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Original Article

Development of an asthma risk factors scale (ARFS) for risk assessment asthma screening in children

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Background: The study objective was to create asthma risk factors scale (ARFS) score that would be correlated with the increased risk of asthma in Lebanese children. This scale would eventually be used both to identify children at risk and assess early diagnosis of asthma.
Methods: A case-control study (study 1) of 1276 children (976 controls and 300 cases) and a cross-sectional study (study 2) of 1000 children were conducted using a parental questionnaire. Children aged between 3 and 16 years were screened for possible enrollment. The ARFS was created by combining the following risk factors: child's exposure to pesticides, detergent mixing, alcohol, smoking and drug intake during pregnancy and breastfeeding, the actual paternal and maternal smoking status and history of asthma, and the types of food the child consumes.
Results: There was a significant increase in the risk assessment screening for asthma per 15 points increments of ARFS ($p < 0.001$ for trend). The score category 0—14.99 best-represented control individuals (88.8% controls), while a score higher than 45 represented asthmatic children best (98.4% asthmatics). The positive predictive value (disease positive/

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all positive by scale) came out as 94.02%, whereas the negative predictive value (disease negative/all negative by scale) was found to be 90.47%. These results were confirmed in the second study sample.

Conclusion: The ARFS is a simple and easy-to-use tool, composed of 15 questions, for the clinician risk assessment of asthma in children, taking into account the environmental exposure, parental history of asthma and dietary habits of the child. Its value for asthma diagnosis remains to be confirmed in future prospective studies, especially in children with chronic respiratory symptoms.

1. Introduction

Symptoms of asthma may begin in early childhood, often in the first few years of life. Around 30—50% of children experience episodes of wheezing, less than half of whom will have continuing childhood asthma.[1] Preschool asthma-like symptoms (wheezing, dry cough, expectoration, chest congestion) are nonspecific; therefore, it is difficult to determine which preschool children with asthma-like symptoms currently have or will develop asthma at school age.[2] Many predictive scores, such as the Asthma Predictive Index (API),[3] PIAMA risk score,[2] and CAPS score[4] have been created to predict the presence of asthma in patients with non-specific respiratory symptoms based on the clinical parameters of the symptom-sign score.

On the other hand, environmental factors seem to play a major role in the development of asthma symptoms in children. If simple environmental factors could be identified, this would allow for better prevention of the asthma. A number of factors have already been identified as triggering factors for asthma symptoms; there is convincing evidence that maternal smoking during pregnancy and breastfeeding, leading to in utero and perinatal exposures to environmental tobacco smoke, are associated with increased risk of asthma.[5] Furthermore, even exposure to passive smoking significantly increased the risks of asthma, wheeze, lower respiratory infections, and reduced lung function in children.[6] Another study showed that alcoholic drinks, particularly wines, appeared to be important triggers for asthmatic responses, probably due to the sensitivity to the sulfite additives[7] and yeast in wine.[8] Children of pesticide workers (storing working equipment in the house, contamination of clothes, etc.), residing near pesticide treated areas or in agricultural regions, and outdoor and indoor spraying of pesticides also contributes to children's exposure, which was associated with chronic respiratory symptoms and asthma in children.[9,10] Domestic use of cleaning products, in particular those in spray form, has been also suggested as a risk factor for asthma.[11] Moreover, in utero exposures to several xenobiotics have been linked to an increased risk of asthma. The literature is replete with evidence of a relationship between drugs intake by the mother during pregnancy and asthma in children.[12] From another perspective, asthma also has significant genetic contributions, with heritability estimates varying between 35% and 95% for asthma.[13,14] Thus, the situation becomes more complex because of the multiplicity of exposures for a single child; we hypothesize that this may lead to a cumulative risk of asthma.

Cumulative risk, as defined in the Environment Protective Agency (EPA) Framework for Cumulative Risk Assessment as "the combined risks from aggregate exposures to multiple agents or stressors", is growing and evolving for asthmatic patients in general. It has existed in some form for many years, such as in the consideration of multiple chemical exposures and sensitive sub-populations.[15] Cumulative risk assessment has been proposed as an approach to evaluate the health risks associated with simultaneous exposure to multiple chemical and non-chemical stressors.[16] Increased knowledge of the greater sensitivity of the unborn baby, the infant and the child has led to general recognition that a higher degree of precaution is now needed in regulating for multiple stressors on the young.[17]

