

# Asthma exacerbations in the pediatric emergency area: evaluation and prospects for improvement of pre-hospital care

Victor Gonzalez-Uribe<sup>1</sup>, Elsy Navarrete<sup>1</sup>, Fernando Angeles-Tellez<sup>2</sup>, Jose Montiel-Gonzalez<sup>2</sup>, Jorge Colin-Rubio<sup>2</sup>, Clara Fernanda Gonzalez-Chavarria<sup>2</sup>, and Zaira Selene Mojica-Gonzalez<sup>2</sup>

<sup>1</sup>Hospital Infantil de Mexico Federico Gomez

<sup>2</sup>Universidad La Salle Facultad Mexicana de Medicina

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## Abstract

**Introduction.** - The frequency of emergency department visits for asthma is a major public health problem in pediatrics. The aim of this study is to identify the characteristics of children who visit the pediatric emergency department for asthma exacerbation and to evaluate their therapeutic management before admission. **Methods.** - A prospective study conducted over a 6-month period in the pediatric emergency departments of 5 hospitals on children aged 1 to 16 years who were admitted to the department with a clinical diagnosis of asthma exacerbation. **Results.** - 143 patients were enrolled in the study. Asthma episodes were moderate to severe in 69.2% of cases (n = 99). Initial therapeutic treatment before admission to the emergency department was appropriate in 17.5% of cases (n = 25). Hospitalizations greater than 24 hours only occurred in 18.2% (n = 26). In children under 3 years of age, the viral context was present in 91.4% (n = 64) & exacerbations were more severe in younger patients (P = 0.002) and economically disadvantaged children (P = 0.025). Only 17.4% (n=25) were found to be positive by an antigen test or PCR test for SARS-CoV-2, suggesting that the involvement of traditional respiratory viruses in asthma exacerbation continues even in pandemic times. Regarding the pre-hospital care, 70.6% (n=101) had received prior treatment, but this treatment was inappropriate in 53.1% (n=76). **Conclusions.** - This study shows that asthmatic children and their families know little about the disease and that physicians are not sufficiently aware of current recommendations for the management of asthmatic children. Admission to the emergency department for asthma could be partially avoided by better diagnosis and therapeutic education.

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severe in younger patients ( $P = 0.002$ ) and economically disadvantaged children ( $P = 0.025$ ). Only 17.4% ( $n=25$ ) were found to be positive by an antigen test or PCR test for SARS-CoV-2. suggesting that the involvement of traditional respiratory viruses in asthma exacerbation continues even in pandemic times.

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**Keywords:** asthma, asthma exacerbation, children, demographics, risk

### Key points:

The high proportion of children under study allowed for a more thorough analysis of this age group's features, which are frequently understudied. It also supports previously reported findings, such as the role of viral infections of the airways in the development of exacerbations. Additionally, there is a connection between viruses and the amount of allergenic exposure in hypersensitive children and more severe exacerbations in poor socioeconomic instances.

The research shows a link between the exacerbations and poor socioeconomic status. This high rate may be due to both the poor health status of disadvantaged populations and the lack of monitoring, education, and therapeutic adherence among those in this socioeconomic group, who may be more likely to seek care in hospitals without first consulting a doctor. Additionally, research has demonstrated a link between asthma control and socioeconomic status. Additionally, it was shown that there is an inversely proportionate relationship between education level and the usage of emergency treatment.

## 1 | INTRODUCTION

Asthma is a pathology with global prevalence that has been increasing in the last three decades in all regions of the world and all ages, although with some geographical disparities.<sup>1, 2</sup> Currently, almost 300 million people are affected according to the WHO.<sup>3, 4</sup> It is the most common chronic pathology in children, and in Mexico, its prevalence is currently estimated at around 6.8-19.7%.<sup>5, 6</sup> Half of asthma hospitalizations are of concern in the pediatric population.<sup>6-8</sup>

Therefore, asthma is a major public health problem in pediatrics due to its prevalence, emergency care rate, high-cost hospitalizations, and high rates of induced school absenteeism.<sup>9-11</sup> In addition, the excessive use of healthcare services and the morbidity of asthma could be partially avoided. They are explained by a lack of initial crisis support, poor control of the disease, deficits in education and risk identification, and the importance of obesity in other asthma subtypes.<sup>3, 8, 12-14</sup>

Several studies conducted in emergency departments have made it possible to specify the characteristics of the hospitalized pediatric population for asthma exacerbation.<sup>15-17</sup> The authors have highlighted the need to improve therapeutic education in these children but have not been able to study the population of consultants in non-emergency departments. Therefore, we did a multicentric transversal study to identify characteristics of children who were treated in pediatric emergency rooms for asthma exacerbation. The secondary objective was to evaluate their pre-hospital management to determine what improvements could be put in place to reduce the need for emergency care.

