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Low prevalence of asthma in Mexican children and adults with a positive rtRT-PCR test for SARS-CoV-2: a cross-sectional study during the 2020 pandemic

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Abstract
Background: It has recently been argued that asthma does not increase the risk of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. If so, the prevalence of asthma in subjects diagnosed with COVID-19 should be lower than in the general population.
Objective: To determine the prevalence of asthma in Mexican children and adults with SARS-CoV-2 infection.
Methods: A public database of the Epidemiological Surveillance System for Viral Respiratory Disease in Mexico was analyzed. Those who underwent the real-time reverse transcriptase-polymerase chain reaction-SARS-CoV-2 (rtRT-PCR-SARS-CoV-2) test from February 27 to June 21, 2020, were included. In addition to the prevalence of asthma, some factors associated with it were investigated.
Results: Data from 417,366 subjects were analyzed. Asthma prevalence in children, adults, and global were 3.7%, 3.3%, and 3.3%, respectively. Although the asthma prevalence was lower in SARS-CoV-2 positive over negative patients, significant differences were only found in adults (2.8% vs. 3.7% respectively; odds ratio (OR)=0.74; 95% confidence interval (CI): 0.71–0.77); but not in children (3.5% vs. 3.8%, respectively; OR=0.91; 95%CI: 0.76–1.10). Multivariate analysis showed in younger than 18 years that girls and immunosuppression were factors associated with a decrease in the odds to develop asthma. In adults, asthma was positively associated with females, obesity, smoking, immunosuppression, chronic obstructive pulmonary disease, arterial hypertension, and cardiovascular disease.

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Conclusion: The prevalence of asthma in child and adult were lower than those previously reported. Our study seems to support the hypothesis that asthma patients have a lower risk of SARS-CoV-2 infection. Further studies are required to demonstrate the consistency of our findings. © 2021 Codon Publications. Published by Codon Publications.

Introduction

About 350 million people suffer are asthmatic worldwide.[1] Its prevalence in children and adults range from 9.4% to 12.6%[2] and 4.3%[3], respectively.

In early 2020, World Health Organization declared the new coronavirus strain, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), as a public health issue. The main transmission of COVID-19 virus (*Coronavirus disease 2019*) is through exposure to respiratory secretion drops and contact with infected people. However, they can also spread from contaminated objects, air in closed places, and possibly fecal-oral transmission.[4] The chances of this virus affecting asthmatic patients are high as they are easily susceptible to viral respiratory infections. [5] Nevertheless, it seems it is not like that. First clinical and epidemiological reports at the beginning of the pandemic, have suggested that allergic diseases and asthma, among them, are not risk factors for SARS-CoV-2 infection.[6,7]

Due to scarce evidence of asthma in pandemic. The need of epidemiological studies demonstrating higher consistency in populations different from those where COVID-19 was first reported (Wuhan, China). This study aims to determine asthma prevalence in Mexican children and adult samples who underwent a real-time reverse transcriptase-polymerase chain reaction (rtRT-PCR) test to detect SARS-CoV-2 and compare them to national and worldwide asthma.

Material and methods

Design and subjects

A cross-sectional study was conducted based on open data from the Epidemiological Surveillance System of Respiratory Viral Disease in México, from February 27 to June 21, 2020. This system includes 475 monitor units of respiratory viral disease distributed all over the Mexican territory and can be used as sample representativeness, as they comprise patients from communitarian health centers and general hospitals of different socioeconomic status. The Epidemiological Surveillance System of Respiratory Viral Disease system follows a sentinel surveillance model, which collects samples from 10% of the acute respiratory ambulatory cases, severe cases, and 100% viral deaths. Open data published by "Dirección General de Epidemiología" (https://www.gob.mx/salud/documentos/datos-abiertos-152127), is available to the general population for use and reuse. But the only limitation is that the information collected lacks variables to identify subjects as they are not recorded.

