Allergol Immunopathol (Madr). 2021;49(1):40-49 eISSN:1578-1267, pISSN:0301-0546

Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

ORIGINAL ARTICLE

Prevalence of asthma, its correlates, and validation of the Pre-School Asthma Risk Factors Scale (PS-ARFS) among preschool children in Lebanon

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Received: 16 January 2020; Accepted: 13 July 2020
Available online 2 January 2021

KEYWORDS
Asthma;
Preschool;
Children;
ARFS score

Abstract
Objectives: The Asthma Risk Factor Scale (ARFS) is used to screen for asthma in Lebanese preschool children (aged 3-16 years). The study objective was to describe factors associated with asthma, confirm ARFS score validity among Lebanese preschool children, and develop a risk score for asthma diagnosis in this age group (Pre-School Asthma Risk Factor Scale [PS-ARFS]).
Methods: A cross-sectional study enrolled 515 preschool children (November 2018 and March 2019). The ARFS is a 15-item tool that assesses children's environmental exposure, parental history of asthma, and dietary habits.
Results: The percentage of asthmatic children was 8.2%. Higher odds of asthma in children were associated with living near a prairie sprayed with pesticides (odds ratio [OR]=2.33), playing outdoors (OR=2.89), having a heater in the bedroom (OR=10.73), attending a nursery (OR=2.91), having a mother who smokes cigarettes (OR=3.35) or water pipe (OR=2.46), a sister with a history of seasonal allergy (OR=6.81), and a parental history (mother and father) of asthma (OR=6.15 and OR=9.83, respectively). Higher ARFS scores (OR=1.144) were associated with higher odds of asthma. Accordingly, the PS-ARFS was created according to the following formula: ARFS score+(playing outdoor×2.4)+(heating system in the bedroom×12.9)+(having attended a nursery×2.5) (area under the curve=0.908 [0.860-0.957]; P<0.001); at value: 14.20, Se=84.3% and Sp=90.9%.
Conclusion: PS-ARFS is suggested for screening of asthma in preschool children in an epidemiological setting and in the absence of spirometry.

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https://doi.org/10.15586/aei.v49i1.25

Introduction

Asthma is one of the most common etiologies of respiratory illness worldwide.[1] It usually occurs early in life[2] and is associated with airway hyperresponsiveness and variable, but largely reversible, airflow obstruction.[1] Narrowing of airway is caused by different factors, including inflammatory mediators, airway edema, and airway remodeling.[1] According to the International Study of Asthma and Allergies in Childhood (ISAAC),[3] the prevalence of asthma in children varies between 13.2% and 13.7%, and according to an Italian study[4] between 9.1% and 9.5% with stabilization or decline in the prevalence and mortality rates in recent years.[5] According to nationally representative studies, in Lebanon, the prevalence of diagnosed asthma some 14 years ago was 4.8% in 5–12-year-old[6] and 5.6% in 13–14-year-old[7] schoolchildren, while nothing is known about its prevalence in younger, 3–5-year-old, children.

Asthma in children is mainly diagnosed clinically and usually confirmed by spirometry. It is difficult to achieve in preschool children (2–6 years old), for their inability to perform voluntary breathing maneuvers as efficiently as done by older children and adults.[8] Despite the availability of new techniques,[9] spirometry constitutes an adjunct test not always performed for the diagnosis of asthma and remains mainly clinical. In this case, the difficulty of diagnosing asthma in preschool children is more related to different clinical phenotypes of the disease at that age.[10] It is therefore essential to identify children who are likely to develop asthma using simpler means: knowing the risk factors of the disease may be a way to identify children at high risk of asthma, which would help physicians to screen for asthma at earlier stages, thereby decreasing its burden and severity.

Factors associated with asthma have been studied extensively in schoolchildren and include parental asthma,[9] maternal use of medications during pregnancy (antibiotics and paracetamol),[9] environmental and prenatal smoking,[11-13] preterm delivery,[14] number of older siblings,[15] gastroesophageal reflux disease,[16] and atopy.[17] Furthermore, the association between breastfeeding and asthma in children is still controversial, for no definitive conclusion could be made in this regard.[18] In addition, exposure to indoor pollutants represents a potentially modifiable cause of allergic sensitization and asthma.[19] A recent meta-analysis has found that the children aged 3–5 years who attend nurseries have lower odds of asthma.[20]

Although many studies[21,22] have focused on creating a predictive score for asthma based on children's symptoms, the Asthma Risk Factor Scale (ARFS) created in 2018 is based on children's exposure to toxics, and is utilized to screen for the disease in Lebanese children aged 4–17 years.[23] The ARFS is a simple, easy-to-use 15-item tool that helps clinicians assess children's environmental exposure, parental history of asthma, and dietary habits; it has demonstrated adequate validity and predictive properties. The ARFS was generated by studying multiple risk factors in children: exposure to pesticides (presence in the house of a person working with pesticides, living in an area sprayed with pesticides, and use of pesticides in the house), mixing detergents, exposure to maternal medication intake, alcohol drinking, and smoking during pregnancy and/or breastfeeding (number of cigarettes per day or number of waterpipes per week), current parental smoking status, history of asthma, and the types of food (red meat, fast-food, nuts, dairy products, chocolate, milk, pastry, fish, legumes, fruits, olive oil, fried food, chips, and caffeinated beverages).

