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Prevalence and Risk Factors of Asthma and Allergic Diseases in Primary Schoolchildren Living in Bushehr, Iran: Phase I, III ISAAC Protocol

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ABSTRACT

Asthma and allergic diseases present a major health burden. Information on the prevalence of these diseases indicates that these diseases are increasing in various parts of the world. It was hoped that this study would be helpful to health system policy-makers in planning allergy prevention programs in the region.

The prevalence of asthma and allergic diseases and relation between the various risk factors involved were assessed among schoolchildren in the city of Bushehr, Iran. The ISAAC Phase I and III questionnaires were completed by parents of 1280 children aged 6-7 years and self-completed by 1115 students aged 13-14 years.

The prevalence of atopic eczema, allergic rhinitis and asthma among 6-7 year-old students were 12.1%, 11.8% and 6.7%, respectively. While, the prevalence of these diseases among 13-14 year-old students were found to be 19%, 30% and 7.6%, respectively. There was an association between asthma and allergic rhinitis as well as eczema ($p < 0.05$). Consumption of fast food as a risk factor was significantly associated with asthma ($p = 0.03$).

The prevalence of asthma and allergic diseases was high among schoolchildren in the city of Bushehr, Iran. Also an association was observed between the fast food consumption and asthma.

Keywords: Allergic rhinitis; Asthma, Atopic eczema; Children; ISAAC; Prevalence

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INTRODUCTION

The prevalence of asthma and allergic diseases has increased worldwide, especially in the more developed countries in the past two to three decades.¹⁻³ The results of various studies showed that the prevalence of asthma and allergic diseases varied in different countries from 1% to 40%.^{3,4} Changes in the prevalence of these diseases were associated with genetic and environmental factors, mainly in the form of allergens, air pollution, exposure to cigarette smoking and diet that would influence the prevalence of allergic diseases.^{5,6} International assessment of asthma and allergic diseases was for the first time carried out using standardized questionnaires which was presented by the International Study of Asthma and Allergies in Childhood (ISAAC) survey.⁴ The prevalence of asthma in Iran has been reported to vary from 2.7% to 35.2%.⁷ In addition, the prevalence of allergic rhinitis in children between 6-7 years of age was reported to be 11.9% and in children aged 13-14 was 21.2%.⁸

Because few studies have been conducted on asthma and allergies in southwest part of Iran, the epidemiology of these diseases is still not fully understood. This study was therefore designed to determine the prevalence of asthma and allergic diseases and to find out the possible risk factors among schoolchildren living in the city of Bushehr, Iran.

MATERIALS AND METHODS

Location and Population

This cross sectional study was conducted in 2011/2012 in Bushehr. The city with 247,706 people is situated in the southwestern part of Iran, with hot, humid and semi-desert climate. Dusty air pollution (events) has been a problem since the year 2008. The study was approved by the ethics committee of Bushehr University of Medical Sciences (BPUMS).

Study Design

The subjects were selected from all the primary public schools in the city of Bushehr. We used a Persian version (translated by National Research Institute of Tuberculosis and Lung Disease, Tehran, Iran) of the standardized questionnaire of ISAAC protocol phase I written and video questionnaire (only shown to children aged 13-14 years).⁴ Instructions were given by us and the teachers before the questionnaires

were completed. All the students with the age 6-7 and 13- 14 years were invited to participate in the study. Totally, 2540 questionnaires were distributed among the students. The children were studying in 42 primary and secondary schools. Ten medical students of BPUMS helped completing the questionnaires by the children and explained the wheezy breathing to them. The questionnaires for 1280 children aged 6-7 years were completed by their parents at home, and 1115 children aged 13-14 years filled the questionnaires themselves. The rate of participation in the survey was above 94.2%.

Statistical Analysis

Global descriptions of eczema, allergic rhinitis, and asthma prevalence were computed. Data were characterized with standard descriptive statistics. The association between asthma, allergic rhinitis and eczema was assessed by using 95% confidence intervals. Also the risk factors for them were examined. The Chi-square test was used to determine association between the groups. Missing and inconsistent responses were excluded from subsequent analysis. Results were considered significant at $p < 0.05$. The SPSS version 16 (SPSS Inc. Chicago, IL, USA) was used.

RESULTS

Out of 2540 students, 2395 (1280 students aged 6-7 and 1115 aged 13-14 years old) responded to the questionnaires. In the group of 6-7 years old, 667 (52.1%) were boys and 613 (47.9%) were girls, and in the group of 13- 14 years old, 471 (42.2%) were boys and 644 (57.8%) were girls. There was no sex difference between the groups ($p > 0.05$).

