Original Article

Risk Factors Associated With Pediatric Asthma Hospitalization: A Retrospective Case-Control Study

Lucy Grace de los Angeles Luna Muñoz; M.D.[1], Silvia Ursula Revoredo Llanos; M.D.[2], Karina Ordaya-Gonzales; M.D.[3], Liliana Arriola-Montenegro; M.D.[4], Andres Chaponan-Lavalle; M.D.[5], Jose Arriola-Montenegro; M.D.[6]

1 Escuela de Medicina, Universidad Privada Antenor Orrego, Trujillo, Perú
2 Hospital Belén de Trujillo, Trujillo, Perú
3 Departamento de Medicina, Universidad Científica del Sur, Lima, Peru
4 Department of Pediatrics, University of South Alabama, Mobile, United States
5 Departamento de Medicina, Universidad Peruana de Ciencias Aplicadas, Lima, Peru
6 Department of Medicine, University of Minnesota, Minneapolis, United States

Abstract
Objective: To evaluate the risk factors associated with asthma in children hospitalized at Hospital Belen de Trujillo.
Materials and methods: An analytical study of retrospective cases and controls was carried out in which 258 clinical histories of children between 5 to 14 years of age who were hospitalized in the Hospital Belen de Trujillo (HBT) during the period 2015-2019 were included, which were grouped into 129 histories of children who had been hospitalized for asthma (cases) and 129 histories of children hospitalized for a different cause (controls). The frequency distribution will be calculated, the Chi-square statistical test will be used, the odds ratio will be obtained and the 95% confidence interval will be calculated; finally, a multivariate analysis will be performed by means of logistic regression to determine whether the influence of other variables generates a greater risk of developing asthma in children.
Results: The multivariate analysis showed that the factors: cesarean delivery, non-exclusive breastfeeding, history of bronchiolitis, obesity and maternal age together predict 92. 0% of the cases of asthma; however, taking the influence of all the factors at the same time, it was found that the cesarean delivery route, non-exclusive breastfeeding, obesity and maternal age are significant for the regression ($p<0.05$), while the factor history of bronchiolitis is not significant ($p>0.05$). Likewise, when the bivariate analysis of the five variables studied was performed and the Chi-square test was applied, it was found that all five factors were significant ($p<0.05$) for asthma in children at Hospital Belen de Trujillo.
Conclusion: The factors cesarean delivery route, non-exclusive breastfeeding, history of bronchiolitis, obesity and maternal age are associated with asthma in children hospitalized at HBT.

Keywords: Asthma; Risk Factors; Child

Introduction

The incidence of asthma has a significant rise in recent decades, emerging as a global public health concern. While the highest prevalence has been reported in Westernized nations, Latin American countries also exhibit notable rates, such as 32.1% in Costa Rica (1). Peru falls within the category of

Correspondence:
Dr. Andres Chaponan-Lavalle
Email: andreschaponan460@gmail.com

countries with intermediate prevalence rates ranging from 20.7% to 28.2% in low-altitude regions, with a decline observed in higher altitude areas (2).

Multiple factors are implicated in the onset of asthma. During the first year of life, rapid maturation of the respiratory tract and immune system occurs, leaving infants susceptible to viral infections. This susceptibility, coupled with various biological mechanisms, underlies the association between bronchiolitis and wheezing/asthma (3, 4). In addition, maternal age correlates with placental and fetal growth, potentially influencing organ development and predisposing individuals to chronic conditions like asthma (5). Another contributing factor is the mode of delivery, particularly cesarean section, which has been linked to allergic diseases like asthma. Vaginal delivery exposes newborns to maternal probiotics and microbiota crucial for mitigating atopic diseases, whereas cesarean delivery introduces hospital and environmental bacteria to the sterile neonate, bypassing the beneficial maternal microbiota (6). Moreover, obesity, particularly truncal adiposity, can reduce functional residual capacity (7). Adipose tissue, functioning as an endocrine organ, secretes hormones such as adiponectin, leptin, and resistin. Elevated serum concentrations of leptin and leptin/adiponectin ratios correlate directly with asthma severity (8). Breastfeeding also plays a pivotal role; human milk contains live microbes and oligosaccharides that foster intestinal microbiota development, thereby influencing immune function and potentially mitigating asthma risk (9).

This study aims to investigate the influence of maternal and pediatric variables on asthma development in children, with the objective of integrate these findings into medical practice. This proactive approach seeks to mitigate asthma risk factors early on, ultimately benefiting pediatric populations and reducing the burden on healthcare systems.

Materials and methods

A retrospective observational case-control study was conducted on children aged 5 to 14 years at Hospital Belen de Trujillo (HBT) hospitalized between 2015 and 2019. We selected 129 asthma patients as the case group and 129 patients hospitalized for other reasons as the control group, meeting specific criteria. The study ran from January 1, 2023, to September 21, 2023.