Since data on actual exposure levels of multiple sources in the population are scarce, this represents a fundamental lacuna in knowledge underpinning environmental risk regulation and makes assessment of health risk very difficult.[17] Interaction of multiple exposure factors and association with health problems have been assessed in some diseases, but not asthma. All children are clearly exposed to multiple chemicals before and after birth.[17] The concept of multiple exposures has been applied to asthma for specific air pollutants,[18]; however, different factors may increase the probability of asthma-like symptoms development in the child. Although many algorithms to predict the development of asthma in children have been reported previously, these took the symptoms of asthma into consideration, mainly wheezing and cough. Some authors developed a model for use in the general population,[19] while others restricted their analysis to children with early symptoms (wheeze or cough).[20] In our analysis, although we considered children with wheezing, coughing or having expectorations in the absence of flu, we base our selection on these symptoms because they are prevalent in young children and suggestive of childhood asthma.[21] However, we hypothesize that using exposures indices, parental and dietary factors may help health professionals predict the expression of asthma even before symptoms appear. We base our choice of variables on the pilot study that was conducted last year in Lebanon showing factors associated with asthmatic children.[22]

Thus, our objective in this study is to create an asthma risk factors scale score that would be associated with the increased risk of asthma expression in children from 3 to 16 years of age in Lebanon, taking into account multiple toxic exposure, environmental factors, parental history of asthma and the diet followed by the child. The aim of this study was to work on the first 2 steps, in order to evaluate the performance of the scale in a separate sample in a future study.

2. Methods

2.1. Ethical aspect

The Institutional Review Board of the Lebanese University Faculty of Pharmacy waived the need for an approval based on the fact that it was an observational study that respected participants' autonomy and confidentiality and caused minimal harm.

2.2. Study design

2.2.1. Study 1

This case-control study was conducted between December 2015 and April 2016. In addition to cases (asthmatic) and controls (healthy), a third group of participants (undiagnosed/probable asthma) was defined as the presence of respiratory symptoms (wheezing, cough, excess bronchial secretions, respiratory distress), but without a physician's diagnosis of asthma.

2.2.2. Participants' characteristics

Controls were chosen using a sample of healthy Lebanese students from schools in all districts of Lebanon including children from different socioeconomic levels. Directors of the schools were contacted to obtain permission to enter classrooms to distribute the questionnaires. Children were then given the questionnaire to be filled out at home by their parents after parental written informed consent was obtained. Classification into a control (healthy child) required the absence of a diagnosis of a respiratory disease by a physician and absence of respiratory symptoms (wheezing, cough, dyspnea).

Asthma cases were taken from a specialized center for the treatment of asthma in children, which provides free services to children with respiratory diseases from all areas of the country. Children visited the center either as new patients or for follow-up visits on their asthma symptoms and not for any other reason. After the administration's approval, the questionnaire was distributed in the Asthma Center to asthmatic children's parents after a written informed consent was obtained. Classification into the diagnosed asthma group was defined as the child having asthma-related symptoms (chronic wheezing, cough, and dyspnea), as well as an affirmative answer to the question "Has your doctor ever told you that your child has asthma?" No matching was done for cases and controls regarding any variable.

2.2.3. Study 2

This was a cross-sectional study conducted on Lebanese students in public and private schools from January to June 2017 using the International Study of Asthma and Allergies in Childhood (ISAAC).[23] The list of schools provided from the Lebanese Ministry of Higher education was used to randomly select the centers.

Seventeen public schools were contacted from all Lebanese geographic areas: 5 in Beirut; 3 in South Lebanon; 1 in Nabatieh; 2 in Mount Lebanon; 5 in North Lebanon; and 1 in Bekaa. In the case of private schools, 17 were contacted: 6 in Beirut, 6 in Mount Lebanon; 2 in North Lebanon; 1 in Nabatieh; and 2 in Bekaa. Eight schools (1 public and 7 private ones) refused to participate, while 26 out of 34 (73.3%) agreed to distribute the questionnaires among their students between the 1st and 9th grades. Students had to take the questionnaires home to be filled in by their parents and returned back to school before collection by the inquirer.