Clinical data were obtained from an epidemiological survey that included the following variables: sex, age, state of residence, current self-report of smoking, and personal asthma history. Coexistent diseases included: obesity, systemic arterial hypertension (SAH), diabetes, chronic obstructive pulmonary disease (COPD), chronic renal disease, cardiovascular disease (cardiac insufficiency, cardiac arrhythmias, or coronary artery disease), and immunosuppression (usage of chemotherapy in patients with cancer, systemic steroids, or AIDS).

SARS-CoV-2 detection

In Mexico, SARS-CoV-2 presence is detected through rtRT-PCR technique. Each lab performing tests is officially certified by the "Instituto de *Diagnóstico y Referencia Epidemiológicos*."

Ethics

This study followed ethical principles for medical research in humans as per the Helsinki Declaration. This research is a retrospective analysis of open data provided by the Mexican Government for public access, usage, reuse, and redistribution. It is considered 'not risky,' according to Mexican legislation and article 17 of "*Reglamento de la Ley General de Salud en Materia de Investigación para la Salud*" as they do record the personal information of any individual. The participating researchers did not receive any special payment for this study and declared that they had no conflicts of interest.

Once unloaded, data were exported from Microsoft Excel (Redmond, WA) to IBM SPSS Statistics for Windows (Armonk, NY). Some inconsistencies and lost values were detected prior to the analysis; thus, reclassification of variables was performed for its introduction in multivariate models.

Statistical analysis

The descriptive and inferential statistic was performed. Asthma prevalence was assessed globally and in children and adults from Mexico and combined groups (at the national level and state by state). Confidence intervals of 95% for proportions, were calculated. Comparison of sex, age, smoking, diabetes background, COPD, immunosuppression, SAH, cardiovascular disease, obesity, and chronic renal disease between subjects with and without asthma, was assessed by chi-square test. Multivariate models utilizing logistic regression were created separately for the whole sample, children, and adults using IBM SPSS Statistics

for Windows, Version 23, Armonk, NY. The independent variable was asthma presence, and covariates were sex, age, obesity, smoking, COPD, immunosuppression, SAH, and cardiovascular disease. A $p \leq 0.05$ was considered statistically significant.

Results

During the period of analysis, a total of 479,528 children or adults underwent rtRT-PCR test to identify SARS-CoV-2 infection, but finally, only 417,366 subjects were analyzed (Figure 1) due to the following reasons: no results in rtRT-PCR (56,590); foreigners (2563); and incomplete data or mistakes in codification (3009).

Of the total population selected, women constituted 50.6% and men 49.4%. Adult population resulted in 95.6%, and pediatric was 4.4%. Mean age in adults and children were 44.1 ± 15.2 and 8.4 ± 5.8 years, respectively.

Table 1 provides the prevalence of asthma at the national level in children, and adults who requested the performance of the rtPCR-SARS-CoV-2 test. The global prevalence of asthma was 3.3%. The states of Mexico with the highest prevalence were: Sonora (6.2%), Yucatan (5.7%), and Quintana Roo (5.3%); at the same time, the ones with the least prevalence were: Hidalgo (2.2%), Puebla (1.9%), and Tlaxcala (1.7%).

As shown in Table 1 the asthma prevalence in children of Mexico is was 3.7%. States of the country with the highest asthma frequency were: Sonora (9.4%), Nayarit (8.4%), and Chihuahua (7.8%); and with the least frequency: Coahuila (2.3%), Michoacan (2.0%), and Tlaxcala (1.2%).

Asthma in adults showed a prevalence of 3.3% (Table 1). Once again, Sonora was the state with the highest asthma prevalence (6.2%), followed by Yucatan (5.6%), and Quintana Roo (5.3%). On the other hand, Estado de Mexico (2.2%), Tlaxcala (1.7%), and Puebla (1.9%) were the states with the least prevalence.

