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Comparison of physical fitness between healthy and mild-to-moderate asthmatic children with exercise symptoms: A cross-sectional study

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Abstract

Objective: Asthma is a chronic disease that may affect physical fitness, although its primary effects on exercise capacity, muscle strength, functionality and lifestyle, in children and adolescents, are still poorly understood. This study aimed to evaluate the differences in cardiorespiratory fitness, muscle strength, lifestyle, lung function, and functionality between asthmatics with exercise symptoms and healthy children. In addition, we have analyzed the association between clinical history and the presence of asthma.

Study Design: Cross-sectional study including 71 patients with a diagnosis of asthma and 71 healthy children and adolescents (7–17 years of age). Anthropometric data, clinical history, disease control, lifestyle (KIDMED and physical activity questionnaires), lung function (spirometry), exercise-induced bronchoconstriction test, aerobic fitness (cardiopulmonary exercise test), muscle strength and functionality (timed up and go; timed up and down stairs) were evaluated.

Results: Seventy-one patients with asthma (mean age 11.5 ± 2.7) and 71 healthy subjects (mean age 10.7 ± 2.5) were included. All asthmatic children had mild to moderate and stable asthma. EIB occurred in 56.3% of asthmatic children. Lung function was significantly ($p < .05$) lower in the asthmatic group when compared to healthy peers, as well as the cardiorespiratory fitness, muscle strength, lifestyle and functionality. Moreover, asthmatic children were more likely to have atopic dermatitis, allergic reactions, food allergies, and a family history of asthma when compared to healthy children.

Verónica Sanz-Santiago and Ignacio Diez-Vega contributed equally to this study.

Conclusions: Children with mild-to-moderate asthma presenting exercise symptoms show a reduction in cardiorespiratory fitness, muscle strength, lung function, functionality, and lifestyle when compared to healthy peers. The study provides data for pediatricians to support exercise practice aiming to improve prognosis and quality of life in asthmatic children.

KEYWORDS
aerobic fitness, asthma, muscle function, physical fitness

1 | INTRODUCTION

Asthma is a chronic inflammatory disease characterized by variable airway obstruction, leading to hyperresponsiveness, inflammation, and respiratory symptoms.[1] The disease is highly prevalent in children and a major cause of pediatric hospitalization worldwide.[2] Although there are several different asthma phenotypes and predictive indexes are difficult to establish, clinical risk factors have been identified, including the presence of atopic dermatitis, family history of asthma, being male, high levels of total IgE (>60 kU/l), and exposure to tobacco smoke.[3]

As a consequence of airway alterations, as well as the frequent anxiety profile due to the expectation of symptoms, several factors have been associated with asthma, including physical inactivity, overweight and obesity,[4] unhealthy lifestyle, and lower self-esteem, leading to reduced quality of life. The forced expiratory volume in the first second (FEV_1) is one of the most used clinical parameters for diagnosing and monitoring asthma.[5] Literature data indicate that low FEV_1 values are associated with clinical worsening, exacerbation, and exercise-induced bronchoconstriction (EIB).[2,6] Alternatively, there is evidence that lung function values in asthmatic children are within or close to normal values.[6] Considering the complexity of the disease and the advancements in treatment, patients may present with normal lung function, although deteriorating aerobic fitness, muscle function, and metabolic dysfunctions may be present. To date, there is scarce literature on how asthma affects physical fitness, lifestyle and functionality in children and adolescents.

Asthmatics frequently report symptoms when exercising, as well as lower exercise tolerance, which are associated with multiple factors, including the degree of airway obstruction at rest, decreased ventilatory capacity, a greater sensation of dyspnea, and EIB. However, there is contradictory evidence regarding aerobic fitness levels of asthmatic children and adolescents, and it is not clear whether there are differences in fitness between asthmatics and healthy children.[7] In addition, it is already known that reduced cardiorespiratory and muscular fitness are risk factors for cardiovascular diseases in childhood and adolescence,[8] highlighting the importance of peripheral muscle function. Although decreased peripheral muscle strength has been observed in chronic lung diseases, and are usually associated with chronic use of corticosteroids, sedentary lifestyle, and reduction in aerobic capacity,[9] very little is known about muscular changes in pediatric patients with asthma.

Therefore, the main objective of this study was to evaluate the differences in cardiorespiratory fitness, muscle strength, lifestyle, lung function and functionality between asthmatic and healthy children. In addition, we have also aimed to analyze the association between clinical history and the presence of asthma.

2 | METHODS

A cross-sectional study was carried out in a tertiary children Hospital following all principles described in the Declaration of Helsinki. The study was approved by the Hospital Research Ethics Committee R-031/14. All legal guardians and patients over 12 years signed informed consent to participate in the study. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement[10] was used as a reference to draft the manuscript.