2.2.4. Questionnaire and variables

The detailed questionnaire was distributed randomly by interviewers who were not related to the study. All interviewers received thorough training prior to the start of the data collection to ensure adequacy and standardization of the process. A pretested self-administered questionnaire adapted to local Arabic language (the native language in Lebanon) from the standardized and validated American Thoracic Society chronic respiratory disease questionnaire was used[24] and administered to parents. The same conditions were applied for questionnaires in both cases and controls to evaluate the diagnosis of asthma and respiratory symptoms. The standardized ISAAC questionnaire was used, after translation into Arabic and back-translation into English to ensure accuracy of the questions.[23] More details about the methodology followed can be found in other reports.[22,25–29]

This questionnaire assessed the socio-demographic characteristics, including age, gender, region, number of rooms and the number of persons living in the house, the level of education for both parents, the family history of asthma, and other known risk factors of asthma (the heating system used inside the house, child history of recurrent otitis, humidity inside the house, if the child went to a nursery, etc.). Education level of parents was quantified according to the number of years of study.

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?" while chronic respiratory symptoms was defined as the presence of one of the following symptoms: recurrent wheezing (during the day, evening, night, the whole day or at exercise), a recurrent cough (during the day, evening, night, the whole day or at exercise), a history of more than one dyspnea plus wheezing episode treated by a doctor. Questions regarding wheezing and night cough without having a cold were also taken from the ISAAC questionnaire.[23]

Questions about smoking or alcohol intake during pregnancy and during breastfeeding, the kind of smoking or alcohol and the quantities consumed were included, in addition to the use of any drug during pregnancy or lactation, and occupational, regional, local, and domestic

pesticides exposure and cleaning product use. For pesticide exposure, information was recorded using the following questions: ''Have you ever used pesticides in your work?'' ''Have you ever used pesticides outside work (for house or garden treatment…)?'' ''Do you live in a region heavily treated by pesticides?'' ''Do you live in proximity to a field heavily treated by pesticides?'' along with the duration of exposure during work and the number of times the house or the garden was sprayed by pesticides per week or per year. Parental active smoking was determined by several questions, categorizing parents into non-smokers or current smokers. Passive smoking was determined by the number of smokers at home.

Detergent use was determined by questions about who uses these products at home, the type of detergents used and if there were any mixture of these products during cleaning at home. Information about the heating system used at home, the presence of an air conditioner and a humidifier, the presence of humidity or mold at home as seen on the walls and the child's history of recurrent otitis, tonsillectomy, cardiac problems, premature birth and kindergarten attendance were also recorded. The Forced Expiratory Volume in 1 s (FEV1) was obtained for each asthmatic child aged 6 years and above after an assessment by spirometry in the physician's clinic. Children under 6 years did not undergo that test. It is of note that all asthmatic children were prescribed at least one asthma medication.

2.2.5. Dietary intake assessment

The self-administered questionnaire used in this study included questions related to the socio-demographic background of the children and a short food frequency questionnaire (FFQ) to assess the usual dietary intake. The FFQ was composed of 16 semi-quantitative questions covering different food categories (including the five basic food categories typically consumed by the Lebanese population).[30] The FFQ used in this study was adapted from the questionnaire earlier administered in the Lebanese population[30] and the CDC Global School Health Survey[31]; the finally used items were vegetables, fruits, olive oil, fish and sea food, meats (including cooked meats, poultry, ham, and hotdog), pasta, sweets (cake, ice cream, chocolate), carbonated beverages, fruit, vegetables, fast food (hamburger, pizza, Lebanese pizza (known as Mankouche with thyme or cheese or yogurt based kechek), and fried potatoes and chips. We omitted to ask questions about eggs and dairy products as separate items because they would have been confusing to the parents to record in the FFQ given that these food items are frequently consumed in Lebanon within composite dishes (eggs, cheese, and yogurt within cooked dishes), and fast food meals. The FFQ asked how often each food item, group, or beverage was usually consumed with five possible answers for each of the food categories: (1) never, (2) two times or less per week, (3) three to six times per week, (4) at least one time per day, and (5) at all meals. These five response categories were later merged into four categories for analysis, namely: (1) never, (2) once or twice per week (3) three to six times per week, and (4) consumption on daily basis.

2.3. Asthma risk factor scale creation

To develop a scale, at least three steps seem necessary. First, relevant risk factors need to be identified, second the level of exposure for each factor that constitutes risk should be determined, and third the performance of the scale should be evaluated in a separate sample and setting. Since the existing models depend on different variables related to the environment and the local context, we decided to create a new model that included most variables that correlated with increased asthma risk in Lebanese children.