The prevalence of asthma in patients affected by COVID-19 was 2.8% in positives (4942 people with asthma /178,306) and 3.7% in negative patients (8841 people with asthma /239,060; $p < 0.0001$). Similar prevalence was
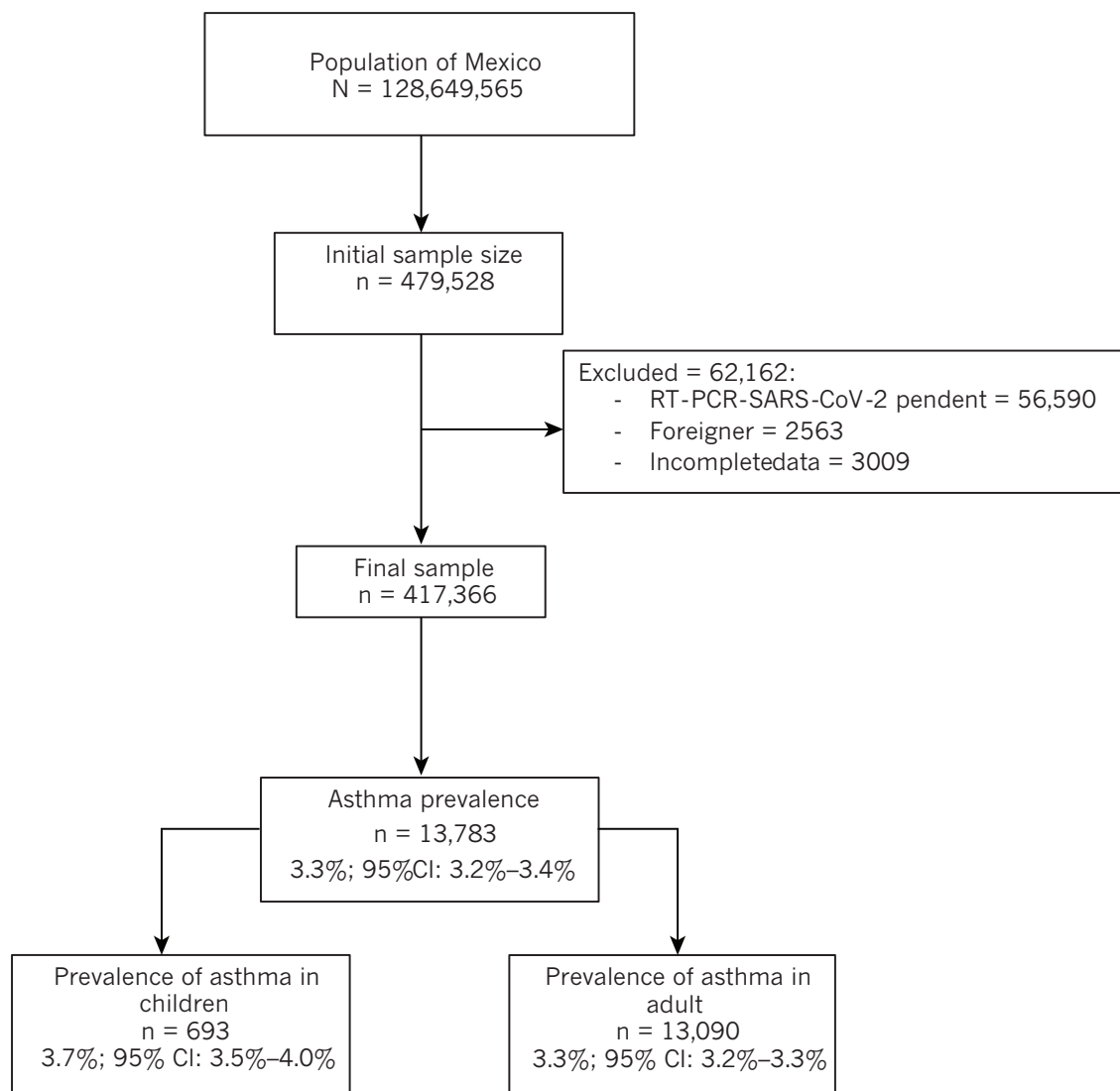

Figure 1   Selection of study subjects and prevalence of asthma in children and adults.

Table 1 Prevalence of asthma in Mexico in subjects who were tested for rtRT-PCR-SARS-CoV-2.