A sample size of 142 participants was estimated considering an α error of .05, a statistical power $(1 - \beta)$ of 0.80 and an intermediate effect size of $d = 0.475$.[11] The effect size was estimated from pilot results of VO_2 peak.

2.1 | Participants

Asthmatic children were selected consecutively in the outpatient clinics of the Pediatric Pulmonology department (Hospital Universitario Infantil Niño Jesús). Healthy children were recruited from schools in the same district as the hospital to avoid significant differences in main environmental conditions (levels of air contamination, presence of environmental allergens and pollens).[12,13]

The following eligibility criteria were used for the asthmatic group: (a) children and adolescents aged 7–17 years old; (b) asthma diagnosis with at least 6 months of evolution; (c) exercise-associated symptoms (a score 0–1 in the Question 2 of the asthma control test [ACT] childhood questionnaire, validated in Spanish,[14] or 2–3 in the Question 7 of the asthma control questionnaire for children-CAN.[15] The exclusion criteria used were: (a) requirement for increase in basal medication use, including an increase in the inhaled corticosteroid dose, long-acting β2 agonist or leukotriene receptor antagonists or oral corticosteroids or omalizumab; (b) respiratory exacerbation that required systemic corticosteroids in the last

3 months or the presence of mild crisis in the last month (need for a higher dose than usual of short-acting beta-agonist); (c) locomotor system problems that would interfere in the protocol of evaluation; (d) irregular use of the medication prescribed by the physician; (e) presence of another chronic respiratory or cardiac disease associated with symptoms during exercise.

The evaluation of the presence of symptoms during exercise was performed based on patients' medical history, considering its presence before inclusion in the study. No medications were withdrawn during the test days and patients kept their usual treatment regimen.

Healthy children were selected by convenience sampling, using a covariate adaptive randomization, to reduce selection bias. A letter was sent to all parents explaining the aims of the study and they voluntarily agreed to enroll their children for testing. Healthy and asthmatic children were matched by sex, age (± 2 years) and tanner stage (± 1 stage) to ensure comparability. Eligibility criteria for the healthy group were: (a) children and adolescents aged 7–17 years old; (b) attending schools in the same district as the hospital; and (c) no positive answers in The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.[16] Exclusion criteria were: (a) muscle-skeletal problems that would prevent adequate performance of tests; and (b) presence of cardiac, neurological, or chronic respiratory disease that would impair cardiorespiratory fitness and muscle function.

2.2 | Assessments

2.2.1 | Clinical history

Clinical data were collected regarding the presence of a medical diagnosis of atopic dermatitis, allergic rhinoconjunctivitis, current or past food allergy, and history of a medical diagnosis of asthma and/or allergic rhinoconjunctivitis in the parents.[17] The presence of passive smoke was also registered.

2.2.2 | Anthropometric data and body composition

Height and weight were measured using a mechanical balance (ASIMED model BARYS PLUS C) equipped with a telescopic height measuring meter to calculate body mass index (BMI). The cut-offs used to describe nutritional status were those proposed for subjects aged 5–19 years according to the World Health Organization converted into *z*-scores. Nutritional status classification used was: obese: ≥+2 *SD*; overweight: >+1 *SD*; normal weight: −1 to +1 *SD*; thin: ≤−2*SD*; severely thin: ≤−3*SD*.[18]

The waist-height ratio, which is a measure of visceral or intra-abdominal fat, was also measured. The ratio was calculated using the waist circumference in centimeters, measured using a KaWe 1.5 m × 8 mm tape at an equidistant point between the lower rib and iliac crest, divided by height in centimeters. The visceral fat distribution cut-offs defined for the pediatric age range are: normal ≤0.47; moderate 0.47–0.50; and excess >0.50.[18]

The participants' body composition was assessed using the bi-frequency mode (at 5/50 kHz) bioimpedance analysis method (BodyStat 1500MDD, Bodystat). Body fat mass index and fat-free mass index were calculated and expressed as percent (%) values.

