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Prevalence and Severity of Adolescent Asthma in Yazd, Iran: Based on the 2020 Global Asthma Network (GAN) Survey

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ABSTRACT

Asthma, as the most common chronic disease in children, encompasses substantial health and socioeconomic burden worldwide. This study aimed to evaluate the prevalence, severity, and management of asthma in adolescents aged 13-14 years.

This cross-sectional study, which was part of the Global Asthma Network (GAN) 2020 survey, was conducted in early 2020 in Yazd, Iran. A total of 48 schools in Yazd city were selected by cluster sampling.

In this study, 5141 students, including 3069 (59.7%) females and 2072 (40.3%) males participated. Prevalence of ever and current wheezing was 19% and 9% respectively. The former was significantly higher in males than females (p<0.001). About 2% of the participants, which was 22.1% of students with current wheezing, had severe asthma. The prevalence of severe asthma was significantly higher in males (p=0.026). Our results showed that 4.8% of students had confirmed asthma by a doctor, significantly predominant in males (p<0.001). The prevalence of using inhaled medicines in the past 12 months was 3.8%, which was significantly higher in males than females (p<0.001). The prevalence of using short-acting β -agonists (SABA) and long-acting β -agonists (LABA) was 2.3% and 1.4% among the students, respectively, with a male predominance (p=0.019). About 1.2% and 0.8% of participants were using inhaled corticosteroids (ICS) and the combination of ICS and LABA, respectively, which was significantly higher in male participants (p<0.001).

According to our findings and in comparison to the previous ISAAC study in Yazd, the prevalence of severe asthma has decreased which indicates better management of asthma during the past two decades.

Keywords: Adolescent; Asthma; Prevalence

INTRODUCTION

Allergic disorders, as the most common chronic

Corresponding Author: Zahra Nafei, MD; Children Growth Disorder Research Center, Shahid Sadoughi diseases in children and adolescents, encompass substantial health and socioeconomic burden worldwide.¹ The Global Burden of Disease studies

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This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/ by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited estimated that about 339 million people around the world have asthma and this disorder cause death of more than 1000 people every day.2-4 Global asthma network (GAN) survey, cross-sectional, multi-center, multi-country, epidemiological research is based on an international study of asthma and allergies in childhood program (ISAAC) in 2012.5 ISAAC was developed in 1991 and used a simple methodology for providing valuable data on the prevalence of the symptoms of childhood asthma, allergic rhinoconjunctivitis, and eczema in different countries.6,7 The GAN survey expands the methodology used in ISAAC phase three and not only studies children (aging 6-7 and 13-14 vears old) but also their parents.⁵ It is now recognized that the prevalence of allergic diseases and asthma has peaked in some areas, especially in developed countries, while it has an increasing trend in developing countries.8,9

Based on the ISAAC questionnaire, several epidemiological studies have been conducted in Iran since 1997 in the age group of 13-14 years, revealing that the prevalence of asthma varies from 1.26% to 8.7% in different regions. This variation can be due to the climate and geographical diversities of Iran.^{10,11} A systematic review of ISAAC studies in Iran showed that the average prevalence of asthma symptoms in children increased from 1998 to 2003 (5.89% vs. 27.16%).¹² The prevalence of adolescent asthma (asthma ever or current wheezing) in Tehran has increased from 13.5% to 16.6% in ten years since 2001.^{11,13} Yazd, as one of the industrial cities of Iran is located as part of a large desert in central Iran, and it is the driest city in Iran due to its long distance from the sea. ISAAC studies conducted in two phases between 2003 and 2015, showed a declining trend in asthma prevalence in this city.^{11,14} To have more accurate estimates and provide evidence for proper planning, we decided to conduct this research as part of the GAN survey in Yazd.

MATERIALS AND METHODS

Questionnaire

This cross-sectional study was conducted as a part of the GAN 2020 study between February 2020 and June 2020 in the city of Yazd, located in central Iran. This study was initiated after being approved by the ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (IR.SSU.REC.1398.244), and obtaining the agreement of the education department. The informed consent form was at the beginning of the electronic questionnaire and each student was completely free to participate in the research.

