



Patterns of allergen sensitization in patients with asthma in Yaqui Valley, Mexico

Diego Hazael Ramirez-Leyva, Leticia Díaz-Sánchez, Maria Citlaly-Ochoa & Jose Manuel Ornelas-Aguirre

To cite this article: Diego Hazael Ramirez-Leyva, Leticia Díaz-Sánchez, Maria Citlaly-Ochoa & Jose Manuel Ornelas-Aguirre (2021): Patterns of allergen sensitization in patients with asthma in Yaqui Valley, Mexico, Journal of Asthma, DOI: [10.1080/02770903.2021.1941086](https://doi.org/10.1080/02770903.2021.1941086)

To link to this article: <https://doi.org/10.1080/02770903.2021.1941086>



Published online: 17 Aug 2021.



Submit your article to this journal [↗](#)



Article views: 10



View related articles [↗](#)



View Crossmark data [↗](#)



Patterns of allergen sensitization in patients with asthma in Yaqui Valley, Mexico

Diego Hazael Ramirez-Leyva, MD, MEd^a, Leticia Díaz-Sánchez, MD^b, Maria Citlaly-Ochoa, MD^c and Jose Manuel Ornelas-Aguirre, MD, MSc^d 

^aFamily Medicine, Instituto Mexicano del Seguro Social, Ciudad Obregón, México; ^bAllergology and Immunology, Instituto Mexicano del Seguro Social, Ciudad Obregón, México; ^cPediatric Pneumology, Instituto Mexicano del Seguro Social, Ciudad Obregón, México; ^dUniversidad de Sonora, Department of Health Sciences, Ciudad Obregón, México

ABSTRACT

Introduction: People who live in highly allergenic regions have a greater risk of being sensitized; therefore, these areas have a higher prevalence of mono and polysensitized patients. The aim of the present study was to investigate the allergen sensitization profiles in patients with asthma in an agricultural zone in Mexico.

Methods: An analytical cross-sectional study was conducted in a secondary care hospital in Obregon City, Mexico. The allergen sensitization pattern profiles were analyzed through a skin prick test (SPT) in 294 patients. Data was collected before SPT: asthma control was classified according to the Global Initiative for Asthma Criteria, nutritional status was assessed with the Body Mass Index (BMI) using Quetelet's index ($BMI = \text{weight}/\text{height}^2$), and comorbidities, asthma, and smoking habits were collected from the patients' medical records.

Results: In this study, in a group of adults with asthma, the prevalence of sensitization was 77%. The most frequent categories of aeroallergens were in indoors, in zones with weeds and abundant trees. A low proportion of monosensitized patients (2%) was observed. House dust mites were the most common allergens.

Conclusions: Our study describes the sensitization pattern among asthma patients. This study will help identify the panel of most common allergens in this region of Mexico, and aid in selection of specific treatment through immunotherapy.

ARTICLE HISTORY

Received 21 January 2021

Revised 29 April 2021

Accepted 4 June 2021

KEYWORDS

Allergenic; asthma; atopy; immunotherapy; skin prick test

Introduction

Variation in allergen sensitivity patterns is conditioned by climate change, the degree of environmental pollution, disruption in the microenvironments, and cultural traits (1). These different patterns may explain discrepancies in the prevalence of asthma, primarily in patients with atopy (2). In Mexico, the prevalence of asthma is 7%, ranging from 1.2% to 15% according to geographical region (urban or agriculture zones, with or without grass, and excess use of pesticides) (3).

Allergy diseases are highly prevalent chronic conditions that can start from an early age and are mediated by type 1 hypersensitivity reactions (4); and respiratory allergies are the most frequent in this group with a prevalence of 10 to 30% in adults worldwide (5). A patient with an allergy produces immunoglobulin E (IgE) against a specific substance that causes an exaggerated response in the immune system: these substances are called allergens and are classified into aeroallergens and food allergens (6).

Allergen exposure is clinically manifested as: rhinitis, urticaria, dermatitis, conjunctivitis, gastrointestinal symptoms, or asthma (7). The most important diagnostic tool in the study of allergies is a thorough medical history, and the identification of allergens involved (8). Knowledge of the sensitization pattern through the skin prick test (SPT) is a key element in defining specific treatment lines (9); and treatment alternatives are focused on administering an allergen-specific immunotherapy that is used in desensitization to allergens, suppression of allergic inflammation, and for allergen-specific immune tolerance (10).

People who live in highly allergenic regions are at greater risk of being sensitized; hence, these areas show a higher prevalence of mono and polysensitized patients (11). The Yaqui Valley, known as the granary of Mexico, is located at the southern end of the state of Sonora between the Gulf of California and the "Sierra Madre Occidental" in Northwest Mexico; and is a land with intense agricultural activity in the middle of desert scrubs and estuarine ecosystems.

The Yaqui Valley has a hot, dry climate with a summer rainy season. The type of vegetation is dry jungle and desert, and the State is considered one of the most allergenic in the country due to the region's wheat monoculture, which is supported by the availability of water from the Yaqui River that feeds the entire region. Another factor that contributes to clinical conditions is the use of agrochemicals which are very reactive and highly allergenic, along with the increased use of fossil fuels and the generation of dusts from agriculture practices. The Yaqui Valley is considered the "cradle of the green revolution" of agriculture in Mexico and is home to the Yaqui indigenous tribes (12). The patterns of sensitization fluctuate among different areas and populations, and in Mexico there is presently no epidemiological data about the sensitization rate of common allergens in the Yaqui Valley. Consequently, we aimed to investigate the allergen sensitization profiles in patients with asthma and the relationship of these profiles with uncontrolled disease in an agricultural zone of Mexico.