2.2.3 | Tanner stage

Tanner Staging, also known as Sexual Maturity Rating (SMR), is a rating system that professionals use to document the development and sequence of secondary sexual characteristics of children during puberty. The scale has five stages on pubic hair (men and women), female breast development. and male external genitalia.[19]

2.2.4 | Asthma-related questionnaires

Disease control was assessed using both the Asthma Control Test (ACT) for those over 12 years of age and the c-ACT pediatric questionnaire for those under 12 years of age. The ACT and c-ACT contains questions that are related to the frequency of both asthma symptoms and required rescue medication use during the previous 4 weeks. The scores in the ACT and c-ACT ranges from 5 (worse control) to 25 (total control).[20] The categorization of disease control was performed according to the Global Initiative for Asthma (GINA): controlled asthma, partially controlled, or uncontrolled.[21]

The ISAAC questionnaire was used to detect symptoms of asthma in healthy participants. The questionnaire was completed by each child under the supervision of the researchers according to the protocol used in prior international studies addressing the prevalence of asthma symptoms among children and adolescents.[22]

2.2.5 | Lung function

Spirometry was performed using a Spirostik spirometer (Jaeger) with a Blue Cherry diagnostic software platform, following the American Thoracic Society-European Respiratory Society (ATS/ERS) guidelines.[22] The data were interpreted using the unified approach of the Global Lung Initiative (GLI) of 2012.[23]

2.2.6 | Fraction of exhaled nitric oxide (FeNo)

FeNo was measured using portable equipment, previously validated (NIOX VERO, Circassia). Before starting the exam, a previous training was carried out with each patient, to demonstrate the technique. A cut-off point for children of 35 ppB was used. A maximum of six maneuvers were performed, two of which had to be considered as acceptable following the criteria of the ATS/ERS.[24]

