




Epidemiology, Sociodemographic Factors and Comorbidity for Allergic Rhinitis, Asthma, and Rhinosinusitis Among 15 to 65-year-Old Iranian Patients

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Abstract

Background: It is well established that upper and lower airways are often clumped together when diagnosing and treating a disease. This study was designed to determine the prevalence of upper and lower airway diseases and to assess the effect of sociodemographic factors on the prevalence and the comorbidity of these disorders.

Methods: This cross-sectional population-based study included patients with ages ranging between 15 to 65 years, who were referred to allergy outpatient clinics in various provinces of Iran from April to September 2020. A modified global Allergy and Asthma European Network (GA2LEN) screening questionnaire was filled out by local allergists of the 12 selected provinces in Iran. Information about the patients and sociodemographic factors was also recorded. Statistical analysis was done by univariate statistical analyses and multiple logistic regressions in SPSS software Version 26.

Results: Out of 4988 recruited patients, 1078 (21.6%) had the symptoms of allergic rhinitis (AR) and 285 (5.7%) met the criteria of asthma. The prevalence of acute rhinosinusitis (ARS) and chronic rhinosinusitis (CRS) was 21.6 % and 22%, respectively. The highest prevalence of AR and ARS was in Tehran with the arateof of 33.9% each. Asthma was more prevalent in Khuzestan (14.2%) and CRS in Baluchestan (57.5%). Our analysis showed that the patients with asthma were most likely to have other allergic diseases as well—CRS (OR = 4.8; 95% CI, 2.02- 5.82), AR (OR= 2.5, 95% CI, 2.10-3), ARS (OR = 1.8; 95% CI, 2.10-3), followed by eczema (OR = 1.4; 95% CI, 1.13-1.67). We found that those individuals with CRS were most likely to have painkiller hypersensitivity (OR= 2.1; 95% CI, 1.21-3.83). Furthermore, smoking has been found more than 1.5 folds in patients with ARS. After adjusting variables, there was no correlation between education, occupation, and ethnicity with the studied diseases.

Conclusion: Rhinosinusitis is a common condition among Iranian patients. This study confirmed that inflammation of the upper and lower airways can occur simultaneously. Gender, education, occupation, and ethnicity were found to be irrelevant in the development

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↑What is “already known” in this topic:

Allergic rhinitis, asthma, and sinusitis represent a major global health problem; to date, there have not been any multiple large sample-sized studies investigating respiratory disease in various provinces of Iran.

→What this article adds:

Rhinosinusitis is a common condition among Iranian patients. Factors such as environmental location and smoking proved to be important in determining the prevalence of AR, asthma, and sinusitis.

of either AR, asthma, ARS, or CRS.

Keywords: Rhinosinusitis, Epidemiology, Population, Asthma, Allergic rhinitis, Iran

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Introduction

Upper and lower airway diseases manifest in forms of various conditions but are not limited to allergic rhinitis (AR), asthma, acute rhinosinusitis (ARS), and chronic rhinosinusitis (CRS).

AR is the most prevalent chronic noncommunicable disease affecting nearly 400 million people worldwide (1, 2). The diagnosis of AR is based on the patient history of nasal symptoms including congestion, rhinorrhea, sneezing, nasal itching, and pruritus of the eyes, and oral mucosa. AR can be a predisposing factor in the development of diseases involving the paranasal sinus cavities, the middle ear, and the nasopharynx. There is an association between AR and asthma due to the pathophysiological continuum between nose and bronchus (3, 4).

It is estimated that around 300 million people have asthma worldwide, and it is likely that a further 100 million may be affected by 2025 (5). An individual with asthma must undergo a physical examination, a medical history review, and a lung function test. Genetic and environmental factors interact to cause asthma to develop. Smoking, using nonsteroidal anti-inflammatory medicines (NSAID) and having had atopic dermatitis as a child are some of the known risk factors for asthma. In patients with asthma, it is crucial to identify whether or not rhinitis, chronic sinusitis, and gastroesophageal reflux are co-existing conditions that may affect asthma control (6-8).

Rhinosinusitis is one of the most common medical conditions with a significant impact on patients' quality of life. Rhinosinusitis is defined as inflammation of the nose and the paranasal sinuses; it is divided into acute rhinosinusitis (ARS) and chronic rhinosinusitis (CRS). ARS is characterized as a temporary infection that usually follows a cold and lasts less than 12 weeks. On the other hand, CRS lasts for longer than 3 or 4 months (9). It is estimated that 16% of adults are diagnosed with ARS annually; this might be an overestimation due to the overlap with allergic rhinitis (9). Recent data have demonstrated that CRS affects about 5% to 15% of the general population of the USA and European countries, with an increased incidence of smokers (10, 11). Common signs and symptoms of both types of rhinosinusitis are nasal inflammation, postnasal discharge, nasal obstruction, pain and tenderness of sinuses, and a reduced sense of smell and taste. A recent study found that there was an association between CRS with asthma, AR, and eczema (12).

Respiratory diseases represent a major global health problem, which could result in disability and morbidity. Iran is the second largest country in the Middle East; to date, there have not been any multiple large sample-sized studies investigating the prevalence of AR, asthma, and rhinosinusitis in its various provinces. This study aims to determine the association between AR, asthma, ARS, and CRS in Iranian patients aged 15 to 65 years while also taking into account comorbidities and sociodemographic factors.

Methods

To investigate the epidemiology and risk factors for AR, asthma, ARS, and CRS in people residing in Iran's 12 major provinces, a cross-sectional, population-based study was done. The study period included April 2020 to September 2020.

Sample Size

The maximum sample size was estimated at $P = 0.15$ (adults' proportion with ARS) (9), $\alpha = 0.05$ ($Z = (0.025) = 1.96$), and $d = 0.01$ using the following formula. Therefore, this study should include a total of 5000 individuals with AR, asthma, and sinusitis.

$$n = \frac{Z_{\alpha}^2 P(1 - P)}{d^2}$$

During the time of the study, all allergists in 18 chosen cities based on classified random sampling regarded eligible patients and continued to complete the overall sample size. Patients between the ages of 15 and 65 who had been in the chosen cities for at least a year, were eligible as long as they did not have a mental disability and could speak Persian.