Material and methods

Study design and population

An analytical cross-sectional study was conducted from March 2017 to December 2018, at the Regional General Hospital #1 in Obregon City, Mexico. Patients diagnosed with asthma according to the Global Initiative for Asthma (GINA) (13), who were over 16 years of age, with at least one positive SPT; residents of the Yaqui Valley, who signed the informed consent letter, were included. Patients with immunosuppression, cancer, diabetes mellitus; rheumatoid arthritis, systemic lupus erythematosus, pregnancy; and intake of tricyclic antidepressants, were excluded.

Data collection was done before the SPT with a standardized data collection form: asthma control was classified according to GINA criteria in three different groups: controlled, partially controlled, and uncontrolled; nutritional status was assessed with the Body Mass Index ($BMI = \text{weight}/\text{height}^2$); active and passive smoking were evaluated by direct question; and the comorbidities such as allergic rhinitis and atopic dermatitis, type of treatment, and the time of evolution with asthma, were collected from the medical records.

Skin prick test

The SPT was performed using a standardized technique (14): before SPT each patient had at least one medical evaluation in the Allergy Division, a clinical history,

and paraclinical studies including complete blood count, nasal cytology, urinalysis; stool ova and parasites, chest x-ray, and spirometry, were performed. The sensitization pattern was implemented with a panel of 47 glycerinated allergens (ROCEL® allergens, México) in a concentration of 1:20 weight-volume: the panel included nine indoor allergens; pollens from six grasses, 15 weeds and nine trees; and seven fungal allergens. All patients were instructed to interrupt (one week prior) medications that may affect the results (antihistamines, systemic steroids, and leukotriene receptor antagonists). Dermographism was evaluated before the SPT. The allergen panel was selected according to the local characteristics and previous studies in Mexico.

Skin prick tests were performed by a trained nurse under the supervision of a certified allergist and immunologist. On the volar surface of the forearms, the application sites of each extract were marked at a distance of 2 centimeters from one another. Subsequently, using the Osterballe technique (15), antigen drops were applied. The punctures were made perpendicular to the skin with Prestige® brand lancets (Nipro, USA), using one for each puncture without causing bleeding to avoid combination of the different extracts. Finally, a puncture was made in the positive control and another in the negative: histamine (10 mg/mL) was used as a positive control, and saline solution as negative control. The size of the wheals was recorded at 15 min by an allergist, and a positive test was defined as an induration of at least 3 mm greater than the negative control.

Allergen panel

Indoor allergens: *dermatophagoides farinae* (*D. farinae*), *dermatophagoides pteronyssinus* (*D. pteronyssinus*), *blomia tropicalis*, *cockroach mix* (*Periplaneta Americana* and *Blattella Germanica*), *mosquito*, *animal hair* (*dog and cat*) and *mix of feather*.

Tree pollen: *acacia spp*, *shinus molle*, *prosopis spp*, *olea europaea*, *populus spp*, *alnus spp*, *pinnus spp*, *fraxinus spp* and *liquidambar styraciflua*.

Weed pollen: *artemisia ludoviciana*, *artemisia tridentata*, *artemisia vulgaris* *salsola pestifer*, *amaranthus palmeri*, *chenopodium album*, *ambrosia trifida*, *ambrosia elatior*, *helianthus spp*, *atriplex bracteosa*, *cosmos spp*, *rumex crispus*, *franseria tenuifolia*, *medicago sativa* and *plantago major*.

Grass pollen: *zea mays*, *phleum pratense*, *holcus halepense*, *lolium perene*, *capriola dactylon* and *agrostis alba*.

Fungal: *fusarium oxysporum*, *monilia sitophila*, *penicillium notatum*, *aspergillus fumigatus*, *candida albicans*, *cephalosporium spp* and *helminthosporium sativum*.

Statistical analysis

Each allergen was measured to detect the prevalence of sensitization. Quantitative variables were described as median and interquartile range (IQR), and qualitative variables were expressed as frequency and percentage. The assumption of normality was made by the Kolmogorov-Smirnov test. The Chi-squared test was used to analyze differences in categorical variables, and the Odds ratio was used to calculate risk. In the multivariate analysis, logistic regression was used to identify the variables associated with uncontrolled asthma according to predictive models, and assumptions of logistic regression were tested. The variables with highest *p* values were eliminated in each model, and logistic regression was carried out again using the remaining variables; while this process was repeated successively and completed when all the variables in the final model were significant ($p < 0.05$). For data analysis, the IBM SPSS program, version 20 (Armonk, NY, USA) was used.

Ethics

The study was approved by the Local Health Research and Ethics Committee #2603 of the *Instituto Mexicano del Seguro Social (IMSS)* in Obregon City, Mexico; with registration number R-2016-2601-32. The research was carried out in accordance with Bioethical Principles, the General Health Law regarding health research in Mexico, and the Declaration of Helsinki. All patients signed a letter of written and informed consent. Patients under 18 years of age signed the written informed agreement along with their legal guardians who also signed the informed consent.

Results

A total of 384 skin tests were performed on patients with asthma from the Yaqui Valley, and 90 were negative for skin reaction ($n = 294$). Two hundred and thirty-eight (81%) were female, and 56 (19%) were male: the median age was 44 (21 IQR) years. The most frequent atopic comorbidities were allergic rhinitis (94%), and atopic dermatitis (13%). Asthma control based on the Global Initiative for Asthma (GINA) was balanced: 110 (37%) controlled, 84 (29%) partially controlled, and 100 (34%) uncontrolled.