Although the previous study was conducted in children aged 3–16 years, preschool children were just a minority. The response to environmental stressors varies in children of different age groups because of the intra- and intergroup differences between them (changes in children's anatomy, physiology, and biochemistry).[24] According to these variances in children's reactions to exposures, diseases develop differently in children.[24] Therefore, it was found interesting to study this age group exclusively. Since there is little information on the involved risk factors of asthma in young children, this paper aimed to describe factors associated with asthma, confirm the Asthma Risk Factors Scale (ARFS) score validity among Lebanese preschool children, and develop a risk score for asthma screening in this age group (Pre-School Asthma Risk Factor Scale [PS-ARFS]).

Methods

Ethical aspect

This study was approved by the Psychiatric Hospital of the Cross Ethics and Research Committee (HPC-007-2019). Each participant was informed about the aims of the study, and a written consent was obtained from the child's parent.

Study design

A cross-sectional study was conducted in a sample of Lebanese schools. Preschool children aged 3–5 years were recruited from three private urban schools of three different governorates (out of a total of five governorates) in Lebanon between November 2018 and March 2019. A detailed questionnaire was addressed to the children's parents. Children whose parents refused to participate in this study were excluded.

Sample size calculation

The following formula was used to calculate the minimal sample size calculation:

$$\boldsymbol{n} = (Z1-\alpha/2)2p(1-p)/d2,$$

where $Z1-\alpha/2=1.96$ for $\alpha=5\%$ (or 95% confidence interval [CI]). A sample of 232 Lebanese children was targeted to allow for adequate bivariate and multivariate analyses based on the Epi info sample size calculations, with a population size of 360,000 children aged below five years[25] and a frequency of diagnosed asthma being 8.2%.[12]

Questionnaire and variables

A pretested self-administered questionnaire, inspired from the ISAAC questionnaire, was used after a forward-back translation.[26] Although no formal validation study was conducted, the same questionnaire was used in the previous studies conducted in Lebanon, showing the cross-cultural suitability of its questions. [27-30]

The first part of the questionnaire assessed the socio-demographic characteristics, including age, gender, region, number of rooms and the number of persons living in the house, education level of both parents, family history of asthma, and other known risk factors for asthma (heating system used in the house, child history of recurrent otitis, humidity in the house, child attending a nursery, etc.). Education level of parents was quantified according to the number of years of schooling (illiterate, primary, complementary, secondary, and university).

The primary diagnosis of declared asthma was defined as an affirmative answer to the question: “Has your doctor ever told you that your child has asthma?” Moreover, food, seasonal, and medication allergies were self-reported by the parent based on a previous physician diagnosis.

Questions about smoking or drinking alcohol during pregnancy and/or breastfeeding, type of smoking or alcohol, and quantities were included, in addition to the use of any medication during pregnancy and/or lactation, occupational, regional, local, and domestic exposures to pesticides, and use of detergents. Passive smoking was characterized by the number of smokers in the house.

The use of detergents was determined by questions about who uses these products in the house, what kind of detergents are used, and whether or not there is a mixture of these products during cleaning in the house. Additional information was also collected: the heating system used in the house, presence of an air conditioner and a humidifier, presence of humidity or mold on the walls of the house, and the child’s history of recurrent otitis, tonsillectomy, cardiac problems, premature birth, and attending nursery.

Asthma Risk Factor Scale (ARFS)

The ARFS score was computed from a previous study conducted in Lebanon on school children aged 4–17 years, using the following equation[23]:

$$\begin{aligned}\text{ARFS} = &(\text{Respiratory infections} \times 10)\\ &+ (\text{playing in dust} \times 2) + (\text{playing on carpets} \times 2)\\ &+ (\text{pulmonary problems in the child for last two years} \times 25.5)\\ &+ (\text{respiratory problems in the child before two years of age} \times 13.5)\\ &+ (\text{humidity in the house} \times 2.1)\\ &+ (\text{asthma in mother} \times 6.3)\\ &+ (\text{asthma in both parents} \times 9)\\ &+ (\text{history of reflux in the child} \times 2.9)\\ &+ (\text{living in pesticides region} \times 2.6)\\ &+ (\text{red meat daily} \times 2.8) + (\text{nuts} < 2 \text{ times/week} \times 0.4)\\ &+ (\text{nuts 3–6 times/week} \times 0.4)\\ &+ (\text{dairy products} < 2 \text{ times/week} \times 0.3)\\ &+ (\text{dairy products 3–6 times/week} \times 0.2).\end{aligned}$$