Study Area and Ethnicity

Iran, the second largest country in the Middle East, has a total area of 1.648 million km² with a population of 82.9 million. The Persian Gulf and the Gulf of Oman border it on the south, and the Caspian Sea also borders it on the north. Iran has 31 different provinces. The weather in Iran varies greatly, from being dry in the desert to subtropical around the Caspian shore.

To understand the epidemiology of AR, asthma, ARS, and CRS within each province, we need to first look at the

population and environment of each province. The map of Iran used in this study was divided into 9 major geographic regions: the center, the north, the south, the west, the east, the northwestern, the northeastern, the southwestern, and the southwestern. Using classified random sampling, 2 cities were chosen at random inside each of the borders for the sample (18 cities). Some cities were located in the same province: Khuzestan with 2 cities of Ahvaz and Dezful; Khorasan with 3 cities of north Khorasan, Mashhad, Golestan; Mazandaran with 2 cities of Mazandaran and Sari; Fars contains Shiraz, Johrom, and Fassa. The data were collected from 12 provinces from April to September 2020. The selected provinces were as follows: (1) Tehran province in the north of the central plateau of the country, with an area of 18,814 km² and population of 13.3 million; (2) Khuzestan province is in the southwest of the country with an area of 64,055 km² and population of 4.7 million; (3) West Azerbaijan province is in the northwest of the country with an area of 37,437 km² and population of 3.27 million; (4) Isfahan province is located in central Iran with an area of 107,018 km² and population of 5.1 million; (5) Ilam province is in the western part of the country with an area of 20,133 km² and population of 580,158; (6) Khorasan province is located in the northeastern region of Iran with an area of 299,231 km² and population of 8.1 million; (7) Sistan and Baluchestan province is in the southeast region of the country with an area of 180,726 km² and population of 2.7 million; (8) Zanjan province is in the northwest of the country with an area of 21,773 km² and population of 1.0 million; (9) Mazandaran province is in the north of the country with an area of 23,833 km² and population of 3 million; (10) Fars province is in southwest of Iran with an area of 122,608 km² and population of 4.8 million; (11) Lorestan province is a province located in the western region of Iran with an area of 28,294 km² and population of 1.7 million; and (12) Hamedan province is in western part of the country with an area of 19,368 km² and population of 1.7 million.

Although almost a dozen other ethnic groups make up more than one-third of Iran's 82.9 million people, Persians constitute the country's largest ethnic group. Turks, Kurds, and Arabs make up Iran's other 3 largest ethnic groupings.

Questionnaire

A questionnaire was created for this study mostly based on the GA²LEN questionnaire (13); it was sent to allergists in selected cities via email. Before mailing the questionnaire, we discussed the questionnaire with multiple allergists. Each physician was required to complete an interview-based questionnaire for patients between the ages of 15 and 65 who had resided in the chosen cities for at least a year. The results were gathered, and any human error was taken into consideration.

The questionnaire was designed to collect information about AR, asthma, ARS, and CRS. A person was assumed to have AR if they indicated that they experienced one or more of the following symptoms on at least 4 consecutive days for at least 4 weeks: sneezing, itching, nasal congestion, and rhinorrhea. The diagnostic criteria for asthma were having a positive response to the following ques-

tions: Have you ever had asthma? And at least a positive answer to one of the following 5 questions: Have you had wheezing or whistling in your chest at any time in the last 12 months? Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? Have you been woken by an attack of shortness of breath at any time in the last 12 months? Have you been woken by a flare-up of coughing at any time in the last 12 months? Have you had wheezing or whistling without cold?

A participant was classified as having ARS in this study if they answered positively to the following question: Did you have at least 1 episode of a congested nose, purulent nasal discharge, and pain or pressure in the sinuses for at least 10 days in the prior 12 months?

CRS was diagnosed according to 2 positive responses to the following questions (with at least a positive answer in either question a or b): (a) Has your nose been blocked for >12 weeks in the last 12 months? (b) Have you had discolored nasal discharge in the throat for >12 weeks in the last 12 months? (c) Have you had pain or pressure around the forehead, nose, or eyes for >12 weeks in the last 12 months? (d) Has your sense of smell been reduced or absent for >12 weeks in the last 12 months? A doctor's diagnosis of CRS was given with a positive response to the following question: Has a doctor ever told you that you have chronic sinusitis?

We added additional questions regarding the participants' age, gender, eczema, adverse reactions to NSAIDs, smoking for up to a year, employment as a health care worker, ethnicity, occupation, and education to the survey.

Statistical Analysis

Statistical analyses were performed using SPSS software Version 26 (IBM, USA). Quantitative and qualitative variables were described with mean \pm SD and frequency (n) and percentages (%), respectively. Univariate statistical analyses such as chi-square, Fisher exact test, and independent sample t test were computed to compare each variable across different provinces. The independent variables with a $p < 0.20$ in the univariate analysis (unadjusted) were selected for multiple analyses (adjusted). To determine the components that impact Asthma, ARS, CRS, and AR individually, multiple logistic regressions as modified methods are fitted using the backward elimination methodology based on likelihood ratio. The association between independent variables was assessed using an odds ratio (OR) and a 95% confidence interval (CI). Correlations were considered to be significant if the $p < 0.05$.

