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

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Abstract
Introduction: The frequency of visits to emergency department for asthma is a significant public health problem in pediatrics. This study aimed to identify the characteristics of children who visited the pediatric emergency department for asthma exacerbation and evaluated their therapeutic management prior to admission.
Methods: A prospective study was conducted over a 6-month period in the pediatric emergency departments of five hospitals involving children aged 1-16 years admitted to the department with a clinical diagnosis of asthma exacerbation.
Results: In all, 143 patients were enrolled in the study. Asthma episodes were moderate to severe in 69.2% of cases (n = 99). Initial treatment prior to admission to the emergency department was adequate in only 17.5% of cases (n = 25). Hospitalization for more than 24 h occurred in 18.2% (n = 26) patients. In children aged <3 years, viral infection was present in 91.4% cases (n = 64) and exacerbations were more severe in younger patients (P = 0.002) and children belonging to low-income stratum (P = 0.025). Only 17.4% (n = 25) were positive for SARS-CoV-2 (antigen test or polymerase chain reaction test), suggesting that the involvement of traditional respiratory viruses in asthma exacerbation continued even during pandemic. Regarding the pre-hospital care, 70.6% (n = 101) had received prior treatment, but this treatment was inadequate in 53.1% cases (n = 76).
Conclusion: This study showed that asthmatic children and their families had little knowledge about the disease and that physicians must be sufficiently aware of current recommendations for managing asthmatic children. Admission to the emergency department for asthma could be avoided partially by better diagnosis and therapeutic education.

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Introduction

Asthma is a globally prevalent pathology that has been increasing during the last three decades in all regions and age groups with some geographical disparities.[1,2] According to the World Health Organization (WHO), currently almost 300 million people are affected with asthma.[3,4] It is the most common chronic pathology in children. In Mexico, its prevalence is currently estimated at around 6.8–19.7%.[5,6] Half of asthma hospitalizations are of concern in the pediatric population.[6–8]

Asthma is a significant public health problem in pediatrics because of its prevalence, emergency care rate, high-cost hospitalization, and high proportions of induced school absenteeism.[9–11] In addition, the excessive use of healthcare services and the morbidity of asthma could be avoided partially. 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.[3,8,12–14]

Several studies conducted in emergency departments have made it possible to specify the characteristics of the hospitalized pediatric population for asthma exacerbation.[15–17] The studies have highlighted the need to improve therapeutic education in asthmatic children but have not been able to study the population of consultants in non-emergency departments. Therefore, we did a multi-centric transversal study to identify the characteristics of children 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.

Methods

We conducted the study that included patients aged 1–16 years with a history of wheezing or dyspnea and were treated in the pediatric emergency departments of five hospitals (two public [IMSS HGZ No. 8 Hospital Ajusco Medio] and three private hospitals [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 and 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, gender, occupation, social security coverage [SSC], family income, passive smoking, and residence–hospital distance).
- Personal or family history (first degree) of type-2 inflammatory diseases (T2D), such as atopic dermatitis, allergic rhino-conjunctivitis, and asthma.
- Triggers of exacerbation: viral, allergic, or exercise-related asthma.
- Treatment prior to arriving to emergency department.
- Past asthma diagnosis (data collected for interrogation or health record following international recommendations).
- For patients with a history of asthma: previous anti-asthmatic treatment, compliance with prescriptions and dosages, medical follow-up for asthma (absent, carried out by a doctor/general practitioner, pediatrician, or pneumo-pediatrician/pediatric allergist), existence of a written or oral crisis action protocol, and existence of an individualized action plan. The physician also collected information from medical archives about this emergency visit.
- Severity of exacerbation according to the Global Initiative for Asthma (GINA) recommendations.[18]
- Duration of exacerbation and need for hospitalization.