The Prevalence and Risk Factors for Eczema

The prevalence of eczema among 6-7 year-old students was 12.1% (155/ 1280) [55.4% boys and 44.6% girls]. In the group of 13-14 years old, it was 19% (220/ 1115) [38.2% boys and 61.8% girls]. The prevalence of eczema in 13-14 year-old group was significantly higher than 6-7 year-old group ($p = 0.001$). Overall prevalence of eczema in both of the groups was 15.6 % (Figure 1). As shown in table 1, among 6-7 year-old students, 41 (3.2%) had an itchy rash which was coming and going for at least 6 months, 28 (2.2%) had the rash at any time during the past 12 months, and 13 (1%) had their lesions cleared completely. In this

age group, 5 (0.4%) had itchy rash for the first time occurring under 2 years old. In the group of 13-14 year-old students, the itchy rash condition was 87 (7.8%), 59 (5.3%) and 31 (2.8%), respectively.

We also examined the association between eczema and allergic rhinitis, wheeze symptoms and asthma. In

the group of 6-7 years old with eczema, 4.5% had allergic rhinitis, 34.1% had wheeze and 12.2% had asthma. Whereas, in 13-14 year-old subjects with eczema, 15% had allergic rhinitis, 32.2% had wheeze and 13.1% had asthma.

Table 1. Demographic Data and Prevalence of Eczema Symptoms in the Schoolchildren of Bushehr

Variables	6-7 year-old students (N= 1280)	13-14 year-old students (N= 1115)
Sex		
Male	667 (52.1%)	471 (42.2%)
Female	613 (47.9%)	644 (57.8%)
Eczema (AD)	155 (12.1%)	220 (19%)
Age onset (If reported)		
≤ 2 y	5 (3.2%)	
2-4 y	9 (5.8%)	
≥ 5	14 (9%)	
Affected area		
Flexor	22 (14.2%)	42 (19%)
Extensor	133 (85.8%)	178 (81%)
Awake at night (If reported)		
Never	15 (9.6%)	32 (14.5%)
≤ one night	6 (3.8%)	18 (8.1%)
≥ one night	6 (3.8%)	12 (5.4%)

Y: year; N: number; AD: atopic dermatitis

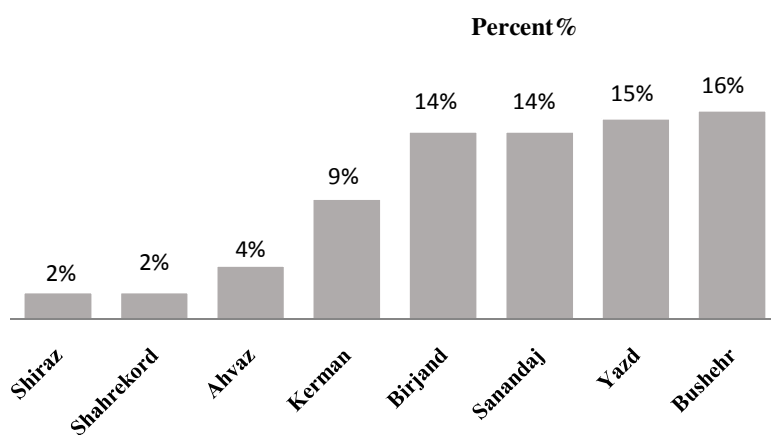


Figure 1. Comparison of prevalence of eczema (Atopic Dermatitis) in Bushehr with other cities of Iran, based on ISAAC Protocol

Prevalence of Asthma and Allergies in Bushehr

Table 2. Prevalence of wheezing and asthma symptoms in the Schoolchildren of Bushehr

Variables	6-7 year old Students (N= 1280)	13-14 year old Students (N= 1115)
Wheeze	254 (19.8%)	200 (17.9%)
Male	132 (51.7%)	96 (48%)
Female	122 (48.3%)	104 (52%)
Asthma	85 (6.7%)	83 (7.6%)
Male	31 (36.5%)	43 (51.8%)
Female	54 (63.5%)	40 (48.2%)
Attacks of wheezing per year		
None	25 (9.8%)	14 (7%)
1-3	94 (37%)	84 (42%)
4-12	18 (7%)	18 (9%)
> 12	2 (0.7%)	15 (7.5%)
Sleep disturbance		
Never	97 (38.1%)	93 (46.5%)
One night	27 (10.6%)	19 (9.5%)
> one night	15 (5.9%)	14 (7%)