## 2 | METHODS

We conducted a study that included patients aged 1 to 16 years with a history of wheezing or dyspnea who were treated at the pediatric emergency departments of 5 hospitals (2 public [IMSS HGZ No.8-Hospital Ajusco Medio] and/3 private [Hospital San Angel Inn-Hospital Español-Hospital Dalinde]) in Mexico City from November 2021 to April 2022. Patients with other causes of obstructive pulmonary pathology (cystic

fibrosis, bronchopulmonary dysplasia), hemodynamically significant congenital heart disease, or a history of great prematurity were excluded. A standardized questionnaire was applied to all patients by a physician and included the following:

- \* Socio-demographic and environmental parameters (age, sex, occupation, social security coverage (SSC), family-income, passive smoking, and distance home-hospital)
- \* Personal or family history (first degree) of type 2 inflammatory diseases (T2D) like atopic dermatitis, allergic rhino-conjunctivitis, and asthma
- \* Triggers of the exacerbation: viral, allergic, or exercise-related asthma
- \* Treatment before arriving at the emergency room
- \* Severity of exacerbation according to GINA recommendations<sup>18</sup>
- \* The duration of the exacerbation and the need for hospitalization
- \* Previous asthma diagnosis (data collected for interrogation or health record in accordance with the international recommendations)
- \* For patients with a history of asthma: previous anti-asthmatic treatment, compliance with prescriptions and dosages, medical follow-up of asthma (absent, carried out by a doctor general practitioner, pediatrician, or pneumo-pediatrician/pediatric allergist), the existence of a written or oral crisis action protocol and the existence of an individualized action plan

## 2.1 | Data analysis

Children were grouped by age: less 36 months (infant asthma), 3 to 5 years, 6 to 11 years, and over 12 years. Management of exacerbation prior to admission to emergency rooms were considered proper if patients had repeatedly received high doses of beta-2 short-acting agonists (50 mg/kg per dose) with a minimum of 4 and a maximum of 15 puffs of salbutamol equivalent administered every 20 minutes during the first hour or its equivalent dose by nebulized therapy. The management was completed by oral corticosteroids at a dose of 1 to 2 mg/kg per day in case of known severe persistent asthma or with a risk factor for severe acute asthma or severe attack immediately or not responding within an hour to the inhaled treatment. This was in accordance with the recommendations of management of the asthma attack.

Management of the crisis was considered inappropriate when dosages were below recommendations or if it included other treatments prescribed in isolation (antibiotics, cough suppressants, inhaled corticosteroids, physiotherapy respiratory or antihistamines), including use that is not recommended. The children's families were classified as having a low economic level if the household income was equivalent to or lower than the minimum monthly salary (MMS) in Mexico City (\$5258.10 MXP/\$265.30 USD). Hospitalizations were classified as short-term hospitalization (less than 24 hours) or conventional hospitalization (more than 24 hours).

## 2.2 | Statistics

The population was described by numbers/percentages for qualitative and categorical variables and by averages (+/- standard deviation) for quantitative variables. Quantitative data were compared between groups by a student t-test or the Kruskal-Wallis test (if conditions of validity, normality, and equality of variances were not present). Comparison between two qualitative variables was performed via the chi<sup>2</sup> test or the Fisher's exact test if applicable. A multivariate analysis was conducted with a logistic regression model (with a variable of a moderate to severe response versus a mild response). The model considered an adjustment of significant factors in the univariate situation and relevant parameters from a clinical point of view in light of the literature. Interactions between factors were tested. The difference tested was considered as significant at  $p < 0.05$ . All analyses were carried out with IBM(r) SPSS(r) Statistics.