The PS-ARFS was thus created to improve the performance of ARFS. To assess risk factors associated with asthma status, a logistic regression analysis was performed using healthy children versus asthmatic children as the dependent variable. Potential risk factors of asthma (significantly associated), not previously included in the ARFS scale, were added as new variables, and odds ratios (ORs) of these additional risk factors were rounded off and used as coefficient factors in the PS-ARFS formula (results are presented in Table 3, model 2). In the new scale formula, the presence of a variable was coded as 1, and its absence as 0.

Statistical analysis

Data analysis was performed on IBM SPSS Statistics for Windows, version 23.0 (Armonk, NY, USA: IBM Corp.). Descriptive statistics included the frequency (percentage) for categorical variables and mean (standard deviation) for continuous variables. The Chi-square test was used to evaluate association between categorical variables and the presence/absence of asthma, whereas Student’s *t*-test was used to evaluate association between continuous and dependent variables. Furthermore, to minimize possible confounding, a backward logistic regression was conducted, taking the presence/absence of diagnosed asthma as a dependent variable and taking all variables that showed $P<0.2$ in bivariate analysis as independent variables. We applied the Bonferroni corrections to guard against the bias of repeated testing effects; we calculated an adjusted P-value by dividing the desired P-value (0.05) by the number of hypotheses being conducted. Therefore, statistical significance in the bivariate analysis was set at $0.05 \div 23 = 0.002$. Statistical significance in the multivariable analysis was set at $P<0.05$. Moreover, in the model, we included both ARFS and PS-ARFS to automatically select the most appropriate one to predict dependent variable; this method had been used previously for similar purposes in other settings (selecting the most adequate predictors using correlation coefficients when correlations are not high [<0.4]).[32,33]

The Receiver-Operating Characteristics (ROC) curve was sketched to determine the cut-off point of both ARFS and PS-ARFS scores that would be predictive of asthma status in this age group. The sensitivity and specificity as well as the negative and positive predictive values for both scales were calculated to assess criterion validity. All these calculations were performed to compare both scales.

Results

Out of 700 questionnaires distributed, 515 (73.57%) were completed and received back. Details regarding socio-demographic and other characteristics of the participants are shown in Table 1. Patients had a mean age of 4.44 ± 0.83 years; 46.0% of them were females. The majority (75.7%) lived in Mount Lebanon (Table 1). The proportion of asthmatic preschool children was 8.2% (95% CI 5.8-10.5).

Bivariate analysis

Details regarding the bivariate analysis of factors associated with asthma are summarized in Table 2. A significantly higher proportion of asthma was found in preschool

Table 1 Socio-demographic and other characteristics of the participants.

Variable	Frequency (%)
Sex	
Male	278 (54.0%)
Female	237 (46.0%)
Governorate	
Beirut	87 (16.9%)
Mount Lebanon	390 (75.7%)
North Lebanon	38 (7.4%)
Physician-diagnosed asthma	
No	473 (91.8%)
Yes	42 (8.2%)
	Mean ± SD
Age (in years)	4.44 ± 0.83
Number of siblings older than the child	0.85 ± 0.98
Number of siblings younger than the child	0.48 ± 0.82
Wheezing	
No	358 (69.5%)
Yes, when sick	132 (25.6%)
Yes, without cold episodes	24 (4.7%)
Yes, when exercising	1 (0.2%)
Cough without having the flu	
No	450 (87.4%)
Yes, more than 3 days per week	23 (4.5%)
Yes, more than 4 days to 3 months per year	42 (8.2%)
Expectoration without having the flu	
No	467 (90.7%)
Yes, more than 3 days per week	31 (6.0%)
Yes, more than 4 days to 3 months per year	17 (3.3%)|

Table 2 Bivariate analysis taking the presence versus absence of asthma in child as a dependent variable.