An Asthma Risk Factor Scale (ARFS) was created to screen if the symptoms of the disease may vary with the number of risk factors the child has. The ARFS was created by combining the following risk factors: pesticide exposure of the child (presence at home of a person working with pesticides, living in an area sprayed with pesticides, use of pesticides at home); detergent mixing; alcohol drinking during pregnancy and breastfeeding; number of cigarettes per day or number of smoked waterpipes per week during pregnancy and breastfeeding; any drug intake during pregnancy and breastfeeding; the paternal and maternal smoking status and history of asthma; and the types of food the child eats (red meat, fast-food, nuts, dairy products, chocolate, milk, pastry, fish, legumes, fruits, olive oil, fried food, chips, caffeinated beverages).

We did a logistic regression analysis using healthy vs. asthmatic status of children as the dependent variable to assess the risk factors associated with the asthma status. The odds ratios (ORs) of the factors associated with the presence of asthma in children were rounded and used as coefficient factors in the ARFS formula. For multiple logistic regression model with one continuous outcome (ARFS) and a set of k independent predictors (i.e., Xi's which may be continuous or categorical), the equation is usually expressed as: $Y = \text{alpha} + B_1X_1 + B_2X_2 + B_3X_3 + \ldots + B_KX_K$

The parameters - alpha and beta's (B) represent an intercept and odds ratios, respectively. The ORs taken from the logistic regression predicted asthma in the epidemiological setting best. The questions pertaining to the formula are summarized in Supplementary Table 1.

The diagnostic score for asthma (DS-asthma) was computed using the following equation: Asthma risk factors scale = (respiratory infections × 10) + (playing in dust × 2) + (playing on carpets × 2) + (pulmonary problems in the child in the last 2 years × 25.5) + (respiratory problems in the child before 2 years of age × 13.5) + (humidity in the house × 2.1) + (asthma in mother × 6.3) + (asthma in both parents × 9) + (history of reflux in the child × 2.9) + (living in pesticides region × 2.6) + (red meat daily × 2.8) + (nuts <2 times/week × 0.4) + (nuts 3–6 times/week × 0.4) + (dairy products <2 times/week × 0.3) + (dairy products 3–6 times/week × 0.2).

In this formula, the presence of the variable is replaced by 1. If both parents have asthma, then replace that variable with 1 and replace asthma in the mother by 0. For nuts and dairy products consumption, choose the higher frequency of eating the type of food and replace the variable

by 1. The scale has a minimum of 0 and a maximum of 73.1 points. In the sample, the minimum was 0 and the maximum was of 64.6. We divided the continuous score into 4 categories based on a 15-point increment (divided in quartiles) as follows: category 1 reflects the control group (0–14.99), category 2 (15–29.99) and category 3 (30–44.99) for undiagnosed/probable asthma and category 4 (more than 45) for diagnosed asthma.

We calculated the reliability of the scale to assess the quality of our data. High Cronbach alphas were as follows: ARFS (0.823) and ISAAC questionnaire (0.872). Since we obtained high internal consistency, the results are considered reliable and robust.

To ensure the validity of the results, the score that was created in study 1 was tested on the other sample (study 2) which was independent from the first one.

2.4. Statistical analysis

Data analysis was performed on SPSS software, version 23. Percentages were shown for qualitative variables, while means and standard deviation were given for quantitative variables. We used the Shapiro Wilk test to check the normality of variables distribution. Two-sided statistical tests were used to compare between group percentages: Wilcoxon test for quantitative variables with non-homogeneous variances or non-normal distribution, and Student's t test for quantitative variables of normal distribution and homogeneous variances. Moreover, a backward logistic regression was performed, using asthmatic vs. healthy children as dependent variable and taking into account the variables in the bivariate analysis that showed a p-value < 0.2.

3. Results

3.1. Sociodemographic characteristics

Out of 1680 questionnaires distributed in schools, 1503 (89.46%) were collected from parents of the children aged 3–16 years old. There were missing values in our results since not all questions were answered by all parents. In this study, 976 children had no respiratory problems (64.9%; 95% CI 62.65–67.48), with 300 having diagnosed asthma (20%; 95% CI 17.937–21.983) respectively. The 227 children having undiagnosed/probable asthma (15.1%; 95% CI 13.29–16.92) were excluded from the analysis (Supplementary Table 2).

