

# Hygiene Hypothesis: Association between Hygiene and Asthma among Preschool Children in Lebanon

**Souheil Hallit** (✉ [souheilhallit@hotmail.com](mailto:souheilhallit@hotmail.com))

Universite Saint-Esprit de Kaslik Faculte de Medicine et des Sciences Medicales <https://orcid.org/0000-0001-6918-5689>

**Hala Sacre**

Ordre des Pharmaciens du Liban

**Nelly Kheir**

Holy Family University

**Eva Hobeika**

Universite Saint-Esprit de Kaslik

**Rabih Hallit**

Universite Saint-Esprit de Kaslik Faculte de Medicine et des Sciences Medicales

**Mirna Waked**

University of Balamand Faculty of Medicine and Medical Sciences

**Pascale Salameh**

Universite Libanaise

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## Research article

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# Abstract

**Background** Our objective was the validation of a scale to assess the hygiene hypothesis and the link between hygiene, and asthma among 3 to 5 years old Lebanese children in preschool.

**Methods** Between November 2018 and March 2019, this cross-sectional study was carried out, enrolled 515 preschool children' asthma and potential risk factors, including hygiene, were assessed using a standardized questionnaire. A specific hygiene hypothesis related scale was generated and validated for this purpose.

**Results** Items related to the hygiene hypothesis scale have led to a convergence over a nine factors solution, having over than 1 Eigenvalue, which explains the variance total of 65.86%. Cronbach's alpha values corresponding to the hygiene hypothesis related scale (0.696) was deemed acceptable. The backward logistic regression, taking as dependent variable the asthma's presence or absence in child, showed that living in prairie (ORa=2.42), playing outside (ORa=2.80), having respiratory problems (ORa=4.18), attending a kindergarten (ORa=2.76), and having a sister with seasonal allergy (ORa=6.86) had significant association with increased odds of occurrence of children's asthma. The hygiene hypothesis related score was not found to be associated with increased asthma odds ( $p=0.663$ ).

**Conclusion** Current findings suggested that home cleaning and personal cleanliness were not correlated with asthma in preschool children. Future studies will require more in-depth analyses of microbial exposure, allowing proper identification of unequivocal species and functional characteristics.

## Background

One of the foremost common causes of respiratory disease worldwide is asthma <sup>1,2</sup>, and its prevalence range varies between 2% and 30% according to an international multicenter study <sup>3</sup>. Numerous questions were raised revolving around the reasons behind the increase in asthma and allergies prevalence, in spite of improved treatments and health care. In industrialized countries, a widely accepted explanation on the increase of asthma prevalence is provided by the "hygiene hypothesis", affirming that: the reduction in exposure to certain micro-organisms at an early age is purported to increase allergic disease risk at a later stage of life <sup>4</sup>. The U.S. Food and Drug Administration explains the hygiene hypothesis to lay public as "the probable increase in the risk of allergic diseases, due to extremely cleansed household environments, frequently found throughout the developed world" <sup>5</sup>; for decades, it has been suggested that prenatal exposure to the farm environment through pregnancy or living on a farm during childhood might behold protective effects against asthma by deviating the immune system in schoolchildren to non-allergic pathways, therefore modulating it <sup>6,7</sup>. This theory underwent several changes: at first it stated that "during early childhood, unhygienic contact with older siblings transmitted infection, which prevented allergic diseases" <sup>8</sup>; more recently, increasing use of detergents/disinfectants in homes has shifted the focus from the infection theory to that of "sterile" houses, paving the way toward a kind of "cleanliness hypothesis."

Inconsistent findings between studies<sup>9</sup> may be explained by the use of different definitions and phenotypes of asthma (e.g. atopic vs non-atopic) and various comparison groups<sup>10</sup>; it may as well reflect on diverse underlying mechanisms and related environmental exposures. Formerly low-risk, low- and middle-income countries may now be witnessing an increase in the prevalence of asthma, whereas in many high-risk, high-income countries: it reached a plateau<sup>11</sup>. Some low-income cities have been reporting high asthma rates<sup>11</sup>, where conditions of overcrowding, poor hygiene, and a high burden of infectious diseases predominate. In Germany, links have been founded between personal or household cleanliness and the process of allergies development<sup>12</sup>.