Data analysis

Children were grouped by age as follows: <36 months (infant asthma), 3–5 years, 6–11 years, and >12 years. Management of exacerbation prior to admission to emergency rooms was considered proper if patients had repeatedly received high doses of beta-2 short-acting agonists with a minimum of four and a maximum of 20 puffs of salbutamol metered dose inhaler (MDI) or equivalent administered every 20 min during the first hour, or its equivalent dose by nebulized therapy.[18] The management was completed by oral corticosteroids with a dose of 1–2 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, following the recommendations of management of asthma attack by GINA guidelines.[18]

Management of crisis was considered inappropriate if dosages were below recommendations or if it included another therapy prescribed in isolation (antibiotics, cough suppressants, inhaled corticosteroids, respiratory physiotherapy, or antihistamines), including the use not recommended. Families of asthmatic children were classified as low-income if the household income was equivalent to or lower than the minimum monthly salary (MMS) in Mexico City (MXP$5258.10 or US$265.30).[19] Hospitalization was classified as short-term hospitalization (<24 h) or conventional hospitalization (>24 h).

Statistics

The population was described by numbers/proportions for qualitative and categorical variables and by averages (±SD) for quantitative variables. Quantitative data were compared between groups by Student's *t*-test or Kruskal–Wallis test (if conditions of validity, normality, and equality of variances were absent). Comparison between two qualitative variables was performed via Chi square test or 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 a univariate situation and relevant parameters from a clinical point of view considering the literature. Interactions between factors were tested. The tested difference was

considered significant at $P < 0.05$. All analyses were carried out with SPSS Statistics (IBM®, Armonk, NY, US).

Ethics approval and consent to participate

The study was conducted according to the rules of good practice and international epidemiological research. The authors obtained informed parental consent for each questionnaire from the parents/guardians of participants. All procedures were carried out in accordance with the ethical standards of the Institutional Committee on Human Investigation, the World Medical Association, and the Helsinki Declaration.

The study was approved by the Institutional Review Board (IRB), and the protocols used in the study were approved by the Committee of Human Subjects Protection & BioEthics with registrations and approvals CEI-007504/jicsanotice.aut.1492 and LSPP-13:03CdhEvV120820221203ber_t324 in December 2021 and January 2022, respectively, in accordance with the guidelines of the institution. The data analysis abided by confidentiality according to the National Personal Data Law and privacy notices.

Results

In all, 195 patients were identified as candidates to participate in the study, of which 26 patients were excluded from the study for not having complete epidemiological data, 10 had a history of bronchopulmonary dysplasia, and 16 refused to participate. Finally, 143 patients were enrolled with a mean age of 3.9 ± 3.3 years, and 60.1% (n = 86) were males; 49.6% (n = 71) were aged <3 years, 25.9% (n = 37) were aged 3–5 years, 20.3% (n = 29) were aged 6–11 years, and 4.2% (n = 6) were aged >12 years. Previous asthma diagnosis was found in 87.4% (n = 125) children. In all age categories combined, 69.2% (n = 99) had a moderate or severe exacerbation.

Data regarding management prior to arrival to the emergency department and having previous treatment are summarized in Table 1, including the sub-analysis of patients aged 1–3 years. No significant differences in the treatment were observed between subgroups.

The time between the first clinical signs of crisis and the time elapsed for management in the emergency department was prolonged, and only 8.3% (n = 12) arrived in the emergency department in <6 h (Figure 1). The median time was 16 h across all age categories. Regardless of the distance between the patient's residence and the hospital, in 60.2% (n = 86) of patients their residence was within a radius of no more than 5 km, and in 39.8% (n = 57) patients, it ranged between 5 and 15 km. No record was found about patients residing at more than 15 km from the hospital. No statistical significance was found between the distance from the hospital and the time of arrival to the emergency department.

In a sample of 125 children with a documented asthmatic history, 48.8% (n = 61) received a control medication prior to the visit; 70.9% (n = 39) of these patients were estimated to follow a prescribed treatment. In 32.2% of pediatric patients (n = 40), asthma was regularly monitored by a pediatrician or specialist in pediatric allergy or pulmonology, whereas in most cases (45.2%; n = 56), asthma monitoring was not performed frequently. In 36.5% of cases (n = 45), the protocol for managing asthma exacerbations was communicated orally to families (n = 25), and a written plan was provided by a physician (n = 20). An individualized action plan was implemented in 22.7% of the total sample (n = 27); Table 2 provides summary of the data.