GAN standard written questionnaire is developed from ISAAC questionnaires. It includes the main ISAAC questions that assess the prevalence and severity of asthma and other allergic diseases and associated factors. Moreover, the GAN has added some questions related to asthma management and confirmed asthma by a doctor, rhinitis, and eczema. The core questions are both sensitive and specific, have good content, construct, and concurrent and predictive validity.¹⁵

In this study first, the English version of the GAN questionnaire builds on the findings of ISAAC, was translated into Persian, and validated by some experts familiar with the specialized language. To evaluate the translated version, a pilot study was performed on 100 randomly selected adolescents. The questions were on the adolescents' revised based comments. Cronbach's alpha was used to evaluate the reliability of the translated questionnaire. The alpha coefficient was 0.862 for asthma symptoms, which indicates the high internal consistency of the cases. Then it was translated back into English. The latest version was emailed to the main coordinator of the GAN survey in New Zealand and it was approved.

Sampling

According to GAN recommendations, at least a sample size of 3000 subjects is required to obtain a good prevalence estimate. The study power at a 1% level of significance to detect the one-year prevalence of wheezing and severe asthma between the two centers will be 99% and 90% respectively.⁶ Since the sampling unit was school and the questionnaire was completed by the students, it would likely have a cluster effect. According to the number of male and female students aged 13-14 years old and the required sample size, 48 public and private schools in urban areas of Yazd and from both educational districts were selected by simple random sampling. Schools with non-Iranian students were excluded from the study. Due to the closures of schools during the COVID-19 pandemic, an electronic questionnaire, based on the GAN standard questionnaire, was designed and an access link to the electronic questionnaire was provided

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to school principals to be uploaded in students' virtual education groups. All students aged 13-14 years from selected schools were asked to complete the questionnaire.

Concerning response rate, 5, 141 out of 7, 214 students completed the questionnaire (71.3%). Unacceptable demographic data were re-checked on the phone and corrected if necessary.

Definition of Items

In this study, the prevalence of asthma symptoms was assessed based on answers to questions related to wheezing in the past year. Severe asthma is defined as \geq 4 attacks of wheeze, or night sleep disturbance \geq 1 per week from wheeze, or wheeze affecting speech in the past 12 months. The prevalence of asthma is considered based on confirmed asthma by a doctor. Those who answered "yes" to the question "have you ever had asthma?" were considered as "asthma ever".

Statistical Analyses

The output data were received through an Excel spreadsheet. All analyses were done using SPSS, version 23.0 (IBM, Armonk, NY). Pearson Chi-square test was used to determine the relationship between variables that were expressed as percentages. p-value<0.05 was considered statistically significant.

RESULTS

Prevalence of Asthma Symptoms, Severity and Hospitalization

Out of 7,214 students aged 13-14 in selected schools, 5,141 ones, including 3069 (59.7%) females and 2072 (40.3%) males, answered the questionnaires. Data on the prevalence of asthma symptoms as well as the emergency department and hospital admissions and severity of asthma are summarized in Table 1.

Confirmed asthma by a doctor was reported by 4.8% of students with male predominance (p<0.001), which was considered the prevalence of asthma in this study. On the other hand, confirmed asthma by a doctor was present in 86% of participants with "asthma ever".

In this study, 54% of students with confirmed asthma by a doctor had an action plan with no sex predominance (p=0.1). The prevalence of urgent visits by a physician, admission in the emergency department

without hospitalization, and hospitalization during the last year was 2.6%, 1.7%, and 0.6%, respectively. The prevalence of school absenteeism due to breathing problem was 3.4% of participants in the last year, and it was significantly higher in males (p<0.001).

Prevalence of Severe Asthma Symptoms in Current Wheezers

In this study, 6.3% of participants reported a wheezing attack in the past year, while only one percent reported \geq 4 wheezing attacks. Among those who reported wheezing in the last year, 69.8% had wheezing attacks and 10.8% had \geq 4 wheezing attacks; the latter was significantly higher in male participants (*p*=0.019). Sleep disturbance and speech-limiting wheezing were seen in 2.5% and 0.93% of participants, without any significant differences between males and females (Table 2).

Prevalence of Using Asthma Medications

The prevalence of using inhaled medications was summarized in Table 3. In our study, 2.3% and 1.4% of participants were using short-acting β - agonists (SABA) and long-acting β -agonists (LABA); respectively, which was significantly higher in male participants. It was also found that 29% and 38% of participants with asthma by a doctor were using ICS and a combination of ICS and LABA, respectively, and 24.5% and 30% of them were using Ketotifen syrup and Montelukast tablet, respectively, in short courses or every day. About 2% of the participants used ICS or a combination of ICS and LABA over the past year, which was more prevalent in male participants. The use of oral medications to help to breathe was reported by 7.6% of participants, which was significantly higher in males (p < 0.001). The prevalence of using oral medications, such as Salbutamol, theophylline, montelukast, and Ketotifen was 2.3%, 2.7%, 2.6%, and 5.1% in the past year, respectively.