The major problem with the assessment of hygiene behavior is the difficulty in measuring it. As with self-reporting, direct observation is difficult and, the participant's necessity to reflect socially alluring hygiene standards can plausibly influence it<sup>13</sup>. The hand hygiene behavior measurement relies upon self-reporting, surveillance and representative measures (e.g. rates of disease, use of a cleanser like soap)<sup>14</sup>. A validated scale, originally developed by Stevenson et al., was created taking into consideration all aspects of hygiene hypothesis, including hygiene behavior in its various related forms<sup>15</sup>. Another scale using some similar and some newer items compared to that of Stevenson et al. was created by Weber et al<sup>12</sup>; it allows the measurement of food-related cleanliness, overall, household, hand and individual hygiene by self-reporting. In studies of household dust composition, routine cleaning protocols like the sampling location's floor sweeping or changing bed linens have been appraised<sup>16-19</sup>.

In Lebanon, to the best of our knowledge, there have been no studies carried out to evaluate the association between hygiene hypothesis and asthma in Lebanese children. In this paper, we adapted and validated the scale created by Weber et al. to assess the hygiene hypothesis related behavior and the link between hygiene, and asthma among 3 to 5 years old children in Lebanese preschool.

## Methods

### Study design

The conduction of this retrospective cohort study was done in a random Lebanese schools sample. Preschool children aged 3 to 5 were recruited from three private schools in three different governorates in Lebanon between November 2018 and March 2019. All parents having 3–5 year old children were sent a detailed questionnaire. Parents who refused to be part of this study were excluded.

### Sample size calculation

Since similar studies are absent in Lebanon, sample size was computed employing Epi info and the subsequent criteria: a 5 million population size, the theoretical 50% application frequency of hygiene measures, and a 5% confidence limits. A target sample of 384 children was selected, insuring proper bivariate and multivariate analyzes power<sup>20</sup>.

### Questionnaire and variables

The questionnaire used, previously tested and self-administered, was adapted from the validated International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire to the local native language in Lebanon: Arabic <sup>21</sup>. To guarantee the questions' accuracy, translation was done to Arabic then back to English <sup>22</sup>. The same questionnaire was used in previous studies conducted in Lebanon among older children <sup>23-29</sup> and university students <sup>30</sup>.

The first part of the questionnaire included the assessment of socio-demographic characteristics. They are enumerated as follows: age, gender, region, number of individuals living in the house and number of rooms, both parents' educational level, history of asthma in the family, among other known asthma risk factors such as: heating system used and humidity inside the house, child's recurrent otitis history, child attending a nursery, etc.). The educational level of parents was quantified by the number of schooling years (illiterate, primary, complementary, secondary, university).

The second part included questions on the diagnosis and symptoms of asthma. A positive answer to the inquiry "Has your doctor ever told you that your child has asthma?" has defined the declared asthma diagnosis. Whereas the occurrence of one of the subsequent symptoms: recurrent wheezing and cough (amid the day, evening, night, the entire day or at exercise), history of over than one episode (treated by a physician specialist) of dyspnea alongside wheezing has defined: chronic respiratory symptoms. Additionally taken from the ISAAC questionnaire were the questions about night coughing, without experiencing a cold, and wheezing <sup>22</sup>.

