as administering probiotics to newborns have been proposed.^{16,17}

Finally, there has been an increase in the percentage of births by cesarean section in recent years,^{18,19} with a cesarean section rate of 25.7% in Europe¹⁹ and 27.3% in Spain.²⁰ The increase of cesarean section birth, which could lead to altered development of the child's intestinal flora as stated by the hygiene hypothesis, together with the parallel growth of prevalence of asthma, could support the theory of cesarean section birth as a risk factor for asthma development.

Justification

Both asthma and the percentage of cesarean sections have increased in parallel in recent years.

The fact of being born by cesarean section versus vaginal delivery does not fully explain the overall increase in asthma prevalence. Furthermore, cesarean delivery is indicated for urgent reasons but also for other non-medical reasons,²⁵ including social and lifestyle factors, which could be confounding variables. Therefore, this might be an association without a causal character. However, literature on the topic suggests that cesarean section birth could be a risk factor to consider for developing asthma. Moreover, this risk could be related to the hygiene hypothesis.

We find it relevant to conduct a research study to assess the association between cesarean section birth and asthma development in our Health Area.

Objectives

The objective is to analyze the risk of asthma admission after cesarean section birth compared to vaginal delivery in the pediatric population.

Hypotheses

We hypothesize conceptually that being born by cesarean section increases the risk of developing asthma in the pediatric age.

We formulate an operational hypothesis through a null hypothesis, where there is no association between being born by cesarean section versus vaginal delivery and the increased incidence of admissions for asthma in the pediatric age, over the 28 years of the study, compared to

patients hospitalized for other reasons. We also propose an alternative hypothesis in which there is an association.

Population and Methods

We conducted a retrospective observational analytical case-control study from 1993 to 2020, both inclusive.

All cases and controls are obtained from the Minimum Basic Data Set (MBDS) of the Río Carrión Hospital in Palencia.

1. Inclusion criteria for cases

- Cases include all discharges for patients aged 7-16 diagnosed with asthma. Patients under 7 years of age have not been included as they may originate diagnostic doubts as they can have wheezing due to other causes different from asthma.
- Asthma is defined as any firm diagnosis of asthma, its subtypes, phenotypes, or morbidities, in the primary or secondary diagnosis in MBDS.

2. Exclusion criteria for cases

- We do not include diagnoses that may originate diagnostic doubts, such as bronchitis, pneumonia, or respiratory infection.

3. Inclusion criteria for controls

- For each case, a control of the same age is selected, which has also caused an episode of admission and discharge.
- To ensure similar ages between the case and control, the control recruited is born on the same day as the case or the nearest subsequent day to the case's birth date.

4. Exclusion criteria for controls

- Controls cannot be diagnosed with asthma, its subtypes, phenotypes, or morbidities in the primary or secondary diagnosis in MBDS, medical history, or telephone survey. Doubtful cases such as pneumonia, respiratory infection, bronchitis, bronchial hyperreactivity, or wheezing are excluded.
- In any case, to avoid repeated instances, for patients who generate multiple admission episodes, only each repeat patient's last admission episode is considered.

Variables recorded

Variables recorded include the type of delivery (vaginal or cesarean), asthma admission (yes or no), date of birth, date of admission, and age.

Data is obtained from the MBDS registry, paper and electronic medical records, and telephone surveys with verbal informed consent.

All diagnostic codes came from the International Classification of Diseases, which was in its 9th version (ICD-9 CM) until 2015 and its 10th version (ICD-10) until 2020.

Sample size

In the Río Carrión Hospital of the University Hospital Complex of Palencia (CAUPA), the estimated cesarean section rate relative to the total number of births is 20% on average between the years of birth of the study patients (1977-2013).

We considered a difference of 35% in the asthmatic group and 20% in the control group in cesarean section proportions relative to total births to be significant.

Assuming an alpha risk of 0.05 and a beta risk of 0.2 in a bilateral test, 137 subjects are required in the first group and 137 in the second to detect the difference between the two proportions as statistically significant. This difference is expected to be 0.2 in the first group and 0.35 in the second. A follow-up loss rate of 0% has been estimated. The ARCOSENO approximation has been used.

On the other hand, we include all patients admitted in a period of 28 years (1993-2020 both included) whose patients were born in a period of 36 years according to inclusion criteria, ranging from 1977 (those who were 16 years old in 1993) to 2013 (those who were 7 years old in 2020).