The sample size, determined using a case-control formula, included 258 participants: 129 cases (children with asthma) and 129 controls (children without asthma). Criteria for cases and controls included complete medical records of patients aged 5 to 14 years. Exclusions were cystic fibrosis, pulmonary tuberculosis, HIV infection, congenital heart disease, and respiratory malformations

The study involved reviewing medical records with permission from the HBT Director. Random sampling selected the records, and data was recorded on a collection sheet. Information bias was considered due to potential incomplete clinical records, possibly affecting research outcomes.

The data were organized in Excel 2019 and analyzed using SPSS version 26. To determine if cesarean delivery, non-exclusive breastfeeding, history of bronchiolitis, maternal age, and obesity are risk factors associated with asthma, the Chi-square test was employed with a significance level of < 0.05. Odds Ratio (OR) will be obtained, and the 95% confidence interval will be calculated, along with the execution of multivariate analysis through logistic regression.

Results

The primary objective of this study was to assess asthma risk factors among hospitalized children at HBT. A multivariate logistic regression was conducted to analyze five factors collectively associated with asthma. Results presented in Table 1 reveal a significant association ($p<0.05$) of cesarean delivery, non-exclusive breastfeeding, obesity, and maternal age with asthma, collectively predicting 92.0% of cases. However, a history of bronchiolitis was not found to be significant ($p>0.05$).

As a principal objective, we determine the association between cesarean delivery and asthma in children, as depicted in Table 2. Of the children with asthma, 27.9% were delivered via cesarean section, while 36.8% of non-asthmatic children were not. A significant association ($p<0.05$) between cesarean delivery and childhood asthma was identified through the Chi-square test, with $X^2 = 23.123$. The OR was calculated to be 3.53 (95% CI: 2.09 - 5.96).

Addressing the second objective, we aimed to determine the association between non-exclusive breastfeeding and childhood asthma, as detailed in Table 3. Results indicate that 40.7% of children with asthma were not exclusively breastfed, with the same percentage among non-asthmatic children.

Table 1: Risk Factors Associated with Asthma in Children Hospitalized at HBT (2015-2019)

Risk Factors	B	Standard error	Wald	df	p-value
Cesarean delivery	2.798	0.797	12.320	1	<0.001
Non-Exclusive Breastfeeding	3.556	0.858	17.196	1	<0.001
History of Bronchiolitis	24.223	3167.441	0.000	1	0.994
Obesity	4.041	0.904	19.998	1	<0.001
Maternal age	3.328	1.032	10.400	1	0.001
Constant	-6.257	1.034	36.622	1	<0.001

df: Degrees of freedom

Table 2: Association between Cesarean Delivery and Asthma in Children Hospitalized at Hospital Belen de Trujillo 2015–2019

Cesarean delivery	Asthma				Total	
	Yes		No			
	N	%	N	%	N	%
Yes	72	27.9	34	13.2	106	41.1
No	57	22.1	95	36.8	152	58.9
Total	129	50.0	129	50.0	258	100
X^2 = 23.125 (p-value< 0.05), Odds Ratio =3.53 (2.09; 5.96)						

A significant association (p<0.05) between non-exclusive breastfeeding and childhood asthma was confirmed by the Chi-square test (X^2 = 101.721). The OR was 19.14 (95% CI: 10.22 - 35.84) (p < 0.05).

Table 3: Association between Non-Exclusive Breastfeeding and Asthma in Children Hospitalized at Hospital Belen de Trujillo 2015–2019

Non-Exclusive Breastfeeding	Asthma				Total	
	Yes		No			
	N	%	N	%	N	%
Yes	105	40.7	24	9.3	129	50.0
No	24	9.3	105	40.7	129	50.0
Total	129	50.0	129	50.0	258	100
X^2 = 101.721 (p-value< 0.05), Odds Ratio = 19.14 (10.22; 35.84)						

The third objective aimed to determine the association between a history of bronchiolitis and childhood asthma, as presented in Table 4. Among children with asthma, 36.0% had a history of bronchiolitis, compared to 50.0% of non-asthmatic children without such a history. A significant association (p<0.05) between a history of bronchiolitis and childhood asthma was observed through the Chi-square test (X^2 = 145.418). The Odds Ratio (OR) was calculated as 4.58 (95% CI: 3.43 - 6.12) (p<0.05).

For the fourth objective, Table 5 illustrates that 20.9% of children with asthma were obese, while 45.7% of non-asthmatic children were not obese. A significant association (p < 0.05) between obesity and

childhood asthma was identified through the Chi-square test (X^2 = 38.03).