## 2.3 | Ethics

The study was conducted according to the rules of good practice and international in epidemiological research. Parental consent was obtained for each questionnaire. The submission and approval of the ethics and good practices committee were obtained as well as the validation of the questionnaires by the corresponding IRB. The data analysis respected confidentiality according to the National Personal Data Law and Privacy Notices.

### 3 | RESULTS

143 patients were enrolled with a mean age of 3.9  $\pm$  3.3 years, and 60.1% (n = 86) were male. 49.6% (n = 71) were under three years old, 25.9% (n = 37) were three to five years old, 20.3% (n = 29) were six to 11 years old, and 4.2% (n = 6) were over the age of 12. Previous asthma diagnosis was found in 87.4% (n = 125). In all age categories combined, 69.2% (n = 99) had a moderate or severe exacerbation.

The demographic aspects and treatment prior to emergency management are presented in Table 1. No significant differences in the treatment were observed between the subgroups. The time between the first clinical signs of the crisis and the time elapsed for management in the emergency department was prolonged, and only 8.3% (n = 12) arrived at the emergency department in less than six hours (Fig. 1). The median time was 16 hours across all age categories and in children under three years of age.

In children with a history asthma (n = 125), 48.8% (n = 61) had control treatment, with adherence estimated in 70.9% of cases (n = 39). There was routine monitoring of asthma by a pediatrician, pediatric allergist/pulmonologist in 32.2% (n = 40), but was most often not done [45.2% (n = 56)]. An asthma plan protocol for exacerbation was explained to families in 36.5% of cases (n = 45), orally in 20.0% of cases (n = 25), and in written form in 16.5% of cases (n = 20). An individualized action plan was implemented in 22.7% of cases (n = 27) (Table 2).

#### 3.1 | Exacerbations

Across all ages, approximately 22% of patients (n = 31) had SSC, and 42% (n = 56) were from a low-economic background. 60.1% (n = 86) of patients lived within 15 km of the hospital, second-hand smoke was reported for 54.9% (n = 73), and T2D was present in 68.1% of cases (n = 94) for all ages. The crisis occurred in the aftermath of an effort (n = 10) in 7% of cases (n = 10) and in the context of respiratory virus in 75.7% of cases (n = 106) at all ages. In children under three years of age, the viral context was present in 91.4% of cases (n = 64). Information collected on the severity of exacerbations upon admission to the emergency department, medical treatments implemented, and hospitalizations following management are summarized in Table 3.

Moderate and severe exacerbations were more common in children belonging to the youngest age groups (p = 0.002). Similarly, the average age was significantly lower (p < 0.001) in children with moderate to severe exacerbation on admission (3.5  $\pm$  3.0 years) compared to those with a mild exacerbation (5.1  $\pm$  3.6). Being from a low economic background was also a risk factor for severity of exacerbation (p = 0.025, OR: 1.13).

The relation between male sex and severity of exacerbations was not significant (p = 0.099), although boys were more represented in more severe exacerbations. Treatment in the emergency department included beta-2 agonist aerosols/more restricted nebulization (p < 0.001) and less frequently corticosteroid use (p < 0.001) in mild exacerbation. Multivariate analysis confirmed that moderate and severe exacerbations were more common under three years of age compared to the upper age group (p = 0.024). Low socioeconomic background represented a non-significant risk of severity of exacerbations (p = 0.061) (Table 4).

### 4 | DISCUSSION

The purpose of this study was to characterize children with asthma who use pediatric emergency departments. One of the interests of this study was the factors that lead seeking care in emergency departments, which was carried out directly in the emergency department, so it represents both children who were hospitalized and those were not hospitalized after their passage. The high rate of participation in the study and the complete responses to standardized questionnaires leave little missing data overall. The number of patients

included over the period is relatively high given the number of annual treatments for asthma in the pediatric emergency room of the hospital.

The high representation of infants in the population studied made it possible to analyze the characteristics of this age group more precisely, which are often less known. The results are in line with already known data.<sup>19-21</sup> It also confirms other known data, including viral infections of the airways as factors triggering exacerbations.<sup>22-24</sup> There is also a link between viruses and the level of allergenic exposure in sensitized children<sup>22, 25</sup> and more severe exacerbations in cases of low socio-economic level.<sup>26-28</sup>

Something worth mentioning in this study is that even though it was conducted during the COVID-19 pandemic using the national care model, most hospitals in Mexico City requested screening for SARS-CoV-2 for lower respiratory symptoms. Only 17.4% (n=25) of patients were found to be positive by either an antigen test or PCR test for SARS-CoV-2. This suggests that the involvement of traditional or already described respiratory viruses remains preponderant in the epidemic of asthma exacerbation.