A significant proportion of children (n = 59) in the cohort aged <3 years had a documented medical history of asthma or medical history of persistent early wheezing, accounting for approximately 83.1% of the patients. In 55.0% of these patients, the treatment was determined as correct. In 47.5% (n = 28) of asthma cases, there was a lack of follow-up. Table 2 reveals that the protocol outlining appropriate actions to be taken during an exacerbation was explained to only 20.3% cases (n = 12), and a written plan was provided in less than 8.5% of cases (n = 5).

In the study, 22% of the patient population (n = 31) had an SSC, while 42% (n = 56) were from low-income households with no SSC. About 21% of the children were from families with incomes below or equal to the MMS. During the study, 24% (n = 16) of these patients were diagnosed at SSC centers, whereas 57% (n = 37) of the patients belonged to the families with low socioeconomic status and having no SSC. Most children, specifically 60.1% (n = 86), aged 1–16 years, and 67.1% (n = 69) aged <3 years, resided less than 5 km from the hospital. A prevalence rate of 54.9% (n = 73) was observed for in children aged 1–16 years affected by passive smoking, whereas a prevalence rate of 63.1%

Table 1 Treatment prior to emergency management.

	1–16 years, n (%)
Pre-emergency treatment	
Beta-2 agonist	80 (55.9)
OCS	34 (23.7)
Beta-2 agonist + OCS/SCS	29 (20.3)
Pre-hospital management	
Appropriate	25 (17.5)
Inappropriate	76 (53.1)
Absent	42 (29.3)

OCS: oral corticosteroids; SCS: systemic corticosteroids.

Table 2 Characteristics of patients by age with a history of asthma attending the emergency department.

	1–16 years (%)
Present	48.8
Absent	51.2
Appropriate	32.2
Inappropriate	22.6
Absent	45.2
Written	16.5
Oral	20
Absent	63.5
Present	22.7
Absent	77.3

(n = 41) was observed in case of children aged <3 years. T2D was found in 68.1% of cases (n = 94) across all age groups and in 59.4% of cases (n = 41) among patients aged <3 years.

The crisis occurred due to exercise in 7% (n = 10) patients. Moreover, the crisis occurred in 75.7% of patients (n = 106) across all age groups in the context of respiratory viral infection. With a total sample size of 64, the viral infection was discovered in 91.4% of cases in the cohort of children aged <3 years. SARS-CoV2 antigen and polymerase chain reaction (PCR) tests revealed that only 17.4% (n = 25) patients where positive for the virus.

Table 3 provides a summary of the data collected concerning the severity of exacerbations at the time of admission to emergency department, the medical treatment administered, and the subsequent hospitalizations. Moderate and severe exacerbations were more prevalent than mild exacerbations among the youngest of children (P = 0.002). Similarly, the mean age was significantly less in children (3.5 ± 3.0 years) with moderate to severe exacerbation at admission (P < 0.001) than in those with mild exacerbation (5.1 ± 3.6 years).

Low socioeconomic status of the family was also a risk factor for the severity of exacerbations (P = 0.025). Correlation between male children and severity of exacerbations was not statistically significant (P = 0.099), although boys were more likely to experience severe exacerbations. In patients with mild exacerbation, fewer beta-2 agonist aerosols and corticosteroids were administered in the emergency department (P < 0.001). In patients with moderate to severe exacerbation, the number and duration of hospitalization was significantly more important (P < 0.001). A multivariate analysis confirmed that moderate and severe exacerbations were more prevalent in the <3-year age group than in the older age group (P = 0.024). Table 4 confirms, although not statistically (P = 0.061), that a low socioeconomic background is associated with an increased risk of severe exacerbations.

Table 3 Hospital management of exacerbation by age.