3.2. Multivariable analysis for asthma diagnosis as dependent variable

The multivariable analysis taking the children's status of asthma versus healthy as the dependent variable showed that children with a history of respiratory infections (bacterial or viral) had significantly higher odds of having asthma (ORa = 10.015), while children who played outside in dusty conditions and on carpets significantly had almost twice the odds of having asthma (ORa = 1.963 and ORa = 1.982), respectively. Children with pulmonary problems in the last 2 years had a significant 25 fold increase in having asthma (ORa = 25.518), while those with respiratory problems before the age 2 years had significantly increased odds of asthma (ORa = 13.473). High humidity at home would significantly increase the odds of asthma (ORa = 2.140), while a history of asthma in the mother only and in both parents would significantly increase the odds of asthma in the child (ORa = 6.324 and ORa = 9.037), respectively. A history of reflux in the child, living in a region sprayed with pesticides would significantly increase the odds of asthma (ORa = 2.919 and ORa = 2.6) respectively. Concerning food types, eating red meat on a daily basis would significantly increase the odds of asthma compared to no meat consumption (ORa = 2.826), while eating nuts less than 2 times per week (ORa = 0.41) would significantly decrease the odds of asthma compared to no consumption of nuts, whereas eating nuts 4–6 times per week (ORa = 0.351) would decrease these odds even more. Furthermore, eating dairy products 4–6 times per week (ORa = 0.161) and on a daily basis (ORa = 0.181) would significantly decrease the odds of asthma compared to no dairy products consumption (Supplementary Table 1).

3.3. Asthma risk factors scale and risk assessment screening of asthma

In Fig. 1, we present the risk assessment screening for asthma in the whole sample; there was a significant increase in risk assessment screening for asthma per 15 points increments of ARFS ($p < 0.001$ for trend). The score category 0–14.99 best represented control individuals, while a score higher than 45 represented asthmatic children best.

When considering children with chronic respiratory symptoms only, the results showed that 82.8% would belong to the control group (category 1), 7.5% would be in category 2, 8.4% in category 3 and 1.3% in category 4, with categories 2–4 referring to moderate, moderate-severe and severe asthma groups. This indicates that 17.2% of these symptomatic children might be underdiagnosed for asthma (they had a total score that would not place them in the asthma category).

For the percentage of expected FEV1, we found: $r = -0.083$; $p < 0.001$ and the equation was: [Percentage of expected FEV1] = 87.09 − (0.04 × [Asthma Risk Factors Scale]) (Supplementary Fig. 1).

The higher the ARFS score, the lower was the FEV and the more severe the asthma. It is also worth noting that a significant and negative correlation was found between the ARFS and the FEV1 values ($r = -0.516$; $p < 0.0001$).

3.4. Scale properties

The sample was normally distributed. In individuals with asthma, the mean was 24.07 ± 17.60, and the median was 20.70. In controls, the mean was 4.07 ± 5.27, and the median was 2.4. Moreover, children with respiratory disease had a mean score of 9.08 ± 12.06 and a median of 4.40 ($p < 0.001$). The positive predictive value (disease positive/all positive by scale) came out as 94.02%, whereas the negative predictive value (disease negative/all negative by scale) came out as 90.47%.

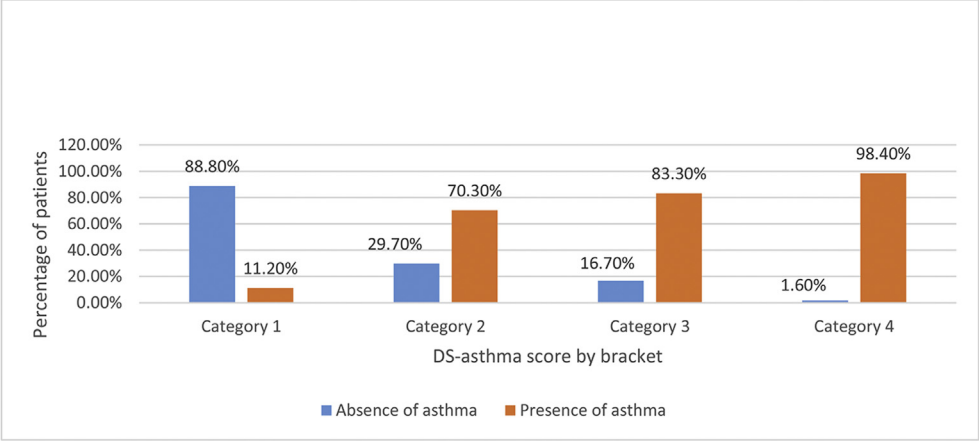

Figure 1 Percentages of children with diagnosed asthma by 2 points category of exposure to toxics index among children with or without diagnosed asthma. * Category 1 = Asthma Risk Factors Scale from 0 to 14.99, category 2 = score from 15 to 29.99, category 3 = score from 30 to 44.99; category 4 = score more than 45.