Y: year; N: number;

The Prevalence and Risk Factors for Rhinitis

The prevalence of rhinitis in 6-7 year-old group was 151 (11.8%) which included 83 (54.9%) boys and 68 (45.1%) girls, and in 13-14 year old group was 334 (30%) with 147 (44%) boys and 187 (56%) girls. The prevalence of allergic rhinitis in different cities of Iran is shown in figure 2. Conjunctivitis accompanied by rhinitis (Rhino-conjunctivitis) was 121 (12.5%) in 6-7 year old group and it was 245 (22%) in 13-14 year old

group with the symptom. There was statistical difference between these two groups according to allergic rhinitis and rhino-conjunctivitis ($p=0.001$). The symptom of allergic rhinitis in both the groups during spring, summer, fall and winter were 31.7%, 22.5%, 86.7% and 41.7% respectively. The rhinitis symptom affected daily activities of the students with the conditions as never, slightly, moderately and frequently was 30.4%, 37.8%, 19.9% and 11.9%, respectively.

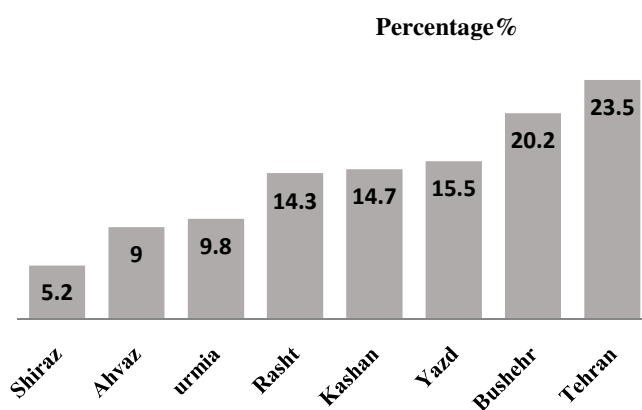


Figure 2. Comparison of prevalence of Allergic Rhinitis in Bushehr with other Cities of Iran, based on ISAAC Protocol

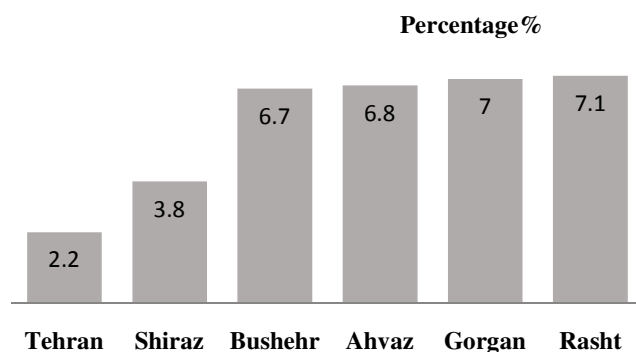


Figure 3. Prevalence of asthma in 6-7 year-old Group based on ISAAC protocol in comparison with cities of Iran

The Prevalence and Risk Factors for Ever Wheeze and Asthma in Both Groups

In 6-7 year-old group (1280 subjects), the prevalence of asthma was 6.7% (63.5% boys and 36.5% girls). Male gender was a significant risk factor for asthma (OR =1.65 and, CI=1.03, 2.68; $p=0.029$). In addition, the prevalence of ever wheeze in the group of 6-7 year-old students was 254 (19.8%) and that of the current and exercise wheeze in the previous 12 months were 139 (10.9%), and 35 (2.7%), respectively. Wheeze limiting speech and dry cough at night in the previous 12 months were determined to be 8 (0.6%) and 80 (6.2%), respectively.

In 13- 14 year-old group (1115 subjects), the prevalence of asthma was 83 (7.6%), including boys as 40 (48.2%) and girls as 43 (51.8%). There was no gender difference regarding asthma between males and females ($p>0.05$). The prevalence of ever wheeze in this group was 200 (17.9%) and that of the current and exercise wheeze in the previous 12 months were 127 (11.4%), and 175 (15.7%), respectively. Wheeze limiting speech and dry cough at night in the last 12 months in this group was found to be 33 (3%) and 90 (8.1%), respectively. The overall prevalence of asthma and ever wheeze in the students living in the city of Bushehr were 7% and 18.9%, respectively.