	Total		
	Sample size n	With asthma	Prevalence (%)	95% CI (prevalence %)
All	417,366	13,783	3.3	3.2 to 3.4
Children	18,487	693	3.7	3.5 to 4.0
Adults	398,879	13,090	3.3	3.2 to 3.3

95%CI: 95% confidence interval; rtRT-PCR-SARS-CoV-2: real-time reverse transcriptase-polymerase chain reaction to SARS-CoV-2.

noted in adults too: 2.8% in positive adults (4797 /174,166) and 3.7% in negative adults (8293 /224,713; $p<0.0001$). However, no significant differences were found in children: 3.5% in positive children (145/4140) and 3.8% in negative children (548 /14,347; $p=0.344$). Table 2 provides the univariate analysis of factors associated with asthma in subjects who carried rtRT-PCR-SARS-CoV-2. Here, asthma prevalence was significantly more frequent in women (odds ratio (OR)=1.71, $p<0.0001$), in age groups from 6 to 11 years and 12 to 19 years (OR=2.02, $p<0.0001$ and OR=2.07, $p<0.0001$, respectively), current smokers (OR=1.08, $p=0.012$), COPD patients (OR=2.26, $p<0.0001$), immunosuppression (OR=1.69, $p<0.0001$), SAH (OR=1.22, $p<0.0001$), cardiovascular disease (OR=1.60, $p<0.0001$), or obesity (OR=1.73, $p<0.0001$).

The multivariate analysis showed that asthma prevalence was 1.7 times more frequent in women than in men (Table 3). Adults showed 22% fewer odds to suffer asthma

Table 2 Univariate analysis of factors associated with asthma in subjects who underwent rtRT-PCR-SARS-CoV-2.

	Total n=417,366		With asthma n=13,783				
	n	%	n	%	OR	95% CI	p*
Sex							
Male	211,151	50.6	5211	2.5	1		
Female	206,215	49.4	8572	4.2	1.71	1.65-1.77	<0.0001
Age, years							
≤5	6918	1.7	154	2.2	1		
6-11	4761	1.1	214	4.5	2.02	1.64-2.49	<0.0001
12-19	11,088	2.7	510	4.6	2.07	1.72-2.48	<0.0001
20-39	170,053	40.7	6258	3.7	1.65	1.41-1.94	<0.0001
40-64	181,521	43.5	5673	3.1	1.40	1.19-1.65	<0.0001
≥65	43,025	10.3	974	2.3	1.02	0.86-1.21	0.848
Current smoker							
No	380,961	91.3	12,496	3.3	1		
Yes	36,405	8.7	1287	3.5	1.08	1.02-1.14	0.012
Diabetes	52,369	12.5					
No	364,997	87.5	12,058	3.3	1		
Yes	52,369	12.5	1725	3.3	0.99	0.95-1.05	0.911
COPD	6632	1.6					
No	41,0734	98.4	13,297	3.2	1		
Yes	6632	1.6	486	7.3	2.26	2.06-2.49	<0.0001
Immunosuppression							
No	410,451	98.3	13,401	3.3	1		
Yes	6915	1.7	382	5.5	1.69	1.52-1.88	<0.0001
Systemic arterial hypertension							
No	349,124	83.6	11,130	3.2	1		
Yes	68,242	16.4	2653	3.9	1.22	1.17-1.27	<0.0001
Cardiovascular disease							
No	407,638	97.7	13,277	3.3	1		
Yes	9728	2.3	506	5.2	1.60	1.46-1.75	<0.0001
Obesity							
No	348,706	83.5	10,282	2.9	1		
Yes	68,660	16.5	3501	5.1	1.73	1.66-1.80	<0.0001
Chronic kidney disease							
No	408,862	98.0	13,528	3.3	1		
Yes	8504	2.0	255	3.0	0.91	0.80-1.03	0.115

rtRT-PCR-SARS-CoV-2: real-time reverse transcriptase-polymerase chain reaction to SARS-CoV-2; COPD: chronic obstructive pulmonary disease; OR: odds ratio calculated in a tetrachoric table (the reference group is indicated as OR=1); 95% CI: 95% confidence interval.
*Statistical analysis was performed using the chi-square test.

Table 3   Multivariate analysis of factors associated with asthma in subjects who underwent rtRT-PCR-SARS-CoV-2.