3.5. ROC curve

In Supplementary Fig. 2, we present the ROC curves of asthma prediction, comparing asthmatic patients with control individuals. The area under the curve (AUC) was high = 0.879 [0.852−0.906] ($p < 0.001$); at value 6.3, Se = 82.6% and Sp = 85.1%.

3.6. Bivariate analysis associated with the ARFS scale

The bivariate analysis results of the sociodemographic and the socioeconomic factors with the ARFS showed that the ARFS was significantly associated with the paternal and maternal levels of education, the socioeconomic status and the district ($p < 0.001$ for all these variables). Furthermore, a significantly higher mean asthma risk factors scales score was found in wheezing as compared to non-wheezing children ($p < 0.001$). The same applies for the presence of recurrent otitis ($p < 0.001$) and heart problems ($p = 0.003$) in the child, premature child's birth ($p < 0.001$), and the child having gone to a nursery at earlier age ($p = 0.005$) (Supplementary Table 2).

3.7. ARFS validation (study 2)

A total of 1000 students were enrolled in study 2. The results of study 2 showed that the sample included 49.6% boys and 50.4% girls. The mean age of the children was 10.34 ± 3.96, with almost similar distribution across the country. Half of the fathers and 35.7% of the mothers smoked, with the highest proportion of both parents having a secondary level of education. The ARFS score ranged from 0 to 54 in this sample. The ROC curve of asthma prediction comparing asthmatic patients with control individuals gave similar results, as follows: the Area under the curve (AUC) was high = 0.860 [0.822−0.897] ($p < 0.001$); at value 2.05, Se = 75.7% and Sp = 70.9%. The validation of the ARFS score on the sample of study 2 showed similar results (92.4% in category 1 and 0% in category 4 for controls; 7.6% in category 1 and 100% in category 4 for asthmatic children) respectively ($p < 0.0001$). (see Tables 1 and Supplementary Table 3).

4. Discussion

In this study we were able to create and validate an asthma risk factors score (ARFS) associated with respiratory disease, mainly asthma in children. To our knowledge, this is the first study to take environmental exposure factors, parental history and dietary factors into consideration for the prediction of asthma in children, since previous studies observed positive associations between asthma and each of the scale factors (pesticides, alcohol, cigarette and waterpipe smoking, detergents) alone.[9–12] The ARFS could be helpful in primary care when preschool children present with symptoms suggestive of asthma for the first time. Our tool will thus help identify communities at risk of multiple chemical exposure to predict relative risk across regions and communities in the country, and to assess and rank magnitude and contributions of multiple stressors.[32]

In this analysis we could demonstrate that cumulative exposures to toxics, along with parental history of asthma and consumption of specific types of food, were associated with higher odds of asthma, asthma-like symptoms, similar to the Respiratory Toxics Exposure Score (RTES) validated by Salameh et al. for COPD screening.[33] This method could be considered non-conventional, since exposures were assessed concomitantly. Since the ORs increased with every added risk factor, we could say that the probability of disease is multiplied. Conventional risk assessment methodology has relied on simplifying assumptions, both implicit and explicit, about combined effects from exposure to environmental mixtures. In general, these simplifying assumptions, such as evaluating the risks of chemicals separately and adding resultant risks are meant to foster conservative (protective) risk estimates.[34]

As for correlates of exposure to toxics, the ARFS was significantly and negatively associated with the parents'

Table 1 Multivariate logistic regression taking asthmatic vs. healthy children as dependent variable (Study 1).