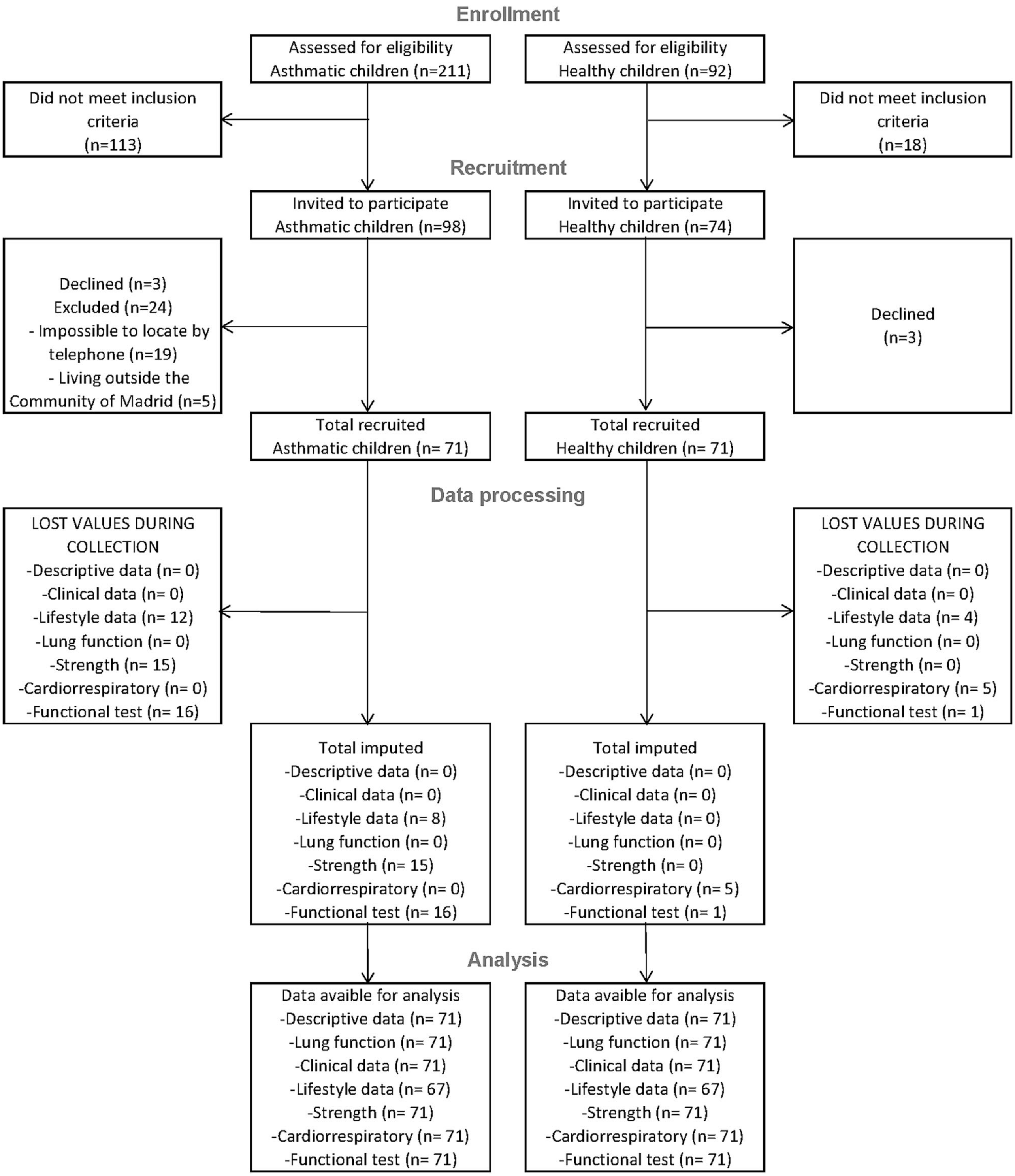

FIGURE 1 Flow chart of the study

2.2.7 | Exercise-induced bronchoconstriction

A bronchial challenge test was performed on a treadmill (Burdick T600 with Burdick TA620 Control Unit Inc.) using an incremental load, following the ATS/ERS recommendations for the assessment of bronchial hyperresponsiveness. After the exercise stress test, lung function was measured by serial spirometry at 3, 5, 10, 15, and 30 min. A positive EIB test was considered when there was a decrease in the FEV_1 of more than 10% in any of the postexercise measures.[25]

TABLE 1 Descriptive data of participants in the study

	Asthmatic		Healthy		
	Mean ± *SD*	95% CI	Mean ± *SD*	95% CI	*p* value
Age (y)	11.5 ± 2.7	(10.9; 12.1)	10.7 ± 2.5	(10.1; 11.3)	0.081
Tanner stage	2.3 ± 1.3	(2.0; 2.6)	1.9 ± 1.2	(1.6; 2.2)	0.076
Height (cm)	146.7 ± 16.2	(142.9; 150.6)	144.9 ± 14.1	(141.5; 148.2)	0.463
Height (*z*-score)	0.14 ± 1.03	(−0.10; 0.39)	0.47 ± 0.90	(0.26; 0.68)	0.046
Weight (kg)	43.8 ± 14.4	(40.4; 47.2)	39.2 ± 10.8	(36.6; 41.7)	0.033
Weight (*z*-score)	0.51 ± 1.12	(0.25; 0.78)	0.52 ± 0.97	(0.29; 0.75)	0.981
BMI (kg/m^2)	19.8 ± 3.7	(18.9; 20.7)	18.3 ± 2.5	(17.7; 18.9)	0.005
BMI (*z*-score)	0.65 ± 1.31	(0.34; 0.96)	0.40 ± 1.02	(0.16; 0.64)	0.212
Waist-height ratio	0.48 ± 0.06	(0.47; 0.50)	0.46 ± 0.05	(0.45; 0.47)	0.044
Fat-free mass (%)	73.4 ± 6.3	(71.9; 74.9)	73.0 ± 8.7	(71.0; 75.1)	0.739
Body fat mass (%)	26.6 ± 6.2	(25.1; 28.1)	27.0 ± 8.61	(24.9; 29.0)	0.755
FeNo	30.4 ± 27.4	(23.9; 36.9)	15.4 ± 16.7	(11.4; 19.3)	<0.001

Note: Values expressed as mean ± *SD*.
Abbreviations: BMI, body mass index; CI: confidence interval; FeNo, fraction of exhaled nitric oxide.

2.2.8 | Cardiopulmonary exercise testing (CPET)

To evaluate the cardiorespiratory fitness, a treadmill (Technogym Run Race 1400HC) maximum test was used. The protocol used started with an initial speed and slope of 2.5 $km\ h^{-1}$ and 0.5%, respectively. Increases in both variables of 0.1 $km\ h^{-1}$ and 0.5%, respectively, were used every 15 s. Gas exchange data were measured breath-by-breath using open-circuit spirometry (Vmax 29C; SensorMedics). The peak oxygen consumption (VO_2 peak) was recorded as the highest value obtained for any continuous 20 s period.[26] The ventilatory threshold (VT1) was determined using the criteria of an increase in both the ventilatory equivalent for oxygen consumption (V_E/VO_2) and end-tidal pressure of oxygen with no increase in the ventilatory equivalent for carbon dioxide production (V_E/VCO_2). The test was considered as maximum if the following criteria were met: (i) heart rate greater than 180 beats per minute and (ii) respiratory exchange ratio above 1.0.[27]

2.2.9 | Muscle strength

After familiarization with the techniques of the movements involved (low paddle, pull ahead, chest press, leg press, knee extension, and knee flexion lying down), tests were performed for the direct calculation of 5RM (maximum repetition). The test protocol consisted of performing two series of warm up at 50% and 70% of the perceived 5RM (15 and 10 minimum repetitions, respectively), with a resting period of 1 min between series. After 2 min of rest, a third series was performed aiming for 5RM at 90%–105%, depending on the effort used in the last warm-up series. If the first attempt of 5RM was achieved, the resistance was increased by 2.5%–5% and, after another 2 min of rest, a new attempt was performed. If the first attempt of 5RM was not successful, the resistance was reduced by 2.5%–5% and, after 2 min of rest, another attempt of 5RM was performed. If this second attempt was successful, the resistance achieved was considered as 5RM.[28] As the age of the population studied is wide, results were normalized by calculating the relative strength, that is, the weight (kg) achieved in each muscle group by the weight (kg) of the subject.[28] All tests were performed using pediatric resistance machines (STRIVE).