Results

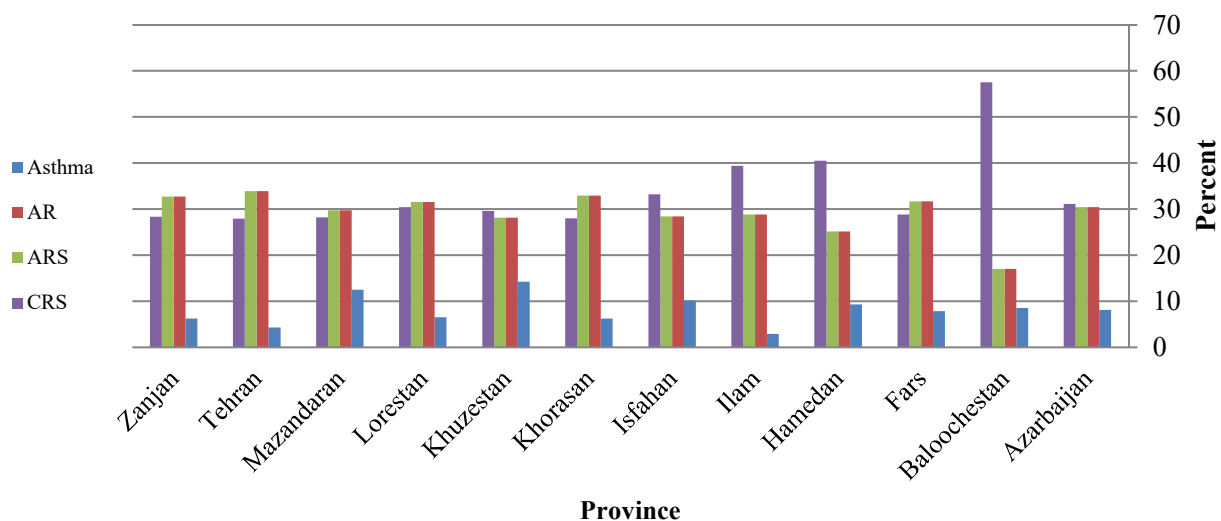
A total of 5000 questionnaires were filled out even though 12 were excluded because of filling errors. The mean age of responders was 38.2 ± 11.5 years and the female to male ratio was 3049 to 1940 (1.57 to 1), respectively. Out of 4988 referral patients, 1078 (21.6%) had the symptoms of for AR, and 285 (5.7 %) met the criteria of asthma. A total of 2180 patients met the criteria for ARS, of whom 1102 also met the criteria for CRS. Those 1102 patients were excluded from the ARS group since they were considered as having CRS. The prevalence of ARS and CRS were 21.6 % (1078/4989 and 22.1%

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Table 1. Comparison of the prevalence of asthma, allergic rhinitis, acute rhinosinusitis and chronic rhinosinusitis in various provinces of Iran, the year 2020

Disease	Azərbayjan	Baluchestan	Fars	Hamedan	Ilam	Isfahan	Khorasan	Khuzestan	Lorestan	Mazandaran	Tehran	Zanjan
Asthma	36 (8.1)	9 (8.5)	41 (7.8)	21 (9.3)	3 (2.9)	21 (10.1)	46 (6.2)	38 (14.2)	12 (6.5)	34 (12.5)	10 (4.3)	14 (6.2)
AR	135 (30.4)	18 (17)	167 (31.7)	57 (25.1)	30 (28.8)	59 (28.4)	245 (32.9)	75 (28.1)	58 (31.5)	81 (29.7)	79 (33.9)	74 (32.7)
ARS	135 (30.4)	18 (17)	167 (31.7)	57 (25.1)	30 (28.8)	59 (28.4)	245 (32.9)	75 (28.1)	58 (31.5)	81 (29.7)	79 (33.9)	74 (32.7)
CRS	138 (31.1)	61 (57.5)	152 (28.8)	92 (40.5)	41 (39.4)	69 (33.2)	208 (28)	79 (29.6)	56 (30.4)	77 (28.2)	65 (27.9)	64 (28.3)
Total	444 (100)	106 (100)	527 (100)	227 (100)	104 (100)	208 (100)	744 (100)	267 (100)	184 (100)	273 (100)	233 (100)	226 (100)

**Fig. 1.** Comparison of the prevalence of asthma, allergic rhinitis (AR), acute rhinosinusitis (ARS), and chronic rhinosinusitis (CRS) in different provinces of Iran in 2020.

(1102/4989), respectively. **Table 1** and **Figure 1** illustrate the frequency of AR, asthma, ARS, and CRS in the 12 provinces of Iran. The highest prevalence of AR was in Tehran (33.9%), followed by Khorasan (32.9%). Asthma was more prevalent in Khuzestan (14.2%). The prevalence of ARS and CRS was significantly higher in Tehran (33.9%) and Baluchestan (57.5%), respectively. The results of the chi-square test showed a significant difference between the prevalence of asthma, AR, ARS, and CRS in 12 provinces of Iran ($p < 0.001$).

The number of patients with a doctor's diagnosis of CRS was significantly higher than the patients who fit the criteria of CRS (1102 vs 564; $p \leq 0.001$).

The results of multiple logistic regression in **Table 2** indicated that the risk of AR was significantly higher in responders with asthma (OR, 2.59; $p < 0.001$), ARS (OR, 2.48; $p < 0.001$), CRS (OR, 2.39, $p < 0.001$), eczema (OR, 1.74; $p < 0.001$), NSAID hypersensitivity (OR, 1.52; $p < 0.001$), and those with increased age (OR, 1.20; $p < 0.001$).

Table 3 shows how the risk of asthma was significantly higher in responders with CRS (OR, 4.84; $p < 0.001$). There was no relationship between asthma and participants' level of education, occupation, and ethnicity.

The results of multiple logistic regression in **Table 4** showed that the risk of ARS was significantly higher in responders with CRS (OR, 4.84; $p < 0.001$), and AR (OR, 2.51; $p < 0.001$).

Table 5 illustrates the risk of CRS as significantly higher in responders with NSAID hypersensitivity (OR, 2.15; $p < 0.001$).