	Absence of Asthma in child N = 473 (91.8%)	Presence of asthma in child N = 42 (8.2%)	p-value
Gender			**0.007**
Male	247 (52.2%)	31 (73.8%)	
Female	226 (47.8%)	11 (26.2%)	
Living in prairie sprayed with pesticides			**0.039**
Yes	76 (16.1%)	12 (28.6%)	
No	397 (83.9%)	30 (71.4%)	
Playing outdoors			**0.010**
Yes	240 (50.7%)	30 (71.4%)	
No	233 (49.3%)	12 (28.6%)	
Respiratory problems forbidding activities			**0.006**
Yes	27 (5.7%)	7 (16.7%)	
No	445 (94.3%)	35 (83.3%)	
Premature birth			**0.006**
Yes	27 (77.8%)	66 (22.2%)	
No	451 (94.3%)	36 (7.4%)	
Hospitalization after birth			**0.080**
Yes	25 (5.3%)	5 (11.9%)	
No	447 (94.7%)	37 (88.1%)	
Nursery			**0.028**
Yes	254 (53.8%)	30 (71.4%)	
No	218 (46.2%)	12 (28.6%)	
Mother smoking			**0.048**
No	331 (70.1%)	21 (50.0%)	
Cigarette	41 (8.7%)	7 (16.7%)	
Waterpipe	98 (20.8%)	14 (33.3%)	
Cigarette and waterpipe	2 (0.4%)	0 (0.0%)	
Both parents smoking status			**0.012**
Neither of them smoke	209 (44.6%)	15 (35.7%)	
One of them smokes	163 (34.8%)	10 (23.8%)	
Both parents smoke	97 (20.7%)	17 (40.5%)	
Father food allergy			<**0.001**
Yes	6 (1.3%)	4 (9.5%)	
No	466 (98.7%)	38 (90.5%)	
Brother food allergy			**0.024**
Yes	4 (0.8%)	2 (4.8%)	
No	468 (99.2%)	40 (95.2%)	
Father medication allergy			**0.002**
Yes	2 (0.4%)	2 (4.8%)	
No	471 (99.6%)	40 (95.2%)	
Sister seasonal allergy			**0.005**
Yes	10 (2.1%)	4 (9.5%)	
No	463 (97.9%)	38 (90.5%)	
Asthma in family member (mother)			**0.001**
Yes	8 (1.7%)	4 (9.5%)	
No	465 (98.3%)	38 (90.5%)	
Asthma in family member (father)			**0.005**
Yes	6 (1.3%)	3(7.1%)	
No	467 (98.7%)	39 (92.9%)	
Both parents asthma status			<**0.001**
No	459 (97.0%)	36 (85.7%)	
Yes	14 (3.0%)	6 (14.3%)	
Asthma in family member (sister)			<**0.001**
Yes	1 (0.2%)	3 (7.1%)	
No	472 (99.8%)	39 (92.9%)	
Asthma in family member (brother)			**0.019**
Yes	8 (1.7%)	3 (7.1%)	
No	465 (98.3%)	39 (92.9%)	
Asthma in family member (others)			**0.002**
Yes	13 (2.7%)	5 (11.9%)	
No	460 (97.3%)	37 (88.1%)	
Allergic rhinitis family members (sister)			<**0.001**
Yes	0 (0.0%)	3 (7.1%)	
No	473 (100%)	39 (92.9%)	
Allergic rhinitis family members (brother)			**0.009**
Yes	3 (0.6%)	2 (4.8%)	
No	470 (99.4%)	40 (95.2%)	
Child reflux			**0.009**
Yes	35 (7.4%)	8 (19.0%)	
No	437 (92.6%)	34 (81.0%)	

(*Continued*)

Table 2 (*Continued*)

	Absence of Asthma in child N = 473 (91.8%)	Presence of asthma in child N = 42 (8.2%)	p-value
Eczema before 2 years			0.036
Yes	28 (5.9%)	6 (14.3%)	
No	445 (94.1%)	36 (85.7%)	
Skin rash for at least 6 months			0.066
Yes	24 (5.1%)	5 (11.9%)	
No	449 (94.9%)	37 (88.1%)	
Heating system using wood			0.086
Yes	33 (7.0%)	6 (14.3%)	
No	440 (93.0%)	36 (85.7%)	
Heating system using electricity/power			0.060
Yes	326 (68.9%)	23 (54.8%)	
No	147 (31.1%)	19 (45.2%)	
Place heating system			**0.001**
Sitting room	165 (35.4%)	15 (37.5%)	
Bedroom	6 (1.3%)	4 (10.0%)	
All the house	295 (63.3%)	21 (52.5%)	
	Mean ± SD	Mean ± SD	
Alcohol glasses per week during pregnancy	0.08 ± 0.30	0.03 ± 0.17	0.092
Alcohol glasses per week during breastfeeding	0.04 ± 0.27	0.001 ± 0.001	**<0.001**

*Numbers in bold indicate a significant p-value (p<0.002) after Bonferroni correction.

children whose fathers had food allergy (9.5% vs. 1.3%) and an allergy to medication (4.8% vs. 0.4%); whose sisters had allergic rhinitis (7.1% vs. 0%); and mothers and sisters had asthma (9.5% vs. 1.7% and 7.1% vs. 0.2%, respectively); and had a heater in the bedroom compared to other rooms in the house (10.0% vs. 1.3%). Finally, a higher mean ARFS score was found in asthmatic children compared to healthy controls (18.66 vs. 5.66; P<0.001).