Regarding nutritional status, the median BMI was 28.1 (IQR 7.8) kg/m²: 114 (38%) had obesity, 90 (31%) were overweight (and this was identical for normal weight); and there were no underweight patients recorded. Active or passive smoking was found in 88

(30%) patients. The time since asthma diagnosis had a median of 6 (IQR 13) years, and most patients (56%) had had this disease for more than 6 years. Characteristics of the patients are described in Table 1. The number of positive skin tests had a median of 10 (IQR 5). According to positive results, they were classified as monosensitized (2%), and polysensitized (98%); and most participants were sensitized to more than 10 allergens (53%). The prevalence of main allergens by category is described in Figure 1.

The most frequent indoor allergens were: *D. pteronyssinus* 44%, *D. farinae* 43%, *Blomia tropicalis* 40%, and *cockroach mix* 39%. In pollens, the most frequent were: *Amaranthus palmieri* (weed) 37%, *prosopis spp* (tree) 33%, *ambrosia trifida* (weed) 30%, *European olea* (tree) 29%, *salsola pestifer* (weed) 27%, *plantago major* (weed) 26%, and *phleum pratense* (grass) 25%. In fungi, greater sensitization was found to *Aspergillus fumigatus* 27%, *candida albicans* 6%, and *cephalosporium spp* 2%. Only five patients were monosensitized to *mosquito* ($n = 3$) and *cockroach mix* ($n = 2$) (Table 2).

There were 110 (37%) patients with controlled asthma, and 184 (63%) uncontrolled (including partially controlled) asthma. Table 3 specifies the association between the most common allergens and uncontrolled asthma: *Blomia tropicalis* and *D. pteronyssinus* allergens had the highest OR values. Table 4 identifies the clinical characteristics associated with uncontrolled asthma. The multivariate analysis and the models are shown in Table 5, demonstrating that the variables with the highest association were obesity (OR = 4.0; 95% CI = 2.2 to 7.4), tree pollen (OR = 3.3; 95% CI = 2.0 to 5.6), *Blomia tropicalis* (OR = 4.3; 95% CI = 2.4 to 7.7),

Table 1. Baseline characteristics of patients.

Characteristic ($n = 294$)	n (%)	95% CI
Age – yr	44 (21) ^a	–
Asthma evolution time – yr	6 (13) ^a	–
Body Mass Index – kg/m ²	28.1 (7.8) ^a	–
Positive SPT	10 (5) ^a	–
Sex		
Male	56 (19)	(9 to 29)
Female	238 (81)	(76 to 86)
Nutritional status		
Normal weight	90 (31)	(21 to 41)
Overweight	90 (31)	(21 to 41)
Obesity	114 (38)	(29 to 47)
Asthma control		
Controlled	110 (37)	(28 to 46)
Partially controlled	84 (29)	(19 to 39)
Uncontrolled	100 (34)	(25 to 43)
Smoking	88 (30)	(20 to 40)
Atopic comorbidity		
Allergic rhinitis	276 (94)	(91 to 97)
Atopic Dermatitis	38 (13)	(2 to 24)
Monosensitization	5 (2)	(–10 to 14)

yr = years, kg/m² = Quetelet index, a = median (interquartile range), n = frequency, % = percentage, SPT = skin prick test, 95% CI = 95% Confidence interval.

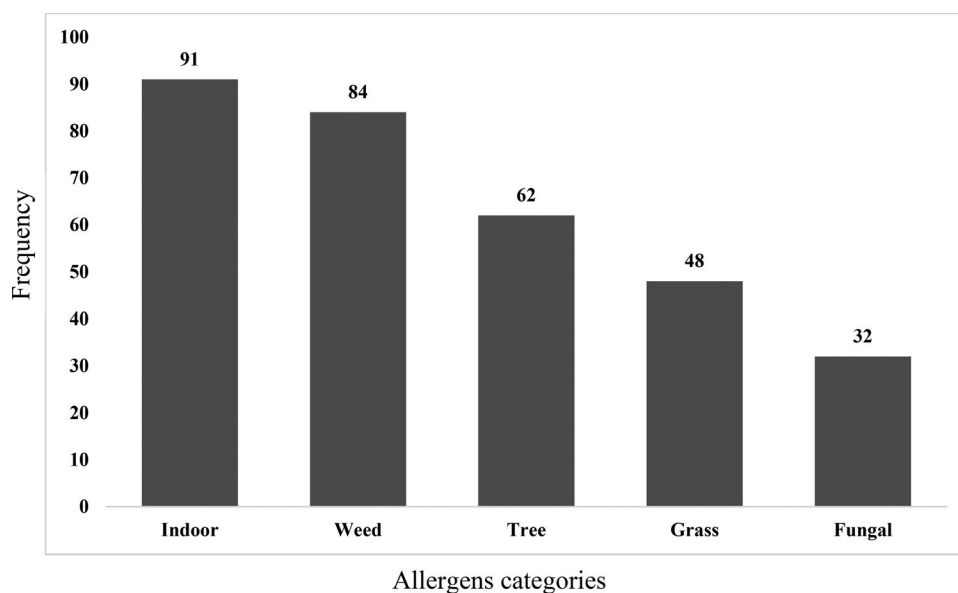


Figure 1. Frequency of allergen sensitization by category.

Table 2. Sensitization frequency to main allergens in the Yaqui Valley.