Discussion

We evaluated the prevalence of AR, asthma, ARS, and CRS and their risk factors in the 12 different provinces of Iran. This study found that the rate of respiratory and allergic disorders was more prevalent in women by approximately 1.5 folds. Boys had a higher risk of developing an allergy in childhood. However, it appears that from puberty on, women are more frequently concerned about atopic illnesses (14). There has been recognition of the relationship between sex hormones and the possibility of allergy sensitivity throughout the past few decades. It has been revealed that sexual hormone receptors on lymphocytes and leucocytes may regulate the type of immune reaction and inflammation associated with an allergic response (15, 16).

According to the study, the prevalence of CRS was 22%

Table 2. The results of univariate (unadjusted) and multiple logistic regressions (adjusted) models on factors associated with allergic rhinitis

Characteristics	Level	n (%)	Univariate logistic regression		Multivariate logistic regression	
			OR (95%CI)	P- value	OR (95%CI)	P- value
Age				<.001 [^]	1.20 (1.10-1.30)	<.001
Gender	Male	609 (31.4)	1.05 (0.92-1.18)	0.485		
	Female	986 (32.3)	-			
Asthma	Yes	200 (63.5)	4.10 (3.22-5.19)	<.001	2.59 (1.91-3.50)	<.001
	No	1395 (29.8)	-			
Eczema	Yes	556 (47.2)	2.39 (2.09-2.73)	<.001	1.74 (1.49-2.05)	<.001
	No	1039 (27.3)	-			
CRS	Yes	605 (54.9)	3.60 (3.10-4.10)	<.001	2.39 (2.01-2.85)	<.001
	No	989 (25.5)	-			
ARS	Yes	629 (58.3)	4.27 (3.71-4.92)	<.001	2.48 (2.07-2.95)	<.001
	No	966 (24.7)	-			
NSAID hypersensitivity	Yes	51 (55.7)	2.73 (1.82-4.10)	<.001	1.52 (0.87-2.66)	0.145
	No	1541 (31.5)	-			
Smoking	Yes	170 (30.9)	0.94 (0.78-1.14)	0.551		
	No	1425 (32.1)	-			
Health worker	Yes	470 (36.5)	1.34 (1.17-1.54)	<.001	0.81 (0.66-0.99)	0.035
	No	960 (30.0)	-			
Education	Advanced	1059 (35.0)	-			
	High school	325 (30.3)	1.24 (1.07-1.44)		0.74 (0.40-1.38)	0.351
	Primary school	207 (24.3)	1.67 (1.41-1.99)		0.94 (0.76-1.13)	0.520
	Illiterate	4 (11.4)	4.17 (1.47-11.83)	<.001	0.82 (0.65-1.03)	0.092
Occupation	Employed	454 (33.8)	-			
	Self-employed	648 (27.5)	1.35 (1.17-1.54)		0.89 (0.73-1.08)	0.241
	Student	285 (44.7)	0.63 (0.53-0.76)		1.13 (0.88-1.45)	0.339
	Retired	40 (24.5)	1.57 (1.08-2.28)	<.001	1.02 (0.64-1.61)	0.947
	Other	77 (34.7)	0.96 (0.72-1.29)		0.3 (0.65-1.33)	0.684
Ethnicity	Turk	278 (33.5)	1.07 (0.91-1.26)			
	Persian	1067 (31.9)	0.95 (0.76-1.99)			
	Kurd	322 (29.8)	0.91 (0.71-1.20)	0.78	-	
	Arab	35 (31.8)	0.91 (0.71-1.16)			
	Other	119 (30.9)	-			

^Independent Sample t-test

Table 3. The results of univariate (unadjusted) and multiple logistic regression (adjusted) models on factors associated with asthma

Characteristics	Level	n (%)	Univariate logistic regression		Multivariate logistic regression	
			OR (95%CI)	P- value	OR (95%CI)	P- value
Age (year), mean± SD				<.001	0.99 (0.98-1.01)	0.207
Gender	Male	128 (6.6)	0.92 (0.73-1.17)	0.511	1.15 (0.96-1.39)	0.135
	Female	187 (6.1)	-			
Eczema	Yes	120 (10.2)	2.38 (2.21-2.75)	<.001	1.38 (1.13-1.67)	0.001
	No	195 (5.1)	-			
AR	Yes	200 (12.5)	4.10 (3.22-5.19)	<.001	2.51 (2.10-3.00)	<.001
	No	115 (3.4)	-			
ARS	Yes	170 (4.3)	3.42 (2.71-4.32)	<.001	1.78 (1.31-2.41)	<.001
	No	145 (13.5)	-			
CRS	Yes	544 (50.5)	3.15 (2.49-3.98)	<.001	4.84 (2.02-5.82)	<.001
	No	533 (14.3)	-			
NSAID hypersensitivity	Yes	33 (34.0)	8.43 (5.45-13.05)	<.001	1.32 (0.72-2.36)	0.375
	No	282 (5.8)	-			
Smoking	Yes	45 (8.2)	1.30 (0.99-1.91)	0.058		
	No	270 (6.1)	-			
Health workers	Yes	96 (7.4)	1.49 (1.15-1.93)	0.003	0.81 (0.66-0.99)	0.035
	No	164 (5.1)	-			
Education	Advanced	198 (6.5)	-	0.340		
	High school	57 (5.3)	1.24 (0.92-1.69)			
	Primary school	59 (6.9)	0.93 (0.69-1.27)			
	Illiterate	1 (2.9)	2.38 (0.32-17.46)			
Occupation	Employed	110 (6.8)	-			
	Self-employed	123 (5.2)	1.33 (1.02-1.73)		1.25 (0.83-1.89)	0.293
	Student	55 (8.6)	0.78 (.55-1.09)	0.018	0.93 (0.61-1.42)	0.734
	Retired	13 (8.0)	0.84 (0.46-1.54)		1.38 (0.89-2.15)	0.151
	Other	14 (6.3)	1.08 (0.61-1.93)		1.06 (0.52-2.15)	0.873
Ethnicity	Turk	188 (22.7)	1.26 (0.73-2.17)			
	Persian	717 (22.4)	-			
	Kurd	52 (16.1)	1.64 (0.74-3.60)	0.134		
	Arab	24 (21.8)	1.54 (1.08-2.19)			
	Other	67 (14.4)	1.16 (0.64-2.09)			

among Iranian patients, followed by AR and ARS at each 21.6%. A population-based survey revealed a prevalence of 13% and 17% in the USA (17). Our study suggests that