The third section included questions related to factors generally associated with asthma namely parental asthma <sup>31,32</sup>, prenatal exposure to medications (antibiotics, paracetamol) <sup>32-34</sup>, alcohol and smoking <sup>27,29,35</sup>, preterm delivery <sup>36</sup>, passive smoking and environmental exposure to toxics <sup>27,29,35</sup>, number of older siblings <sup>37</sup>, medication or alcohol intake during breastfeeding <sup>38</sup>, reflux <sup>39</sup>, atopy <sup>40</sup>, exposure to pesticides (local, regional, occupational, and household), as well as cleaning products usage at home. Regarding the exposure to pesticides, registration of information was done via these questions: "Do you live in a region heavily treated by pesticides?" "Do you live in the proximity of a heavily pesticides treated field?" "Have you ever used pesticides in your work?" "Have you ever used pesticides outside of your work (for garden or house treatment...)" (Which represent the para-occupational exposure that can bring pesticides home through particles sticking to clothes), alongside the duration of work-time exposure in addition to the number of times (per week or year) pesticides were sprayed in the garden or house. At home, the number of smokers characterized passive smoking. Questions regarding who utilizes detergent products at home, detergents type and whether or not these products are mixed when cleaning the house: have determined the use of detergents. Additional information was also recorded regarding the in house choice of heating system, the presence of humidifier and air conditioner, the presence on the home walls of humidity or mold, a child's history of cardiac problems, recurrent otitis, premature birth, tonsillectomy, as well as attending kindergarten.

This last section was dedicated to the hygiene hypothesis and comprised 46 questions: 32 were taken from a previous study<sup>12</sup>, and 14 were added based on the Lebanese experience. Some examples include

“how many times to you clean the bathroom per week? How many times to you clean the kitchen per week? How many times do you wash the child’s hands after playing outside? After using the toilet? Do you clean his hands with or without soap?” The sum of answers computed the total score to all questions, with higher scores indicating more home cleanliness.

## Statistical analysis

Version 23 of the SPSS software was used to carry out data analysis. Missing data represented < 10% of the whole database, therefore, were not replaced. Descriptive statistics included for categorical variables: the frequency (percentage), as for continuous variables: the mean (standard deviation). Evaluation of the association between categorical variables and presence/absence of asthma was done using the Chi-square test, whereas the association between continuous variables and dependent variable was evaluated by the Student t-test. To confirm the construct validity of hygiene hypothesis related questionnaire among the Lebanese population, the principal component analysis (PCA) technique was used in order to perform the factor analysis, with a promax rotation since there was a significant correlation between extracted factors. Verified to be adequate were Bartlett’s test of sphericity and the Kaiser-Meyer- Olkin measure of sampling adequacy. The number of factors retained conformed to Eigenvalues over one. Furthermore, the computation of Cronbach’s alpha helped in assessing the total score reliability as well as subscale factors reliability. Conducting the backward logistic regression, the dependent variable taken was: the presence/absence of asthma whereas the independent variable was: all variables in the bivariate analysis showing a  $p < 0.1$ ; allowing us to minimize possible confounding factors. A p-value of less than 0.05 delineated significance.

## Results

Seven hundred questionnaires were handed out, from which 515 (73.57%) were completed and collected back. The average age of participants was  $43.11 \pm 16.69$  years; 76.3% of them were females. Moreover, 107 (44%) patients possessed an education equal to university level, whereas the majority was married (62.8%), having a low (less than 1000 USD) monthly income (48.2%). The participants had a mean BMI of  $26.30 \pm 5.22$  kg/m<sup>2</sup> (Table 1). Asthmatic children percentage was 8.2% [CI 95% 5.8–10.5].

## Factor analysis

Twenty-two items were removed from the hygiene hypothesis related scale. Since no items over-correlated to each other ( $r > 0.9$ ), had low factors loading ( $< 0.3$ ) or due to low communality ( $< 0.3$ ), then all items can be extracted from the list. PCA corresponding to the hygiene hypothesis related questions was run over the entire sample (with a noted total  $n = 515$ ). Scale items converged over a nine factors solution, having a higher than 1 Eigenvalue, unfolding a total variance of 65.86%. A 0.621 Kaiser-Meyer-Olkin measure of sampling adequacy was computed for the scale, alongside a significant Bartlett’s test of sphericity ( $p < 0.001$ ). Furthermore, Cronbach’s alpha value was deemed acceptable with regards to the hygiene hypothesis scale (0.696) (Table 2).