Allergens (n = 294)	n (%)	95% CI
Indoors		
Dermatophagoides pteronyssinus	130 (44)	(35 to 53)
Dermatophagoides farinae	126 (43)	(34 to 52)
Blomia tropicalis	116 (40)	(31 to 49)
Cockroach mix	114 (39)	(30 to 48)
Trees		
Prosopis spp	96 (33)	(23 to 42)
Europaeana olea	86 (29)	(19 to 39)
Alnus spp	58 (20)	(10 to 30)
Weeds		
Amaranthus palmeri	108 (37)	(28 to 46)
Ambrosia trifida	88 (30)	(20 to 40)
Salsola pestifer	78 (27)	(17 to 37)
Plantago major	76 (26)	(16 to 36)
Artemisia vulgaris	68 (23)	(13 to 33)
Grass		
Phleum pratense	74 (25)	(15 to 35)
Zea mayz	54 (18)	(8 to 28)
Agrostis alba	44 (15)	(4 to 26)
Fungal		
Aspergillus fumigatus	78 (27)	(17 to 37)
Candida albicans	18 (6)	(−5 to 17)
Cephalosporium spp	6 (2)	(−9 to 13)

n = frequency, % = percentage, 95% CI = 95% Confidence interval.

Atriplex bracteosa (OR = 4.4; 95% CI = 2.0 to 9.4) and *Olea europaea* (OR = 3.1; 95% CI = 1.5 to 6.2). The final model (Table 6), which is based on the previously described covariates, identifies the main factors associated with uncontrolled asthma.

Discussion

The most important finding in our study was the high prevalence of aeroallergens in the Yaqui Valley. These allergens could be strongly associated with the

development of asthma without being the sole or main cause. A description of the most frequent allergens was the main objective of this investigation, and, like previous studies, the presence of obesity was found to be an associated factor for uncontrolled asthma in combination with some common allergens in the Yaqui Valley (16). There were important differences between groups according to disease control: patients with uncontrolled asthma were older, had a higher body mass index, a higher number of allergens in the SPT, and a longer time since asthma diagnosis.

In order to develop, the allergy sensitization mechanism requires a combination of factors such as atopy, abundant presence of allergens in the environment, and continuous exposure time: some allergens can be universal due to their characteristics, and others are locally specific according to weather and vegetation.

The prevalence of sensitization to at least one allergen in adults with asthma can be up to 82% (9), a result that is similar to our study (77%) where the most frequent categories of aeroallergens were indoors, weeds and trees, which correlates with other studies in Western Mexico (1), China (17), and the Middle East (18).

Asthma and allergic rhinitis

The global prevalence of allergic rhinitis in patients with asthma is 80 to 90% (5), and the present study had similar findings (93%). Some epidemiological and pathophysiological studies suggest a close relationship of this binomial distribution and have shown that allergic rhinitis is a risk factor for asthma (19). The prevalence of both diseases in the same person has

Table 3. Prevalence of skin prick test reactivity to common allergens according to GINA.

Allergen	Asthma control			
	Uncontrolled* <i>n</i> (%)	Controlled <i>n</i> (%)	Odds ratio (95% CI)	<i>p</i> value
<i>D. pteronyssinus</i>	98 (53)	32 (29)	2.7 (1.6 to 4.5)	<0.001
<i>D. farinae</i>	92 (50)	34 (31)	2.2 (1.3 to 3.6)	<0.001
<i>Blomia tropicalis</i>	96 (52)	20 (18)	4.9 (2.7 to 8.6)	<0.001
Cockroach mix	60 (33)	54 (49)	0.5 (0.3 to 0.8)	0.005
<i>Amaranthus palmeri</i>	78 (42)	30 (27)	1.9 (1.1 to 3.2)	0.009
<i>Aspergillus fumigatus</i>	38 (21)	40 (36)	0.45 (0.2 to 0.7)	0.003
<i>Prosopis</i> spp	70 (38)	26 (24)	1.9 (1.1 to 3.3)	<0.001

* = uncontrolled and partially controlled, *n* = frequency, % = percentage, *p* = Chi-Squared test, 95% CI = 95% Confidence interval, spp=species.

Table 4. Clinical characteristics associated with uncontrolled asthma.

Allergen	Asthma control			
	Uncontrolled* (<i>n</i> = 184)	Controlled (<i>n</i> = 110)	Odds ratio (95% CI)	<i>p</i> value
Age ^a	46 (17)	40 (17)	–	<0.001 ^c
BMI ^a	30.3 (7.2)	25.1 (5.6)	–	<0.001 ^c
Number of allergens ^a	12 (6)	9 (6)	–	<0.001 ^c
Time since diagnosis ^a	8 (12)	5 (12)	–	0.002 ^c
Sex ^b				
Male	34 (19)	22 (20)	0.9 (0.4 to 1.6)	0.74 ^d
Female	150 (81)	88 (80)		
Obesity ^b	96 (52)	18 (16)	5.5 (3.1 to 9.9)	<0.001 ^d
Allergic Rhinitis ^b	172 (94)	104 (95)	0.8 (0.3 to 2.2)	0.71 ^d
Atopic Dermatitis ^b	12 (7)	26 (24)	0.2 (0.1 to 0.4)	<0.001 ^d
Smoking ^b	62 (34)	26 (24)	1.6 (0.9 to 2.8)	0.06 ^d

* = uncontrolled and partially controlled, a=median (interquartile range), b=frequency (percentage), c=Mann-Whitney U test, d=Chi-squared test, BMI=body mass index, 95% CI = 95% Confidence interval.

Table 5. Multivariate model of factors associated with uncontrolled asthma.

