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Exposure to toxics during pregnancy and childhood and asthma in children: A pilot study

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Study adds: The results of this study showed an increased risk of asthma in children with waterpipe smoking in pregnancy and an increased risk of respiratory problems (diagnosed and probable asthma) with alcohol intake during pregnancy, waterpipe smoking during pregnancy and parents respiratory problems. Spreading awareness by health care professionals (doctors and pharmacists) is needed to reduce the prevalence of this disease in children.

Keywords:
Asthma
Detergents
Pesticides
Alcohol
Smoking
Pregnancy
Infancy

ABSTRACT

Environmental factors, pesticides, alcohol and smoking are linked to asthma in children. The association of toxic substances exposure with asthma has not been evaluated. Our objective is to assess such associations among children aged less than 16 years old. This is a cross-sectional study, conducted between January and May 2015, using a sample of Lebanese students from private schools in Beirut and Mount Lebanon. Out of 700 distributed questionnaires, 527 (75.2%) were returned to us. Verbal informed consent was also obtained from all parents prior to participating in the study. A significant association was found between waterpipe smoking and diagnosed asthma ($p = 0.003$; $OR_a = 13.25$; 95% CI 2.472–71.026). Alcohol during pregnancy, waterpipe smoking during pregnancy and parents respiratory problems significantly increased the risk of respiratory problems by approximately 5 times, 6 times and 2 times respectively ($p = 0.016$; $OR_a = 4.889$; 95% CI 1.339–17.844, $p = 0.021$; $OR_a = 6.083$; 95% CI 1.314–28.172, $p = 0.004$; $OR_a = 1.748$; 95% CI 1.197–2.554 respectively). Waterpipe smoking, alcohol during pregnancy, recurrent otitis and humidity at home seem to be significantly correlated with asthma in children. Spreading awareness by health care professionals is needed to permit a reduction of the prevalence of these allergic diseases, especially asthma, in children.

1. Introduction

Asthma is a chronic disease characterized by recurrent attacks of breathlessness and wheezing, chest tightness, and cough, which vary in severity and frequency from person to person as defined by the World Health Organization and the Global Initiative for Asthma (GINA) guidelines. Childhood asthma is one of the most important diseases of childhood, causing substantial morbidity [1–3].

The incidence, prevalence and severity of asthma have been increasing in the general population worldwide between 1970s and 80s [4]. There are 14 million people in the USA suffering from asthma. The prevalence of self-reported asthma increased by 75% in the USA from 1980 to 1994 [5]. Asthma prevalence ranged from a low of 0.7% in Macau to 18.4% in Scotland [5–8]. It is also estimated that 300 million people worldwide had asthma, and this number is projected to increase to 400 million by 2025, as countries became more urbanized [6].

The International Study of Asthma and Allergies in Childhood (ISAAC) is a unique worldwide epidemiological research program established in 1991 to investigate asthma, rhinitis and eczema in children due to considerable concern that these conditions were increasing in Western and developing countries [1,2,9]: In 1998,

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research on schoolchildren in Beirut, aged 12 to 14 years was carried out according to the ISAAC program [10], reporting a prevalence of 11.9% for asthma. Using the same method in 2006, the prevalence of physician-diagnosed asthma was 5.3% in 13–14 year-old school children in Lebanon, with high prevalence of ever wheezing (21.4%), wheezing on effort (12.7%) and night cough (22.8%) [11].

However, the natural history and etiology of asthma and allergies remains poorly understood [8], despite a large volume of clinical and epidemiological research within populations which has been directed at explaining why some individuals and not others develop asthma and allergies [2,9–11]. Investigation of the reasons for variations in prevalence between populations may be a more fertile source of new etiological clues, but little is known about worldwide variations in the prevalence of asthma and allergic diseases [2].