## Bivariate analysis

Details regarding the bivariate factors analysis, associated to asthma, are summed up in Table 3. Significantly higher proportion of boys (11.2%) had asthma, as compared to girls (4.6%). A significantly increased proportion of children living in prairie (13.6% vs 7.0%), playing outdoor (11.1% vs 4.9%), having respiratory problems (20.6% vs. 7.3%), born premature (22.2% vs. 7.4%), attending a kindergarten (10.6% vs. 5.2%), having a father and brother with food allergy (40.0% vs. 7.5% and 33.3% vs. 7.9% respectively), having a mother who smokes cigarette, having a father with an allergy to medication (50.0% vs. 7.8%), having a sister with seasonal allergy (28.6% vs. 7.6%), having a sister and a brother with allergic rhinitis (100.0% vs. 7.6% and 40.0% vs. 7.8% respectively), having reflux (18.6% vs. 7.2%), having had eczema before the age of 2 (17.6% vs. 7.5%), and having a heater in the bedroom rather than in other rooms of the house, had asthma. Finally, no significant difference was found among children with or without asthma, with respect to the hygiene hypothesis total score or any of its nine factors ( $p > 0.05$  for all variables), and no noteworthy difference was recorded among hygiene score and the respiratory symptoms (wheezing, cough and bronchial secretions) ( $p > 0.05$  for all variables) (data not shown).

## Multivariable analysis

Considering asthma's presence/absence in child as dependent variable, the backward logistic regression showed that living in prairie (ORa = 2.42), playing outside (ORa = 2.80), having respiratory problems (ORa = 4.18), attending a kindergarten (ORa = 2.76), and having a sister with seasonal allergy (ORa = 6.86) were significantly associated to increased asthma odds among children. Increased asthma odds were found not to be associated with the hygiene hypothesis related score ( $p = 0.663$ ) (Table 4).

## Discussion

Throughout the study, we were not capable of demonstrating the hygiene measures' effect on asthma, but we found other factors to be associated with it. The multivariable analysis findings showed an association between placing a heating system only in the bedroom and higher asthma occurrence in preschool children, whereas installing the heating system in the whole house was associated with lower asthma, in agreement with previous findings<sup>41</sup>. Indeed, insulation of the house provides a warmer and drier indoor environment, therefore leading to amelioration in wheezing, school absenteeism, and trips to the hospital caused by respiratory conditions<sup>42</sup>.

In addition, a significant association was found between smoking cigarettes and waterpipe inside the house, and the increased asthma odds in children. These results consolidate ones from previous studies in Lebanon<sup>27,29</sup>. Amid children with asthma, the ones exposed to second-hand smoke are about twice as likely hospitalized for an acute episode of asthma, having poorer results of pulmonary function test, as estimated by a systematic review<sup>43</sup>. Asthma prevalence is higher among children living with smokers in their homes, and the likelihood of asthma development increases proportionally with the number of smokers at home<sup>44</sup>. Despite this available evidence, waterpipe is still wrongly considered by smokers to

be less dangerous and less toxic than cigarettes<sup>45</sup>. In fact, pregnant and nursing women may stop smoking cigarettes but not waterpipe, and this was proven to lead to higher risks of allergies and asthma among Lebanese children<sup>29,46</sup>. Furthermore, children are frequently allowed to play in closed rooms with ongoing waterpipe smoking. There is a misconception about waterpipes compared to cigarettes, waterpipes being perceived as less addictive and containing less nicotine.

The likelihood of parents having a history of seasonal allergy or asthma was significantly associated with increased asthma odds in preschoolers, in accordance with preceding studies demonstrating that a risk factor associated with atopic wheeze in children is parental asthma<sup>47,48</sup>.

As for the hygiene hypothesis, this is the first study using a validated scale to assess the association between the hygiene hypothesis related behaviors and asthma in preschool children; to the best of our knowledge. We investigated cleaning behaviors (related to cleaning the house) and individual cleanliness habits (related to washing the child's hands, showering, etc.) using an extensive questionnaire enfolded over 40 relevant items. After adjusting all sociodemographic, socioeconomic and other factors described in the literature as being associated with asthma, the results of the multivariable analysis showed that hygiene hypothesis related scale was not significantly associated with asthma among this population group.