Factor	p-value	ORa	Confidence interval	
History of respiratory infections in the child	<0.0001	10.015	5.948	16.861
Child playing outside (in the dust)	0.024	1.963	1.095	3.521
Child playing on carpets	0.007	1.982	1.203	3.265
Pulmonary problems in the child during the last 2 years	<0.0001	25.518	11.736	55.486
Respiratory problems in the child before 2 years (no vs. yes)	<0.0001	13.473	7.361	24.657
Humidity at home as seen on walls	0.004	2.140	1.269	3.609
History of rhinitis in parents	0.067			
Father	0.437	1.364	0.624	2.979
Mother	0.078	2.358	0.908	6.120
Both parents	0.065	0.191	0.033	1.110
History of asthma in parents	<0.0001			
Father only	0.125	1.679	0.866	3.254
Mother only	<0.0001	6.324	2.993	13.362
Both parents	<0.0001	9.037	3.050	26.774
History of reflux in the child	0.004	2.919	1.412	6.033
Living in pesticides region	0.028	2.600	1.106	6.113
Red meat category[a]	0.043			
1–2 times per week	0.904	1.048	0.491	2.235
3–6 times per week	0.588	1.223	0.590	2.535
Daily	0.024	2.826	1.145	6.978
Nuts category[a]	0.006			
1–2 times per week	0.004	0.410	0.225	0.748
3–6 times per week	0.009	0.351	0.160	0.770
Daily	0.848	0.913	0.358	2.325
Dairy products category[a]	0.017			
1–2 times per week	0.058	0.286	0.079	1.042
3–6 times per week	0.003	0.161	0.048	0.540
Daily	0.004	0.181	0.056	0.579
Pastry category[a]	0.069			
1–2 times per week	0.130	0.386	0.112	1.324
3–6 times per week	0.078	0.294	0.076	1.145
Daily	0.940	0.943	0.204	4.355

- Variables entered in the model: gender, age category, education father and mother categories, history of child's respiratory infections, presence of pets at home, number of smokers at home, play in the dust, play on carpet, pulmonary problems, respiratory problems before 2 years of age, eczema before 2 years of age, history of recurrent otitis, heart problems, premature birth, humidity at home as seen on walls, smoking mother, history of rhinitis in parents, history of eczema in parents, history of asthma in parents, history of reflux in the child, smoking kind during pregnancy, alcohol during breastfeeding, person at home using pesticides, child living in region sprayed with pesticides, pesticides use at home, detergent mixing, father type of smoking, fast food category, fish category, red meat category, nuts category, fruits category, vegetables category, dairy products category, olive oil category, fried food category, chips category, pastry category, caffeinated beverages category, milk category.

[a] As compared to never eating these kinds of food.

high level of education. Our results confirm the solid findings of multiple previous studies: it is plausible that parents with high literacy levels were likely to take an active role and intensively engage in the shared decision process, leading to an increase in their satisfaction with shared decision-making.[35] This implies that if physicians improve the interactions with their patient and ensure a better patient's and parents' understanding for the asthma treatment plan, the likelihood of avoiding the exposure to toxics is high. Inversely, lower educational level was significant determining factor of a poorer quality of life in asthmatic patients, in line with the study of Gonzalez-Barcala et al.[36] This is to be expected since lower educational level was linked to poorer access to health care or less adherence to healthy lifestyles, contributing to the worsening of patients' quality of life.[6]

The low goodness-of-fit between ARFS and FEV1 value using current regression analysis can be explained by the fact that in clinical practice and in epidemiological studies,[37] it is common not to use objective measures of airflow obstruction but to rely on symptoms to assess disease control; however, some reports[38] showed that there may be a poor correlation between asthma symptoms and lung function measurements. It is noteworthy that the prediction intervals are wide due to the sample size.

Chronic exposure to various types of pesticides may aggravate or enhance asthmatic symptoms (wheeze, phlegm, flu-like symptoms) through interaction with functional irritant receptors in the airway and promoting neurogenic inflammation, or can cause airway hyperreactivity via a common mechanism of disrupting negative feedback control of cholinergic regulation in the lungs, thus

making pesticides an overlooked contributor to asthma risk.[39] Child exposure to pesticides (in an area surrounding his house) was significantly associated with asthma in our study, which was in agreement with a previous study that showed chronic exposure to pesticides in children was moderately associated with chronic respiratory symptoms and diseases, especially asthma.[40]

Our model could not be compared to other existing models since it is more comprehensive than others (taking into account more variables than previous models), and because our items are more applicable to the Lebanese population. In addition, some of the variables included in existing models were not present in our model. We suggest a comparative study of all models to check the advantages of each model compared to the other.

The classification of asthma in this study, using the ISAAC questionnaire, was obtained mainly with two questions: "Has a doctor ever diagnosed your child as asthmatic?" and "During the last 12 months has your child been observed to be wheezing?" Therefore, we are probably excluding children with wheezing during another period of life, which could indicate an asthmatic condition. However, the ARFS may be able to predict the possibility of having asthma at all ages, depending on some environmental, parental or dietary factors.