In addition, the severity of the exacerbation was correlated with a low economic background. About 21% of the children belonged to a family with income less than or equal to the MMS. This high rate could come from a deficit in monitoring, education, and therapeutic adherence of people in this socio-economic stratum, who could have a tendency to more easily visit the hospital without a pre-hospital medical consultation, as well as a plus poor health status of disadvantaged populations.<sup>29-32</sup> It has also been shown that there is a correlation between a low economic level and less control of asthma.<sup>32</sup> In addition, an inversely proportional link was established between the level of education and the use of emergency care.<sup>33, 34</sup>

A large majority of children consulting emergencies had a history of asthma (85%), but our study did not really make it possible to make a distinction between children whose asthma was already diagnosed by their doctor and those whose symptoms of asthma were present without a diagnosis of asthma. However, this figure is close of the estimate of 11% having inaugural crises in the emergency department according to Khan et al.<sup>35</sup> Only half of the children with a history of asthma in our study had background treatment, and barely a third had specialized follow-up. This confirms the hypothesis of advanced treatment failure and lack of follow-up of asthma that is found in other studies.<sup>36, 37</sup>

All crises, including inaugural ones, have been included in the study, but statistical analysis on adherence to a background treatment, regular follow-up of the child, existence of an action plan of what to do in the event of a crisis, and the introduction of an individualized reception project concerns only children with a history of asthma before inclusion. In our study, the right adherence to background treatment had a relatively high rate. This adherence was assessed by questioning about regular treatment substantively when it was introduced. It is presumably overestimated, and the actual quality of compliance remains difficult to assess in an emergency department. In effect, the evaluation of adherence to background treatment requires specific questions that often appear secondary for the patient's family and the doctor in an emergency context. Even if several exacerbations inevitably remain, the high rate of emergency room visits despite an observance that remains correct could nevertheless reflect insufficient treatment of the disease.

Patients with a history of asthma had a protocol for what to do in the event of a crisis in 36% of cases. It was in written form in only 16% of cases, and an individualized reception project had been set up in 23% of cases. But even if the beneficial effect of the implementation of a written action plan remains controversial in pediatrics,<sup>38-40</sup> in adults, a lack of implementation of a written action plan is a factor recognized as being associated with repeated emergency room visits, probably from a lack of knowledge of the disease and particularly warning signs of the crisis and initial treatment<sup>31</sup>. Taken together, these results clearly demonstrate that improved education of asthma patients and of their surroundings is necessary.

Regarding the pre-hospital care, 70% of children included in our study had received prior treatment, but this treatment was inappropriate in 53% of cases. Only 17% had received appropriate consistent treatment with current recommendations, with a beta-2 agonist being used in 58% of cases and in combination with oral corticosteroids in 20% of cases. The support expected before medical consultation is of course not identical in the case of a first attack or in the case of asthma that is already known. These figures, however, point to

a persistent use of inappropriate treatment in the asthma crisis.

In addition, the time between the onset of respiratory symptoms and emergency management was most often very long (in less than 10% of cases, patients consulted the emergency department within six hours following the onset of symptoms). Recommendations encourage taking medical advice in the absence of improvement of symptoms after a suitable treatment with a beta-2 agonist<sup>16</sup>. The time between the first clinical signs and the beginning of possible pre-hospital medical care could not be collected. This information was non-existent for nearly 30% of patients. We did not find a relationship between the remoteness of the domicile in relation to the pediatric emergency department, which confirms that this very high delay does not come from a lack of access to care but more likely from an underestimation of symptoms by the patient or the patient's family.