CRS is prevalent, but it is still challenging to distinguish between persistent AR and CRS using only symptoms and without diagnostic procedures such as a nasal endoscopy,

Table 4. The results of univariate (unadjusted) and multiple logistic regression(adjusted) models on factors associated with acute rhinosinusitis

Characteristics	Level	n (%)	Univariate logistic regression		Multivariate logistic regression	
			OR (95%CI)	P- value	OR (95%CI)	P- value
Age (year), mean± SD				<0.001	0.99 (0.98-1.01)	0.207
Gender	Male	383 (19.7)	1.20 (1.04-1.38)	0.011	1.15 (0.96-1.39)	0.135
	Female	695 (22.8)	-	-	-	-
Asthma	Yes	145 (20.0)	3.4 (2.71-4.32)	<.001	1.99 (1.45-2.74)	<.001
	No	933 (46.0)	-	-	-	-
Eczema	Yes	400 (34.0)	2.38 (2.21-2.75)	<.001	1.38 (1.13-1.67)	0.001
	No	678 (17.8)	-	-	-	-
AR	Yes	629 (34.9)	4.21 (3.71-4.92)	<.001	2.51 (2.10-3.00)	<.001
	No	449 (13.2)	-	-	-	-
CRS	Yes	544 (50.5)	6.1 (5.2-7.12)	<.001	4.84 (2.02-5.82)	<.001
	No	533 (14.3)	-	-	-	-
NSAID hypersensitivity	Yes	43 (43.0)	2.98 (1.98-4.49)	<.001	1.32 (0.72-2.36)	0.375
	No	1035 (21.2)	-	-	-	-
Smoking	Yes	139 (25.2)	1.26 (1.02-1.54)	0.029	1.52 (1.16-1.99)	0.002
	No	939 (21.2)	-	-	-	-
Health workers	Yes	436 (27.5)	2.54 (2.20-2.95)	<.001	0.81 (0.66-0.99)	0.035
	No	536 (18.8)	-	-	-	-
Education	Advanced	783 (25.9)	-	-	-	-
	High school	187 (17.4)	1.65 (1.38-1.97)	-	0.74 (0.40-1.38)	0.351
	Primary school	106 (12.5)	2.45 (1.97-3.05)	<.001	0.94 (0.76-1.13)	0.520
	Illiterate	2 (5.7)	5.75 (1.38-14.02)	-	0.82 (0.65-1.03)	0.092
Occupation	Employed	434 (26.9)	-	-	-	-
	Self-employed	354 (15.2)	2.06 (1.76-2.41)	-	1.25 (0.83-1.89)	0.293
Ethnicity	Student	204 (32.0)	0.78 (0.64-0.96)	<.001	0.93 (0.61-1.42)	0.734
	Retired	24 (14.7)	2.14 (1.37-3.34)	-	1.38 (0.89-2.15)	0.151
	Other	58 (28.8)	1.04 (0.76-1.43)	-	1.06 (0.52-2.15)	0.873
	Turk	188 (22.7)	1.02 (0.85-1.22)	-	0.81 (0.55-1.19)	0.283
	Persian	717 (22.4)	-	-	1.02 (0.68-1.54)	0.910
	Kurd	52 (16.1)	0.67 (0.49-0.91)	0.023	1.02 (0.53-1.80)	0.958
	Arab	24 (21.8)	0.97 (0.62-1.53)	-	0.95 (0.75-1.18)	0.602
Other	67 (14.4)	0.73 (0.56-0.96)	-	-	-	

Table 5. The results of univariate (unadjusted) and multiple logistic regression(adjusted) models on factors associated with chronic rhinosinusitis

Characteristics	Level	n (%)	Univariate logistic regression		Multivariate logistic regression	
			OR (95%CI)	P- value	OR (95%CI)	P- value
Age (year), mean± SD				<.001^	0.99 (0.98-1.01)	0.061
Gender	Male	400 (20.6)	1.15 (1.0-1.32)	0.047	1.08 (0.90-1.30)	0.396
	Female	702 (23.0)	-	-	-	-
Asthma	Yes	141 (44.9)	3.15 (2.49-3.98)	<.001	1.62 (1.18-2.22)	0.002
	No	961 (20.6)	-	-	-	-
Eczema	Yes	376 (32.0)	2.0 (1.73-2.31)	<.001	1.44 (1.90-1.73)	<.001
	No	726 (19.0)	-	-	-	-
AR	Yes	605 (54.9)	3.56 (3.10-4.09)	<.001	2.41 (2.02-2.87)	<.001
	No	989 (25.5)	-	-	-	-
ARS	Yes	544 (50.5)	6.1 (5.2-7.12)	<.001	4.69 (3.90-5.63)	0.01
	No	533 (14.3)	-	-	-	-
NSAID hypersensitivity	Yes	56 (57.7)	5.02 (3.34-7.56)	<.001	2.15 (1.21-3.83)	0.009
	No	1046 (21.4)	-	-	-	-
Smoking	Yes	153 (27.8)	1.42 (1.16-1.73)	0.001	1.19 (0.92-1.54)	0.196
	No	949 (21.4)	-	-	-	-
Health workers	Yes	354 (27.5)	1.63 (1.64-1.90)	<.001	1.04 (0.85-1.27)	0.730
	No	602 (18.8)	-	-	-	-
Education	Advanced	697 (23.0)	-	-	-	-
	High school	228 (21.2)	1.11 (0.93-1.31)	-	-	-
	Primary school	170 (20.0)	1.20 (0.99-1.45)	0.238	-	-
	Illiterate	7 (20.0)	1.20 (0.52-2.75)	-	-	-
Occupation	Employed	382 (23.7)	-	-	-	-
	Self-employed	467 (19.8)	1.26 (1.10-1.46)	-	1.01(0.81-1.26)	0.956
	Student	169 (26.5)	0.86 (0.70-1.06)	-	0.94(0.70-1.25)	0.665
	Retired	20 (12.3)	2.22 (1.37-3.60)	<.001	0.62(0.34-1.15)	0.128
Ethnicity	Other	64 (28.8)	0.77 (0.56-1.04)	-	1.26(0.85-1.89)	0.248
	Turk	180 (21.7)	0.96 (0.80-1.15)	-	-	-
	Persian	751 (22.5)	-	0.129	-	-
	Kurd	81 (25.2)	1.16 (0.89-1.51)	-	-	-
	Arab	23 (20.9)	0.91 (0.57-1.45)	-	-	-
Other	67 (17.4)	0.73 (0.55-0.96)	-	-	-	