	Asthma			Asthma in children			Asthma in adults		
	aOR	95% CI	p	aOR	95% CI	p	aOR	95% CI	p
Sex									
Male	1			1			1		
Female	1.71	1.65-1.78	<0.0001	0.69	0.59-0.81	<0.0010	1.80	1.74-1.87	<0.0001
Age									
Child, <18 years	1			-	-	-	-	-	-
Adults, ≥18 years	0.78	0.71-0.83	<0.0001	-	-	-	-	-	-
Obesity									
No	1			1			1		
Yes	1.70	1.64-1.78	<0.0001	2.84	2.12-3.80	<0.0010	1.69	1.62-1.76	<0.0001
Current smoker									
No	1						1		
Yes	1.09	1.03-1.16	0.003	-	-	0.796	1.11	1.04-1.17	0.001
COPD									
No	1			-	-	-	1		
Yes	2.04	1.85-2.25	<0.0001	-	-	-	2.03	1.84-2.24	<0.0001
Immunosuppression									
No	1			1			1		
Yes	1.51	1.36-1.68	<0.0001	0.49	0.28-0.83	0.009	1.63	1.46-1.82	<0.0001
Systemic arterial hypertension									
No	1						1		
Yes	1.05	1.00-1.10	0.039	-	-	0.870	1.05	1.00-1.10	0.040
Cardiovascular disease									
No	1						1		
Yes	1.31	1.19-1.44	<0.0001	-	-	0.196	1.34	1.21-1.47	<0.0001

aOR: adjusted odds ratio obtained by binary logistic regression. All variables were introduced in a dichotomous way by the Forward Conditional method. According to this method, those variables that meet the output criteria and are excluded from the model are not considered for the calculation of OR; rtRT-PCR-SARS-CoV-2: real-time reverse transcriptase–polymerase chain reaction to SARS-CoV-2; 95% CI: 95% confidence interval; COPD: chronic obstructive pulmonary disease.
rtRT-PCR-SARS-CoV-2: real-time reverse transcriptase–polymerase chain reaction to SARS-CoV-2;
95% CI: 95% confidence interval;
COPD: chronic obstructive pulmonary disease.

than the pediatric population; obesity, smoking, COPD, SAH, cardiovascular disease, and immunosuppression factors were significantly associated ($p < 0.01$) with asthma. Additionally, girl subjects younger than 18 years and immunosuppression factor decreased the odds to develop asthma but increased the chances to develop obesity. In the adult group, asthma was positively associated with females, obesity, smoking, immunosuppression, COPD, SAH, and cardiovascular disease.

Discussion

To the best of our knowledge, this is the first epidemiological study performed during the pandemic that describes asthma prevalence in the Mexican population taking the trRT-PCR-SARS-CoV-2 test. According to the study results, asthma prevalence in both children and adults was lesser than previously reported.

Interpretation of our findings related to low asthma prevalence in children and adults should considere asthma burden worldwide and locally. . Phase III of 'The International Study of Asthma and Allergies in Childhood,' assessed asthma prevalence in two age groups: 6 to 7 and 13 to 14 years, occurrence worldwide resulted in

9.4% and 12.6%; in Latin America 11.2% and 13.6%; and in Mexico 5.9% and 6.9%, respectively.[2] More recently, similar findings were also recorded in our country. In a local study, in almost 8 thousand children aged 3-15 years in Morelos: asthma prevalence was 11.9%.[8] Two other studies in Jalisco with children aged 6 to 7 and 15 to 18 years demonstrated an 8% and 12.7% asthma prevalence, respectively.[9,10]

Finally, 'Global Asthma Network Mexico' reported the most recent asthma prevalence in children aged 6-7 and 13-14 years: 5.8% and 7.5%, respectively.[11] This prevalence contradicted with the one observed in our study (3.7%).

Besides, in the adult population, the study by To et al.[3] in 70 countries, including more than 178,000 adults aged 18 to 45 years, showed 4.3% global asthma prevalence with minimal variations as 0.2% in China to 21% in Australia; Latin America reported 4.3% and Mexico in particular, had 2.4%.