This could be explained by several factors. Firstly, the hygiene hypothesis's different aspects could not be fully investigated in our study since we could not classify the area of living into rural or urban: in fact, there is no official classification in Lebanon for rural and urban regions. Moreover, the rather small total sample size may not be representative of the entire population; also, this small sample size can result in a power problem (false negative findings). The refusal rate, as well as the fact that the study was conducted in 3 out of 5 districts in Lebanon, can cause a plausible selection bias. The use of a questionnaire in surrogate responders (parents) might not be accurate all the time due to difficulties in comprehending questions, recalling, and symptoms' over- or under-evaluation; leading to a plausible information bias. Due to the retrospective nature of this investigation, a recall bias may be entertained; defining asthma using questions about a physician's diagnosis is acceptable according to the literature, but may nevertheless present a risk of over or under-diagnosis. Various toxics exposure was subjective and quantified as reported by the parents' estimation. For known risk factors of asthma, the recall bias effect can be differential, leading to effects overestimation by parents of children with the disease. Nevertheless, the bias is mainly non-differential for substances that are not acknowledged to be associated to asthma, and the expected association with asthma is underestimated. The hygiene hypothesis being relatively unknown in Lebanon, we expect the bias to be non-differential in this case.

Finally, some other factors related to hygiene may have not been taken into consideration because of the limited funds to accomplish this project. In infants developing allergic disease, differences in the gastrointestinal flora were identified by some investigators<sup>49,50</sup>. Even changes in pregnant women's vaginal microflora were recently associated in early childhood with wheezing outcomes<sup>51</sup>. The association between some parasitic infections and less asthma and allergic diseases in children was

also shown <sup>52,53</sup>, and the immune deviation in early life is somehow influenced by prenatal farm environment exposure <sup>54</sup> leading to a protective outcome when it comes to asthma development in schoolchildren <sup>6,7</sup>. Unfortunately, not being able to measure these factors could be a limitation to this study.

### Limitations and strengths

The number of children with asthma is rather small, which raises the possibility of false positive findings. The findings cannot be extended to imply causation and cannot be generalized to the whole population; in addition to false positive findings, the associations we describe may 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 of higher sample size that override the majority of the drawbacks would be anticipated to ameliorate our results' precision. Future studies that assess the intensity and exposure time for each toxic are also suggested to confirm our findings. Despite all the limitations, we have no reason to doubt the overall validity of our results since our methodology corresponds to other cross-sectional research studies, comprising ISAAC ones that are widely used for international comparisons.

## Conclusion

This study is the first of its kind in Lebanon, and its findings highlight the hygiene hypothesis related behaviors' association with asthma in preschool children. Current findings suggested that home cleaning and personal cleanliness were not correlated with asthma in preschool children. Subsequent studies confirming these findings are necessary, requiring more in-depth analyses of exposure to microbial environment, apprehending the identification of various species and asthma's functional features.

## Abbreviations

ISAAC

International Study of Asthma and Allergies in Childhood

PCA

principal component analysis

## Declarations

### Acknowledgements

We would also like to thank all parents who agreed to take part in these studies.

### Competing interests

There's nothing the authors have to disclose.

## Funding

None.

## Ethics approval and consent to participate

The Ethics and Research Committee at the Psychiatric Hospital of the Cross has approved this study (HPC-007-2019). Informed to each participants were the study's objective and requirement, and the written consent from the child's parent was acquired.

## Authors' contribution

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

## Availability of data and materials

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

## Consent to publish

Not applicable.

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## Tables

<b>Table 1: Sociodemographic characteristics of the participants (N=515).</b>	
<b>Variable</b>	<b>Frequency (%)</b>
<b>Sex</b>	
Male	278 (54.0%)
Female	237 (46.0%)
<b>School type</b>	
Private	512 (99.4%)
Public	3 (0.6%)
<b>Mohafaza</b>	
Beirut	87 (16.9%)
Mount Lebanon	390 (75.7%)
North Lebanon	37 (7.2%)
South Lebanon	0 (0%)
Bekaa	1 (0.2%)
<b>Physician-diagnosed asthma</b>	
No	463 (89.9%)
Yes	52 (10.1%)
<b>Mean <math>\pm</math> SD</b>	
<b>Age (in years)</b>	4.44 $\pm$ 0.83
<b>Number of siblings older than the child</b>	0.85 $\pm$ 0.98
<b>Number of siblings younger than the child</b>	0.48 $\pm$ 0.82

