Prevalence of Asthma, COPD, and Chronic Bronchitis in Iran: A Systematic Review and Meta-analysis

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ABSTRACT

In this study, we aimed to conduct a meta-analysis on the results of eligible studies to estimate the prevalence of asthma, COPD, and Chronic bronchitis in Iran .

International and Iranian databases including PubMed, Scopus, Web of Science, Iranmedex, and scientific information database (SID) were searched for population–based studies that had reported the prevalence of asthma and COPD from 1990 to 2015. We conducted the meta-analysis using metaprop application of Stata statistical software. I-Squared was used for calculating heterogeneity among the studies. To determine causes of heterogeneity, subgroup analysis and meta-regression method were used.

Based on the results of random effect method, the overall prevalence of asthma ever was 4.56% (3.76%-5.36%) among men while it was 4.17% (3.42%-4.91%) among women. Pooled prevalence of current asthma was 7.95% while confidence interval changed from 5.85% to 10.06% (men 5.83% (2.75%-8.92%), women 9.13% (3.35%-14.94%)). Also based on the results of random effect model pooled prevalence of chronic bronchitis of five studies was 5.57%. It seems that the total crude prevalence of current asthma in Iran is less than many other countries such as Kuwait, Lebanon, Thailand, Japan, Australia and Germany and is higher than some other countries such as Oman, Pakistan, South Korea, India, China, Taiwan, Indonesia, Spain, Russia, and Greece. On the other hand, Iran is in middle situation in terms of the prevalence current asthma. Our results can fill the information and knowledge gaps about the status of the prevalence of respiratory diseases in Iran.

Keywords: Asthma; Chronic bronchitis; Iran; Meta-analysis; Prevalence; Systematic review

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INTRODUCTION

The most common chronic respiratory diseases are asthma and chronic obstructive pulmonary disease (COPD) which are among the major causes of morbidity and mortality worldwide.[1,2] Globally, asthma is one of the most common chronic diseases across the world and it affects 300 million people, whereas COPD is the fourth leading cause of death and 10% of adults aged up to 40 years old may be affected by COPD.[3-5] The prevalence of the asthma has increased in some countries during the last decade.[6] Also, due to the increasing number of aged population and increased rates of smoking, it is expected that the global burden of COPD will rise in general population.[7] The prevalence of asthma has become more than double over the past 20 years.[8] According to the reports by the World Health Organization (WHO), the global burden of COPD showed an increasing trend from 1990 to 2010. The COPD was the sixth major cause of death worldwide in 2002. However, its ranking rose to fifth in 2010.[9]

The prevalence of asthma has been reported variously in different countries: 7.6% in the United States,[10] 10% in the United Kingdom, 4.8% in France, 4.8% in Germany, 4.7% in Italy, and 4.8% in Spain.[11] Moreover, the prevalence of COPD was about 9.6% in Rwanda.[12] Chronic bronchitis symptoms, as one of the two key components of COPD along with emphysema,[13] were found in 21.6% of general population in Belgrade.[2] Several systematic reviews were carried out to estimate the prevalence of asthma among children and school-aged people in Iran. The prevalence of childhood asthma has been reported differently at different studies.[14-16] In these studies, the overall prevalence of the asthma has been reported from 3.9% to 13.14% .

The difference in the data about the prevalence of asthma, COPD, and chronic bronchitis among Iranian population may affect the decision of policy makers, insurance organizations and health authorities. Although, there are a few systematic reviews about the prevalence of childhood asthma in Iran, we could not find any systematic review and meta-analysis on the prevalence of the asthma and COPD among Iranian adult population. As a matter of fact, COPD is a chronic respiratory disorder that its key components are chronic bronchitis and emphysema. However, there are not only scare information of COPD in published papers in Iran but also the majority of them have been reported the chronic bronchitis. The aim of the researchers was to carry out a meta-analysis on the results of all conducted studies to present valid information about the prevalence of asthma, COPD, and Chronic bronchitis in Iran