	1-3 years, n (%)	1-16 years, n (%)
Severity		
Mild	12 (16)	44 (30.8)
Moderate	44 (62)	64 (44.7)
Severe	15 (22)	35 (24.5)
Number of beta-2 agonist aerosols		
≤3 aerosols	71 (49.7)	72 (50.3)
>3 aerosols	30 (42)	41 (58)
Oral corticosteroid therapy		
No	125 (87.4)	18 (12.6)
Yes	66 (93)	5 (7)
IV/IM corticosteroid therapy		
No	1 (0.7)	142 (99.3)
Yes	0 (0)	71 (100)
Hospitalization		
No	41 (57)	87 (60.8)
<24 h	16 (23)	30 (21)
>24 h	14 (20)	26 (18.2)

Discussion

This prospective study aimed to characterize asthmatic children using the pediatric emergency department. One of the benefits of this study was its recruitment method, which was conducted directly from emergency departments, and therefore comprised hospitalized children and children not hospitalized but having follow-up visits to hospitals. Given the number of annual asthma admissions to the hospital's pediatric emergency department, the number of patients included over the study period was relatively high.

Table 4 Correlating exacerbation severity with demographic and treatment parameters.

Severity	Mild, n (%)	Moderate-severe, n (%)	Total, n (%)	P[a]	OR	CI 95%	P[b]
Age	44 (30.8)	99 (9.2)	143 (100)				
1-3	12 (27.4)	59 (59.6)	71 (49.6)	0.002	1		
3-6	17 (38.6)	20 (20.2)	37 (25.9)		0.3	[0.11-0.85]	0.024
6-12	11 (25.0)	18 (18.2)	29 (20.3)		0.61	[0.19-1.9]	0.413
12-16	4 (9.1)	2 (2.0)	6 (4.2)		0.16	[002-1-24]	0.081
Gender							
Female	22 (50)	35	57	0.099			
Male	22 (50)	64	86				
Hospitalization							
No	42 (95.4)	45 (45.5)	87 (60.8)	<0.001			
<24 h	2 (4.6)	28 (28.3)	30 (21.0)				
>24 h	0 (0)	26 (26.2)	26 (18.2)				
Favorable economic environment							
No	29	48	77 (57.9)	0.025			
Yes	11	45	56 (42.1)		2.42	[0.96-6.12]	0.061

OR and CI 95%: odds ratio and confidence interval at 95% adjusted for age and economic family level.
[a]Univariate analysis.
[b]Multivariate analysis.

According to the National Health Service (NHS) of Mexico, there were approximately 400 admissions per 20,000 visits per year for 2020 and 2021 (data from medical information departments). A high proportion of infants in the studied population allowed for a more precise analysis of the characteristics of this age group, which typically are less understood.[20] The results are consistent with the previously gathered information regarding the male predominance of asthma in young children and the frequency of exacerbations inversely correlated to age. The study also confirmed other known facts, such as viral airway infections as triggers for exacerbations,[21-25] a link between virus and allergen exposure levels in sensitized children,[23,25] and more severe exacerbations in patients of low socioeconomic status.[26,27] Even though this study was conducted during the COVID-19 pandemic using the national care model, the majority of hospitals in Mexico City requested SARS–CoV-2 screening of patients with lower respiratory tract symptoms, and nearly 10% of patients tested positive for SARS–CoV-2 using either an antigen test or a PCR test, indicating that traditional or previously identified respiratory viruses continued to play a predominant role in the outbreak of asthma exacerbations.

Moreover, in our study, the severity of exacerbations was correlated with a low-income level. Approximately 21% of asthmatic children had benefits of SSC, whereas only 29.5% children aged <15 years had SSC benefits.[19] This high proportion, on the one hand, could be due to deficiency in the monitoring, education, and therapeutic observance of this social class, which inclined to consult hospital more efficiently without pre-hospital consultation, and, on the other hand, to a higher prevalence of poor health in the disadvantaged population.[26,28] It was also demonstrated that low economic status was associated with less effective asthma management.[29-31] In addition, an inversely proportional relationship was established between education level and utilization of emergency care.[30,31] Most consulting children had a history of asthma (85%). However, our study did not allow us to distinguish between children whose asthma was already diagnosed by their physician and those whose asthma symptoms were present prior to the diagnosis. This number was close to the estimate of 11% reached by Khan et al. for initial crises in the emergency department.[32] In our study, only 50% of children with a history of asthma received a disease-modifying treatment, and less than one-third had specialized follow-up. This confirms the hypothesis about the lack of treatment and follow-up for asthma in Latin America.[13]