The results of our study show a flaw that is not negligible in the recognition of the symptoms of asthmatic exacerbation and in its initial management. It reflects a lack of knowledge of the disease in patients and their families and insufficient awareness of health professionals and current treatment recommendations. Concerning this last point, our survey joins other studies conducted in different areas and testifies to the difficulty of implementing conferences consensus. There is sometimes a delay of several years between the development of the recommendations and the evolution of outpatient medical practices.<sup>41-43</sup>

We did not demonstrate a direct correlation between severity of exacerbations and non-compliance, length of time taken to consult the hospital, and lack of initial management of the crisis. However, it seems obvious that the use of emergency care by these children could be reduced through improved control of their illness. This could be done by deliverance and explanation of written action plans of the actions to be taken in case of crisis to families, the functional respiratory follow-up of the patient, and encouraging attendance of asthma classes.

Our work highlights a lack of diagnosis, especially in infant asthma. It strengthens data concerning a lack of knowledge of the disease by the family of the asthmatic child and a poor application of treatment recommendations from health professionals. A consultation in pediatric emergencies can be an opportunity to start education and set up a specialized follow-up if necessary in partnership with the pediatrician or doctor. Improving asthma management would reduce the use of emergencies by improving diagnosis, particularly in infants, increasing awareness of the disease, correction of the current perception of treatments and their use, and an optimization of coordination hospital-city. In this regard, is important to mention the potential interest of training in therapeutic education of doctors in the private sector to improve the current situation. It would be interesting to evaluate this by a new prospective study of the impact of such therapeutic education in terms of asthma control and the use of emergency care.

## 5 | CONCLUSIONS

Exacerbations account for much of the morbidity and cost associated with chronic asthma, and new preventive and treatment approaches are needed. Insights into the immunopathogenesis of asthma have proven efficacy in reducing the risk of exacerbations in patients with mild or moderate to severe asthma. While these developments represent progress in preventing exacerbations, remaining knowledge gaps include developing an evidence base to determine which medication will work best for any given patient.

New initiatives toward understanding different phenotypes of asthma, including those associated with repeated exacerbations, may lead to greater precision in treatment. There are also important obstacles related to cost, obesity, the use of biologics in children, and prevention of exacerbations in patients with type-2-low asthma phenotypes. In addition, better understanding of the contributions of airway viruses and bacteria to exacerbations will lead to new strategies for prevention. Unfortunately, there has been less progress in developing new treatments for exacerbations during acute illness. Evidence implicating mucin hypersecretion and airway inflammatory responses from both infectious and noninfectious sources could lead to new approaches toward achieving this goal.