Models	Multivariate analysis			
	β (SE)	Wald	OR (95% CI)	<i>p</i> value
Clinical factors				
Obesity	1.4 (0.31)	20.45	4.0 (2.2 to 7.4)	<0.001
Age (<35 yr)	−0.8 (0.30)	6.92	0.4 (0.2 to 0.8)	0.009
Evolution (1-5 yr)	0.6 (0.27)	4.73	0.5 (0.3 to 0.9)	0.03
Allergen categories				
Tree pollen	1.2 (0.25)	22.70	3.3 (2.0 to 5.6)	<0.001
Indoor allergens				
<i>D. pteronyssinus</i>	0.8 (0.27)	8.95	2.2 (1.3 to 3.8)	0.003
Dog hair	1.1 (0.49)	4.90	3.0 (1.1 to 7.9)	0.02
<i>Blomia tropicalis</i>	1.4 (0.29)	24.57	4.3 (2.4 to 7.7)	<0.001
Grass and weed pollen				
<i>Capriola dactylon</i>	0.9 (0.49)	3.74	2.6 (0.9 to 6.9)	0.04
<i>Atriplex bracteosa</i>	1.4 (0.38)	14.73	4.4 (2.0 to 9.4)	<0.001
<i>Plantago major</i>	1.2 (0.39)	10.18	3.5 (1.6 to 7.5)	<0.001
Tree pollen				
<i>Prosopis</i> spp	0.6 (0.28)	5.69	1.9 (1.1 to 3.4)	<0.001
<i>Alnus</i> spp	1.0 (0.43)	5.74	2.8 (1.2 to 6.6)	<0.001
<i>Olea europaea</i>	1.1 (0.34)	10.92	3.1 (1.5 to 6.2)	<0.001

β (SE) = Beta coefficient (standard error), OR=Odds ratio obtained through logistic regression, yr=years, 95% CI = 95% Confidence interval, spp=species. All covariates were introduced as categorical variables.

been verified in other studies (1,17,20) and is consistent with our results.

An interesting outcome is the high proportion of polysensitized patients (98%), while apparently the main cause of acquiring multiple sensitivities is high exposure to environmental allergens, for example by occupational exposure or preexisting inflammatory diseases; and sensitization to multiple allergens does

not alone explain the presence of asthma since there are more determining risk factors such as genetics, excessive dietary sugar consumption, indoor air quality, and pollution (21,22). This result is analogous with previous studies done in Mexico (1), although it differs from other studies in the Middle East (18%), South America (36%), Canada (25%), and Europe (17%).

Table 6. Final multivariate model of factors associated with uncontrolled asthma.

Final Model	Multivariate analysis			
	β (SE)	Wald	OR (95% CI)	<i>p</i> value
Obesity	2.2 (0.37)	35.31	9.2 (4.4 to 19.1)	0.001
<i>D. pteronyssinus</i>	1.3 (0.34)	16.13	4.0 (2.0 to 8.0)	0.001
<i>Capriola dactylon</i>	1.3 (0.64)	4.13	3.7 (1.04 to 13.1)	0.04
<i>Atriplex</i>	1.9 (0.44)	18.54	6.7 (2.8 to 15.9)	0.001
<i>Alnus spp</i>	1.3 (0.49)	6.94	3.7 (1.3 to 9.8)	0.008

β (SE) = Beta coefficient (standard error), OR=Odds ratio obtained through logistic regression, 95% CI = 95% Confidence interval, spp=species. All covariates were introduced as categorical variables.

Indoor allergens

Mexico has different climate conditions depending on the zone. The Yaqui Valley (Sonora State) is characterized as being dry and very hot, especially during the summer, and this situation could explain the high prevalence of indoor allergens, especially house dust mites. Previous studies have shown great differences in mite sensitization within Mexico, with the highest rates in humid and semi-hot areas, and the lowest in dry and temperate areas. In the Northwest, in a previous study, the prevalence was 53%, which was close to our results (44%).

In Mexico, house dust mites are the most common allergens present in patients with allergic diseases like asthma (1,23,24). In countries like Iran and in the Asia-Pacific region, these are the main sensitizers (17,25) with higher frequencies than in Mexico. Sensitization to indoor allergens has been described as the main allergen category in asthma, causing bronchial hyperreactivity and uncontrolled disease (24), which agrees with our findings.

The main house dust mites are *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis*, which have a close sensitization frequency among them, and high levels of co-sensitizations due to their homologous amino acid sequence and phylogenetic tree (26); and these allergens are the main sensitizer worldwide in patients with atopy, regardless of age, country, or weather (17,18,24,25). The *D. pteronyssinus* was the third most important risk factor for uncontrolled asthma, and patients sensitized to this allergen had four times more risk of being uncontrolled (OR = 4.0; 95% CI = 2.0 to 8.0).

Other interior allergens are dog and cat hair, for which we found a low prevalence like previous studies in Mexico (6 to 17%) and some regions of France (4%) but differing from Middle East countries where the prevalence is 36 to 78% to any animal hair; whereas China reports 25% to dog hair, and Canada 53% sensitization to cat hair. In the Yaqui Valley, *cockroach mix* was the fifth most frequent interior allergen but the second excluding house dust mites,

whereas the frequency is higher in the Yaqui Valley (40%) than other studies in Mexico (7%), China (31%), France (2%), and the Middle East (32%). The analysis between cockroach mix and uncontrolled asthma showed a close association (OR = 0.5; 95% CI = 0.3 to 0.8), but this result was not significant in the multivariate model.

Pollens and asthma

Concentrations of airborne pollens in the State of Sonora have an inter- and intra-annual variation. A previous study shows that the annual total was 16,243 pollen day/m³ (2016), and 7899 pollen day/m³ (2018) with two peaks: one from March-April, with concentrations around 500 pollen day/m³, and from June-October, with higher concentrations ranging from 800 to 2450 pollen day/m³ (27). Pollens are the most frequent outdoor allergens worldwide (18), and in Yaqui Valley this category placed second in frequency. The pollens were divided into weed, tree and grass: in the sub-category of weed, pollen of the *amaranthus palmeri* was the most frequent; in trees, *prosopis spp*; and in grass, *phleum pratense*, with close frequencies between each one. In Guadalajara (Western Mexico), the pollen category is the main sensitizer in adults with allergic disease, and tree pollen is the most frequent (*Quercus spp*); but in asthma patients, house dust mites are the main sensitizer, followed by cockroaches, and weed pollen (9), which is consistent with our results.