Table 4: Association between Bronchiolitis History and Asthma in Children Hospitalized at Hospital Belen de Trujillo 2015–2019

Bronchiolitis History	Asthma				Total	
	Yes		No			
	N	%	N	%	N	%
Yes	93	36.0	0	0.0	93	36.0
No	36	14.0	129	50.0	165	64.0
Total	129	50.0	129	50.0	258	100
X^2 = 145.418 (p-value< 0.05), Odds Ratio = 4.58 (3.43; 6.12)						

The Odds Ratio (OR) was computed as 7.72 (95% CI: 3.80 - 15.71) (p < 0.05).

Table 5: Association between Obesity and Asthma in Children Hospitalized at Hospital Belen de Trujillo 2015–2019

Obesity	Asthma				Total	
	Yes		No			
	N	%	N	%	N	%
Yes	54	20.9	11	4.3	65	25.2
No	75	29.1	118	45.7	193	74.8
Total	129	50.0	129	50.0	258	100
X^2 = 38.03 (p-value< 0.05), Odds Ratio = 7.72 (3.80; 15.71)						

Regarding the fifth objective, aiming to determine the association between maternal age and childhood asthma, Table 6 demonstrates that 25.2% of children with asthma had mothers under the age of 20, while 46.5% of non-asthmatic children had mothers over the age of 20. A significant association (p < 0.05) between maternal age and childhood asthma was revealed through the Chi-square test (X^2 = 54.42). Furthermore, the Odds Ratio (OR) was calculated as 13.54 (95% CI: 6.33 - 28.96) (p < 0.05).

Discussion

Asthma represents a chronic non-communicable pulmonary condition characterized by airway

inflammation and hyperreactivity, leading to symptoms such as dyspnea, wheezing, and cough, accompanied by variable airflow limitations. It currently stands as a leading cause of childhood respiratory illnesses, with its morbidity burden projected to escalate (10).

Table 6: Association between Maternal Age and Asthma in Children Hospitalized at Hospital Belen de Trujillo 2015–2019

Obesity	Asthma				Total	
	Yes		No			
	N	%	N	%	N	%
Yes	54	20.9	11	4.3	65	25.2
No	75	29.1	118	45.7	193	74.8
Total	129	50.0	129	50.0	258	100
$X^2 = 38.03$ (p-value< 0.05), Odds Ratio = 7.72 (3.80; 15.71)						

Increasing evidence links the association between childhood asthma and maternal factors, including age, obesity, smoking, socioeconomic status, and mode of delivery (11-13).

In concordance with our findings, Clark et al. indicated that characteristics such as hospitalization duration, ICU stay, supplementary oxygen use, and respiratory syncytial virus infection did not exhibit a significant association with asthma (p>0.05) (14). This finding contrasts with Heidy M.'s study in Greece, which suggested that children with respiratory syncytial virus bronchiolitis had a higher likelihood of recurrent wheezing (OR 4.11; 95% CI: 2.24 to 7.56) (15).

Similarly, Liang Y.'s study concluded that the effect of cesarean delivery on asthma and wheezing in children under 2 years was OR = 1.14 (95% CI: 0.73-1.78) and 1.17 in children over 2 years (95% CI: 1.11-1.24, p < 0.001, I2 = 79.38%), with this effect persisting in children under 18 years (16). Additionally, Hou W.'s study which explored the impact of breastfeeding on asthma in children under 12 years, demonstrated a protective effect of breastfeeding against bronchial asthma (OR = 0.875, 95% CI: 0.831–0.922), particularly pronounced in children aged 6 to 12 years (OR = 0.852, 95% CI: 0.794–0.914, p = 7.41×10^{-6}) (17).

Regarding obesity, Azizda B.'s found that patients with a healthy weight exhibited the highest FEV1 percentage (91.46 ± 8.58) and FEV1/FVC ratio (85.75 ± 9.23) (p < 0.001). Conversely, obese patients experienced the highest number of asthma exacerbations (3.22 ± 0.94), followed by underweight patients (2.42 ± 0.59) (p < 0.01). Furthermore, patients with a healthy weight had significantly shorter hospitalization durations (2.0 ± 0.81) (18).

Finally, Laerum B. et al.'s study in Norway examined the association between maternal age at birth and asthma risk, concluding that asthma prevalence decreased as maternal age increased (19).

Conclusion

The factors of cesarean delivery, non-exclusive breastfeeding, history of bronchiolitis, obesity, and maternal age demonstrate significant associations with asthma in children hospitalized at HBT, predicting 92.0% of asthma cases. Furthermore, additional research should investigate other potential factors linked to childhood asthma, to mitigate the burden of this condition on pediatric populations and improve overall health outcomes.