MATERIALS AND METHODS

Definitions

There are different definitions for asthma and COPD in the literature. Asthma is classified as asthma ever, current asthma, exercise-induced asthma, and physician diagnosed asthma. Asthma ever is defined as a history of dyspnea attack and wheezing over the life period; current asthma is a history of one or more attack of dyspnea and wheezing during recent past 12 months; exercise-induced asthma is dyspnea and wheezing triggered by exercise; finally, Physician diagnosed asthma which is a history of diagnosis of asthma over the life time. In this study, COPD was described based on the definition presented by the American Thoracic Society (ATS): "a disease state characterized by the presence of airflow limitation due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive, may be accompanied by airway hyper-reactivity, and may be partially reversible" and chronic bronchitis was characterized by the Global Initiative for Chronic Obstructive Lung Disease as "chronic bronchitis, or the presence of cough and sputum production for at least 3 months in each of two consecutive years".[17-19]

Search Strategy

A sensitive systematic search was separately conducted by two trained researchers to find the studies on asthma and COPD prevalence. The search strategy for English databases was formed using medical subject heading (MeSH terms) and emtree terms of Scopus. The search strategy for Persian databases was formed through the translation of all Mesh and emtree terms with different dictations. English databases included PubMed (from 1985 to 2015), Scopus and Web of Science (from 1990 to 2015). Iranian databases included barakatkns, Irandoc, and scientific information database (SID). We also used conference proceedings that were available online from 1985 to 2015 as a resource of search. All databases (Persian and internationals) were searched for epidemiologic

properties of the asthma and COPD. Explanations about the search strategy and study inclusion protocol are discussed elsewhere.[20]

Data Extraction

Initially, two researchers independently reviewed all the titles and abstracts which were selected by the keywords. In the second phase, full texts of the articles, which were selected from the first phase, were reviewed; finally, the researchers selected the articles whose contents were suitable for data extraction. Disagreements between the two reviewers about selecting articles were resolved by a third reviewer via discussion and consensus. The criteria for data extraction were described by authors elsewhere in a previously published paper.[20] Extracted information included name of the first author, year of publication, study region, type of study (local study or survey), total sample size, response rate, age and sex groups of the participants, urban/rural areas, point prevalence, and 95% confidence interval of point prevalence (CI).

Study Quality Assessment

The global burden of disease quality assessment checklist was used for assessing the quality of studies. Total study quality score was achieved by summing up the sampling method (1-4 score), the sample size (0-3), and the response rate (0-6).[21]

Statistical Analysis

We used Stata statistical software (Texas, USA, version 11) to analyze the data in this study. Standard error of the prevalence of asthma, COPD and chronic bronchitis was calculated for each study using binomial distribution formula.[22] I-Squared was used for calculating heterogeneity among the studies. To determine causes of heterogeneity, subgroup analysis and meta-regression method were used. The subgroup analysis was performed based on age groups (≤18 years and >18 years).

Variables that cause heterogeneity were determined using meta-regression models. In multivariate meta-regression analysis years of publication (1996-1999, 2000-2003, 2004-2007, and 2008-2012), regions within Iran (central, north-northeast, southeast, and west), age-group (≤18 years and >18 years), size of city (big cities was defined as above 1 million population, moderate as between 400000 to 1 million population, and small as a below 400000 population), urban versus rural, quality assessment score, and sample size were entered into the model for asthma; moreover, quality assessment score, sample size and sex were used for COPD.

In the meta-analysis, random effect model was used to estimate the prevalence of asthma and chronic bronchitis in different age groups. We used forest plot to obtain the point estimates of pooled prevalence of the asthma and chronic bronchitis.

RESULTS

Characteristics of Included Studies

In the first phases, a total of 1624 studies on asthma and 773 studies on COPD were found through searching in international and Iranian databases. In the second phase, 1346 study about the asthma were excluded after reading the titles and abstracts and finally, after reviewing texts, 39 eligible papers were included in our study for analysis.[19,23-59] In addition, after reviewing titles, abstracts, and full-text 593 articles about the prevalence of COPD were discarded as they were irrelevant. Finally, five papers were included in the meta-analysis and summarized in Figure 1 and Table 1.[52,60-63]

Twenty two out of 39 papers about asthma had been written in English and 14 papers had been written in Persian. Four papers about COPD had been written in English. All the included articles had been carried out as cross-sectional surveys. Overall, the total population who had been involved in the studies of asthma and COPD were 119130 and 9202 individuals, respectively. The population who had been studied in the selected researches was from different parts and regions of Iran (seven studies had been conducted in north, three studies in south, four studies in east and the south east, and the remaining studies had been carried out in the central provinces of Iran).