In the Yaqui Valley, Mesquite (*Prosopis spp*) is distributed extensively; and so, it was the most frequent tree pollen among asthma patients, but in the final model this type of pollen was not associated with uncontrolled asthma. Pollens that showed association to asthma were: *alnus spp* (tree pollen) which gives three times more risk for uncontrolled asthma; *capriola dactylon* (grass pollen), conferring three times more risk; and *atriplex bracteosa* (weed pollen), conferring six times more risk. This result shows the diversity of factors associated with uncontrolled asthma in the final model (Table 6); and in this model, the risk factors were distributed as one clinical factor, one indoor allergen, one tree pollen, one weed pollen, and one grass pollen.

A study done in Western Mexico in children with asthma showed a similar pattern in the frequency of sensitization to pollen from weeds, grasses, and trees (1). In weed pollen, Middle East countries report high frequencies (64 to 77%) (28), which are similar to our findings since these countries have comparable

climate conditions. In China, there is a higher frequency of sensitization to *Artemisia* (13%) and *Ambrosia* (12%), but at a lower percentage than our study (30% and 23%, respectively). In Canada, the most frequent pollen was grass pollen with 39%, resembling Yaqui Valley findings.

Fungal sensitization

Fungal allergy is a common problem worldwide, and sensitization to this allergen is a leading cause of allergic diseases, uncontrolled asthma, and exacerbation of respiratory symptoms (29). In Mexico, some studies found that the most frequent fungi are *Aspergillus fumigatus*, *Candida albicans*, and *Alternaria alternata* (20), in that order. Although the present study did not include *Alternaria alternata*, the same pattern of prevalence in *Aspergillus fumigatus* and *Candida* was found. The prevalence of *Aspergillus fumigatus* was similar to previous studies in Sonora (22%) and Michoacán (23%), but higher than Jalisco (3%), Nuevo Leon (3%), and Mexico City (17%).

There are important differences in the prevalence of *Aspergillus fumigatus* sensitization worldwide: Europe shows a variation from 0.4% (Italy) to 10.3% (Greece), in the United States 10%, Africa 52%, and Central America 16%, which is lower than our results. Countries in the Middle East with high humidity and temperature have a prevalence of 25% (28), like the Yaqui Valley due to weather conditions. *Aspergillus fumigatus* is the fungus that most sensitizes patients with allergic diseases, especially asthma (30).

In *Candida* genus, our findings are lower than other cities in Mexico such as Michoacán (19%), Jalisco (17%), and Mexico City (16%); while in Middle East cities the prevalence is high in asthma patients (53%). *Candida* is a genus of yeasts with many species that are common to the skin and the gastrointestinal and genitourinary tracts. *Candida* is the most frequently isolated species and many studies have suggested that it plays an important role in allergy diseases (31).

Exposure to fungi is mainly in outdoor environments but it can be an indoor allergen in the right conditions and can even grow on interior surfaces and materials. A previous study on fungal airborne concentration in the Yaqui Valley shows that the annual total was 1,690 spores day/m³ and the peaks were recorded in March, July, August, and December, reaching monthly indices of up to 200 spores (32). The high humidity and temperature allow the growth and development of fungi in the Yaqui Valley. In this region of Mexico, the annual relative humidity is, on average, 45%, with a rainfall of about 450 mm annually, which

theoretically supports the fungus proliferation in this environment. Although temperature and humidity are adequate, the category with the lowest prevalence of sensitization was fungi, which could be explained by the geographical location, since being a valley near the coast supports the dispersal of fungi by the wind. On the other hand, pollen from weeds, trees, and grasses predominated in the category of outdoor allergens, in that order, which is consistent with the local ecosystem.

There is a relationship between fungal sensitization and the severity of allergic diseases (31), and in our investigation the severity of asthma was not considered, but in the final model this category was not relevant. The presence of fungi in outdoor and indoor environments is not equivalent to sensitization but given the correct conditions fungi play an important role in triggering respiratory symptoms in patients with asthma.

Obesity and asthma

Asthma control was found to be balanced according to the Global Initiative for Asthma categories. The final dichotomy showed 66% of patients with uncontrolled asthma (uncontrolled and partially controlled). This uncontrolled asthma may be an incidental finding related to the recruitment location, since our hospital is a regional referral center with specialization in allergology, and patients are sent by their initial treating physician in the case of recurrent or poor response to treatment; therefore, an elevated number of patients with uncontrolled asthma is to be expected. Obesity is a risk factor for the development of asthma and impaired mechanical function of the chest, and it influences treatment response and severity of symptoms (33). The role of obesity in severe asthma shows characteristics related to BMI, supporting the theory that severe asthma associated with obesity may represent a new clinical phenotype.

Obesity is associated with poor control and with severity of respiratory symptoms, a result that is consistent with our population, as we found a nine-fold increased risk for uncontrolled asthma in people with obesity, and it is the main risk factor for uncontrolled asthma in our population. Interventions that promote lifestyle modifications and weight loss represent an important area of opportunity that will contribute to symptom and overall clinical improvements.