Multivariable analysis

A backward logistic regression, taking the presence/absence of asthma in children as a dependent variable, showed that higher odds of asthma in children were significantly associated with living near a prairie sprayed with pesticides (OR=2.33); playing outdoors (OR=2.89); having a heater in the bedroom (OR=10.73); attending a nursery (OR=2.91); mother smoking cigarettes (OR=3.35) or a waterpipe (OR=2.46); having a sister with a history of seasonal allergy (OR=6.81); and a parental history (mother and father) of asthma (OR=6.15 and OR=9.83, respectively) (Table 3, Model 1). The second backward logistic regression, taking the presence/absence of asthma in children as a dependent variable and the ARFS score as an independent variable, showed that a higher ARFS score (OR=1.144) was significantly associated with higher odds of asthma in children, in addition to other factors (playing outdoors, heating system in the bedroom, and nursery attendance) (Table 3, Model 2).

Table 3 Multivariable analyses.

Model 1: Logistic regression taking the presence vs. absence of asthma in child as the dependent variable.

Variable name	ORa	p-value	95% CI
Living near a prairie sprayed with pesticides (yes vs. no*)	2.338	0.046	1.014-5.390
Playing outdoors (yes vs. no*)	2.896	0.013	1.257-6.670
Place heating system (bedroom vs. sitting room*)	10.738	0.004	2.143-53.796
Attending a nursery (yes vs. no*)	2.916	0.013	1.251-6.796
Mother smoking cigarette vs. non-smoker	3.350	0.023	1.183-9.493
Mother smoking: waterpipe vs. non-smoker	2.466	0.035	1.067-5.702
History of seasonal allergy in the child's sister (yes vs. no*)	6.810	0.007	1.682-27.576
History of asthma in the mother (yes vs. no*)	6.158	0.011	1.528-24.816
History of asthma in the father (yes vs. no*)	9.838	0.012	1.651-58.615

Variable(s) entered: gender, living prairie, playing outdoor, respiratory problems, wood, electricity, place heating system, premature birth, hospitalization after birth, nursery, mother smoking, family member allergy, food allergy father, food allerg',- brother, medication allergy father, seasonal allergy sister, asthma family members mother, asthma family members father, asthma family members brother, child reflux, eaema before 2 years old, skin rash for at least 6 months, alcohol glasses per week during pregnancy.

Model 2: Logistic regression taking the presence vs. absence of asthma in child as the dependent variable and taking the Asthma Risk Factors Scale score as an independent variable.

Variable name	ORa	p-value	95% CI
Playing outdoors (yes vs. no*)	2.441	0.036	1.058-5.629
Place of the heating system (bedroom vs. sitting room*)	12.934	0.001	2.802-59.690
Attending a nursery (yes vs. no*)	2.471	0.049	1.005-6.077
Asthma Risk Factors Scale score	1.144	<0.001	1.097-1.193

Variable(s) entered: gender, living prairie, playing outdoor, respiratory problems, wood, electricity, place heating system, premature birth, hospitalization after birth, nursery, mother smoking, family member allergy, food allergy father, food allerg', brother, medication allergy father, seasonal allergy sister, asthma family members mother, asthma family members father, asthma family members brother, child reflux, eczema before 2 years old, skin rash for at least 6 months, alcohol glasses per week during pregnancy, asthma risk factors scale score.