We had 115 age-sex data points for analyzing the prevalence of asthma, as well as, 10 age-sex data points for the prevalence of chronic bronchitis were used (because some studies reported the prevalence of disease among several specific age-sex groups).

Table 1. Characteristics of studies included in meta-analysis of Asthma and COPD

Study	Sample size	Location	Quality Assessment Score	Asthma Ever	Current Asthma	Physician Diagnosis Asthma	Exercise Induced Asthma	COPD	Chronic bronchitis
Golshan et al.,2001	3982	Isfahan	11	7.60	3.90		1.80		
Boskabady et al.,2002	5579	Khorasan Razavi	6	2.79					
Golshan et al.,2002	1309	Zarinshahr	9		5.88	1.60	19.44		
khazaei et al., 2003	1286	Sistan v Balochestan	7	16.72					
Masjedi et al.,2004	6127	Tehran	12	1.18					
Hedayatmofidi et al.,2007	580	Golestan	4	1.03					
Shakurnia et al.,2010	2932	Khozestan	13	9.78					
Mohammadzadeh et al.,2008	6494	Mazandaran	9	3.69	11.47		5.83		
Najafizadeh et al.,2008	6074	Gilan	11	5.97					
Varasteh et al.,2009	1751	Khorasan Razavi	10	2.30					
Marefati et al.,2011	1690	Khorasan Razavi	6				12.54		
Sahebi et al.,2011	1508	Azarbayejan Sharghi	10	2.00					
Zobeiri et al.,2011	6000	Kermanshah	7			0.64			
Ghaffari et al.,2012	1818	Mazandaran	7	8.75					
Rejaeefard et al., 2011	600	Kohkiloyeh	4	10.50					
Hassanzadeh et al., 2010	3000	Fars	4	3.86					
Mehrabi et al.,2007	864	Kordestan	3	2.30					
Karimi et al., 2007	3060	Yazd	5		10.48				
Abbasi Ranjbar., 2005	6145	Gilan	11	5.75					
Zohal et al., 2006	5068	Qazvin	9	2.05					
Gharagozlou et al.,2002	3000	Isfahan	6			1.76			
Habibi Khorasani et al., 2002	3060	Kerman	7	2.75					
Hatami et al., 2002	3000	Bushehr	13			6.78			
Golshan et al., 2000	1331	Isfahan	11	5.70					
Farrokhi et al., 2014	2395	Bushehr	13	7.01					
Golshan et al., 2002	994	Isfahan	10	6.13					
Rahimian., 1998	1900	Yazd	10		3.52				
Golshan et al., 1999	3820	Lorestan	10			1.49			
Bazazi et al., 2006	2800	Golestan	4	7.07					
Mirzaei et al., 2007	2740	Yazd	4		5.40				

Tootoonchi., 2004	619	Tehran	6	2.80	19.40	12.00		
Mortazavi Moghadam et al., 2004	3537	Khorasan Jonobi	13		10.03			
Kajbaf et al., 2009	903	Khozestan	12		8.70	3.40		
Masjedi et al., 1996	6061	Khorasan Jonobi	12	5.75				
Masjedi et al., 1996	5582	Gilan	12	3.18				
Masjedi et al., 1996	5522	Zanjan	12	3.22				
Tazesh et al. 2013	5500	Tehran	10		10.80			
Rahimi-Rad et al., 2007	3000	Azarbayejan Gharbi	11	2.03				
Golshan et al.,2001	4636	Isfahan	8				1.68	4.66
Golshan et al.,2002	994	Isfahan	10					4.42
Golshan et al.,2011	1308	Isfahan	6					8.18
Sharifi et al., 2014	271	Tehran	4				10	10.92
Emra et al.,2004	1993	Sharekord	11					1.8