Although genetic predisposition and environmental exposure are thought to lead to the development of these conditions, the nature of such associations remains unclear [12,13]. There are many risk factors linked to asthma in children including familial history of asthma in one of the parents or both. Environmental factors exposure during childhood found associated with asthma in the Lebanese population were the public schools' environment, the presence of molds on bedrooms' walls and pets' possession [16]. Salameh et al. also found that exposure to pesticides was associated with chronic respiratory symptoms and asthma [17]. The effect of parents' smoking on children has been shown to be a triggering factor to express asthma in children even in early life [13–15], in addition to active smoking [18]. In Lebanon, similar results were shown in a post hoc analysis, where passive exposure to mother's smoke from cigarettes and from waterpipe was associated with asthma and allergic diseases [19].

Moreover, association has been found between in utero exposures to several xenobiotics and increased risk of asthma. 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 [20]. However, in utero and young childhood exposures to these toxics have not been fully assessed in Lebanon. While we know that these exposures are common during pregnancy among Lebanese women [21], the association of exposure to toxic substances in utero and during infancy (alcohol, tobacco including cigarette and waterpipe smoke, pesticides, and detergents) with asthma has not been evaluated. Our objective is to assess such associations among children aged less than 16 years old in schools in Beirut and Mount Lebanon; this project is considered as a pilot step to be confirmed by further studies.

2. Methods

2.1. Study design and sample

This is a cross-sectional study that was conducted between January and May 2015 using a sample of Lebanese students from private schools in Beirut and Mount Lebanon, based on the list of schools provided by the Ministry of Education. A sample of 318 students was targeted to allow for adequate power for bivariable and multivariable analyses to be carried out according to the Epi info sample size calculations with a population size of 4 million in Lebanon, an 11.7% expected frequency of asthma, a 5% confidence limits [22]. We decided to distribute 700 questionnaires to take cluster effect and refusals into account.

We contacted the directors of three schools to take the permission to enter classrooms to distribute the questionnaires. Children were given the questionnaire to be filled at home by their parents. Verbal informed consent was also obtained from all parents prior to participating in the study and completing the self-administered questionnaire. Out of 700 distributed questionnaires, 527 (75.2%) were returned to us.

2.2. Data collection and measurement

Data were collected using an Arabic, self-administered questionnaire consisting of 74 questions that assessed 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, if the child went to a nursery, etc.). We also took into account potential confounders such as recurrent otitis and humidity by asking about the child's history of recurrent otitis by asking about the frequency of the otitis per year and the presence of humidity and molds in the house as seen on walls; we considered a child as having recurrent otitis media if he had more than 3 episodes within the last 6 months or more than 4 episodes within the last 12 months [23].

The respiratory health status of the child was assessed using the ISAAC questionnaire [2]. The presence of cough was defined by a positive answer to the questions: "In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?", while the presence of wheezing was defined by a positive answer to the questions "Has your child ever had wheezing or whistling in the chest at any time in the past?". To know if the child had respiratory problems, the questions "Have you found your child bothered to breathe?" and "Currently did you find that your child has difficulty breathing?" were used.

To ask about the presence of bronchial congestion, the following questions "Have you found your child congested?" and "Do you currently see that your child has a chest congestion?" were used. An affirmative answer to these questions as well revealed the presence of the symptom.

A respiratory problem was considered to be present in case of the presence of any of the previously defined symptoms of asthma (wheezing, cough, respiratory bothering, chest congestion), but without physician diagnosis, as stated by the parents.

Diagnosed asthma was defined as a positive answer to the question "Did the doctor tell you that you have asthma?" [2]. The presence of child recurrent otitis and a serious respiratory problem occurrence before 2 years of age were also assessed. We also assessed the parental history of asthma by asking both parents about the presence physician diagnosed asthma.

Questions about smoking or alcohol intake during pregnancy and during breastfeeding, the kind of smoking or alcohol along with the quantity were included, in addition to the use of any drug during pregnancy or lactation, occupational, regional, local, and domestic pesticides exposures and cleaning products use. For pesticide exposure, information was recorded using the following questions: "Have you ever used pesticides in your work?" "Have you ever used pesticides out of your work (for house or garden tr eatment...)?" "Do you live in a region heavily treated by pesticides?" "Do you live in the proximity of a heavily treated field by pesticides?" along with the duration of exposure during work and the number of times the house or the garden get sprayed by pesticides per week or per year. Active smoking was determined by several questions (number of daily cigarettes or weekly waterpipes smoked), categorizing subjects in non-smokers or current smokers. Passive smoking will be characterized by the number of smokers at home.