Strengths and weaknesses

The main strength of the present study is being the first carried-out directly in the Yaqui Valley, and

although there are previous studies done in Northwest Mexico, they do not show data from this important area. Another advantage is in the recruitment of patients during all seasons, which reduces the selection bias secondary to seasonal variation of allergic diseases. With regards to weaknesses, the data about sensitization are only regional, but it could still be useful for people living in other countries. The investigation was conducted in patients with allergic diseases and not in the general population, we didn't follow the population over time, and did not control for variables such as air pollution (pesticides, for example), the presence of mold at home, and the diet. Despite these limitations our results are useful for patients with asthma and allergic rhinitis. The profile of sensitization was made through SPT, and quantitative measurement of the size of wheals, or IgE concentration, could contribute with more information on the allergy profile. Many studies describe the severity of asthma symptoms and their association with allergens, but we focused on disease control, and for this reason comparison with other studies was limited.

Conclusion

In conclusion, we found that indoor allergens (especially house dust mites) and weed pollen were the most frequent allergens in the Yaqui Valley. Our study describes the sensitization pattern among asthma patients, which is an important tool for diagnosis and treatment of allergic diseases. Obesity was found to be another factor associated with asthma. This can be explained by an inflammatory response through diet; with actions directed at encouraging an anti-inflammatory diet as a fundamental part of the treatment. Sensitization to allergens is not enough to diagnose allergic diseases, and the presence of specific symptoms is necessary for finding the source through SPT or specific IgE. This study will help identify the panel of most common allergens in the Yaqui Valley for performing skin prick tests and for identifying specific treatment through immunotherapy.

Acknowledgements

The authors wish to thank the *Instituto Mexicano del Seguro Social* for their support in this project, the authorities of the Regional General Hospital #1 in Obregon City, and the staff of the Allergy Division for their commitment and professionalism. Special thanks to Alan Urbina-Alvarez for the Spanish to English translation.

Author contributions

RLDH and DSL designed the study. RLDH wrote the manuscript. OMC contributed to data collection. RLDH and JMOA performed the statistical analysis and interpretation of the results. All authors read and approved the final manuscript.

Declaration of interest

The authors report no conflicts of interest.

ORCID

Jose Manuel Ornelas-Aguirre  <http://orcid.org/0000-0002-6225-7587>

References

- Alcalá-Padilla G, Bedolla-Barajas M, Kestler-Gramajo A, Valdez-López F. [Prevalence of sensitization to allergens in school children with asthma residents from Guadalajara metropolitan area]. *Rev Alerg Mex*. 2016;63:135–142.
- Pearce N, Pekkanen J, Beasley R. How much asthma is really attributable to atopy? *Thorax*. 1999;54(3):268–272. doi:10.1136/thx.54.3.268.
- Mallol J, Raby P, Cambiazio D, Peñaloza C, Palma R, De Orúe M. [Prevalence of atopy in 1,199 asthmatic children from southern Santiago, Chile]. *Rev Méd Chile*. 2014;142(5):567–573. doi:10.4067/S0034-98872014000500003.
- Gell PG, Coombs R. Clinical aspects of immunology. 2nd ed. Oxford (UK): Blackwell Scientific; 1968.
- PR Sanchez-Borjes M, Bonini S, Kaliner M. The burden of allergic diseases. In: Ruby P, ed. WAO The World Allergy Organization (WAO) white book on allergy: update 2013. 1st ed. Milwaukee (WI): WAO; 2013. p. 27–38.
- Allergens as risk factors for allergic disease. In: Ruby P, ed. WAO The World Allergy Organization (WAO) white book on allergy: update 2013. 1st ed. Milwaukee (WI): WAO; 2013. p. 86–90.
- Sánchez-Caraballo J, Diez-Zuluaga S, Cardona-Villa R. [Sensitization to aeroallergens in allergic patients from Medellín, Colombia]. *Rev Alerg Mex*. 2012;59(3):139–147.
- Fatfeh S, Rekkerth DJ, Hadley JA. Skin prick/puncture testing in North America: a call for standards and consistency. *Allergy Asthma Clin Immunol*. 2014;10(1):44. doi:10.1186/1710-1492-10-44.
- Bedolla-Barajas M, Hernández-Colín DD, Sainz-Hernández J, Morales-Romero J. [Allergen sensitization in Mexican adults with asthma: experience at a teaching hospital]. *Rev Alerg Mex*. 2011;58:133–141.
- Jutel M, Agache I, Bonini S, Burks AW, Calderon M, Canonica W, Cox L, Demoly P, Frew AJ, O'Hehir R, et al. International Consensus on Allergen Immunotherapy II: mechanisms, standardization, and pharmacoeconomics. *J Allergy Clin Immunol*. 2016;137(2):358–368. doi:10.1016/j.jaci.2015.12.1300.
- Til-Pérez G, Carnevale C, Sarría-Echegaray PL, Arancibia-Tagle D, Chugo-Gordillo S, Tomás-Barberán MD. Sensitization profile in patients with respiratory allergic diseases: differences between conventional and molecular diagnosis (a cross-sectional study). *Clin Mol Allergy*. 2019;17:8. doi:10.1186/s12948-019-0112-4.