Estimated Prevalence of Asthma, COPD, and Chronic Bronchitis

Based on the results of random effect method, the overall prevalence of asthma ever was 4.56% (3.76%-5.36%) among men while it was 4.17% (3.42%-4.91%) among women. Pooled prevalence of current asthma was 8.80% while confidence interval changed from 6.48% to 11.12% (men 5.83% (2.75%-8.92%), women 9.13% (3.35%-14.94%)). Also based on the results of random effect model pooled prevalence of chronic bronchitis of five studies was 5.57% (Figure 2). In addition, two studies reported different prevalence rates for COPD i.e. 10.0% and 1.68%. Pooled prevalence of all types of asthma as well as, chronic bronchitis has been shown in Figure 3. Furthermore, prevalence of asthma in terms of age has been indicated in Figure 4.

Subgroup Analysis and Meta-regression

The overall prevalence of asthma ever among the age groups ≤18 and >18 were 4.87 % (4.29%-5.46%) and 2.54% (1.98%-3.10%), respectively. In multivariate meta-regression models, year of
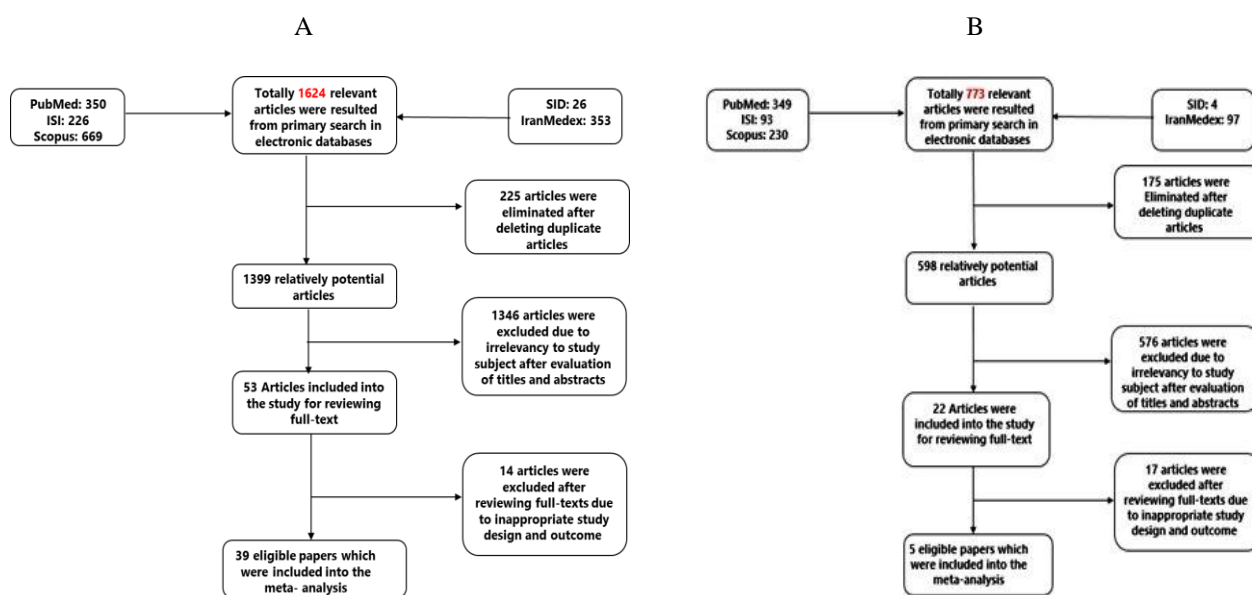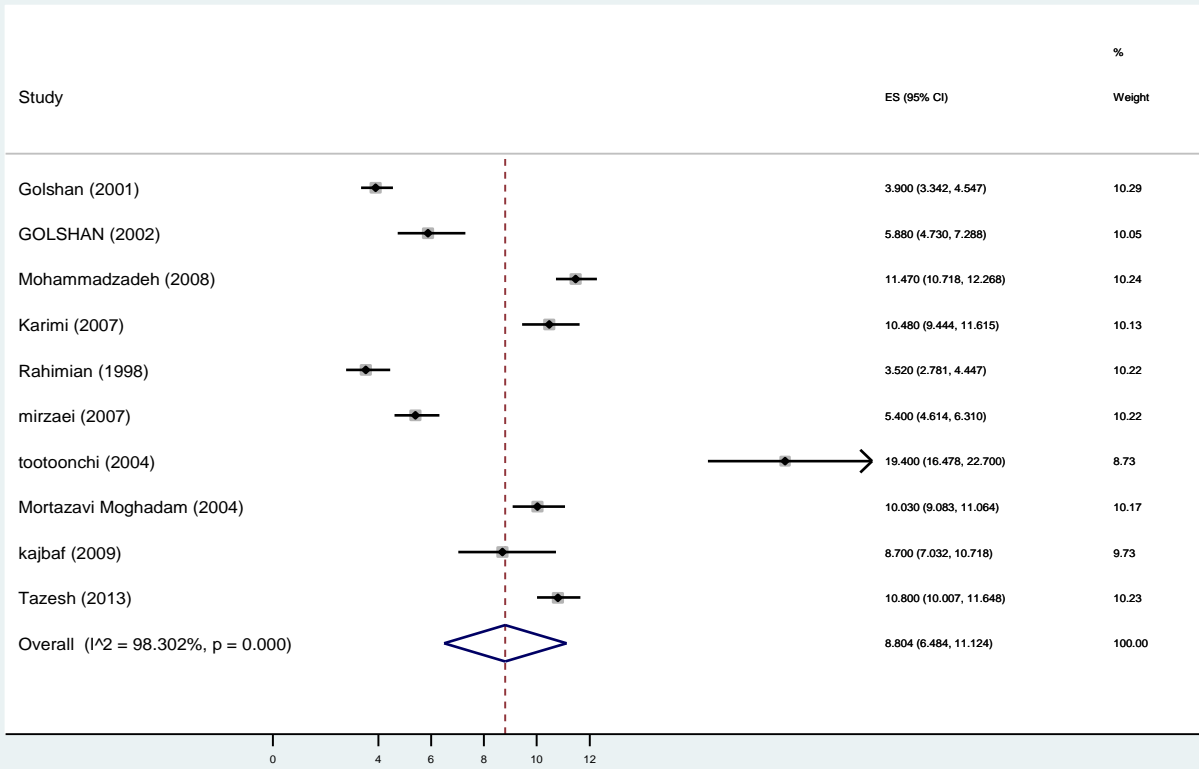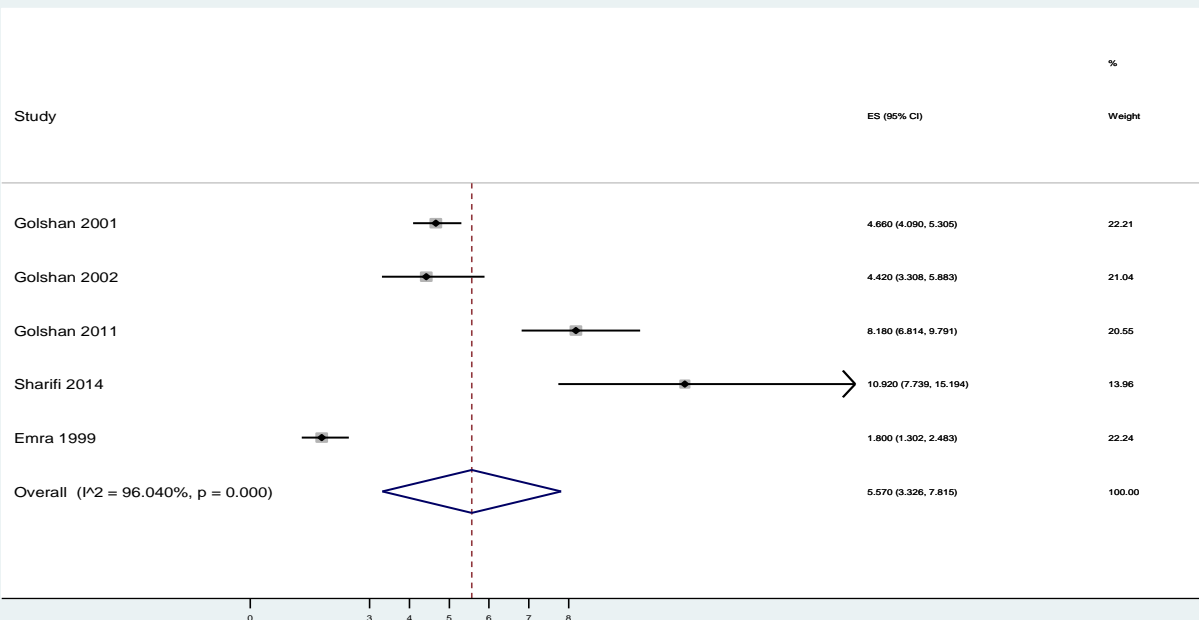
A
B