^Independent Sample t-test

a nasal CT scan, or atopy testing (18). Our results agree with those of research conducted in Bushehr, a city in southwest Iran, where the prevalence of CRS is 28.4% (19).

We found that the prevalence of asthma was 5.7%, ranging from 4.3% to 10.9% among the Iranian population. This difference could be explained by the difference in the age of the studied individuals and the year of

study (20-22).

The province of Tehran, which is home to around 18% of the nation's population, had the greatest prevalence of AR and ARS. The province of Tehran is the most industrialized province in Iran and 86.5% of its population resides in urban areas (23). A recent meta-analysis showed that sensitivity to fungal aeroallergens was higher in Tehran than in any other city in Iran, most likely due to its climate condition (24). In our study, asthma was more prevalent in one province of Khuzestan, which is consistent with the study done by Aidani et al who reported the prevalence of asthma in Khuzestan province to be almost twice as high as any other province in Iran (21). The reason Khuzestan had a high rate of individuals with asthma is thought to be due to the years of being exposed to various pollutants. According to a 2013 study done by the World Health Organization, the city of Ahwaz (the capital of Khuzestan province) is found to be one of the most polluted cities in the world in 2013 (25).

The results of this study indicated a greater prevalence of CRS in patients living in the provinces of Sistan and Baluchestan. One of the driest areas of Iran is this vast province, which is also subject to high winds. Khazaei et al discovered allergens in the area, including home dust mites, fungi, and wind-pollinated plants, and they identified these as the primary contributors to allergic respiratory disorders in this region (26).

The purpose of this study was to distinguish between CRS and a potential CRS diagnosis made by a doctor based on symptoms that patients described using the GA2LEN questionnaire. Compared to what was reported by the patients who fit the criteria for CRS, there was a noticeably higher percentage of patients who received a doctor's diagnosis of CRS. According to these statistics, either our patients or doctors may tend to diagnose CRS more frequently than is necessary.

After adjusting variables in the present study, the prevalence of AR increased with increasing age (OR, 1.2). According to several studies, the prevalence of AR rises from childhood through young adulthood (27). Due to the identical symptoms, nonallergic rhinitis may develop in elderly AR patients yet remains identified as AR (28). The populations of the study would need to be divided into various age groups for better analysis to obtain better outcomes.

Based on the results of multiple logistic regressions, there was no difference between gender in AR, asthma, ARS, or CRS. There was a sex disparity for asthma, with a higher prevalence in boys than in girls before puberty, and female adults had an increased prevalence of asthma when compared with men. In the present study, age ranged from childhood to adulthood, which could explain the lack of a gender difference in patients with asthma in our study (29). Ostovar et al did a study in Bushehr (southwestern Iran) and found no gender differences among patients with CRS, which is consistent with our study (30).

Our analysis showed that patients with AR were more likely to have other allergic diseases. In the community of people with AR, the most frequent comorbidity was asthma,

followed by ARS, which was more common than CRS, and eczema, which was the least common. Asthma had the highest frequency with an OR of 2.6 and eczema had the lowest frequency with an OR of 1.7. AR and asthma are often comorbid conditions; several studies have shown childhood AR to be associated with at least a 2-time increase in the risk of developing asthma at an older age (31, 32).

The frequency of CRS was 4.8 folds higher in each patient with asthma and ARS. A Korean study found that having asthma increased the risk of developing CRS with an adjusted hazard ratio of 1.7 (33); the higher rate discrepancy may be explained by the different regional factors and genetic backgrounds in both the Korean and Iranian populations. A population-based study has shown the prevalence of CRS to be higher in Canadian patients with asthma (34). Although ARS and CRS are 2 different diseases, both occur as secondary complications of infections and allergies. According to a study by Hoffmans et al, people with ARS had a 2.1-fold increased risk of acquiring CRS. (35); some characteristics including age, sex, and ethnicity could be important for higher ratio in our study.

Our study further demonstrated patients with CRS had a greater risk for AR by 2.4 folds, followed by 1.6 folds for asthma, and 1.4 folds for eczema. Allergies can cause chronic inflammation in the mucosal lining of sinuses and thus prevent the usual clearance of bacteria via the sinus cavity (36). This finding supports the concept of a united allergic airway where a common atopic entity manifests symptoms of upper and lower airway diseases (37). The prevalence of asthma in patients with CRS was reported to be in a wide range from 4% to 44% (38-41). A recent study suggests that increased periostin levels may be a reason for the development of asthma in patients with CRS (42).

We found that NSAID hypersensitivity was most common (OR 2.1) in people with CRS. Epidemiological studies established the link between CRS and aspirin sensitivity, as aspirin-exacerbated respiratory disease (AERD). The combinations of diseases may be difficult to treat when using standard medical and surgical interventions (43).

Furthermore, it was found that over 1.5 folds of individuals with ARS admit to smoking. Direct cigarette and other tobacco usage are associated with an increase in the prevalence of both acute and chronic sinusitis in the USA (44). Smoking significantly lowers the ciliary beat frequency of nasal mucosal cells, which has been linked to mucociliary dysfunction in people with sinusitis (44). Large population-based studies have helped establish smoking as a significant risk factor for CRS; nevertheless, our data did not support this topic after adjusting various variables.