Detergents use was determined by questions about who uses these products at home, the type of detergents and if there is any

mixture of these products or not (the use of 2 or more detergents simultaneously).

The term "toxics" was used in our study to include exposure to any of the following: tobacco smoke, alcohol, pesticides, detergents, medications and illicit drug intake. The use of licit and illicit substances was determined by several detailed questions: the pattern of use of licit substances (tobacco, alcohol, medications) or illicit substances (drugs of abuse) by the mother during pregnancy and infancy of the child was assessed.

2.3. Statistical analysis

Data entry and analysis were performed on SPSS statistical software, version 21. A p-value less than 0.05 was considered significant. The Chi-square test was used for comparison between categorical variables, while Student test were used for comparison of means between two groups. For multivariable analysis, several stepwise backward likelihood ratio logistic regressions were performed for asthma, asthma likelihood, allergies, recurrent otitis and respiratory problem before 2 years of age as dependent variables, taking into account the studied socio-demographic and other factors that presented an association in bivariable analysis with a p-value <0.2.

3. Results

3.1. Sociodemographic results

Out of the 700 questionnaires distributed in schools, 527 were collected (75.2%) from parents of children aged between 3 and 15 years of age. There were missing values in our results since not all questions were answered by all parents. In our study, 77 children out of 527 (14.6%; 95% CI 11.65–17.74) had a respiratory problem, with 34 children (6.4%; 95% CI 6.2–11.2) having diagnosed asthma and 43 (8.2%; 95% CI 4.7–9.3) with probable asthma.

Table 1 summarizes the socio-demographic and socioeconomic factors. The results showed that 36.46% of these children were between 7 and 10 years of age; the mean age was 9.54 ± 3.76 years; 59.2% were males; 58.7% lived in Mount Lebanon and 40.2% in Beirut. Parents' university education was 55.8% for fathers and 62.2% for mothers. The percentage of children living in a house with 3 rooms or more was 92.5%, while 82.4% of them lived with more than 4 persons inside the house. The mean height was 1.39 ± 24.44 meters and the mean weight was 37.55 ± 17.5 kg. 34 (6.5%) out of these 527 children had diagnosed asthma while 43 (8.2%) had probable asthma. No association was found between socio-demographic characteristics and health status except for more probable disease in Beirut (p = 0.023).

3.2. Bivariable analysis of known risk factors

The bivariable analysis results for the factors that might be associated with the respiratory problem are summarized in table 2. Our results showed that humidity (p = 0.007), heating system (p < 0.001), premature birth (p = 0.012), eczema (p = 0.049), respiratory problems below two years old (p < 0.001) can significantly affect the children health status. However, parents respiratory problems, being previously in kindergarten or nursery, the presence of smokers at home, and medications used during pregnancy and breastfeeding, were not significantly associated with the health status (p > 0.05 for all).

3.3. Exposure to toxics during pregnancy and infancy

Table 3 summarizes the bivariable analysis performed concerning the exposure of pregnant mothers and infancy to active smoking, alcohol, drug intake and detergent mixing. A significant association was found between waterpipe smoking and alcohol during pregnancy and diagnosed asthma (p = 0.035 and 0.011 respectively), whereas no significant correlation was found for

Table 1
Socio-demographic and socioeconomic factors associated with asthma and probable asthma.