*Reference group

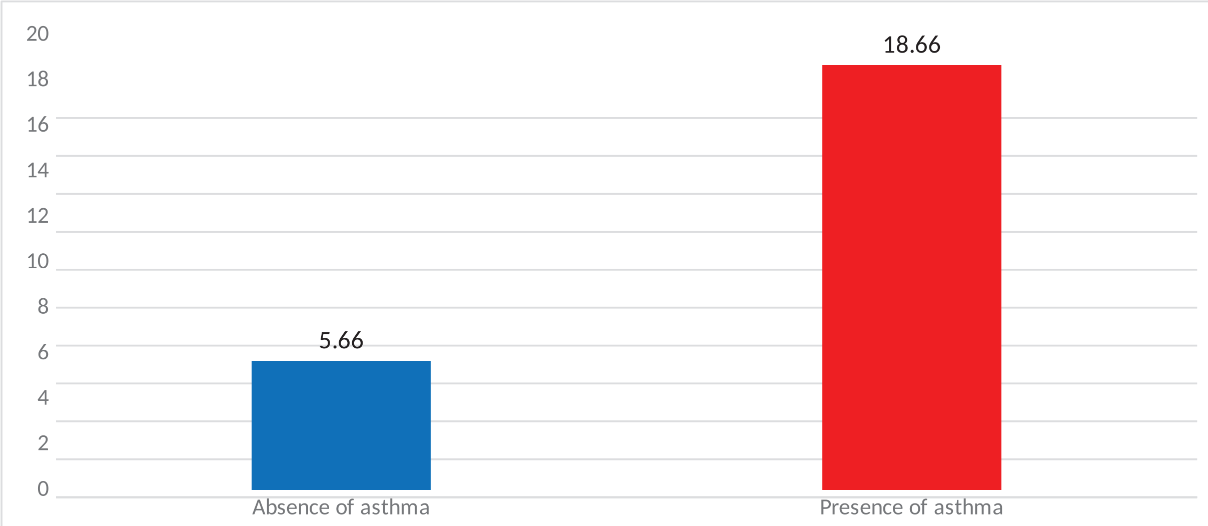

Figure 1 Comparison of the mean ARFS score in children with and without asthma.

Pre-School Asthma Risk Factors Scale score

The new PS-ARFS score for asthma was computed using the following formula based on Model 2:

$$\text{PS-ARFS score} = \text{ARFS score} + (\text{playing outdoors} \times 2.4) + (\text{heating system in the bedroom} \times 12.9) + (\text{having attended a nursery} \times 2.5).$$

In this formula, the presence of a variable is coded as 1, and its absence as 0.

Validity measures

The ROC curves of both ARFS and PS-ARFS scores were sketched, comparing children diagnosed with asthma with healthy children. The optimal ARFS score considered as a cut-off between asthma and healthy children was 8.95. The sensitivity and specificity were good at this cut-off point (80.4% and 87.2%, respectively). The area under the curve was high: 0.859 (0.787–0.932; $P<0.001$). For PS-ARFS, respective results were: area under the curve: 0.908 (0.860–0.957; $P<0.001$); at value: 14.20, Se = 84.3% and Sp = 90.9% (Figure 1).

The predictive values

The positive predicted value (PPV) of the ARFS score at the cut-off point of 8.95 was 87.2% (95% CI [84.32%; 90.08%]), and the negative predicted value (NPV) was 80.4% (95% CI [76.97%; 83.83%]). In parallel, the PPV of the PS-ARFS score at the cut-off point of 14.20 was 88.7% (95% CI [85.97%; 88.7%]), and the NPV was 84.3% (95% CI [81.16%; 87.44%]).

Discussion

To the best of our knowledge, this study is the first one to shed light on the factors associated with asthma and validate a screening scale among preschool children in Lebanon. In this study, the rate of asthma in this age group was 8.2%, a rate higher than that found in older Lebanese children (4.8% in 5–12-year-old,[6] and 5.6% in 13–14-year-old[7] schoolchildren). No studies have been conducted in the Arab countries on asthma in preschool children; one study conducted in Iraq revealed a prevalence of wheezing (15.8%) in Iraqi children.[34] This rate was also lower than that found in Portugal in the same age group (10.7%)[35] but within the global prevalence range established by an international multicenter study (2% to 30%).[36] The results also showed that multiple factors might be associated with asthma in preschool children; some of these factors are modifiable (living near a prairie sprayed with pesticides, playing outdoors, heating system used in the house, attending a nursery, and passive smoking), while others are not modifiable (parental/family history of asthma and seasonal allergy).

Pesticides

In our study, living near a prairie sprayed with pesticides was shown to be associated with higher asthma in children, in agreement with the results of previous findings;[12] a cross-sectional analysis of Lebanese children identified an increased risk of chronic respiratory symptoms, including wheezing, among those exposed to pesticide in the house, or exposed to pesticides due to parent's occupation, and used outside their house. However, given this study's cross-sectional design, it is difficult to assess whether exposure to pesticides preceded the diagnosis of asthma. Owing to controversies,[37] there is a need for studies that include pesticide-specific exposure assessment and markers of biological mechanisms, and take into account the influence of the timing of exposure across the life span.

Heating system in the house

In our study, the results show that placing a heating system in the bedroom rather than in the sitting room was associated with higher odds of asthma in children; in contrast, installing an effective home heating system could increase indoor temperature and reduce asthma symptoms in asthmatic children.[38] The use of HEPA filters in an air-filter review conducted by Sublett et al. concluded that air filtration decreased progression of allergic respiratory diseases.[39] Strategies for reducing indoor allergen or pollution by reducing the penetration of outdoor pollutants into the indoor environment need to be further explored and refined. The results of heating system in the bedrooms versus heating the complete house seem rather surprising. It could be related to other socioeconomic factors or to a previous diagnosis of asthma in children who have heaters in the bedroom. Therefore, inferring a reverse causality or the issue of heating type since the question asked was not clear enough. The CI was wide because of the small effective sample obtained in this study (only 10 children). Further larger studies are needed to confirm our findings.