### Abbreviations:

T2D: type 2 inflammatory diseases

SSC: social security coverage

MMS: minimum monthly salary

IRB: Institutional Review Board

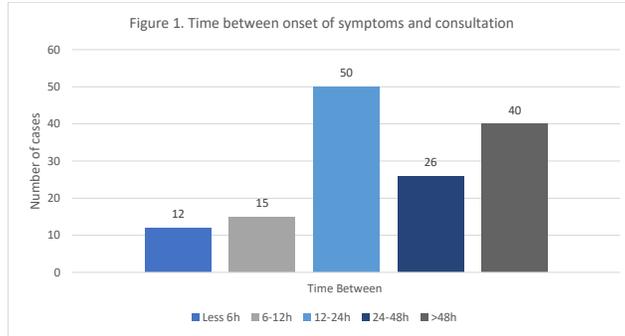
## 6. References

1. Asher MI, Garcia-Marcos L, Pearce NE, Strachan DP. Trends in worldwide asthma prevalence. *Eur Respir J*. 2020;56(6). Epub 20201224. doi: 10.1183/13993003.02094-2020. PubMed PMID: 32972987.
2. Asher MI, Rutter CE, Bissell K, Chiang CY, El Sony A, Ellwood E, et al. Worldwide trends in the burden of asthma symptoms in school-aged children: Global Asthma Network Phase I cross-sectional study. *Lancet*. 2021;398(10311):1569-80. Epub 20211028. doi: 10.1016/S0140-6736(21)01450-1. PubMed PMID: 34755626; PubMed Central PMCID: PMC8573635.
3. Ellwood P, Asher MI, Billo NE, Bissell K, Chiang CY, Ellwood EM, et al. The Global Asthma Network rationale and methods for Phase I global surveillance: prevalence, severity, management and risk factors. *Eur Respir J*. 2017;49(1). Epub 20170111. doi: 10.1183/13993003.01605-2016. PubMed PMID: 28077477.
4. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma P. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004;59(5):469-78. doi: 10.1111/j.1398-9995.2004.00526.x. PubMed PMID: 15080825.
5. Estela DB, Arturo B, Nayely RN, Maureen NE, Roberto GA, Valente MJ, et al. Have asthma symptoms in Mexico changed in the past 15 years? Time trends from the International Study of Asthma and Allergies in Childhood to the Global Asthma Network. *Allergol Immunopathol (Madr)*. 2021;49(1):1-10. Epub 20210102. doi: 10.15586/aei.v49i1.35. PubMed PMID: 33528923.
6. Del-Rio-Navarro BE, Navarrete-Rodriguez EM, Berber A, Reyes-Noriega N, Garcia-Marcos Alvarez L, Grupo Gan Mexico GIM. The burden of asthma in an inner-city area: A historical review 10 years after Isaac. *World Allergy Organ J*. 2020;13(1):100092. Epub 20200108. doi: 10.1016/j.waojou.2019.100092. PubMed PMID: 31934263; PubMed Central PMCID: PMC6953772.
7. Del-Rio-Navarro BE. Asthma in the Region of the Americas. *Int J Tuberc Lung Dis*. 2022;26(1):43-7. PubMed PMID: 36284410.
8. Pozo-Beltran CF, Navarrete-Rodriguez EM, Fernandez-Soto R, Navarro-Munguia J, Hall-Mondragon MS, Sienna-Monge JJ, et al. [Knowledge of asthma: educational intervention with the 2014 GINA guide in primary care physicians]. *Rev Alerg Mex*. 2016;63(4):358-64. doi: 10.29262/ram.v63i4.196. PubMed PMID: 27795216.
9. Larenas-Linnemann D, Salas-Hernandez J, Del Rio-Navarro BE, Luna-Pech JA, Navarrete-Rodriguez EM, Gochicoa L, et al. [MIA 2021, Comprehensive Asthma Management. Guidelines for Mexico]. *Rev Alerg Mex*. 2021;68 Suppl 1:s1-s122. doi: 10.29262/ram.v68i5.880. PubMed PMID: 34311514.
10. Serebrisky D, Wiznia A. Pediatric Asthma: A Global Epidemic. *Ann Glob Health*. 2019;85(1). Epub 20190122. doi: 10.5334/aogh.2416. PubMed PMID: 30741507; PubMed Central PMCID: PMC7052318.
11. Lipstein EA, Perrin JM, Kuhlthau KA. School absenteeism, health status, and health care utilization among children with asthma: associations with parental chronic disease. *Pediatrics*. 2009;123(1):e60-6. doi: 10.1542/peds.2008-1890. PubMed PMID: 19117848.
12. Fernandez-Soto JR, Navarrete-Rodriguez EM, Del-Rio-Navarro BE, Saucedo-Ramirez OJ, Del-Rio-Chivardi JM, Meneses-Sanchez NA, et al. Asma: uso adecuado de dispositivos para inhalacion. *Bol Med Hosp Infant Mex*. 2019;76(1):5-17. doi: 10.24875/BMHIM.18000127. PubMed PMID: 30657469.
13. Fischer GB, Camargos PA, Mocelin HT. The burden of asthma in children: a Latin American perspective. *Paediatr Respir Rev*. 2005;6(1):8-13. doi: 10.1016/j.prrv.2004.11.002. PubMed PMID: 15698808.