2.2.10 | Functional tests

The functional mobility was evaluated by using the Timed Up and Go (TUG) test of 3 m and the Timed Up and Down Stairs (TUDS) test. The 3-m TUG test is a measure of the time needed to stand up from a seated position in a chair, walk 3 m, turn around, return to the chair, and sit down. For the TUDS test, the time spent to ascend and descend 12 stairs was measured.[29] All children used a hand railing in the TUDS test to diminish the risk of falling. Time in both tests was measured by the same investigator with the same stopwatch to the nearest 0.1 s.

2.2.11 | Lifestyle: Mediterranean diet and physical activity levels

The KIDMED questionnaire was used to assess the adherence of participants to the Mediterranean diet. This questionnaire has 16 items or questions that are answered as true or false, of which 12 are related to healthy habits and score +1 point each; the remaining four

TABLE 2 Comparison between asthmatic children and healthy children in the lifestyle, lung function, muscle strength, cardiorespiratory fitness and functionality

	Asthmatic		Healthy				
	Mean ± *SD*	95% CI	Mean ± *SD*	95%CI	*p*	η^2_p	1-β
Lifestyle							
PAQ (score)	2.4 ± 0.6	(2.2; 2.5)	3.1 ± 0.6	(3.0; 3.2)	<0.001	0.275	1
KIDMED (score)	6.1 ± 2.4	(5.6; 6.7)	8.9 ± 2.0	(8.4; 9.4)	<0.001	0.291	1
Passive smoking (% Y)	40	(30; 50)	20	(10; 30)	0.011	0.047	0.729
Lung function (*z*-score)							
FEV_1	−0.67 ± 0.94	(−0.92; −0.42)	−0.10 ± 1.20	(−0.35; −0.16)	0.002	0.066	0.880
FVC	−0.36 ± 1.15	(−0.61; −0.11)	−0.52 ± 0.94	(−0.76; −0.27)	0.371	0.006	0.145
FEV_1/FVC	−0.45 ± 1.25	(−0.74; −0.16)	0.87 ± 1.22	(0.58; 1.16)	<0.001	0.224	1
$FEF_{25\text{-}75\%}$	−1.01 ± 1.06	(−1.31; −0.71)	0.84 ± 1.46	(0.55; 1.14)	<0.001	0.348	1
Relative strength (kg/weight)							
Bench press	0.75 ± 0.22	(0.70; 0.79)	1.02 ± 0.19	(0.97; 1.07)	<0.001	0.300	1
Leg press	1.49 ± 0.56	(1.37; 1.61)	1.89 ± 0.48	(1.77; 2.01)	<0.001	0.129	0.995
High row	0.66 ± 0.22	(0.62; 0.71)	0.99 ± 0.19	(0.94; 1.04)	<0.001	0.396	1
Leg extension	1.00 ± 0.39	(0.91; 1.09)	1.43 ± 0.37	(1.34; 1.52)	<0.001	0.248	1
Low row	0.69 ± 0.21	(0.64; 0.74)	0.94 ± 0.22	(0.89; 0.99)	<0.001	0.263	1
Hamstring curl	0.66 ± 0.33	(0.59; 0.74)	1.04 ± 0.31	(0.96; 1.11)	<0.001	0.253	1
Ventilatory threshold							
VO_2 (mL kg min^{-1})	20.2 ± 4.2	(19.1; 21.2)	27.5 ± 4.8	(26.5; 28.6)	<0.001	0.405	1
V_E (L min^{-1})	23.3 ± 7.5	(21.6; 25.0)	26.3 ± 7.4	(24.6; 28.0)	0.017	0.040	0.668
V_E/VO_2	27.2 ± 3.3	(26.5; 27.9)	25.0 ± 2.7	(24.3; 25.7)	<0.001	0.121	0.992
V_E/VCO_2	31.8 ± 4.0	(30.9; 32.7)	28.5 ± 3.6	(27.7; 29.4)	<0.001	0.158	0.999
VO_2 (%VO_2 peak)	57.4 ± 8.6	(55.2; 59.6)	62.5 ± 10.1	(60.4; 64.7)	0.001	0.071	0.902
Peak exercise							
VO_2 (mL kg min^{-1})	35.3 ± 5.7	(33.8; 36.9)	44.6 ± 7.4	(43.0; 46.1)	<0.001	0.332	1
V_E (L min^{-1})	52.9 ± 18.6	(48.7; 57.0)	51.2 ± 16.7	(47.0; 55.3)	0.568	0.002	0.088
RER	1.10 ± 0.15	(1.07; 1.13)	1.07 ± 0.12	(1.04; 1.10)	0.250	0.009	0.209
Heart rate (bpm)	187.4 ± 13.4	(184.7-190.1)	191.4 ± 8.8	(188.7; 194.0)	0.039	0.030	0.542
Speed	6.4 ± 0.6	(6.3; 6.6)	6.8 ± 0.7	(6.6; 6.9)	0.001	0.079	0.93
Test time (min)	9.6 ± 1.4	(9.3; 10.0)	11.0 ± 1.7	(10.7; 11.4)	<0.001	0.167	1
Functional test (s)							
TUG 3 m (*n* = 67)	3.7 ± 0.4	(3.6; 3.8)	3.7 ± 0.6	(3.6; 3.8)	0.906	<.001	0.052
TUDS (*n* = 67)	6.9 ± 1.4	(6.6; 7.2)	6.3 ± 1.0	(6.0; 6.6)	0.007	0.058	0.772