<b>Factor</b>	<b>Factor 1</b>	<b>Factor 2</b>	<b>Factor 3</b>	<b>Factor 4</b>	<b>Factor 5</b>	<b>Factor 6</b>	<b>Factor 7</b>	<b>Factor 8</b>	<b>Factor 9</b>
Number of times of liquid detergents use on the floor per week	0.834								
Number of times of wiping the floor per week	0.737								
Number of times of dusting the house per week	0.674								
Number of times of liquid detergents use on surfaces per week	0.674								
Number of times of cleaning the bathrooms per week	0.650								
Number of times of whitening products use per week	0.627								
Number of times of cleaning the kitchen per week	0.564								
Number of times of washing the child's hands with soap before eating per day		0.905							
Number of times of washing the child's hands without soap before eating per day		0.891							
Number of times of washing the child's hands with soap after playing outside per day			1						
Number of times of washing the child's hands without soap after playing outside per day			0.991						
Number of times of washing the child's hair with shampoo per week				0.868					
Number of times of showering the child per week				0.844					
Level of the parents' bedroom in the house					0.872				
Level of the child's bedroom in the house					0.856				
Swimming in an indoor pool						0.707			
Number of times of washing the child's hands with soap after using the toilet per day						0.649			
Number of times of washing the child's hands without soap after using the toilet per day						0.645			
Presence of compost containers inside the house							0.838		
Presence of compost containers outside the house							0.682		
Number of pets at home								0.767	
Presence of a fish tank in the house								0.669	
Eating nails									0.726
Number of times of cutting nails per month									0.689
<b>Cronbach alpha</b>	0.805	0.817	0.977	0.691	0.617	0.667	0.290	0.222	0.228
<b>Percentage of variances explained</b>	15.08	11.34	7.17	6.68	6.29	5.78	4.79	4.56	4.17

**Factor 1: cleaning the house; Factor 2: washing hands before eating; Factor 3: washing hands after playing outside; Factor 4: showering (body and hair); Factor 5: level of the bedrooms in the house; Factor 6: indoor swimming pool and washing hands after**

toilet use; Factor 7: presence of compost in/out the house; Factor 8: presence of animals in the house; Factor 9: nails eating and cutting.

<b>Table 3: Bivariate analysis taking the presence/absence of asthma in child as the dependent variable.</b>			
	<b>Absence of Asthma in child N=473 (91.8%)</b>	<b>Presence of asthma in child N=42 (8.2%)</b>	<b>p-value</b>
<b>Gender</b>			0.007
Male	247 (88.8%)	31 (11.2%)	
Female	226 (95.4%)	11 (4.6%)	
<b>Living in prairie</b>			0.039
Yes	76 (86.4%)	12 (13.6%)	
No	397 (93.0%)	30 (7.0%)	
<b>Playing outdoor</b>			0.010
Yes	240 (88.9%)	30 (11.1%)	
No	233 (95.1%)	12 (4.9%)	
<b>Respiratory problems forbidding activities</b>			0.006
Yes	27 (79.4%)	7 (20.6%)	
No	445 (92.7%)	35 (7.3%)	
<b>Premature birth</b>			0.006
Yes	21 (77.8%)	66 (22.2%)	
No	451 (92.6%)	36 (7.4%)	
<b>Hospitalization after birth</b>			0.080
Yes	25 (83.3%)	5 (16.7%)	
No	447 (92.4%)	37 (7.6%)	
<b>Kindergarten</b>			0.028
Yes	254 (89.4%)	30 (10.6%)	
No	218 (94.8%)	12 (5.2%)	
<b>Mother smoking</b>			0.048
No	331 (94.0%)	21 (6.0%)	
Cigarette	41 (85.4%)	7 (14.6%)	
Waterpipe	98 (87.5%)	14 (12.5%)	
Cigarette and waterpipe	2 (100.0%)	0 (0.0%)	
<b>Father food allergy</b>			<0.001
Yes	6 (60.0%)	4 (40.0%)	
No	466 (92.5%)	38 (7.5%)	
<b>Brother food allergy</b>			0.024
Yes	4 (66.7%)	2 (33.3%)	
No	468 (92.1%)	40 (7.9%)	
<b>Father medication allergy</b>			0.002
Yes	2 (50.0%)	2 (50.0%)	
No	471 (92.2%)	40 (7.8%)	
<b>Sister seasonal allergy</b>			0.005
Yes	10 (71.4%)	4 (28.6%)	
No	463 (92.4%)	38 (7.6%)	
<b>Asthma in family member (mother)</b>			0.001
Yes	8 (66.7%)	4 (33.3%)	
No	465 (92.4%)	38 (7.6%)	
<b>Asthma in family member (father)</b>			0.005
Yes	6 (66.7%)	3 (33.3%)	
No	467 (92.3%)	39 (7.7%)	