A population-based study in Mexico City, including more than 1000 adults older than 40, showed an asthma prevalence of 5%.[12] Even more, in Guadalajara, Mexico, asthma prevalence in women went from 4.2% to 8.5% and in men 3.5% to 5.7%.[13,14]

In summary, children and adult's prevalence in our study in most states of Mexico was lower than the disease

burden reported in previous studies, thus, it seems that asthma is not a risk factor for SARS-CoV-2 infection.

Our study has provided three possible outcomes for the low asthma prevalence during the COVID-19 pandemic: (a) Asthma sub-diagnosis, (b) Asthma could protect against COVID-19 disease, and (c) drugs for asthma control could lessen the risk of infection or symptoms of COVID-19.

The study by Halpin et al.[15] showed contradictory outcomes. It reported that asthma patients had a higher probability of severe COVID-19 (up to 40% more) than non-asthmatic patients. Nevertheless, ranking asthma group according to the presence of an allergy, non-allergic asthma group was found to increase this association significantly (OR=1.48; p=0.003). In contrast, allergic asthma did not show a significant statistical association with severe COVID-19 (p=0.09).[16] Even more, the association of asthma and respiratory allergy with the expression ACE2 receptor in airway cells was assessed by Jackson et al.[17] Two relevant facts emerged from this trial: first, the ACE2 receptor expression was less in asthma subjects and allergic sensitization compared to those subjects with no asthma neither allergic sensitization; remarkably, asthma patients with more allergic sensitization expressed ACE2 receptor in a limited quantity compared to those patients with asthma and without allergic sensitization; second, when patients with allergic rhinitis or asthma encountered allergens, expression of ACE2 receptor decreased significantly within the following hours after challenge. Since asthma-associated allergic sensitization represented about 80% and 90% of the cases.[18, 19] In our study, it might be that subjects who underwent an rtRT-PCR-SARS-CoV-2 test could be mainly those with non-atopic asthma.

Interestingly, in our study, it was observed that asthma prevalence was less in adults with a positive test of SARS-CoV-2. Previous studies in China revealed that people with any allergic disease were not more susceptible to develop COVID-19. The clinical findings by the Epidemiology Working Group[6] and Zhang et al.[20] reported that chronic respiratory disease, presented a lesser prevalence of SARS-CoV-2 infection over other comorbidities like SAH, diabetes, and cardiovascular disease. Another study by Li et al.[7] compared clinical characteristics of patients with severe and non-severe COVID-19, the frequency of asthma of 0.7% and 1.1% (p=0.681), respectively. This highly contrasted with asthma prevalence in the Chinese population (6.4%). Authors have suggested that the Th2 immune response in this study population could counteract inflammation induced by SARS-CoV-2. This inference supports our analysis. Other published literature also suggests that few patients with asthma are infected by SARS-CoV-2,[21] but, this infection is not a significant cause of asthma exacerbation leading to hospitalization[22,23] or death.[7,24] However, considering that asthma is a heterogeneous disease, further studies investigating the association between asthma and COVID-19 severity should be performed. Practicing physicians should be alert of this association and continue to provide evidence-based care to these patients according to both international and national guidelines.

Limitations and strengths of the study

Firstly, a little more than 10% of rtRT-PCR-SARS-CoV-2 tests results were missing during the data analysis. Secondly, the open database had no diagnostic certainty of asthma, allergic sensitization, and the survey research may have human errors. Leading and response bias are known factors that could lead respondents to answer incorrectly. Thirdly, more confusing variables may exist in the database that may have been overlooked. Finally, our study sample is not representative of the entire Mexican population as it was limited to people tested by rtRT-PCR to detect the SARS-CoV-2 virus. The study's strength is its data collection, performed by skilled physicians. They followed up the positive cases through active (repeated telephone calls) and passive (records and reports from the hospital) surveillance.

Conclusion

In summary, observed asthma prevalence in children and adults in the present study is significantly lesser than previously suggested global and national studies that strengthens the hypothesis standing for less risk of SARS-CoV-2 infection in asthma patients. More research needs to be performed to support this hypothesis.

Conflict of interest

The authors declare no potential conflicts of interest.

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