12. Why the Yaqui valley?. In: Matson PA, ed. *An introduction. Seeds of sustainability*. 1st ed. Washington (DC): Island Press; 2012. p. 3–12.
13. Global Initiative for asthma (GINA). *Global strategy for asthma management and Prevention (2019 update)* [Internet]. Global strategy for asthma management and Prevention. 2019. <https://ginasthma.org/wp-content/uploads/2019/06/GINA-2019-main-report-June-2019-wms.pdf>.
14. Heinzerling L, Mari A, Bergmann K-C, Bresciani M, Burbach G, Darsow U, Durham S, Fokkens W, Gjomarkaj M, Haahtela T, et al. The skin prick test - European standards. *Clin Transl Allergy*. 2013;3(1):3. doi:10.1186/2045-7022-3-3.
15. Osterballe O, Weeke B. A new lancet for skin prick testing. *Allergy*. 1979;34(4):209–212. doi:10.1111/j.1398-9995.1979.tb01700.x.
16. Peters U, Dixon AE, Forno E. Obesity and asthma. *J Allergy Clin Immunol*. 2018;141(4):1169–1179. doi:10.1016/j.jaci.2018.02.004.
17. Yan YR, Xu YH, Zheng Q, Guo YS. The prevalence and sex difference of allergen sensitization among adult patients with allergic diseases in Shanghai, China. *Asian Pac J Allergy Immunol*. 2019;37(3):147–153. doi:10.12932/AP-150118-0241.
18. Moghtaderi M, Hosseini Teshnizi S, Farjadian S. Sensitization to common allergens among patients with allergies in major Iranian cities: a systematic review and meta-analysis. *Epidemiol Health*. 2017;39:e2017007. doi:10.4178/epih.e2017007.
19. Eriksson J, Bjerg A, Lötvald J, Wennergren G, Rönmark E, Torén K, Lundbäck B. Rhinitis phenotypes correlate with different symptom presentation and risk factor patterns of asthma. *Respir Med*. 2011;105(11):1611–1621. doi:10.1016/j.rmed.2011.06.004.
20. Fernández-Soto R, Navarrete-Rodríguez EM, Del-Rio-Navarro BE, Sienna-Monge JLL, Meneses-Sánchez NA, Saucedo-Ramírez OJ. Fungal allergy: pattern of sensitization over the past 11 years. *Allergol Immunopathol (Madr)*. 2018;46(6):557–564. doi:10.1016/j.aller.2018.01.005.
21. Padilha LL, Vianna EO, Vale ATM, Nascimento JXPT, da Silva AAM, Ribeiro CCC. Pathways in the association between sugar sweetened beverages and child asthma traits in the 2nd year of life: findings from the BRISA cohort. *Pediatr Allergy Immunol*. 2020;31(5):480–488. doi:10.1111/pai.13243.
22. Tiotiu AI, Novakova P, Nedeva D, Chong-Neto HJ, Novakova S, Steiropoulos P. Impact of air pollution on asthma outcomes. *Rev Int J Environ Res Public Health*. 2020;17(17):6212. doi:10.3390/ijerph17176212.
23. Bedolla-Barajas M, Valdez-López F, Arceo-Barba J, et al. [Frequency of sensitization to pollens of the subclass Rosidae in patients with respiratory allergy]. *Rev Alerg Mex*. 2014;61:327–335.
24. Raj D, Lodha R, Pandey A, Mukherjee A, Agrawal A, Kabra SK, New Delhi Childhood Asthma Study Group. Aeroallergen sensitization in childhood asthmatics in northern India. *Indian Pediatr*. 2013;50(12):1113–1118. doi:10.1007/s13312-013-0304-9.
25. Park SC, Hwang CS, Chung HJ, Purev M, Al Sharhan SS, Cho H-J, Yoon J-H, Kim C-H. Geographic and demographic variations of inhalant allergen sensitization in Koreans and non-Koreans. *Allergol Int*. 2019;68(1):68–76. doi:10.1016/j.alit.2018.07.005.
26. Xu C-X, Zhang M-L, Li B-Z, He Y, Zou Z-H, Wu Q-R, Tao A-L, Lai H, Sun J-L. Efficacy of sublingual immunotherapy with dermatophagoides farinae extract in monosensitized and polysensitized patients with allergic rhinitis: clinical observation and analysis. *Biomed Res Int*. 2015;2015:187620. doi:10.1155/2015/187620.
27. Ortega-Rosas CI, Meza-Figueroa D, Vidal-Solano JR, Gonzalez-Grijalva B, Schiavo B. Association of airborne particulate matter with pollen, fungal spores, and allergic symptoms in an arid urbanized area. *Environ Geochem Health*. 2021;43(5):1761–1782. doi:10.1007/s10653-020-00752-7.
28. Moghtaderi M, Hejrati Z, Kolahi N, Heidari B. Sensitization to aeroallergens in patients with allergic rhinitis, asthma, and atopic dermatitis in Shiraz, Southwestern Iran. *Indian J Allergy Asthma Immunol*. 2015;29(2):79. doi:10.4103/0972-6691.178272.
29. Denning DW, Pashley C, Hartl D, Wardlaw A, Godet C, Del Giacco S, Delhaes L, Sergejeva S. Fungal allergy in asthma-state of the art and research needs. *Clin Transl Allergy*. 2014;4:14. doi:10.1186/2045-7022-4-14.
30. Nazari Z, Ghaffari J, Ghaffari N, Ahangarkani F. A review on hypersensitivity reactions to fungal aeroallergens in patients with allergic disorders in Iran. *Curr Med Mycol*. 2019;5(1):42–47. doi:10.18502/cmm.5.1.537.
31. Fukutomi Y, Taniguchi M. Sensitization to fungal allergens: resolved and unresolved issues. *Allergol Int*. 2015;64(4):321–331. doi:10.1016/j.alit.2015.05.007.
32. Moreno-Sarmiento M, Peñalba MC, Belmonte J, Rosas-Pérez I, Lizarraga-Celaya C, Ortega-Nieblas MM. Airborne fungal spores from an urban locality in southern Sonora, Mexico. *Rev Mex Mic*. 2016;44:11–20.
33. Kim M, Cho S-H, Jung J-W, et al. Association between obesity and lung function changes by sex and age in adults with asthma. *J Asthma*. 2020;1–11. doi:10.1080/02770903.2020.1839904