Disease status/Factors	Total number of subjects N = 527(100%)	Healthy subjects N = 447(85.3%)	Diagnosed asthma N = 34(6.45%)	Probable asthma N = 43(8.15%)	p-Value
Age category					0.097
[3–6] years	131 (25.4%)	102 (43.2%)	12 (35.3%)	17 (40.5%)	
[7–10] years	182 (35.3%)	161 (36.46%)	9 (26.5%)	12 (28.6%)	
[11–13] years	91 (17.6%)	83 (18.9%)	5 (14.7%)	3 (7.1%)	
>14 years	112 (21.7%)	94(21.4%)	8 (23.5%)	10 (23.8%)	
Male sex	310 (59.2%)	260 (58.2%)	24 (70.6%)	26 (60.5%)	0.359
District					0.023
Beirut	208 (40.2%)	170 (38.4%)	14 (43.8%)	24 (55.8%)	
Mount Lebanon	304 (58.7%)	269 (60.7%)	17 (53.1%)	18 (41.9%)	
Education of the father					0.534
Low*	8 (1.6%)	7 (1.6%)	0 (0%)	1 (2.5%)	
Intermediate**	214 (42.6%)	186 (43.2%)	15 (48.5%)	13 (32.5%)	
High***	280 (55.8%)	238 (55.2%)	16 (51.6%)	26 (65%)	
Education of the mother					0.195
Low	7 (1.4%)	5 (1.2%)	0 (0%)	2 (5%)	
Intermediate	183 (36.5%)	162 (37.6%)	11 (35.5%)	10 (25%)	
High	312 (62.2%)	264 (61.3%)	20 (64.5%)	28 (70%)	
Room Number at home					0.924
<2 rooms	39 (7.6%)	33 (7.5%)	2 (6.1%)	4 (9.5%)	
[3–4] rooms	232 (45%)	201 (45.6%)	14 (42.4%)	17 (40.5%)	
>5 rooms	245 (47.5%)	207 (46.9%)	17 (51.5%)	21 (50%)	
Persons at home					0.404
<3 persons	91 (17.6%)	81 (18.3%)	3 (9.1%)	7 (16.7%)	
>4 persons	427 (82.4%)	362 (81.7%)	30 (90.9%)	35 (83.3%)	

* Low education: education for 8 years or less.
** Intermediate education: education for more than 8 years but no university degree.
*** High education: university degree.

Table 2
Bivariable analysis for the factors associated with the health status.

Disease status/ Factors	Total number of patients N = 527 (100%)	Healthy patients N = 447 (85.3%)	Probable asthma N = 43 (8.2%)	Diagnosed asthma N = 34 (6.5%)	p-Value
Heating					<0.001
No heating	2 (0.4%)	1 (0.2%)	–	1 (3.1%)	
Gas	149 (29.3%)	129 (29.5%)	14 (35.0%)	6 (18.8%)	
Electricity	261 (51.3%)	233 (53.3%)	24 (40%)	8 (25%)	
Other	97 (19.1%)	74 (16.9%)	6 (15%)	17 (53.1%)	
Premature birth					0.012
No	478 (93.2%)	416 (94.50%)	35 (85.4%)	27 (84.4%)	
Yes	35 (6.8%)	24 (5.50%)	6 (14.6%)	5 (15.6%)	
Any drug during pregnancy					0.339
No	416 (903.3%)	357 (93.00%)	32 (91.4%)	27 (100%)	
Yes	30 (6.7%)	27 (7.00%)	3 (8.6%)	–	
Any drug during infancy					0.751
No	505 (98.2%)	433 (98.2%)	40 (97.6%)	32 (100%)	
Yes	9 (1.8%)	8 (1.8%)	1 (2.4%)	–	
Smokers at home					0.739
No	271 (51.8%)	234 (52.5%)	20 (46.5%)	17 (50%)	
Yes	255 (48.2%)	212 (47.5%)	23 (53.5%)	17 (50%)	
Kindergarten					0.367
No	291 (57.2%)	247 (56.7%)	22 (53.7%)	22 (66%)	
Yes	218 (42.8%)	189 (43.3%)	19 (46.3%)	10 (31.2%)	
Parents respiratory problems					0.063
No	458 (89.9%)	399 (91.1%)	36 (87.8%)	23 (74.2%)	
Father	27 (5.3%)	20 (4.6%)	3 (7.3%)	4 (12.9%)	
Mother	24 (4.7%)	18 (4.1%)	2 (4.9%)	4 (12.9%)	
Heart problems					0.262
No	506 (98.6%)	435 (98.9%)	40 (9.6%)	31 (96.9%)	
Yes	7 (1.4%)	5 (1.1%)	1 (2.4%)	1 (3.1%)	
Eczema before 2 years old in children					0.049
No	494 (96.3%)	427 (97%)	37 (90.2%)	30 (93.8%)	
Yes	19 (3.7%)	13 (3%)	4 (9.8%)	2 (6.2%)	
Respiratory problems in children before 2 years old					<0.001
No	489 (95.7%)	427 (97.5%)	36 (87.8%)	26 (81.2%)	
Yes	22 (4.3%)	11 (2.5%)	5 (12.2%)	6 (18.8%)	

medications intake, detergent mixing during pregnancy and none of the factors during infancy.