Interestingly, the present study found that the likelihood of AR, asthma, and ARS among health care workers was much lower. One explanation is that tolerance to various allergens and irritants could occur in an occupational environment (45).

Although it appears that education may affect reporting

of symptoms, we did not have any association between education and studied diseases. After adjusting the variables, there was no correlation between one's occupation and occurring AR, asthma, ARS, and CRS.

We found no correlation between ethnicity and sinusitis, asthma, or AR in our multivariate study. However, several studies have found a link between various ethnicities and AR (46, 47). It's plausible that such differences cannot be detected because of the diverse environmental elements in the different provinces. Multicenter surveys could help determine the exact prevalence of AR, asthma, and sinusitis in Iran. A drawback of the current study would be that it relied solely on self-reported symptoms rather than objective tests like spirometry, allergy skin tests, and computed tomography scans of the nose.

Conclusion

Rhinosinusitis is a common condition among Iranian patients. This study confirmed that inflammation of the upper and lower airways can occur simultaneously. Factors such as environmental location and smoking proved to be important in determining the prevalence of AR, asthma, ARS, and CRS. However, based on our results, factors such as gender, education, occupation, and ethnicity were found to not contribute to these conditions.

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Ethical Considerations

The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1398.239).

Conflict of Interests

The authors declare that they have no competing interests.

References

- Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic rhinitis. *Lancet*. 2011;378(9809):2112-2122.
- Pawankar R, Bunnag C, Khaltaev N, Bousquet J. Allergic Rhinitis and Its Impact on Asthma in Asia Pacific and the ARIA Update 2008. *World Allergy Organ J*. 2012;5(Suppl 3):S212-217.
- Baumann LM, Romero KM, Robinson CL, Hansel NN, Gilman RH, Hamilton RG, et al. Prevalence and risk factors for allergic rhinitis in two resource-limited settings in Peru with disparate degrees of urbanization. *Clin Exp Allergy*. 2015;45(1):192-199.
- Meng Y, Wang C, Zhang L. Recent developments and highlights in allergic rhinitis. *Allergy*. 2019;74(12):2320-2328.
- Nunes C, Pereira AM, Morais-Almeida M. Asthma costs and social impact. *Asthma Res Pract*. 2017;3:1.
- Kaplan A, Szefer SJ, Halpin DMG. Impact of comorbid conditions on asthmatic adults and children. *NPJ Prim Care Respir Med*. 2020;20: 30(1):36.
- Nabavizadeh SH, Moghtaderi M, Esmailzadeh H, Hosseini Teshnizi S, Sarasadat Nabavizadeh SS. Socio-Demographic and environmental factors in children with asthma: A cross-sectional study from southwestern Iran. *Zahedan J Res Med Sci*. 2019;21(2):e88388.
- Lo PC, Tsai YT, Lin SK, Lai JN. Risk of asthma exacerbation associated with nonsteroidal anti-inflammatory drugs in childhood asthma: A nationwide population-based cohort study in Taiwan. *Medicine (Baltimore)*. 2016;95(41):e5109.
- DeBoer DL, Kwon E. Acute Sinusitis. In: StatPearls [Internet]. 2020. Treasure Island (FL): StatPearls Publishing.
- Dietz de Loos D, Lourijsen ES, Wildeman MAM, Freling NJM, Wolvers MDJ, Reitsma S, et al. Prevalence of chronic rhinosinusitis in the general population based on sinus radiology and symptomatology. *J Allergy Clin Immunol*. 2019;143:1207.
- Leo G, Triulzi F, Incorvaia C. Diagnosis of chronic rhinosinusitis. *Pediatr Allergy Immunol*. 2012;23 Suppl 22:20-26.
- Cho SH, Ledford D, Lockey RF. Medical Management Strategies in Acute and Chronic Rhinosinusitis. *J Allergy Clin Immunol Pract*. 2020;8(5):1559-1564.
- Bousquet J, Burney PG, Zuberbier T, Cauwenberge PV, Akdis CA, Bindslev-Jensen C, et al. GA2LEN (Global Allergy and Asthma European Network) addresses the allergy and asthma epidemic. *Allergy*. 2009;64:969-977.
- Dharmage SC, Perret JL, Custovic A. Epidemiology of Asthma in Children and Adults. *Front Pediatr*. 2019;7:246.
- Fuseini H, Newcomb DC. Mechanisms Driving Gender Differences in Asthma. *Curr Allergy Asthma Rep*. 2017;17(3):19.
- Jensen-Jarolim E, Untermayr E. Gender-medicine aspects in allergology. *Allergy*. 2008;63(5):610-615.
- Plis JR, Lucas JW, Ward BW. Summary health statistics for U.S. adults: National Health Interview Survey, 2008. *Vital Health Stat*. 2009;10(242):1-157.
- Tan BK, Kern RC, Schleimer RP, Schwartz BS. Chronic rhinosinusitis: the unrecognized epidemic. *Am J Respir Crit Care Med*. 2013;188(11):1275-1277.
- Ostovar A, Pordel S, Movahed A, Kaboodkhani R, Akhlaghi A, Darabi A, et al. The prevalence of asthma in adult population of southwestern Iran and its association with chronic rhinosinusitis: a GA2LEN study. *Clin Transl Allergy*. 2019;9(43).
- Fazlollahi MR, Najmi M, Fallahnezhad M, Sabetkish N, Kazemnejad A, Bidad K, et al. The prevalence of asthma in Iranian adults: the first national survey and the most recent updates. *Clin Respir J*. 2018;12(5):1872-1881.
- Idani E, Raji H, Madadzadeh F, Cheraghian B, Haddadzadeh Shoshtari M, Dastoorpoor M. Prevalence of asthma and other allergic conditions in adults in Khuzestan, southwest Iran. *BMC Public Health*. 2018;19(1):303.
- Mohammadbeigi A, Hassanzadeh J, Mousavizadeh A. Prevalence of asthma in elementary school age children in Iran—a systematic review and meta-analysis study. *Pak J Biol Sci*. 2011;14(19):887-893.
- National census 2016. amar.org.ir. Retrieved 2017-03-14.
- 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.
- Dastoorpoor M, Idani E, Goudarzi G, Khanjani N. Acute effects of air pollution on spontaneous abortion, premature delivery, and stillbirth in Ahvaz, Iran: a time-series study. *Environ Sci Pollut Res*. 2018;25(6):5447-5458.
- Khazaei HA, Hashemi SR, Aghamohammadi A, Farhoudi F, Rezaei N. The study of type 1 allergy prevalence among people of South-East of Iran by skin prick test using common allergens. *Iran J Allergy Asthma Immunol*. 2003;2(3):165-168.
- Warm K, Hedman L, Lindberg A, Lötval J, Lundbäck B, Rönmark E. Allergic sensitization is age-dependently associated with rhinitis, but less so with asthma. *J Allergy Clin Immunol*. 2015;136(6):1559-1565.e2.
- Nyenhuis SM, Mathur SK. Rhinitis in older adults. *Curr Allergy Asthma Rep*. 2013;13(2):171-177.
- Postma DS. Gender differences in asthma development and progression. *Genet Med*. 2007;4(Suppl B):S133-146.
- Ostovar A, Fokkens WJ, Vahdat K, Raeisi A, Mallahzadeh A, Farrokhi S. Epidemiology of chronic rhinosinusitis in Bushehr, southwestern region of Iran: a GA2LEN study. *Rhinology*. 2019;57(1):43-48.
- Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 2000;106(5 Suppl):S201-205.
- Thomas M. Allergic rhinitis: evidence for impact on asthma. *BMC Pulm Med*. 2006;6 Suppl 1(Suppl 1):S4.
- Tsilochristou OA, Douladiris N, Makris M, Papadopoulos NG. Pediatric allergic rhinitis and asthma: can the march be halted? *Paediatr Drugs*. 2013;15(6):431-440.
- Ryu G, Min C, Park B, Choi HG, Mo JH. Bidirectional association