Figure 1. Process of search and analysis for selection of studies conducted on (A) asthma and (B) COPD

A

B

Figure 2. Forest plot of the prevalence of (A) current asthma (B) chronic bronchitis among Iranian people
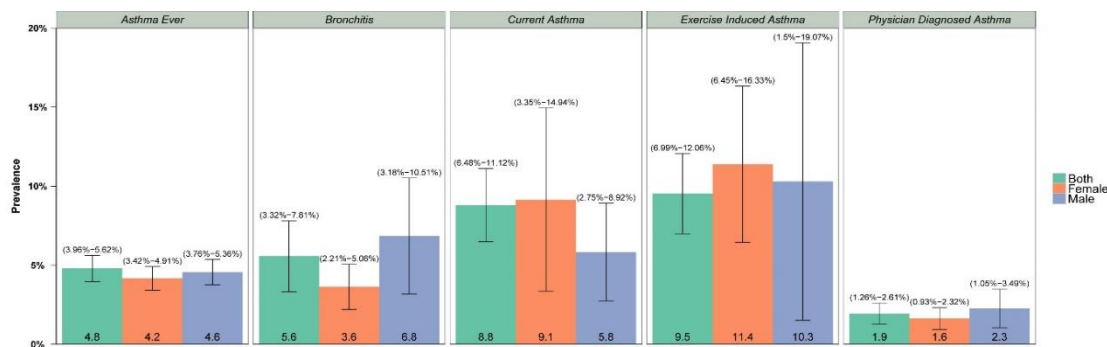
Figure 3. Prevalence of asthma and chronic bronchitis by gender
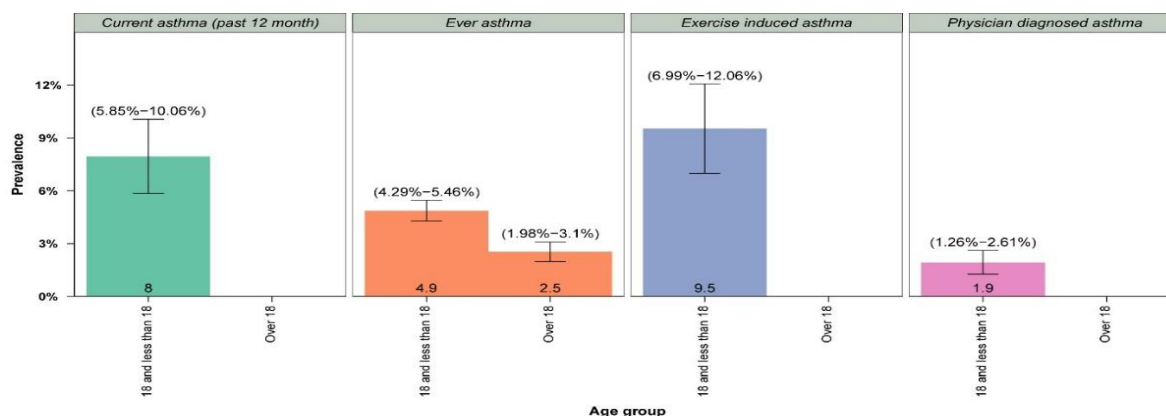

Figure 4. Prevalence of Asthma in terms of Age

publication, region of Iran, age-group, size of city, urban versus rural, quality assessment score, and sample size were entered into the model for assessing asthma; in addition, quality assessment score and sample size were used for assessing COPD. It should be noted that the effect of these factors did not significantly remove heterogeneity in our study, while they changed the results obtained for chronic bronchitis. The results of multivariate meta-regressions analysis for various types of the asthma are presented in table 2.