3.4. Multivariable analysis

When considering diagnosed asthma as a dependent variable, the multivariable analysis showed that the smoking type during pregnancy was significantly associated with asthma in the child: waterpipe smoking during pregnancy appeared to significantly increase the asthma risk in children, as shown in table 4 ($p = 0.003$; $OR_a = 13.25$; 95% CI 2.472–71.026).

When considering allergies as dependent variable, the multivariable analysis showed that alcohol consumption during infancy and the presence of humidity at home increased the risk of allergies ($p = 0.007$; $OR_a = 14.121$; 95% CI 2.087–95.559 and $p = 0.001$; $OR_a = 3.164$; 95% CI 1.556–6.432 respectively) as shown in table 4. To note that age tended to significance with a p-value of 0.057.

When considering the presence of a respiratory problem as a dependent variable, the multivariable analysis (table 4) showed that alcohol during pregnancy, waterpipe smoking during pregnancy and parents respiratory problems were significantly associated with probable asthma diagnosis in children and would increase that risk by approximately 5 times, 6 times and 2 times respectively ($p = 0.016$; $OR_a = 4.889$; 95% CI 1.339–17.844, $p = 0.021$; $OR_a = 6.083$; 95% CI 1.314–28.172, $p = 0.004$; $OR_a = 1.748$; 95% CI 1.197–2.554 respectively). Age appeared to be a protective factor against respiratory problems in children by 6.7% ($p=0.035$; $OR_a=0.943$; 95% CI 0.893–0.996).

When considering respiratory problems in children before 2 years old as a dependent variable, the multivariable analysis showed that waterpipe smoking during pregnancy significantly increased the odds of a respiratory problem before two years of age by around 10 times as shown in Table 4 ($p = 0.002$; $OR_a = 9.611$; 95% CI 2.221–41.591). Parents respiratory problems also increased the risk of respiratory problems in children before 2 years old significantly by more than 2 times ($p = 0.006$; $OR_a = 2.299$; 95% CI 1.266–4.173).

4. Discussion

This is a cross sectional pilot study carried out on schoolchildren in Lebanon (Beirut and Mount Lebanon) to assess potential risk factors for asthma, respiratory diseases and allergy, especially the effect of exposure to toxic substances during pregnancy and infancy.

Our results showed that waterpipe smoking was significantly associated with the asthma diagnosis and other respiratory problems. Alcohol during infancy and humidity at home were significantly associated with allergies. Age, alcohol and waterpipe smoking during pregnancy, smoking during infancy and parents' respiratory problems were all significantly associated with probable asthma. Respiratory problems in children before 2 years of age were significantly correlated with alcohol during infancy, the kind of smoke during pregnancy and parents respiratory problems. Finally, recurrent otitis in children was significantly associated

Table 3
Association between exposure to toxics during pregnancy and infancy and disease state.