Results

In the 28-year study period, there were 290 admission episodes with asthma diagnoses. These episodes were caused by 155 patients, some of whom were admitted several times. To avoid repeated cases, only the last admission episode of the repeated patients was taken into account. Regarding these 155 patients, there were only 145 cases with documented delivery type. Therefore, only 145 patients were finally included in the case group (asthmatics). For cases, 155 controls (non-asthmatics) were selected.

The historical proportion of cesarean sections in this series, including asthmatic and nonasthmatic patients, is 16.3% of the total births.

The historical proportion of cesarean sections in the case group (asthmatics) is 18.6%, compared to 14.2% in the control group (non-asthmatic), i.e., there is a difference of 4.4% more cesarean sections in the asthmatic group compared to those of the control group. However, this difference is statistically non-significant. (Table 1).

Table 1. The proportion of cesarean sections by type of delivery.

Type of delivery	Asthma		Total
	no	yes	
Vaginal	133	118	251
% within asthma	85.8%	81.4%	83.7%
Cesarean	22	27	49
% within asthma	14.2%	18.6%	16.3%
Total	155	145	300
% within asthma	100.0%	100.0%	100.0%

Significance level $p=0.3$

Discussion

In our health area, the historical percentage of cesarean sections relative to total births is 16.3%, a figure much lower than observed today in our country. This may be because the birth registry in our study covers 36 years, from 1977 (the year of birth of those who were 16 years old in 1993) to 2013 (the year of birth of those who were 7 years old in 2020).

We have not found an association between being born by cesarean section and an increased risk of admission for asthma, given that the difference found in the percentage of cesarean sections between admissions of asthmatics and non-asthmatics is not statistically significant. Therefore, we cannot assume the alternative hypothesis that there is an association is valid. Based on this finding, we cannot conclude that there is an association between being born by cesarean section and a higher risk of suffering from asthma, unlike what has been postulated in other research studies.

If an association had been found, it could not be said that being born by cesarean section was an independent risk factor for developing asthma because there could be other variables or confounding factors, such as family history of asthma or atopy, habitat, physical activity or lifestyle, tobacco exposure, or nutritional status, that would not have been taken into account in this study. A multivariate analysis was not performed because multivariate data were not available in the medical records as it was a retrospective study. A prospective study could have been designed that included multiple variables; however, a retrospective study was chosen, feasible for the 36 years that cover the patients' births, to increase the sample size of the independent variable, the type of delivery, which does appear in the medical history, and the dependent variable, asthma, which does appear in the diagnosis at discharge from the MBDS. However, the fact that an association was not found makes the study valid despite not having carried out a multivariate analysis including these possible risk factors. These factors would be considered risk factors per se and not confounding variables for an association that was not found.

Similarly, given that there is no association between being born by cesarean section and an increased risk of suffering from asthma, we cannot conclude from this study that the different mechanism in the acquisition of the intestinal flora of a child born by cesarean section versus vaginal delivery poses an increased risk of asthma in our health area. Nor can we conclude an increased risk of other atopic diseases after being born by cesarean section, as suggested by other studies based on the hygiene hypothesis. In the same way as previously stated, if an association had been found, a multivariate analysis would be necessary to clarify whether the acquisition of intestinal flora would be related to the risk of asthma or other atopic diseases, but the fact that there is no association makes it unnecessary to consider the mode of acquisition of intestinal flora in cesarean delivery as a risk factor for atopic diseases or asthma. This is important because treatments to modify the intestinal flora, such as the

administration of probiotics, would not be necessary for newborns delivered by cesarean section.

We conclude that there is no association between being born by cesarean section and a higher risk of developing asthma in our health area and, for all these reasons, different treatments would not be necessary for newborns born by cesarean section compared to newborns born vaginally to prevent the development of asthma.

Conflict of Interest

The authors declare no conflict of interest.

Funding

Research Project funded by the Ernesto Sánchez Villares Foundation. The results of this research project were presented as an oral communication at the XXXIV Guillermo Arce and Ernesto Sánchez Villares Memorial of the Society of Pediatrics of Asturias, Cantabria, and Castilla y León, held in Valladolid on November 10 and 11, 2023.

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