Table 2. Univarate meta-regression analysis for detecting sources of heterogeneity

Type of Asthma	Variable	Coefficient	Standard Error	*p*-Value	Adj R-Squared
Asthma Ever	Year category	0.007483	0.0031977	0.022 *	18.17%
	Region	0.010817	0.0043388	0.015 *	
	Size of city	0.126905	0.0055736	0.025 *	
Current Asthma	Year category	0.0145632	0.0172689	0.421	-20.47%
	Region	0.009142	0.0213459	0.679	
	Size of city	0.0042106	0.0212385	0.847	
Exercise Induced Asthma	Year category	0.0077926	0.366548	0.838	29.64%
	Region	0.0202134	0.0210395	0.369	
	Size of city	0.290236	0.337558	0.418	
Physician Diagnosed Asthma	Year category	0.289506	0.0043916	<0.001 *	76.78%
	Region	0.048115	0.0088959	0.001 *	
	Size of city	0.0011441	0.0042441	0.795	
Chronic bronchitis	Quality assessment score	0.0135414	0.0056906	0.098	57.32%

* Significant at the 5% level

DISCUSSION

Asthma is considered as a reversible inflammatory process which occurs in airways, particularly in small and moderate airways. [64] We estimated the prevalence of four defined types of asthma, asthma ever, current asthma, physician diagnosed asthma, and exercise induced asthma. However, because of the scarcity of data and overlaps of definitions, we could not estimate the prevalence of asthma symptoms. Furthermore, most of Iranian studies on the prevalence of asthma have used clinical asthma and asthma symptoms interchangeably.

This study presented a comprehensive report that is the first quantitative summary of the prevalence of asthma (in all ages), COPD, and chronic bronchitis in Iran. The results of this meta-analysis showed that pooled prevalence estimates varied depending on the definitions of asthma and ranged from 2% (physician diagnosed asthma) to 9% (exercise induced asthma).

This study estimated the prevalence of asthma according to different definitions; for instance, the prevalence of current asthma was reported to be higher than that in asthma ever and physician diagnosed asthma. It could be due to the increase in physicians' and patients' awareness of asthma disease. Furthermore, pooled prevalence of current asthma was higher among females, while the prevalence of asthma ever and physician diagnosed asthma was higher among males.

Using subgroup analysis, the results showed that the prevalence of asthma was higher in Bushehr and other cities located at the southeast of Iran than the other regions. It could be due to higher rate of smoking or other environmental factors like Hookah Smoking.[65] Highest rate of smoking among women in Iran is reported by Amiri et al in Bushehr (south of Iran).[66] Higher levels of air pollution or humidity in the mentioned regions may be the other justification for the higher prevalence of asthma in the mentioned regions. There is a positive relationship between the increased rate of asthma and smoking. [67] Furthermore, we found some other factors that are effective in the pathogenesis of asthma; such factors could justify the differences in the prevalence of asthma in different communities. For example, some environmental factors such as air pollutants, infectious agents particularly viral infections, and some individual factors such as obesity have a role in triggering and exacerbation of clinical symptoms of asthma. [68] All these factors could increase heterogeneity in the prevalence of asthma in different sites and among different populations.