- between asthma and chronic rhinosinusitis: Two longitudinal follow-up studies using a national sample cohort. *Sci Rep*. 2010;10(9589).
34. Chen Y, Dales R, Lin M. The epidemiology of chronic rhinosinusitis in Canadians. *Laryngoscope*. 2003;113(7):1199-1205.
 35. Hoffmans R, Schermer T, van Weel C, Fokkens W. Management of rhinosinusitis in Dutch general practice. *Prim Care Respir J*. 2011;20(1):64-70.
 36. Scadding GK. Rhinitis and Sinusitis. *Clin Respir Med*. 2008:409-423.
 37. Giavina-Bianchi P, Aun MV, Takejima P, Kalil J, Agondi RC. United airway disease: current perspectives. *J Asthma Allergy*. 2016;9:93-100.
 38. Chapurin N, Pynnonen MA, Roberts R, Schulz K, Shin JJ, Witsell DL, et al. CHEER National Study of Chronic Rhinosinusitis Practice Patterns: Disease Comorbidities and Factors Associated with Surgery. *Otolaryngol Head Neck Surg*. 2017;156(4):751-756.
 39. Benninger MS, Sindwani R, Holy CE, Hopkins C. Impact of medically recalcitrant chronic rhinosinusitis on incidence of asthma. *Int Forum Allergy Rhinol*. 2016;6(2):124-129.
 40. Yoshimura K, Kawata R, Haruna S, Moriyama H, Hirakawa K, Fujieda S, et al. Clinical epidemiological study of 553 patients with chronic rhinosinusitis in Japan. *Allergol Int*. 2011;60(4):491-496.
 41. Jarvis D, Newson R, Lotvall J, Hastan D, Tomassen P, Keil T, et al. Asthma in adults and its association with chronic rhinosinusitis: the GA2LEN survey in Europe. *Allergy*. 2012;67(1):91-98.
 42. Asano T, Kanemitsu Y, Takemura M, Yokota M, Fukumitsu K, Takeda N, et al. Serum Periostin as a Biomarker for Comorbid Chronic Rhinosinusitis in Patients with Asthma. *Ann Am Thorac Soc*. 2017;14(5):667-675.
 43. Graefe H, Roebke C, Schäfer D, Meyer JE. Aspirin sensitivity and chronic rhinosinusitis with polyps: a fatal combination. *J Allergy (Cairo)*. 2012;2012:817910.
 44. Lieu JE, Feinstein AR. Confirmations and surprises in the association of tobacco use with sinusitis. *Arch Otolaryngol Head Neck Surg*. 2000;126(8):940-946.
 44. Christensen DN, Franks ZG, McCrary HC, Saleh AA, Chang EH. A systematic review of the association between cigarette smoke exposure and chronic rhinosinusitis. *Otolaryngol Head Neck Surg*. 2018; 158(5):801-816.
 45. Chaari N, Sakly A, Amri C, Mahfoudh A, Henchi MA, Khalfallh T, et al. Occupational allergy in healthcare workers. *Recent Pat Inflamm Allergy Drug Discov*. 2010;4(1):65-74.
 46. Gillam SJ, Jarman B, White P, Law R. Ethnic differences in consultation rates in urban general practice. *BMJ*. 1980;299(6705):953-957.
 46. Hoffmans R, Wagemakers A, van Drunen C, Hellings P, Fokkens W. Acute and chronic rhinosinusitis and allergic rhinitis in relation to comorbidity, ethnicity and environment. *PloS One*. 2018;13(2):e0192330.
 47. Salo PM, Calatroni A, Gergen PJ, Hoppin JA, Sever ML, Jaramillo R, et al. Allergy-related outcomes in relation to serum IgE: results from the National Health and Nutrition Examination Survey 2005-2006. *J Allergy Clin Immunol*. 2011;127(5):1226-35.e7.