Disease status/ Factors	Total number of patients N = 527 (100%)	Healthy patients N = 447 (85.3%)	Probable asthma N = 43	Diagnosed asthma N = 34 (6.5%)	p-Value
Smoking during pregnancy					0.035
No	493 (93.5%)	361 (95%)	103 (91.2%)	29 (85.3%)	
First trimester	33 (6.3%)	19 (5%)	9 (8%)	5 (14.7%)	
Smoking kind during pregnancy					0.008
Smoking cigarette only	21 (4%)	12 (3.2%)	8 (7.1%)	1 (2.9%)	
Smoking waterpipe only	12 (2.3%)	6 (1.6%)	2 (1.8%)	4 (11.8%)	
Smoking both cigarette and waterpipe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Not smoking either	494 (93.7%)	362 (95.3%)	103 (91.2%)	29 (85.3%)	
Alcohol during pregnancy					0.011
No	502(97.1%)	434(98.4%)	37(90.2%)	31(96.9%)	
First trimester	12(2.3%)	7(1.6%)	4(9.8%)	1(3.1%)	
Any drug during pregnancy					0.339
No	416 (93.3%)	357 (93%)	32 (91.4%)	27 (100%)	
Yes	30 (6.7%)	27 (7%)	3 (8.6%)	0 (0%)	
Alcohol during infancy					0.1
No	507(98.6%)	436(98.9%)	41(100%)	30(93.8%)	
Yes	7(1.4%)	5(1.1%)	–	2(6.2%)	
Smoking during infancy					0.594
No	498 (94.5%)	360 (94.7%)	107 (94.7%)	31 (91.2%)	
Yes	29 (5.5%)	20 (5.3%)	6 (5.3%)	3 (8.8%)	
Smoking kind during infancy					0.136
Cigarette	17 (3.2%)	13 (3.4%)	4 (3.5%)	0 (0%)	
Waterpipe	11 (2.1%)	6 (1.6%)	2 (1.8%)	3 (8.8%)	
No smoking	499 (94.7%)	361 (95%)	107 (94.7%)	31 (91.2%)	
Any drug during infancy					0.751
No	505 (98.2%)	433 (98.2%)	40 (97.6%)	32 (100%)	
Yes	9 (1.8%)	8 (1.8%)	1 (2.4%)	0 (0%)	
Direct exposure to detergents during pregnancy					0.07
No	454 (88.7%)	395 (89.9%)	31 (77.5%)	28 (87.5%)	
Yes	58 (11.3%)	45 (10.2%)	9 (22.5%)	4 (14.5%)	

Table 4
Multivariable analysis Dependent variable: Diagnosed asthma.

Factors	p-Value	OR_a	95% Confidence Interval	
Smoking kind in pregnancy	0.011			
Cigarette versus no smoking	0.999	0	0	
Waterpipe versus no smoking	0.003	13.25	2.472	71.026
Dependent variable: Allergies				
Factors	**p-Value**	**OR_a**	**95% Confidence Interval**	
Age	0.057	1.088	0.998	1.186
Alcohol during infancy	0.007	14.121	2.087	95.559
Humidity at home	0.001	3.164	1.556	6.432
Dependent variable: Respiratory problem (diagnosed or probable asthma)				
Factors	**p-Value**	**OR_a**	**95% Confidence Interval**	
Age	0.035	0.943	0.893	0.996
Alcohol during pregnancy	0.016	4.889	1.339	17.844
Smoking kind in pregnancy	0.044			
Cigarette versus no smoking	0.063	3.677	0.933	14.499
Waterpipe versus no smoking	0.021	6.083	1.314	28.172
Smoking during infancy	0.080	0.295	0.075	1.157
Parents respiratory problems	0.004	1.748	1.197	2.554
Dependent variable: Respiratory problems before 2 years of age				
Factors	**p-value**	**OR_a**	**95% Confidence Interval**	
Alcohol during infancy	0.062	5.655	0.918	34.848
Smoking kind in pregnancy	0.007			
Cigarette versus no smoking	0.222	2.71	0.548	13.399
Waterpipe versus no smoking	0.002	9.611	2.221	41.591
Parents respiratory problems	0.006	2.299	1.266	4.173

with alcohol and the kind of smoke during pregnancy, humidity at home and parents respiratory problems.

We found that age was not significantly associated with asthma or allergy but in significant correlation with probable asthma, in opposite to the observation made by Porsbjerg et al. [24]. Living in Beirut was significantly associated with a higher risk of asthma versus Mount Lebanon while there was no significant difference between the 2 districts with probable asthma. This might be

explained by the fact that air pollution is more important in Beirut. This finding is in line with the observation of Salameh et al. [16]. Diagnosis of asthma was more frequently done in males compared to females but this difference was not significant in opposite to the results of Waked and Salameh [16] and as shown previously in the literature that male sex is predominant in asthma population in the first decade [12,13]. This was not confirmed by our study. Familial history for parents respiratory problems has been shown in previous studies to be a risk factor for asthma and allergy [12,13]; it was a significant risk factor for respiratory problems in children under 2 years of age and recurrent otitis in children according to our results.