Adolescents Asthma Prevalence in Central Iran

		Female	Male	Total	р
Wheezing ever	Yes	517(16.8%)	460(22.2%)	977(19%)	<0.00
	No	2552(83.2%)	1612(77.8)	4164(81%)	
Wheezing in the past 12	Yes	247(8%)	214(10%)	461(9%)	0.7
Months (current wheezing)	No	2822(92%)	1858(90%)	4680(91%)	
Asthma ever	Yes	130(4.2%)	161(7.8%)	291(5.7%)	<0.00
	No	2939(95.8%)	1911(92.2%)	4850(94.3%)	
The number of emergencies	None	3004(97.9%)	2002(96.6%)	5006(97.4%)	0.035
visits by a doctor in the past 12 months	1-3	60(2.0%)	67(3.2%)	127(2.5%)	
	4-12	4(0.1%)	2(0.1%)	6(0.1%)	
	>12	1(0.0%)	1(0.0%)	2(0.0%)	
The number of emergency department visits without	None	3026(98.6%)	2030(98.0%)	5056(98.3%)	0.2
hospitalization in the past 12 months	1-3	39(1.3%)	37(1.8%)	76(1.5%)	
	4-12	1(0.0%)	3(0.1%)	4(0.1%)	
	>12	3(0.1%)	2(0.1%)	5(0.1%)	
The number of hospitalizations in the past 12 months	None	3053(99.5%)	2057(99.3%)	5110(99.4%)	0.2
	1	15(0.5%)	13(0.6%0	28(0.6%)	
	2	1(0.0%)	0(0.0%)	1(0.0%)	
	>2	0(0.0%)	2(0.1%)	2(0.0%)	
School missed days in the past 12 months	None	2993(97.5%)	1975(95.3%)	4968(96.6%)	<0.00
	1-3	67(2.2%)	81(3.9%)	148(9.9%)	
	4-12	5(0.2%)	11(0.5%)	16(0.3%)	
	>12	4(0.1%)	5(0.2%)	9(0.2%)	
Severe asthma	Yes	50(1.7%)	52(2.5%)	102(2%)	0.026
	No	3019(98.3%)	2020(97.5%)	5039(98%)	
Exercise-induced wheeze	Yes	474(15.4%)	342(16.5%)	816(15.9%)	0.3
in the past 12 months	No	2595(84.6%)	1730(83.5%)	4325(84.1%)	
Night dry cough without cold in the past 12 months	Yes	361(11.8%)	274(13.2%)	635(12.4%)	0.1
	No	2708(88.2%)	1798(86.8%)	4506(87.6%)	

Table 1. Prevalence of asthma symptoms and hospital and emergency department admission in the aged group of 13-14 years by gender

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		Female	Male	Total	р
Wheezing attacks	None	83(33.6%)	56(26.2%	139(30.2%)	
	1-3 attacks	145(58.7%)	127(59.3%)	272(59%)	0.07
	4-12 attacks	11(4.5%)	20(9.3%)	31(6.7%)	
	> 12attacks	8(3.2%)	11(5.1%)	19(4.1%)	
Sleep disturbance	Never	182(73.7%)	151(70.6%)	333(72.2%)	0.7
in the past	<1night/week	49(19.8%)	47(22%)	86(20.8%)	
12 months	\geq 1night/week	16(6.5%)	16(7.5%)	32(6.9%)	
Speech limiting wheezing	Yes	26(10.5%)	22(10.3%)	48(10.4%)	0.9
in the past 12 months	No	221(89.5%)	192(89.7%)	413(89.6%)	
Severe asthma	Yes	50(20.3%)	52(24.3%)	102(22.1%)	0.3
	No	197(79.7%)	162(75.7%)	359(77.9%)	

Table 2. Asthma severity symptoms and severe asthma in current wheezers in the aged group of 13-14 years by gender

Table 3. Prevalence of using inhaled medications in the aged group of 13-14 years by gender