In addition, the ISAAC questionnaire assesses current asthma, while the ARFS tries to predict asthma before it happens by assessing the related previous exposure to risk factors. Prospective studies are necessary to confirm the value of our risk scale.

In general, to improve the consistency and quality of information, measurement instruments need to be continuously validated because, though they are the standardized ones, it is important to remember that language, culture, and accessibility can affect the results. Our scale is tailored specifically to the Lebanese population; future studies are needed to assess the use of this scale in other neighboring countries, with a similar culture.

4.1. Implications for future research and practice

The implementation of a simple risk index in daily care is beneficial to both physicians and parents. It allows physicians to provide tailored medical care and follow-up in children at high risk of developing asthma, and to follow-up in those with a low or intermediate risk of asthma. The increased likelihood of predicting which children will develop asthma will help physicians reduce diagnostic uncertainties, communicate better with parents to avoid children's environmental exposure and improve adherence to their treatment. Prospective studies are suggested to confirm our finding and further validate our scale. A predictive tool for asthma diagnosis may be chiefly useful in very young children (i.e., aged 5 years and below) who are more likely to have transient wheezing due to their smaller airway size rather than to persistent asthma.

4.2. Limitations

Our study may suffer from several drawbacks. This current work cannot identify whether the risks for persistent asthma remain constant throughout childhood, or if risk factors change once transient wheezing of early childhood subsides. Since our model includes several environmental risk factors such as exposure to pesticides, these characteristics cannot be assessed with sufficient reliability by parental report or environmental measurements in daily clinical practice. Adequate measure exposure to simultaneous factors over time requires a longitudinal design and carefully designed measures, as the questionnaires are subjected to recall and reporting bias. Furthermore, the duration of each risk factor was not taken into account. Although the total sample size is acceptable and might be representative of the Lebanese population as it was drawn from all districts in Lebanon, a selection bias is still possible because of the ten percent refusal rate. The questionnaire used in our methodology, including ISAAC ones, is necessary for international comparisons. The retrospective aspect of the study may constitute a low level of evidence due to the possibility of recall bias. The use of a questionnaire to parents may not always be accurate due to the possible problems in understanding the questions, recall deficiency and over- or underevaluation of symptoms, as well as a possible underestimation of toxics exposure, which can lead to a possible information bias. The wide age range for evaluated children (3—16 years old) may also be a limitation since some of the exposure factors investigated may become more or less significant as a risk depending on the age of the child. Asthma outcome was based on parent-reported questionnaires. In our study, misclassification could have taken place because of underreporting of symptoms. To take into account for these limitations, we recommend that future prospective studies validate and update the ARFS in other populations and countries. In addition, qualitative approaches may sometimes be the only practical means to overcome the problems of complexity and data deficiencies and provide some insight into the nature and magnitude of cumulative risks. A nested-cohort study and studies specifically for each age group, particularly the preschool children, would be necessary to determine the incremental utility of using this score versus usual clinical practice alone, validated against an objective measure of airway reactivity or lung function. This model will be the topic for future researches; it will be tested in different age groups and genders and will allow us to determine the threshold of each category of this scale.

These limitations might cause an over- or underestimation of the results; however, since the information bias is non differential, it would have probably directed our results towards the null. Future researches should be designed to overcome them by a more precise estimation/dosage of the exposure, through a cohort in Lebanon with a stricter follow-up on children from birth to adulthood and on their mothers during pregnancy.

5. Conclusion

Although many studies focused on creating an asthma predictive score out of children's symptoms, we were able to create a predictive index for asthma based on the child's exposure to toxics. This study shows associations between

the exposure risk factors and respiratory symptoms. The ARFS is a simple and easy-to-use tool composed of 15 questions for the clinician to assess the child's environmental exposure, parental history of asthma and dietary habits. The clinician would be able at that time to evaluate the child's risk of having asthma symptoms. The index had good ability to differentiate between asthmatic and non-asthmatic children. This tool might be useful in settings where asthma diagnosis might be uncertain. Its value for asthma diagnosis remains to be confirmed in future prospective studies, especially in children with chronic respiratory symptoms and in all categories, especially the preschool age.

Conflicts of interest

The authors have nothing to disclose.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.pedneo.2018.05.009.

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