4.1. Environmental and family-related factors

We found that living in a humid home, as reflected by mold on the wall, is associated with the development of asthma. This is in line with other researches that had similar results [13,27–29].

Parents' respiratory problems appear to be a risk factor for recurrent otitis and respiratory problems in children before 2 years of age in our study. The known risk factors for recurrent ear infections include atopy, male gender, and day care attendance [30], while few studies have showed a positive strong association between asthma and recurrent ear infections per se among children [31].

In addition, heart problems were not found correlated to higher risk of asthma in this study in opposite to what Massin and collaborators showed that a substantial proportion of children with congenital heart disease have significant non cardiac co morbidities, among which asthma was found the most frequent [31].

4.2. Pesticides, detergents, medication intake

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 hyper-reactivity via a common mechanism of disrupting negative feedback control of cholinergic regulation in the lungs [32], thus making pesticides an overlooked contributor to asthma risk [33]. Child exposure to pesticides (either at home, or in an area surrounding his house) was not significantly associated to asthma in our study, in opposite to the one of Salameh et al. that showed chronic exposure to pesticides in children was moderately associated with chronic respiratory symptoms and diseases, especially asthma [34]. This might be due to the fact that the children recruited in this study were not exposed enough to pesticides in opposite to other studies or due to a small sample size.

On the other hand, domestic use of cleaning products, in particular those in spray form, has been also suggested as a risk factor for asthma [34,35]. Despite encapsulation, sensitisation to detergent enzymes remains an important cause of occupational asthma. The use of these enzymes, mainly amylases, cellulases and lipases, has been described to cause occupational asthma [36]. Our results did not show any correlation between asthma and detergent use at home by the mother or the maid in opposite to what Vizcaya et al. suggested that cleaning workers with asthma or asthma symptoms are characterized by non-reversible airway obstruction and non-eosinophilic inflammation [37]. This difference might be due to the fact that children may not be exposed to detergents for a long period of time during their life, assuming that the mothers clean their home probably when the child is at school or not at home to avoid exposure.

Furthermore, the results of this study did not show a correlation between drug intake during pregnancy and infancy with asthma and allergies. This might be due again to the fact that the data retrieved from mothers were not accurate. The literature is replete with evidence of a relationship between drugs intake by the mother during pregnancy and asthma in children [38–40].

4.3. Smoking

Our study did show a correlation between exposure to smoking during pregnancy especially waterpipe smoking, and asthma, probable asthma, respiratory problems in children before 2 years of age and recurrent otitis in children as well. Cigarette smoking may modify inflammation that is associated with asthma. The evidence points towards a combination of both heightened and suppressed inflammatory responses in smokers compared with nonsmokers with asthma. Constituents of tobacco smoke can cause loss of cilia along with a hypertrophy in the mucus gland in the upper airways. Inflammation, epithelial changes, fibrosis and secretory congestion can occur in the peripheral airways, and alveoli are destroyed with loss of gas exchange surface area and airways flexibility. Vascular changes to the small arteries and capillaries of the bronchioles and the alveoli also occur [41].

A number of genes involved in xenobiotic detoxification systems, antioxidant responses, and damage repair mechanisms for tobacco smoke have been identified to explain this toxicity [42,43]. Glutathione *S*-transferase (GST) M1 enzyme product is involved in detoxification of both reactive tobacco metabolic intermediates and reactive oxygen species [44]. The genes identification was beyond the scope of this study. Simons et al. discovered that the exposure of a pregnant mother to passive smoking increases the risk of physician diagnosed asthma in their children [45]. Active maternal smoking during pregnancy was previously correlated with asthma in children as well [45]. These results were further strengthened by the study done by Neuman et al. (2012), showing an increased risk for preschool wheeze and for asthma among children exposed to cigarette smoke by their mothers during pregnancy [46].