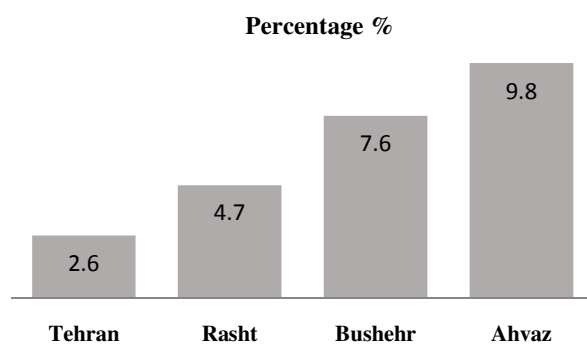


Figure 4. Prevalence of asthma in 13-14 year-old group based on ISAAC protocol in comparison with cities of Iran

DISCUSSION

The prevalence of allergic diseases and asthma is increasing in Iran as well as other countries in the world.^{9,10} ISAAC protocol has provided outstanding conditions to determine and compare the prevalence of asthma and allergic diseases in different populations of the world.⁴ Our study showed that overall prevalence of atopic dermatitis, allergic rhinitis and asthma of the students in the city of Bushehr were 15.6%, 20.2% and 7%, respectively.

Eczema (Atopic Dermatitis)

The prevalence of eczema among students in the city of Bushehr as compared to other parts of the world was high (15.6%). The worldwide mean frequency rate of eczema symptoms is 7.6% (range: 0.1 to 19.9).¹¹⁻¹³ The overall prevalence of current eczema symptoms among the schoolchildren of Bushehr remains highest as compared with other 10 cities in Iran (Figure 1).¹² Also, we conducted a survey about the potential etiologic factors including BMI, fast food or seafood consumption, the level of parents education, parents smoking, house heating system (electricity, gas or wood), pets, sib ship size, acetaminophen (Paracetamol) or antibiotic ingestion to find any relation between eczema and the above mentioned factors. However, we did not find associations between eczema symptoms and the environmental or nutritional factors. There was, however an association between eczema (atopic dermatitis), and allergic rhinitis as well as asthma ($p=0.01$ for both) in 13-14 year-old students, while this finding in 6-7 year-old students was not significant ($p=0.05$).

Interestingly, our study showed that among 6-7 year old students, the prevalence of medical diagnosis and symptoms among boys was higher as compared with the girls. This is in line with an ISAAC steering committee study,⁵ in which male gender showed a significantly higher prevalence than females.¹⁴ The results of a survey about the 13-14 year old students in the schools of Bushehr showed that the prevalence of current eczema increased in the year 2012 as compared with that of 2002 (19.7% vs 9.7%).⁹ In addition, our results showed that the prevalence of eczema (atopic dermatitis) in 13-14 year old group was higher than 6-7 year old group. The increased prevalence of eczema may be as the result of westernized lifestyle and fast food consumption.

Rhinitis (Allergic Rhinitis)

Previous studies indicated that the prevalence of allergic rhinitis in Iran is high.¹³ The results of a pooled study has shown that the prevalence of allergic rhinitis in students aged 6-7 year old was 11.9% and in the subjects aged 13-14 was 21.2%.¹⁵ Moreover, some studies reported that the mean prevalence rate of allergic rhinitis in students aged 13 to 14 was 13.7% (range: 1.6% to 39.7%).^{13,15,16} In our study the prevalence of allergic rhinitis among 6-7 year-old group and 13-14 year-old group was 11.8% and 30%, respectively. In agreement with other studies,^{15,16} allergic rhinitis was the most frequent atopic disorder among the students in the city of Bushehr (figure 2). We found no gender preponderance for allergic rhinitis. However, some studies have reported the higher prevalence of allergic rhinitis in boys.^{8,17}

In recent decades, the incidence of allergic rhinitis has increased in synergism with the growing incidence of allergy throughout the world. This can have a huge negative impact and comorbidities, particularly in children that have a significant health impact on the quality of life. In fact, allergic rhinitis is considered to have impact on asthma.¹⁸ However, our findings indicated that allergic rhinitis was associated with eczema and asthma. Also, in our study, bread and rice consumptions as risk factors, were significantly associated with rhinitis in 6-7 year-old students ($p=0.00$ and $p=0.026$, respectively).