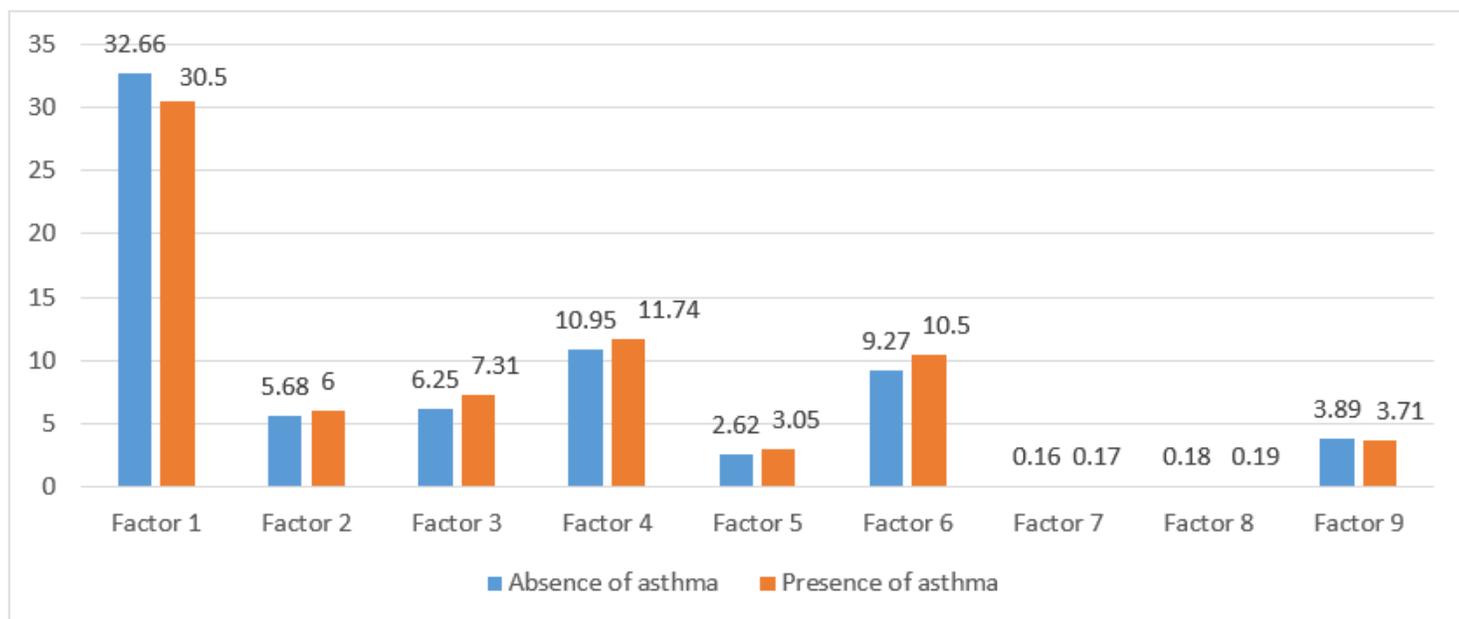
<b>Asthma in family member (sister)</b>			<0.001
Yes	1 (25.0%)	3 (75.0%)	
No	472 (92.4%)	39 (7.6%)	
<b>Asthma in family member (brother)</b>			0.019
Yes	8 (1.7%)	3 (7.1%)	
No	465 (98.3%)	39 (92.9%)	
<b>Asthma in family member (others)</b>			0.002
Yes	13 (72.2%)	5 (27.8%)	
No	460 (92.6%)	37 (7.4%)	
<b>Allergic rhinitis family members (sister)</b>			<0.001
Yes	0 (0.0%)	3 (100.0%)	
No	473 (92.4%)	39 (7.6%)	
<b>Allergic rhinitis family members (brother)</b>			0.009
Yes	3 (60.0%)	2 (40.0%)	
No	470 (92.2%)	40 (7.8%)	
<b>Child reflux</b>			0.009
Yes	35 (81.4%)	8 (18.6%)	
No	437 (92.8%)	34 (7.2%)	
<b>Eczema before 2 years</b>			0.036
Yes	28 (82.4%)	6 (17.6%)	
No	445 (92.5%)	36 (7.5%)	
<b>Skin rash for at least 6 months</b>			0.066
Yes	24 (82.8%)	5 (17.2%)	
No	449 (92.4%)	37 (7.6%)	
<b>Heat home using wood</b>			0.086
Yes	33 (84.6%)	6 (15.4%)	
No	440 (92.4%)	36 (7.6%)	
<b>Heat home using electricity</b>			0.060
Yes	326 (93.4%)	23 (6.6%)	
No	147 (88.6%)	19 (11.4%)	
<b>Place of the heating system</b>			0.001
Sitting room	165 (91.7%)	15 (8.3%)	
Bedroom	6 (60.0%)	4 (40.0%)	
All the house	295 (93.4%)	21 (6.6%)	
	<b>Mean ± SD</b>	<b>Mean ± SD</b>	
<b>Alcohol glasses per week during pregnancy</b>	0.08 ± 0.30	0.03 ± 0.17	0.092
<b>Alcohol glasses per week during breastfeeding</b>	0.04 ± 0.27	0.001 ± 0.001	<0.001
<b>Hygiene hypothesis related total score</b>	74.76 ± 18.91	76.21 ± 16.30	0.630