COPD is a slowly progressive disease characterized by airflow limitation that is generally irretrievable.[69] The pathogenesis of COPD is mainly affected by inhalation of cigarette smoke in the lungs; indeed, cigarette smoke is identified as an important determinant of COPD development.[70]

Data about the prevalence of COPD and chronic bronchitis is scarce and this is the first systematic study to assess the prevalence of these diseases in Iran. The prevalence rate of COPD is reported differently in other countries; for instance, the estimated prevalence of this disease in Spain, Brazil, Greece, China, Vietnam, and Singapore are 10.2%, 15.2%, 8.4%, 6.5%, 6.7%, and 3.5%, respectively.[71-73] In this study, we only found two studies reporting different estimates for COPD. It could be due to the differences in the geographic areas where these studies had been conducted. Furthermore, the controversies in the COPD estimated could be attributed to differences in sampling methods and response rates in the two mentioned studies.

Our findings differ from the results of other systematic reviews on the prevalence of COPD over the world; for instance, a study reported the prevalence of disease to be 9% to 10%.[5] The low prevalence rate of chronic bronchitis which was observed in our study could be due to the fact that COPD is a general word used for describing both chronic bronchitis and emphysema; in our study, we only reported the prevalence of chronic bronchitis. According to Spon et al, the prevalence of chronic bronchitis among Kashmiri population was 5.4%.[74]

In our meta- analysis, the results showed a significant heterogeneity between studies on asthma and COPD which was determined by high I^2. The differences between asthma prevalence rates reported by different studies could be due to differences in data collection methods, sampling methods, time, and regions where the studies had been carried out. Another source of inconsistency was the ambiguity in the criteria used for the diagnosis of asthma. For example, in some of the studies it was unclear whether ever asthma or current asthma had been investigated or not. Moreover in some of the articles, the age distribution of the participants was unclear.

The subgroup analysis was not able to completely explain the heterogeneity. One of the most important

sources of inconsistency in the estimated prevalence of asthma and COPD was the differences in definitions. Our results were relatively in line with the findings of some other researchers. According to Hassanzadeh et al, the prevalence of asthma ever among Iranian senior high school children was 4.4%. Moreover, according to the results of a systematic review by Mohammadbeigi et al, the prevalence of asthma among children aged 6-12 years old in Iran was 3.9%. However, Entezari et al estimated the pooled prevalence of the asthma to be 13.14% in the same age group. [15,79] In addition, according to Ghaffari et al, the estimated prevalence rates of asthma ever and current asthma were 3.04% (95% CI: 2.5 to 3.6) and 9.3% (95% CI: 7.9 to 10.8), respectively.[16] Comparing the prevalence of current asthma in Iran with other parts of the world, our estimated rate is lower than that in Kuwait, Lebanon, Thailand, Japan, Australia, and Germany. On the other hand, our estimated value is higher than that in some countries like Oman, Pakistan, South Korea, India, China, Taiwan, Indonesia, Spain, Russia, and Greece.[76]

The differences in the age range of people who were enrolled in different studies could be introduced as another source of heterogeneity. In addition, several published studies limited their study population only to one sex. For example 34.2% of reviewed studies did not report the prevalence of asthma for males and females separately. Since, some of the studies did not report the prevalence by age or sex, these studies were omitted from our subgroup analysis. As a result of scarcities in the results, there was not enough point data for some subgroup analyses.

In this research, only published studies were reviewed; as a result, unpublished studies and gray literature were not included in our analyses because they were not accessible. Such sets of data could have a great impact on our results.

In conclusion, although, previously published studies have considered the prevalence of childhood asthma in Iran, the present review is a comprehensive report that provides the first quantitative summary of the prevalence of asthma (in all age groups), COPD, and chronic bronchitis in Iran. The results of this study showed that the overall prevalence of asthma ever and chronic bronchitis was 4.8% and 5.6%, respectively. Comparing the prevalence of current asthma in Iran with other parts of the world, our estimated rate is lower than that in Kuwait, Lebanon, Thailand, Japan, Australia, and Germany, while it is higher than that in

some other countries like Oman, Pakistan, South Korea, India, China, Taiwan, Indonesia, Spain, Russia, and Greece. These results can fill the knowledge gaps about the prevalence of respiratory diseases in Iran, and it can help policy makers, specialists, insurance companies, and all stockholders to make plans and evaluate medical services required for reducing the prevalence of respiratory diseases.

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