All crises, including initial ones, were included in the study. However, statistical analysis on the observance of substantive treatment, regular follow-up of the child, existence of an action plan in the event of crisis, and introduction of an individualized reception plan only applied to children with a history of asthma prior to inclusion. Good adherence to disease-modifying treatment was observed in 70.9% of cases (n = 39) of all ages and 54.8% of infants and toddlers (n = 17). This compliance was evaluated in response to the questioning about the regular intake of the introduced treatment background. This likely appeared as an exaggeration, as it remained challenging to assess the actual quality of compliance in emergency departments. Assessing compliance with a disease-modifying treatment requires specific questions that often appear secondary to the entourage and the doctor in an emergency. While many exacerbations are unavoidable, the high proportion of emergency department visits, although the observation remains accurate, could indicate inadequate treatment of the disease.

Only 16% of patients with a history of asthma had a written protocol, and 23% had an individualized care plan, compared to 36% of patients who have a general exacerbation action plan. In adults, the absence of a written action plan was known as a factor associated with repeated visits to emergency department, probably due to a lack of knowledge of the disease and the warning manifestations of the crisis and initial treatment.[34] However, the beneficial effects of implementing a written action plan must be debated in pediatrics.[29,30]

These findings unequivocally demonstrate the need for improvement in educating asthmatic patients and those attending them. Only 17% of the children in our study consistently received appropriate pre-hospital care according to current recommendations,[16] with the use of beta-2 agonist in 58% and oral corticosteroids in 20% cases. Concerning pre-hospital care, 70% of the children in our study had received prior treatment, which was, however, inappropriate in 53% of patients. Naturally, the care anticipated prior to seeking medical advice differed depending on whether it was the first attack or an existing case of asthma. These statistics highlight the persistent inappropriate treatment used in asthma crises. Additionally, even though the recommendations encouraged seeking medical advice immediately if symptoms did not improve after appropriate treatment with beta-2 agonist, the time between the onset of symptoms and emergency care was oftentimes very long (in less than 10% cases, patients sought emergency care within 6 h of onset of symptoms.[16]

It was impossible to determine the time elapsed between the onset of the first clinical symptom and the commencement of any potential pre-hospital medical care. For almost 30% of patients, this was by no means nonexistent. This confirmed that the cause of long delay was most likely an underestimation of symptoms by the patient or their attendants, rather than a lack of access to care. We did not find any relationship between the distance of patient's residence to SSC centers and the consultation time, nor did we find any relationship between patients without an SSC and arrival to emergency department.

The results of our study showed a lack of recognizing symptoms of asthmatic exacerbation and initial management of the same, reflecting a lack of knowledge of the disease in patients and their families and insufficient awareness of current treatment recommendations with health professionals.[30] Concerning the last point, our survey was in accordance to other studies conducted in different fields but testifying also the difficulty of applying the association of consensus, sometimes with a lag of several years between the development of recommendations and the evolution of outpatient medical practices.[32,34]

We did not demonstrate a direct correlation between the severity of exacerbations and noncompliance, the length of delay in consultation at the hospital, and the lack of initial crisis management. However, it was evident that the delivery and explanation to the families the written action plans of what to do in the event of crisis, respiratory

function monitoring of the patient, and encouraging attendance at asthma schools could reduce the use of emergency care by these children through improved disease control.

Our work highlighted the lack of diagnosis, especially in infant asthma. It strengthened bibliographical data concerning the lack of knowledge of attendants of asthmatic children about the disease, and a poor application of therapeutic recommendations by health professionals. A consultation in pediatric emergencies could be an opportunity to start education and set up specialized follow-up, if necessary, in partnership with the pediatrician or doctor treating the patients. Improving asthma management would reduce the use of emergencies through improved diagnosis, particularly in infants, increase disease awareness, correct the current perception of treatments and their use, and optimize the coordination with city hospital. In this respect, it is essential to mention the interest potential of training in the therapeutic education of doctors from private sector to improve the current situation. It would be interesting to evaluate with a new prospective study the impact of such therapeutic education in terms of asthma control and the use of urgent care.