		Female	Male	Total	р
Using any inhalator in the	Yes	91(3.0%)	106(5.1%)	197(3.8%)	<0.00
past year	No	2978(97.0%)	1966(94.9%)	4944(96.2%)	
Using SABA*	As needed	36(1.2%)	44(2.1%)	80(1.6%)	0.019
in the past year	Short courses	16(0.5%)	17(0.8%)	33(0.6%)	
	Every day	1(0.0%)	2(0.1%)	3(0.1%)	
	No use	3016(98.3%)	2009(97%)	5025(97.7%)	
Using LABA+	As needed	23(0.75%)	30(1.5%)	53(1.05%)	0.019
in the past year	Short courses	7(0.23%)	8(0.4%)	15(0.3%)	
	Every day	0	2(0.1%)	2(0.06%)	
	No use	3039(99.02)	2032(98%)	5071(98.6%)	
Using ICS#	As needed	14(0.45%)	22(1.08%)	36(0.7%)	<0.001
in the past year	Short courses	5(0.16%)	13 (6.84%)	18(0.35%)	
	Every day	1(0.03%)	5(0.24%)	6(0.12%)	
	No use	3049(99.3%)	2032(98%)	5081(98.8%)	
Using combination ICS	As needed	7(0.23%)	16(0.77%)	23(0.45%)	<0.00]
and LABA in the past	Short courses	4(0.13)	10(0.48%)	14(0.27%)	
year	Every day	1(0.03%)	5(0.24%)	6(0.11%)	
	No use	3057(99.6%)	2041(98.5%)	5098(99.1%)	

* SABA (Short-acting β- agonists), +LABA(long-acting β- agonists), # ICS(inhaled corticosteroids)

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DISCUSSION

This study was conducted in Yazd as the first report based on a GAN survey in Iran. According to the findings of this study, the prevalence of current wheezing, and the symptoms of severe asthma decreased compared to that reported in the 2003 ISAAC study in Yazd, while the prevalence of asthma ever increased slightly.¹⁴ One reason for the increase in the prevalence of asthma ever compared to previous years may be due to the better acceptance of asthma title as a chronic disease in our society.

The prevalence of two important asthma criteria, including wheezing in the last 12 months and asthma ever was 9% and 5.7%, respectively, in our study, which both were higher in male participants, but this difference was only significant in asthma ever. The mentioned results were consistent with findings of a study by Fazlollahi et al, which was a national population-based study in Iran and conducted in 2016.¹¹ The lower prevalence of asthma ever in female participants in both studies could be attributed to the lower tendency to accept the label of asthma due to cultural and social factors among females in our country.

According to the results of our study, the prevalence of current wheezing and asthma ever was significantly lower in Yazd compared to northern Iran. Regarding the study by Mohammadzadeh et al, in 2008 showed that the prevalence of current wheezing and asthma ever was 13% and 4.4%, respectively. In another study by Zamanfar et al, the prevalence of current wheezing and asthma ever was 30.5% and 13%, respectively, in northern Iran which could be due to higher humidity and plant diversity.^{16,17} In another study performed based on the GAN questionnaire in Kosovo, the prevalence of asthma symptoms such as wheezing ever, wheezing in the past year, and asthma ever was lower than that in our study (12.7%,6.4%, and 3.7% respectively).¹⁸

According to the ISAAC phase III study conducted in 97 countries, the prevalence of current wheezing in the age group of 13-14 years ranged from 32.6% in New Zealand to 0.8% in China. That large study showed a significant trend towards a higher prevalence of wheezing in the past 12 months in affluent countries among adolescents, while the trend of severe asthma symptom prevalence has been reversed among current wheezers in these high-income countries.¹⁹ Fazlollahi et al, showed 4.7 % of total students in this age group had severe asthma with male gender predominance, which was higher than our study.¹¹ This difference can be attributed to the inclusion of students from different parts of Iran with different climatic conditions and plant diversity in this study.

Compared to the study of Karimi et al, in which the prevalence of wheezing attack \geq 4, sleep disturbance \geq 1nights a week, and speech-limiting wheezing were 2.4%, 1.8%, and 2.84% of the total population respectively, it was 0.97%, 0.6%, and 0.93%, respectively in our study.¹⁴ So the lower prevalence of severe asthma symptoms in our study compared with Karimi et al, study results could be indicated better management of asthma by physicians, the availability of more effective medications, and increased public awareness due to the widespread use of media over the years. Similar results were obtained by comparing our study findings with one performed by Masjedi et al, which was conducted in Tehran.¹³

Two indicators of severe asthma, including sleep disturbance and Speech limiting wheezing, had a higher prevalence in the Kosovo study than in our study (2.8% vs. 2.3% and 2% vs. 0.93% respectively). Since having an action plan in the Kosovo study was significantly lower than in our study, (0.58% vs. 2.6%), it seems that having an action plan could be effective in reducing severe asthma.¹⁸

Over the past year, 1.7% of total students were admitted to the emergency department without hospitalization, 0.6% were hospitalized, and 2.6% had urgent visits by a doctor in our study. According to Anderson's study, hospital admissions for adolescents with asthma in high-income countries ranged from 3.71-27.39 per 10,000, with most hospitalization rate in Australia and the lowest rate in Portugal. In the aforementioned study, they used the ISAAC Phase data Three questionnaire and national on hospitalization due to asthma. The hospitalization rate, compared to our study, was significantly lower in developed countries, confirming a lower prevalence of severe asthma, as mentioned in previous studies.²⁰ Since the emergency and hospital admission rate has not been reported based on the GAN questionnaire, it was not possible to compare our results with other studies. The results of future studies could be effective in government planning to reduce the health and economic burden of asthma.