Attending a nursery

Our findings showed that attending a nursery was associated with increased risk of asthma in preschool children, consistent with a Taiwanese study.[40] Indeed, the risk of infections in children increases after attending nursery and may be one of the many triggers for exacerbation and early development of asthma.[38] The symptoms of asthma have a seasonal variation, with peaks during winter and early spring, and a decrease in summer. Seasonal variations in symptoms of cough in both physician-diagnosed asthma groups and non-asthma groups may be partly explained by the seasonality of the epidemiology of the virus.[40]

Passive smoking

In this study, exposure to maternal cigarette and waterpipe smoking during pregnancy, and passive smoking, were significantly associated with an increased risk of asthma in children. Passive smoking can result in a variety of respiratory symptoms, such as cough, phlegm production, breathlessness, and wheezing in preschool children, in addition to hospitalizations and poorer lung function.[41] The prevalence of asthma increases in children who live with smokers, and the risk of developing asthma increases in proportion to the number of smokers in the house,[42] although there is insufficient evidence to link exposure to passive smoking with allergic sensitization.[43] However, some studies suggest that there may be a synergy between hereditary risk of allergy and exposure to second-hand smoke.[44] One large study has reported that chronic respiratory symptoms may persist into adulthood among children who live with a smoker, regardless of subsequent exposure to second-hand smoke.[41]

Playing outdoors

Our study showed that playing outdoors was associated with an increased risk of asthma, contrary to previous findings showing that playing outdoors often helps asthmatic children cope with periods of aggravated symptoms.[45,46] We hypothesize that this result may be driven by outdoor exposures to pollutants: although the outdoor playing could not be quantified and further identified, the high pollutant level in Lebanon[47] could be suggested as a reason for this association, as shown in a previous study conducted on teenagers.[48] The future studies are needed to evaluate the actual link between playing outdoors and asthma in children.

Family history

Our findings also showed that a parental history of asthma was significantly associated with higher odds of asthma in children, in line with international findings.[49] Our results consolidate previous findings, confirming that a family history of asthma was an obvious risk factor for preschool children.

Validity of the PS-ARFS score

Our results showed that the PS-ARFS score could be a good option for detecting the possible presence of asthma in an epidemiological setting, despite the diversity of phenotypes and the absence of spirometry. The sensitivity, specificity, and positive and negative predictive values were found to be excellent, particularly after adding the variables specific to this age group (playing outdoors, having a heating system in the bedroom, and attending a nursery). This is the first study to take into consideration environmental exposure factors, parental history, and dietary factors for the prediction of asthma in children. PS-ARFS may be helpful in screening for asthma in primary care when preschool children present with symptoms suggestive of asthma. Our tool will help to identify communities at risk of exposure to multiple chemicals in regions and communities across the country. The tool may also help decision makers raise awareness about various aspects of asthma. Nevertheless, these results would benefit from further validation in clinical settings, particularly to improve the scale criterion validity. Prospective studies would also be useful to confirm the prediction of asthma over time using this scale. It should be noted that the PS-ARFS score is used in an endeavor to predict a history of ever having a diagnosis of asthma, but does not predict current and the future asthma diagnosis. The ISAAC questionnaire remains the gold standard for epidemiological evaluation of asthma; results obtained from PS-ARFS should be evaluated carefully. Based on the findings presented in Figure 2, it seems that both ARFS and PS-ARFS have similar performances and can be used to screen for the possibility of presence of asthma; however, PS-ARFS is specifically meant for preschool children (for the age range of 3–5 years) and shows a slightly higher area under the curve. Compared with the Asthma Predictive Index (API), one of the most used indexes to predict asthma in children,[50] PS-ARFS takes into consideration environmental, parental, and dietary factors (not just respiratory and cutaneous factors like the API) and does not require blood withdrawal (unlike the API). The metrics within the PS-ARFS score require parental observation and not physician documentation like the API.[50]

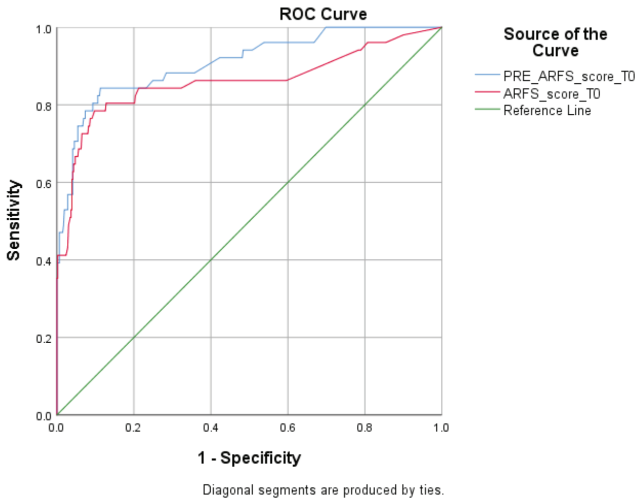

Figure 2 ROC curve of ARFS and PS-ARFS. Children with asthma versus healthy ones were analyzed. For the ARFS (red curve): area under the curve=0.859 (0.787-0.932; $P<0.001$); at value: 8.95, Se=80.4% and Sp=87.2%. For PS-ARFS (blue curve): area under the curve=0.908 (0.860-0.957; $P<0.001$); at value: 14.20, Se=84.3% and Sp=90.9%.