Ever Wheeze and Asthma

The findings of our study indicated that the prevalence of asthma among the schoolchildren is high (6.7% in 6-7 year-old students and 7.6% in 13-14 year-old students) as compared with the same population in other parts of the Middle East, according to the Global Initiative for Asthma (5.8%).¹⁹ The results from previous ISAAC study conducted in Bushehr in the year 2002 showed that the prevalence of asthma in 13-14 year-old students was reported to be 6.7%.¹⁹ The increase in the rate of asthma in this group may be because of the current dusty air pollution, higher humidity, changes in diet and less understanding about risk factors associated with asthma and allergic symptoms in Bushehr. The prevalence of asthma reported from other Iranian cities which have been determined by using ISAAC protocol range from 2.1% to 7.1%, in 6-14 year-old subjects¹⁶ (Figures 3 and 4). The prevalence of asthma in the city of Bushehr as

compared to other cities in Iran was higher except in Ahvaz¹⁶ and that was due to the above mentioned causes. Comparing with the reports from neighboring countries, including Saudi Arabia (23%), Iraq (22.3%), Kuwait (16.8%) and the United Arab Emirates (13%),¹⁶ the prevalence of asthma is significantly lower in the city of Bushehr.

In general, the results of our study showed that the prevalence of asthma in boys of 6-7 year-old age group was significantly higher compared to girls. This is similar to the study conducted by ISAAC steering committee⁴ in which boys showed a significantly higher prevalence of asthma than girls. It has been reported that after puberty period, asthma becomes more prevalent in girls.²⁰ This was not in agreement with our results which showed that female gender predominance of asthma was not significant in 13-14 year-old students. In addition, overall prevalence of ever-, current- and exercise-wheeze as the main symptoms of asthma were 17.9%, 11.4% and 15.7%, respectively. These findings are similar to the previous study conducted in the city of Bushehr in the year 2002.¹⁶ Asthma severity was also assessed by using ISAAC questionnaire in which sleep disturbance and wheeze limiting speech were considered. The differences in rate of wheeze limiting speech and sleep disturbance were not significant in the groups.

Eczema in infancy is associated with development of asthma and rhinitis, and it is one of the strongest risk factors for asthma.²¹ Also, it has been reported that atopic dermatitis and rhinitis are more common in people with asthma.¹⁴ In agreement with these studies, our findings showed that there was an association between eczema and asthma. We also found that fast food consumption, as a risk factor, was significantly associated with asthma in both age groups ($p= 0.03$). Previous epidemiological studies have reported that a higher consumption of fast foods and low vegetables, fruit and rice increased asthma risks in children.²² In addition, Mediterranean dietary pattern was inversely associated (protective effect) with asthma.²³

The results from the present study showed no association between asthma and BMI, seafood consumption, acetaminophen (Paracetamol) or antibiotic ingestion, parents smoking, sib ship size, house heating system, housekeeping animals, as risk factors. Recent epidemiological studies reported an inverse association between sib ship size and asthma, while frequent use of acetaminophen (Paracetamol)

was positively associated with asthma.^{14,24,25}

In conclusion, our study indicated that the prevalence of asthma and allergic diseases based on the ISAAC protocol were relatively high among the students in the city of Bushehr as compared to other cities of Iran. Moreover, the survey showed that the rate of allergic diseases is increasing as compared to the survey conducted in the year 2002. Finally we suggest that the results of our study to be used by authorities responsible for planning allergy prevention programs in the region. We also suggest that potential risk factors to be determined in future studies.

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REFERENCES

1. Banac S, Rozmanic V, Manestar K, Korotaj-Rožmanic Z, Lah-Tomulic K, Vidovic I, et al. Rising trends in the prevalence of asthma and allergic diseases among school children in the north-west coastal part of Croatia. *J Asthma* 2013; 50(8):810-4.
2. Kim SY, Jung JY, Park MS, Kang YA, Kim EY, Kim SK, et al. Increased prevalence of self-reported asthma among Korean adults: an analysis of KNHANES I and IV data. *Lung* 2013; 191(3):281-8.
3. Von Mutius E. The rising trends in asthma and allergic disease. *Clin Exp Allergy* 1998; (28 Suppl 5):45-9.
4. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; 8(3):483-91.
5. Kimber I. Allergy, asthma and the environment: an introduction. *Toxicol Lett* 1998; 102-3:301-6
6. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12(2):315-35.
7. Entezari A, Mehrabi Y, Varesvazirian M, Pourpak Z, Moin M. A systematic review of recent asthma symptom surveys in Iranian children. *Chron Respir Dis* 2009; 6(2):109-14.
8. Mohammadzadeh I B-SR, Alizadeh-Navaei R. The prevalence of allergic rhinitis in Iranian children: A systematic review and descriptive meta-analysis. *J Pediatr Rev*, 2013:19-24.
9. Shakurnia AH, Assar S, Afra M, Latifi M. Prevalence of