14. Gonzalez-Uribe V, Martinez-Tenopala R, Baro-Alvarez Pd, Mojica-Gonzalez Z. Frequency of ADIPOQ 276 and ADIPOQ 45 Polymorphisms in Obese and Eutrophic Adolescents with and without Asthma and their Relationship with Serum Adiponectin Levels. *Medical Research Archives*. 2022;10(9). doi: 10.18103/mra.v10i9.3121.
15. Camp PG, Norton SP, Goldman RD, Shajari S, Smith MA, Heathcote S, et al. Emergency department visits for children with acute asthma: discharge instructions, parental plans, and follow-through of care—a prospective study. *CJEM*. 2014;16(6):467-76. doi: 10.1017/s1481803500003481. PubMed PMID: 25358278.
16. Walsh-Kelly CM, Kelly KJ, Drendel AL, Grabowski L, Kuhn EM. Emergency department revisits for pediatric acute asthma exacerbations: association of factors identified in an emergency department asthma tracking system. *Pediatr Emerg Care*. 2008;24(8):505-10. doi: 10.1097/PEC.0b013e318180fdcb. PubMed PMID: 18645538.
17. Haktanir Abul M, Phipatanakul W. Severe asthma in children: Evaluation and management. *Allergol Int*. 2019;68(2):150-7. Epub 20190114. doi: 10.1016/j.alit.2018.11.007. PubMed PMID: 30648539.
18. Asthma Gif. Global Strategy for Asthma Mangement and Prevention2019. Available from:[www.ginasthma.org](http://www.ginasthma.org).
19. Park S, Jung SY, Kwon JW. Sex differences in the association between asthma incidence and modifiable risk factors in Korean middle-aged and older adults: NHIS-HEALS 10-year cohort. *BMC Pulm Med*. 2019;19(1):248. Epub 20191216. doi: 10.1186/s12890-019-1023-3. PubMed PMID: 31842862; PubMed Central PMCID: PMC6916451.
20. Rosychuk RJ, Ospina M, Zhang J, Leigh R, Cave A, Rowe BH. Sex differences in outcomes after discharge from Alberta emergency departments for asthma: A large population-based study. *J Asthma*. 2018;55(8):817-25. Epub 20171016. doi: 10.1080/02770903.2017.1373805. PubMed PMID: 28872981.
21. Brigham EL, Goldenberg L, Stolfi A, Mueller GA, Forbis SG. Associations Between Parental Health Literacy, Use of Asthma Management Plans, and Child's Asthma Control. *Clin Pediatr (Phila)*. 2016;55(2):111-7. Epub 20150520. doi: 10.1177/0009922815587089. PubMed PMID: 25994320.
22. Saraya T, Kurai D, Ishii H, Ito A, Sasaki Y, Niwa S, et al. Epidemiology of virus-induced asthma exacerbations: with special reference to the role of human rhinovirus. *Front Microbiol*. 2014;5:226. Epub 20140526. doi: 10.3389/fmicb.2014.00226. PubMed PMID: 24904541; PubMed Central PMCID: PMC4033317.
23. Sears MR. Epidemiology of asthma exacerbations. *J Allergy Clin Immunol*. 2008;122(4):662-8. doi: 10.1016/j.jaci.2008.08.003. PubMed PMID: 19014756.
24. Johnston NW, Sears MR. Asthma exacerbations . 1: epidemiology. *Thorax*. 2006;61(8):722-8. doi: 10.1136/thx.2005.045161. PubMed PMID: 16877691; PubMed Central PMCID: PMC2104697.
25. Tan WC, Xiang X, Qiu D, Ng TP, Lam SF, Hegele RG. Epidemiology of respiratory viruses in patients hospitalized with near-fatal asthma, acute exacerbations of asthma, or chronic obstructive pulmonary disease. *Am J Med*. 2003;115(4):272-7. doi: 10.1016/s0002-9343(03)00353-x. PubMed PMID: 12967691.
26. Bentley R, Simons K, Kvalsvig A, Milne B, Blakely T. Short-run effects of poverty on asthma, ear infections and health service use: analysis of the Longitudinal Study of Australian Children. *Int J Epidemiol*. 2021;50(5):1526-39. doi: 10.1093/ije/dyab059. PubMed PMID: 33880535.
27. Caron C, Gjelsvik A, Buechner JS. The impact of poverty on prevention practices and health status among persons with asthma. *Med Health R I*. 2005;88(2):60-2. PubMed PMID: 15816249.
28. Cooper PJ, Rodrigues LC, Barreto ML. Influence of poverty and infection on asthma in Latin America. *Curr Opin Allergy Clin Immunol*. 2012;12(2):171-8. doi: 10.1097/ACI.0b013e3283510967. PubMed PMID: 22391754; PubMed Central PMCID: PMC7612855.