Finally, the PS-ARFS score showed higher sensitivity compared with the API.[50]

Limitations

Our study has several limitations. This is a cross-sectional study with retrospective reports, and consequently a low level of evidence regarding causality. The total sample size was small and might not be a representative of the whole population, since the schools selected were private urban institutions from three of the five districts in Lebanon; this predisposes to a selection bias. The number of children with asthma being rather small raises the possibility of false positive findings; the results cannot be extended to imply causation. A selection bias is also possible because of the refusal rate; this is expected to overestimate the percentage of children with asthma. An information bias is a possibility, since the use of a questionnaire for surrogate respondents (parents) may not always be accurate: problems in understanding questions, recalling, and over- or under-evaluating symptoms are possible; being non-differential, this bias is expected to drive the results toward the null. Another limitation resides in the fact that the entire analysis was based on the diagnosis of asthma, being defined by the question of ever doctor-diagnosed asthma only: defining asthma through questions about a physician's diagnosis is acceptable according to literature, but may still carry a risk of over- or under-diagnosis; also, children aged 3-5 years have a high degree of transient wheezing, and 60% of children that have wheezing at three years will no longer have wheezing by the age of six years.[49] Furthermore, the timing of diagnosis of respiratory symptoms was not obtained in this study; therefore, the results obtained should be treated with caution. Moreover, asking parents about timing of symptoms and diagnosis of disease might complicate the scale and lead to inadequate results because of the increased risk of recall bias in this matter. In all cases, the scale is a screening tool that can be used in nurseries and other epidemiological settings to identify high risk subgroups of children, lead parents to reach for clinical care, and try to decrease childhood exposure to asthma risk factors; however, it does not replace an appropriate diagnosis conducted by a physician in a clinical setting.

The possibility of recall bias might further be plausible because of the retrospective nature of our investigation regarding risk factors: exposure to different toxics could not be quantified objectively and was obtained according to parents' estimation; nevertheless, as stated above, the practicability of the tool requires it to be simple. Nevertheless, for the known risk factors of asthma, the effect of the recall bias could be differential and may lead to the overestimation of effects by parents of children with the disease. However, for the substances that are not known to be associated with asthma, the bias is mainly non-differential, and an underestimation of the association with asthma is to be anticipated. The associations described may also have arisen by confounding or be reverse causation (the latter especially may explain the association with playing outdoors and having a heater in the bedroom). In all cases, prospective studies that override the recall bias would be expected to improve the precision of our results.

Despite all limitations, our methodology is that of other cross-sectional studies, including that of ISAAC, which is widely used in international comparisons. The future studies, conducted in clinical settings and measuring the intensity and duration of exposure to each toxic element, are suggested to confirm and refine the findings of our study. In addition, a prospective follow-up cohort is ongoing; additional validation methods would then be employed to confirm the usefulness of this scale, including exploratory factor analysis, confirmatory factor analysis, and analyses intended to assess the construct validity, criterion validity, test-retest reproducibility, sensitivity to change, and usability.

Conclusion

The results of this study shed light on some factors that are associated with asthma among preschool children in Lebanon. Specific risk factors to this age group (playing outdoors, having a heating system in the bedroom, and attending a nursery), added to the earlier factors found for older children, were found to improve the validity of ARFS, which resulted in generating PS-ARFS. The new scale (PS-ARFS) is suggested for screening of asthma in preschool children in epidemiological settings.

Authors contribution

SH and PS conceived and designed the study. NK performed data collection and entry. SH and PS were involved in data interpretation and statistical analysis. SH and HS wrote the manuscript. HS, RH, and MW helped in the writing and critically revising the manuscript for intellectual content. All authors read and approved the final manuscript.

Acknowledgments

The authors would like to thank Mrs. Desirée Ghanem, Father Valentino Da Silva Ghoul, Mr. Joseph Chahine, Dr. Marie-Claude Fadous Khalife and all other schools directors for their help in data collection. A special thank you for all the parents who participated in this study.

Conflict of Interest

The authors disclose no conflicts of interest.

Funding

This study was funded by the Lebanese University. The funder had no role, whatsoever, in the designing of the study; collection, analysis, and interpretation of data; and writing the manuscript.

Availability of data and materials

There is no public access to the data generated or analyzed during this study to preserve privacy and identity of the individuals. The dataset that supports the conclusions is available from the corresponding author upon request.

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