- asthma among schoolchildren in Ahvaz, Islamic Republic of Iran. *East Mediterr Health J* 2010; 16(6):651-6.
10. Golshan M, Mohamad-Zadeh Z, Zahedi-Nejad N, Rostam-Poor B. Prevalence of asthma and related symptoms in primary school children of Isfahan, Iran, in 1998. *Asian Pac J Allergy Immunol* 2001; 19(3):163-70.
 11. Hassanzadeh J, Mohammadbeigi A, Mousavizadeh A, Akbari M. Asthma prevalence in Iranian guidance school children, a descriptive meta-analysis. *J Res Med Sci* 2012; 17(3):293-7.
 12. Williams H, Robertson C, Stewart A, Ait-Khaled N, Anabwani G, Anderson R, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999; 103(1 Pt 1):125-38.
 13. Anderson HR, Ruggles R, Strachan DP, Austin JB, Burr M, Jeffs D, et al. Trends in prevalence of symptoms of asthma, hay fever, and eczema in 12-14 year olds in the British Isles, 1995-2002: questionnaire survey. *Bmj* 2004; 328(7447):1052-3.
 14. Rad MH, Hamzadeh A. Allergic disease in 6-7-year-old schoolchildren in Urmia, Islamic Republic of Iran. *East Mediterr Health J* 2008; 14(5):1044-53.
 15. Mirsaid Ghazi B, Imamzadehgan R, Aghamohammadi A, Darakhshan Davari R, Rezaei N. Frequency of Allergic Rhinitis in School-age Children (7-18 Years) in Tehran. *Iran J Allergy Asthma Immunol* 2003; 2(4):181-4.
 16. Behbehani NA, Abal A, Syabbalo NC, Abd Azeem A, Shareef E, Al-Momen J. Prevalence of asthma, allergic rhinitis, and eczema in 13- to 14-year-old children in Kuwait: an ISAAC study. *International Study of Asthma and Allergies in Childhood. Ann Allergy Asthma Immunol* 2000; 85(1):58-63.
 17. Masjedi MR, Fadaizadeh L, Najafizadeh K, Dokouhaki P. Prevalence and Severity of Asthma Symptoms in Children of Tehran- International Study of Asthma and Allergies in Childhood (ISAAC). *Iran J Allergy Asthma Immunol* 2004; 3(1):25-30.
 18. Berger WE. Allergic rhinitis in children : diagnosis and management strategies. *Paediatr Drugs* 2004; 6(4):233-50.
 19. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59(5):469-78.
 20. Rahimi-Rad MH, Gaderi-Pakdel F, Salari-Lak S. Smoking and asthma in 20-44-year-old adults in Urmia, Islamic Republic of Iran. *East Mediterr Health J* 2008; 14(1):6-16.
 21. Von Kobyletzki LB, Bornehag CG, Hasselgren M, Larsson M, Lindström CB, Svensson Å. Eczema in early childhood is strongly associated with the development of asthma and rhinitis in a prospective cohort. *BMC Dermatol* 2012; 12:11.
 22. Lee SC, Yang YH, Chuang SY, Liu SC, Yang HC, Pan WH. Risk of asthma associated with energy-dense but nutrient-poor dietary pattern in Taiwanese children. *Asia Pac J Clin Nutr* 2012; 21(1):73-81.
 23. de Batlle J, Garcia-Aymerich J, Barraza-Villarreal A, Antó JM, Romieu I. Mediterranean diet is associated with reduced asthma and rhinitis in Mexican children. *Allergy* 2008; 63(10):1310-6.
 24. Kinra S, Davey Smith G, Jeffreys M, Gunnell D, Galobardes B, McCarron P. Association between sibship size and allergic diseases in the Glasgow Alumni Study. *Thorax* 2006; 61(1):48-53.
 25. Suarez-Varela MM, Garcia-Marcos L, Fernandez-Espinar JF, Bercedo-Sanz A, Aguinaga-Ontoso I, González-Díaz C. Is acetaminophen use associated with atopic eczema and other allergic diseases in adolescents? *Iran J Allergy Asthma Immunol* 2013; 12(2):115-23.