Note: Values expressed as mean ± *SD*.

Abbreviations: $FEF_{25-75\%}$, forced expiratory flow between 25% and 75% of vital capacity; FEV_1, forced expiratory volume in one second; FEV_1/FVC, ratio between forced expiratory volume in 1 s and forced vital capacity; FVC, forced vital capacity; HR, heart rate; KIDMED, Mediterranean Diet Quality Index for children and teenagers; PAQ, Physical Activity Questionnaire; RER, respiratory exchange ratio; TUDS, timed up and down stairs test (12 stairs); TUG, timed up and go test of 3 m; VE, minute ventilation; VE/VCO_2, ventilatory equivalent for carbon dioxide production; VE/VO_2, ventilatory equivalent for oxygen uptake; VO_2, oxygen uptake; Y, yes.

are related to incorrect habits and negative score −1 point each. A total score below 3 indicates a poor adherence, from 4 to 7 indicates intermediate adherence and greater than 8 indicates an optimal adherence to the Mediterranean diet.[30]

The questionnaire Physical Activity Questionnaire for Children (PAQ-C) and Physical Activity Questionnaire for Adolescents (PAQ-A) were used to assess the levels of daily physical activity. This instrument refers to the past 7 days, comprising questions on frequency and time spent walking and doing moderate- and vigorous-intensity activities, as well as time spent sitting. The final score ranges from 1 to 5 and values lower than 2.33 indicate a low physical activity level, from 2.33 to 3.66 moderate level, and higher than 3.66 indicates a high level. All participants who answered yes to the question "Have you been ill over this past week?" were excluded from the analysis.[31]

2.2.12 | Statistical analysis

The distribution of variables was evaluated using the Kolmogorov-Smirnov test. Considering a normal distribution, continuous variables were presented as mean and standard deviation. Categorical variables were presented in absolute and relative frequency. Multivariate analysis of variance (MANOVA) was used to compare the differences in cardiorespiratory capacity, strength level, lung function and functional tests between asthmatic and healthy children. Partial eta squared (η^2_p) was used as effect size measure, considering $\eta^2_p < 0.06$ as low effect, $\eta^2_p < 0.14$ as medium effect, and $\eta^2_p > 0.14$ as large effect. Clinical variables, as well as RERpeak and HRpeak (CPET) were considered as covariates. Considering that no significant changes to the results were found, the multivariate analysis of covariance results are not presented. Two logistic regression models (bivariate and full-adjusted) was used to analyze the relationship between clinical history and the presence of asthma. Missing values of the main variables were imputed through multiple imputation, using linear regression models. Five models were estimated and it was found that the results did not vary with respect to the original data. To simplify the results section of the article, only the data of one imputed model was presented. All statistical analysis were performed with SPSS 21.0.[32] Significant level was set up at $p = .05$.

3 | RESULTS

A total of 71 asthmatic and 71 healthy children were recruited. Figure 1 presents the complete flow chart of the study. In both groups, there was a predominance of girls (57.7%) over boys (42.3%). The mean age was 11.5 years for asthmatics and 10.7 for healthy children. Table 1 presents the descriptive results of the participants.