Conflict of Interests

Authors declare no conflict of interests.

Acknowledgments

None.

References

1. Mushtaq A. Asthma in the USA: the good, the bad, and the disparity. Lancet Respir Med. 2018;6(5):335-336.
2. Cotrina K. Control de asma bronquial en niños y adolescentes atendidos en establecimientos de salud de Chiclayo. Revista Cubana de Pediatría. 2020;92(2).
3. Gao H, Miao C, Li H, Bai M, Zhang H, Wu Z, et al. The effects of different parity and delivery mode on wheezing disorders in the children-a retrospective cohort study in Fujian, China. J Asthma. 2022;59(10):1989-1996.
4. Caixia L, Yang X, Yurong T, Xiaoqun Q. Involvement of epigenetic modification in epithelial immune responses during respiratory syncytial virus infection. Microb Pathog. 2019;130:186-189.
5. Brandão HV, Vieira GO, Vieira TO, Cruz ÁA, Guimarães AC, Teles C, et al. Acute viral bronchiolitis and risk of asthma in schoolchildren: analysis of a Brazilian newborn cohort. J Pediatr (Rio J). 2017;93(3):223-229.
6. Rusconi F, Zugna D, Annesi-Maesano I, Baïz N, Barros H, Correia S, et al. Mode of Delivery and Asthma at School Age in 9 European Birth Cohorts. Am J Epidemiol. 2017;185(6):465-473.
7. Tsai HJ, Wang G, Hong X, Yao TC, Ji Y, Radovick S,

et al. Early Life Weight Gain and Development of Childhood Asthma in a Prospective Birth Cohort. Ann Am Thorac Soc. 2018;15(10):1197-1204.

8. Nasiri Kalmarzi R, Ataee P, Mansori M, Moradi G, Ahmadi S, Kaviani Z, et al. Serum levels of adiponectin and leptin in asthmatic patients and its relation with asthma severity, lung function and BMI. Allergol Immunopathol (Madr). 2017;45(3):258-264.

9. Miliku K, Azad MB. Breastfeeding and the Developmental Origins of Asthma: Current Evidence, Possible Mechanisms, and Future Research Priorities. Nutrients. 2018;10(8):995.

10. Wang G, Han D, Jiang Z, Li M, Yang S, Liu L. Association between early bronchiolitis and the development of childhood asthma: a meta-analysis. BMJ Open. 2021;11(5):e043956.

11. Gómez Real F, Burgess JA, Villani S, Dratva J, Heinrich J, Janson C, et al. Maternal age at delivery, lung function and asthma in offspring: a population-based survey. Eur Respir J. 2018;51(6):1601611.

12. Darabi B, Rahmati S, HafeziAhmadi MR, Badfar G, Azami M. The association between caesarean section and childhood asthma: an updated systematic review and meta-analysis. Allergy Asthma Clin Immunol. 2019;15:62.

13. Deng X, Ma J, Yuan Y, Zhang Z, Niu W. Association between overweight or obesity and the risk for childhood asthma and wheeze: An updated meta-analysis on 18 articles and 73 252 children. Pediatr Obes. 2019;14(9):e12532.

14. Clark AJ, Dong N, Roth T, Douglas LC. Factors Associated With Asthma Diagnosis Within Five Years of a Bronchiolitis Hospitalization: A Retrospective Cohort Study in a High Asthma Prevalence Population. Hosp Pediatr. 2019;9(10):794-800.

15. Makrinioti H, Hasegawa K, Lakoumentas J, Xepapadaki P, Tsolia M, Castro-Rodriguez JA, et al. The role of respiratory syncytial virus- and rhinovirus-induced bronchiolitis in recurrent wheeze and asthma-A systematic review and meta-analysis. Pediatr Allergy Immunol. 2022;33(3):e13741.

16. Liang Y, Zhang J, Bai S, Du S, Yang X, Wang Z. Short-term and long-term effects of cesarean section on asthma and wheezing: A cohort study and meta-analysis. Respir Med. 2023;215:107300.

17. Hou W, Guan F, Xia L, Xu Y, Huang S, Zeng P. Investigating the influence of breastfeeding on asthma in children under 12 years old in the UK Biobank. Front Immunol. 2022;13:967101.

18. Aziz DA, Bajwa RA, Viquar W, Siddiqui F, Abbas A. Asthma exacerbations and body mass index in children and adolescents: experience from a tertiary care center. Monaldi Arch Chest Dis. 2023;94(2).

19. Laerum BN, Svanes C, Wentzel-Larsen T, Gulsvik A, Torén K, Norrman E, et al. Young maternal age at delivery is associated with asthma in adult offspring. Respir Med. 2007;101(7):1431-8.