29. Girard GA. Poverty and inequity in adolescent health care. *Adolesc Med State Art Rev.* 2009;20(3):887-99, viii-ix. PubMed PMID: 20653207.
30. Callander EJ, Schofield DJ. Effect of asthma on falling into poverty: the overlooked costs of illness. *Ann Allergy Asthma Immunol.* 2015;114(5):374-8. Epub 20150326. doi: 10.1016/j.anai.2015.02.017. PubMed PMID: 25817460.
31. Gottlieb DJ, Beiser AS, O'Connor GT. Poverty, race, and medication use are correlates of asthma hospitalization rates. A small area analysis in Boston. *Chest.* 1995;108(1):28-35. doi: 10.1378/chest.108.1.28. PubMed PMID: 7606972.
32. Cantu P, Kim Y, Sheehan C, Powers D, Margerison CE, Cubbin C. Downward Neighborhood Poverty Mobility during Childhood Is Associated with Child Asthma: Evidence from the Geographic Research on Wellbeing (GROW) Survey. *J Urban Health.* 2019;96(4):558-69. doi: 10.1007/s11524-019-00356-2. PubMed PMID: 31049846; PubMed Central PMCID: PMC6890910.
33. Volerman A, Fierstein J, Boon K, Vojta D, Gupta R. Determinants of asthma knowledge and practices among caregivers of children with moderate-to-severe persistent asthma. *Ann Allergy Asthma Immunol.* 2021;127(3):392-4. Epub 20210703. doi: 10.1016/j.anai.2021.06.001. PubMed PMID: 34098112; PubMed Central PMCID: PMC8981792.
34. Chan M, Gray M, Burns C, Owens L, Woolfenden S, Lingam R, et al. Community-based interventions for childhood asthma using comprehensive approaches: a systematic review and meta-analysis. *Allergy Asthma Clin Immunol.* 2021;17(1):19. Epub 20210215. doi: 10.1186/s13223-021-00522-9. PubMed PMID: 33588934; PubMed Central PMCID: PMC7885565.
35. Khan MS, O'Meara M, Henry RL. Background severity of asthma in children discharged from the emergency department. *J Paediatr Child Health.* 2003;39(6):432-5. doi: 10.1046/j.1440-1754.2003.00183.x. PubMed PMID: 12919496.
36. Denlinger LC, Heymann P, Lutter R, Gern JE. Exacerbation-Prone Asthma. *J Allergy Clin Immunol Pract.* 2020;8(2):474-82. Epub 20191122. doi: 10.1016/j.jaip.2019.11.009. PubMed PMID: 31765853; PubMed Central PMCID: PMC6942520.
37. Fleming L. Asthma exacerbation prediction: recent insights. *Curr Opin Allergy Clin Immunol.* 2018;18(2):117-23. doi: 10.1097/ACI.0000000000000428. PubMed PMID: 29406359.
38. Zemek RL, Bhogal SK, Ducharme FM. Systematic review of randomized controlled trials examining written action plans in children: what is the plan? *Arch Pediatr Adolesc Med.* 2008;162(2):157-63. doi: 10.1001/archpediatrics.2007.34. PubMed PMID: 18250241.
39. Pegoraro F, Masini M, Giovannini M, Barni S, Mori F, du Toit G, et al. Asthma Action Plans: An International Review Focused on the Pediatric Population. *Front Pediatr.* 2022;10:874935. Epub 20220426. doi: 10.3389/fped.2022.874935. PubMed PMID: 35592848; PubMed Central PMCID: PMC9113391.
40. Afolabi T, Fairman KA. Association of Asthma Exacerbation Risk and Physician Time Expenditure With Provision of Asthma Action Plans and Education for Pediatric Patients. *J Pediatr Pharmacol Ther.* 2022;27(3):244-53. Epub 20220321. doi: 10.5863/1551-6776-27.3.244. PubMed PMID: 35350158; PubMed Central PMCID: PMC8939274.
41. Aaron SD, Boulet LP, Reddel HK, Gershon AS. Underdiagnosis and Overdiagnosis of Asthma. *Am J Respir Crit Care Med.* 2018;198(8):1012-20. doi: 10.1164/rccm.201804-0682CI. PubMed PMID: 29756989.
42. Bakirtas A. Diagnostic challenges of childhood asthma. *Curr Opin Pulm Med.* 2017;23(1):27-33. doi: 10.1097/MCP.0000000000000338. PubMed PMID: 27801711.
43. Bozzetto S, Carraro S, Zanconato S, Baraldi E. Severe asthma in childhood: diagnostic and management challenges. *Curr Opin Pulm Med.* 2015;21(1):16-21. doi: 10.1097/MCP.0000000000000121. PubMed PMID:

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