We found that 3.4% of our participants missed

school days due to breathing problems in the last year, whose prevalence was significantly higher in male participants. Asthma is one of the leading causes of chronic illness in the United States, with more than 10 million days lost each year. Approximately 59% of children with asthma missed school days, leading to poor academic performance.²¹ Using the modified ISAAC questionnaire, in a study in Korea in 2015, it was found that 9.1% of asthmatics were absent due to asthma problems.²²

The prevalence of exercise-induced wheezing was 15.9% of participants in this study. Compared to studies by Karimi and Masjedi, 22.1% and 16% of adolescents had wheezing during exercise, respectively.^{13,14} The lower prevalence of exerciseinduced wheezing in our city could indicate better control of asthma using new medications, including LABA and leukotriene receptor antagonists (LTRA) in recent years. In addition, greater awareness of school health educators about the early referral of children who experience wheezing and respiratory symptoms during exercise may have contributed to this reduction. The prevalence of exercise-induced wheezing in adolescents was 18.3% and 34% in two recent studies by Fazlollahi and Zamanfar, which was significantly higher than our study.^{11,17} As previously mentioned about studies conducted in northern Iran, the higher prevalence of asthma symptoms and exercise-induced wheezing can be due to climatic differences and plant diversity in that region.

A recent study was done in Bangkok using the GAN questionnaire. According to the aforementioned study, the prevalence of exercise-induced asthma in adolescents aged 13 to 14 was 14.8%, which was consistent with our study.²³

In this study, 12.4% of participants had night dry cough, while its prevalence was 23.8% in a study performed by Karimi et al, in 2003 in Yazd.¹⁴ Given that nocturnal cough can be an important symptom of uncontrolled asthma, its reduced prevalence in our study can be due to the reasons listed above, which have also been effective in reducing other asthma symptoms.

We found that 86% of participants who reported asthma by themselves had confirmed asthma by a doctor, indicating that 14% of students with selfreported asthma might have to wheeze for reasons other than asthma, or for whatever reason their asthma has not yet been diagnosed.

Prevalence of using inhaled medicines in the past 12 months was 3.8% of the participants, mostly as needed, which was significantly higher in male participants (p < 0.001). In this study, 2.3% of participants were using SABA as a quick reliever, and 1.4%, 1.2%, and 0.8% were using LABA, ICS, and a combination of ICS and LABA respectively. The prevalence of these medications consumption was significantly higher in males. In comparison to a study by Gashi V, in Kosovo, the prevalence of consuming inhaled medicines, including controller and reliever medications, in the last year was lower in our study, indicating less acceptance of inhaled medications in our society especially among females, although our patients may have been in the lower steps of asthma, which can be treated with oral drugs such as Montelukast.¹⁸

In the current study, the use of oral medications in the past 12 months to improve respiratory symptoms was three times more than that of inhaled medications. Although inhaled corticosteroids are highly effective in reducing asthma morbidity and mortality, the use of these medications is less acceptable in our society due to various reasons, including fear of dependence and side effects induced by inhaled drugs, such as growth retardation, cardiac complications, and osteopenia.²⁴

The findings of this study showed a low prevalence of current asthma symptoms (current wheeze) in adolescents living in Yazd based on GAN classification. Contrary to what was previously thought, the prevalence of asthma symptoms has not increased over the past two decades, and even its severity has decreased in Yazd according to our findings. The reduction in the severity of asthma can be explained by the availability of new and effective drugs in the treatment of asthma, increased public awareness as well as the presence of specialists in this field.

Despite the modern lifestyle, it is thoughtprovoking that the prevalence of asthma symptoms in our city has not increased in about two decades. Further epidemiological studies are needed to determine the factors affecting this chronic multifactorial disease, such as changes in indoor environments (such as home architectural style, type of flooring, and type of fuel used), outdoor environments (such as climate and vegetation) as well as their effects on gene expression over time.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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