A water pipe consists of a head that is connected to a bowl containing water and a hose with mouthpiece. A tobacco preparation is placed in the head and burning charcoal is placed on top of the tobacco. The smoker inhales through a mouthpiece, which draws air and hot combustion products from the burning charcoal through the tobacco preparation, creating an aerosol consisting of volatilized and pyrolized tobacco components [47]. The resulting smoke then passes through a column of water before being inhaled through the mouth using a pipe [48].

On the basis of smoking machine data, the amount of water pipe tobacco used in a single smoking session was reported to produce 100-fold more tar, 4-fold more nicotine, 11-fold more CO, and 2- to 5-fold more polycyclic aromatic hydrocarbons than did a single cigarette [49]. Indeed, Shafagoj and colleagues found that the water pipe smokers had about 2-fold higher expired CO levels and about 3-fold higher plasma nicotine levels than cigarette smokers [50].

The effect appeared to be particularly strong for smoking during the first trimester of pregnancy with a significant dose-response effect relation 46. Our results showed however prominent effects for waterpipe but no significant results for cigarette smoking: this could be explained by the fact that a low number of mothers consumed cigarettes during pregnancy in our sample (maybe due to its known toxicity), while waterpipe false conception of safety in the Lebanese population induced a higher consumption, the effect of which was easily detected in our study. These alarming results are to be established by further larger scale studies.

4.4. Alcohol

Many persons experience asthma episodes or asthma exacerbation after alcohol consumption. The mechanism of alcohol-induced

asthma occurs in a way that alcohol elevates blood acetaldehyde levels, which leads to degranulation of mast cells. The resultant release of chemical mediators, such as histamine, induces asthma [51]. Alcohol during pregnancy was significantly correlated with probable asthma and recurrent otitis in children, while alcohol intake of the mother during the child infancy was associated with allergies in children. Our results were not in concordance with the results found by Magnus et al. (2014) that the low levels of alcohol exposure during pregnancy or lactation observed in the cohort study they conducted were not associated with increased risk of asthma [52]. Specific studies would be needed to explain these results.

5. Limitations

Our study has several limitations. Being a pilot study, the total sample size is small and might not be representative of the whole population. Furthermore, the number of mothers included in the smoking during pregnancy group is low. A bigger sample in future studies is needed to strengthen the correlation between smoking during pregnancy and asthma in children. This is a cross sectional survey with retrospective reports, and consequently a low level of evidence. The possibility of recall bias might be entertained due to the retrospective nature of our investigation. The effect of the recall bias could be differential and lead to the overestimation of effects for some known risk factors. However, for the substances that are not known to be associated with asthma, the bias is non differential, and an underestimation of the association with asthma is to be expected. Prospective studies that override the recall bias are expected to improve the precision of our results. A selection bias is possible because of the refusal rate. In addition, the study was done in 2 districts out of 6 in Lebanon. An information bias is also possible since the use of a questionnaire in a young population or for surrogate responders (parents) may not always be accurate: problems in question understanding, recall deficiency and over or under evaluating symptoms may still be possible. The exposure to the different toxics was subjective and was quantified according to the parents' estimation. Unfortunately, there was no possibility to measure the quantity and time of exposure to each toxic. Concerning medications categorization, we did not divide them into safe and unsafe drugs since in the literature review, we found that any medication taken by the mother during pregnancy could be associated with respiratory disease in children. Our goal was to check if any medication intake can influence the status of the disease in these children. Moreover, we could not categorize due to the small sample size; further studies with larger sample sizes will allow us to do so. However, our methodology is that of other cross-sectional studies, including ISAAC ones, which is necessary for international comparisons. It is also considered as a pilot study that will orient further larger scale studies.

6. Conclusion

Asthma and related diseases seem to be affected by several risk factors in our population of Lebanese school children across Lebanon. Our findings show that waterpipe smoking and alcohol during pregnancy, along with recurrent otitis and humidity at home seem to be significantly correlated with asthma in children. Since some of these factors are preventable, spreading awareness by health care professionals is needed to permit a possible reduction of the prevalence of these allergic diseases, especially asthma, in children. Additional larger scale studies are necessary to confirm the preliminary results we were able to find, particularly for waterpipe and alcohol exposures.

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