The high representation of infants in the population studied made it possible to analyze more precisely the lesser known characteristics of this age group. The results were in line with and confirmed the prior known data,[19-21] including viral infections of the airways as factors triggering exacerbations.[22-24] There was also a link between viruses and the level of allergenic exposure in sensitized children and more severe exacerbations in patients from low socioeconomic stratum.

In addition, the severity of exacerbation was correlated with a low economic background. This high proportion could result from a deficit in monitoring, education, and therapeutic adherence of patients in low socioeconomic stratum, who tend to more easily visit a hospital without a pre-hospital medical consultation, as well as the poor health status of the disadvantaged population.[25-28] Moreover, a correlation was demonstrated between low economic level and less asthma control.[28] In addition, an inversely proportional link was established between the level of education and the use of emergency care.[29,30]

Most children (85%) consulting emergencies had a history of asthma. However, our study did not distinguish between asthmatic children diagnosed by a physician and symptomatic children without a diagnosis of asthma. However, according to Khan et al., this number could be close to an estimate of 11% having inaugural crises in the emergency department.[32] Only half of the children with a history of asthma in our study had a background of treatment, and scarcely one-third had a specialized follow-up. This confirmed the hypothesis of advanced treatment failure and lack of follow-up of asthma established in other studies.[33-35]

However, even if the beneficial effects of the implementation of a written action plan remained controversial in pediatrics,[32,34] in adults, a lack of implementation of a written action plan was the factor recognized as being associated with repeated emergency room visits. This was probably due to the lack of knowledge of the disease, and particularly not discerning the warning signs of the crisis and merit of initial treatment.[35] Overall, these results clearly demonstrate that improved education of asthma patients and of their surroundings is necessary.

In addition, the time between the onset of respiratory symptoms and emergency management was often very long (in less than 10% of cases, patients consulted the emergency department within 6 h following the onset of symptoms). Recommendations encourage taking the medical advice if no improvement in condition was discovered after treatment with a beta-2 agonist or long beta-2 agonist + corticosteroid.[9,18]

Conclusions

Exacerbations account for much of the morbidity and cost associated with chronic asthma; hence, new preventive and treatment approaches are required. Understanding the immunopathogenesis of asthma has proven efficacious 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 the medication that would work best for particular patients.

New initiatives toward understanding different asthma phenotypes, including those associated with repeated exacerbations, could lead to greater precision in treatment. Obstacles are discovered relating to cost, obesity, the use of biologics in children, and prevention of exacerbations in patients with type-2 low-asthma phenotypes. In addition, a better understanding of the role of airway viruses and bacteria to exacerbations could lead to new strategies for preventing asthma. Unfortunately, less progress is observed in developing new treatment strategies to control exacerbations during acute illness. Evidence implicating mucin hypersecretion and airway inflammatory responses from infectious and noninfectious sources could lead to new approaches toward achieving this goal.

Author Contributions

Victor Gonzalez-Uribe: Contributed to conception, design, acquisition of data, and drafting of the manuscript.

Elsy Maureen Navarrete-Rodríguez: Contributed to conception, drafting, and analysis of the manuscript.

Fernando Sebastián Angeles-Tellez: Contributed to design, acquisition of data, and drafting of the manuscript.

Jose Angel Montiel-Gonzalez: Contributed to acquisition of data, interpretation of data, and drafting of the manuscript.

Jorge Colin-Rubio and Clara Fernanda Gonzalez-Chavarria: Contributed to design and acquisition of data.

Zaira Selene Mojica-Gonzalez: Contributed to analysis and drafting of the manuscript.

Competing interests

The authors declared that they had no conflict of interest to declare in relation to the methods and materials

employed in this study. All authors consented to the publication of this article.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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