Asthmatic children presented ACT values of 20.48 ± 3.35 (95% CI = 19.68; 21.27). According to the GINA score, 16 (22.5%) children were in treatment Level 1; 7 (9.9%) at treatment Level 2; 12 (16.9%) at treatment Level 3; and 36 (50.7%) at treatment Level 4. No child was at treatment Level 5. All asthmatic children had mild-to-moderate and stable asthma and 40 (56.3%) patients presented with EIB.

Comparison between asthmatic and healthy children revealed differences in lifestyle factors, $F(3, 133) = 33.14$; $p < .001$; $\eta^2_p = 0.428$; $1 - \beta = 1$, lung function, $F(5, 136) = 19.15$; $p < .001$; $\eta^2_p = 0.595$; $1 - \beta = 1$, muscle strength, $F(6, 135) = 24.82$; $p < .001$; $\eta^2_p = 0.524$; $1 - \beta = 1$, cardiorespiratory function, $F(13, 128) = 12.15$; $p < .001$; $\eta^2_p = 0.552$; $1 - \beta = 1$, and in the functional tests $F(2, 139) = 5.83$; $p = .004$; $\eta^2_p = 0.078$; $1 - \beta = .866$, when a MANOVA was used. When individual variables for each outcome were compared between asthmatic and healthy children, the results were consistently better in healthy children, with medium to large effect on muscle strength, small to large effect on lifestyle factors, lung function and cardiorespiratory function and small to moderate effect on functional tests (Table 2).

Regression models are presented in Table 3. Asthmatic children were more likely to have atopic dermatitis, allergic reactions, food allergies and a family history of father and mother with asthma when compared to healthy children. In the full-adjusted model, the same associations were obtained, except for food allergies.

4 | DISCUSSION

The results of the present study demonstrated that children with mild-to-moderate stable asthma and exercise symptoms show decreased cardiorespiratory fitness, muscle strength, lung function, functionality, and lifestyle compared to healthy children. These contributions highlight the functional limitations induced by asthma and the need for monitoring and prevention for these patients.

The effects of asthma on aerobic fitness of children and adolescents are still controversial and poorly investigated in the literature. The decrease in cardiorespiratory fitness found in the present study is in accordance with previously reported findings that children with asthma have less cardiorespiratory capacity compared to healthy children,[33,34] although differences were reported for more severe patients and, to the best of our knowledge, this is the first study showing physical fitness alterations in mild-to-moderate patients. On the other hand, there is also evidence showing no differences in cardiorespiratory fitness between patients with mild-intermittent asthma and healthy children,[35,36] which could be related to several factors, including different drug treatment modalities, disease control and previous fitness levels. In our study, the results have shown a decrease in VO_2 at both peak exercise and ventilatory threshold, indicating less exercise capacity in those with asthma. In addition, an increase in V_E/VO_2 and V_E/VCO_2 was found, which might indicate a lower ventilatory efficiency, with a need for greater V_E to eliminate the same amount of CO_2 as compared to healthy children. These changes may contribute to explain shortness of breath and poor exercise performance in children with asthma, even at submaximal levels.[37]

TABLE 3 Regression models for the association of clinical history and the presence of asthma

	Asthmatic	Healthy	Unadjusted model OR (95% CI)	p	Full-adjusted model OR (95% CI)	p
Atopic dermatitis (Y)	41 (57.7)	13 (18.6)	5.99 (2.79; 12.82)	<0.001	4.91 (1.66; 14.48)	0.004
No	30 (13.3)	58 (52.7)	ref.			
Allergic rhinoconjunctivitis (Y)	44 (62.0)	6 (8.6)	17.24 (6.62; 45.45)	<0.001	26.97 (7.52; 96.76)	<0.001
No	27 (9.0)	65 (62.5)	ref.			
Food allergy (Y)	17 (23.9)	3 (4.3)	7.04 (1.96; 25.00)	0.002	3.84 (0.68; 21.76)	0.128
No	54 (47.1)	68 (66.8)	ref.			
Father with asthma (Y)	17 (23.9)	2 (3.0)	10.2 (2.26; 45.45)	0.001	18.56 (2.27; 151.62)	0.006
No	54 (47.1)	69 (68.2)	ref.			
Mother with asthma (Y)	21 (29.6)	4 (5.8)	6.8 (2.20; 21.28)	0.001	13.1 (3.22; 53.26)	<0.001
No	50 (41.4)	67 (65.4)	ref.			
Father with allergic rhinoconjunctivitis (Y)	20 (28.2)	10 (14.9)	2.24 (0.96; 5.21)	0.093	0.59 (0.14; 2.58)	0.484
No	51 (42.8)	61 (56.9)	ref.			
Mother with allergic rhinoconjunctivitis (Y)	15 (21.1)	10 (14.5)	1.58 (0.66; 3.8)	0.421	0.23 (0.05; 1.13)	0.071
No	56 (49.9)	61 (56.9)	ref.			