**Table 4: Multivariable analysis: Logistic regression taking the presence /absence of asthma in child as the dependent variable and the hygiene hypothesis score as an independent variable.**

	ORa	p-value	Confidence interval	
			Lower Bound	Upper Bound
Heating in the bedroom	7.122	0.01	1.606	31.585
Living near a prairie sprayed with pesticides	2.463	0.036	1.061	5.718
Heating in all the house	0.463	0.049	0.215	0.995
Kindergarten	3.466	0.003	1.525	7.876
Father's history of medication allergy	10.728	0.066	0.852	135.124
Sister's history of seasonal allergy	5.424	0.012	1.444	20.367
Mother's history of asthma	7.189	0.004	1.897	27.247
Brother's history of asthma	6.413	0.017	1.394	29.501
Mother's cigarette smoking	3.091	0.041	1.047	9.128
Mother's waterpipe smoking	2.359	0.049	1.017	5.474
Hygiene hypothesis score	0.997	0.805	0.975	1.020

Variable(s) entered: gender, living prairie, playing outside, respiratory problems, Wood, electricity, place heating system, premature birth, hospitalization after birth, kindergarten, mother smoking, family member allergy, food allergy father, food allergy 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 6months, alcohol glasses per week during pregnancy, hygiene hypothesis related score.

## Figures



**Figure 1**

Mean hygiene hypothesis related scale factors scores between asthmatic and non-asthmatic children. Factor 1: cleaning the house; Factor 2: washing hands before eating; Factor 3: washing hands after

playing outside; Factor 4: showering (body and hair); Factor 5: level of the bedrooms in the house; Factor 6: indoor swimming pool and washing hands after toilet use; Factor 7: presence of compost in/out the house; Factor 8: presence of animals in the house; Factor 9: nails eating and cutting.

## Supplementary Files

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- [STROBEchecklist.docx](#)