Abbreviations: CI, confidence Interval; OR, odds ratio to present clinical findings in asthmatic children compared to healthy.

The findings of the present study also demonstrated a decrease in peripheral muscle strength in children with asthma when compared to their healthy peers. Studies have shown a decrease in peripheral muscle strength in chronic respiratory diseases,[9,33,38] which could be associated to chronic use of corticosteroids, sedentary lifestyle and reduced aerobic capacity.[9] In addition, muscle fitness is associated with the present and future cardiovascular health in youth, indicating that it should be monitored to identify youth at risk who could benefit from intervention programs.[39] Although muscle strength is an important factor influencing physical fitness, it has been little studied in children with asthma. Villa et al.[33] reported a reduction in muscle resistance in the quadriceps of asthmatic children. On the other hand, Reimberg et al.[40] did not observe differences in muscle strength between asthmatic and healthy children.[33] Among several factors that may contribute to alter muscle strength, sedentary time is considered as an important one and our results demonstrated a decrease in the levels of daily physical activity in children with asthma when compared to their healthy peers. Although this is in accordance with previous studies,[41] there is also data showing no evidence that children with asthma are involved in less physical activity when compared to healthy peers.[42] However, it is important to highlight that physical activity levels were measured using a questionnaire in the present study, which consists of a subjective assessment measure and may be subjected to bias.

The FEV_1 is one of the most used clinical parameters for the diagnosis and monitoring of asthma,[5] since its decrease is associated with clinical worsening, presence of exacerbation and EIB.[6] On the other hand, there is evidence indicating that lung function may be within or close to normal in children with asthma,[42] as demonstrated in the present study. In addition, respiratory changes and anxiety related to both the appearance of symptoms and the presence of exacerbations, makes many children with asthma have a less healthy lifestyle compared to their peers without the disease.[43] This evidence is also in agreement with data from the present study showing a reduction in both PAQ and KIDMED values. It is already known that a sedentary lifestyle is associated with physical deconditioning.[44] Previous studies in patients with mild-to-moderate asthma have demonstrated that decreased physical activity levels does not seem to be entirely attributable to airflow limitations.[45–47] However, the decrease in physical activity reduces the stimuli to improve muscular and cardiorespiratory fitness, producing a progressive and sustained deconditioning, which further discourages patients to exercise and may contribute to worsen asthma control.[45]

Regarding the association of clinical history with the presence of asthma, our results showed that children with asthma were more likely to have atopic dermatitis, allergic reactions, food allergies, and a positive family history (father and mother) for asthma when compared to healthy children. Our data also demonstrated that those who have asthma increased by 4.9 the risk to develop atopic dermatitis, 26.9 to have allergic rhinoconjunctivitis and 3.8 to have food allergy. Illi et al.[48] have also demonstrated that atopic dermatitis is associated with asthma at school age, although in several of these asthmatic children, wheezing manifested itself before or with the onset of atopic dermatitis.

The present study also has limitations, including the cross-sectional design, which does not allow us to define cause and effects. The assessment of daily physical activity levels using a questionnaire may also be considered a limitation, since it consists of a subjective assessment. On the other hand, as a strength, this is one of the few studies in the literature addressing physical fitness in children with mild to moderate asthma and symptoms to exercise.

In conclusion, results of the present study indicate that children with mild-to-moderate asthma and exercise symptoms show a reduction in cardiorespiratory fitness, muscle strength, lung function, functionality and lifestyle. These results may contribute to better monitoring and development of preventive actions, providing data for pediatricians to support exercise practice aiming to improve prognosis and quality of life in asthmatic children.

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AUTHOR CONTRIBUTIONS

Verónica Sanz-Santiago: Conceptualization (equal), data curation (equal), formal analysis (supporting), funding acquisition (lead), investigation (lead), methodology (lead), supervision (lead), writing original draft (equal), writing review and editing (equal). **Ignacio Diez-Vega**: Data curation (equal), formal analysis (lead), methodology (supporting), visualization (lead), writing original draft (equal), and writing review and editing (supporting). **Márcio Vinícius Fagundes Donadio**: Methodology (supporting), writing original draft (equal), and writing review and editing (lead). **Daniele Schiwe**: Conceptualization (supporting), and writing review and editing (supporting). **Fernanda Maria Vendrusculo**: Conceptualization (supporting) and writing review and editing (supporting).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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